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ORIGINAL RESEARCH

Interaction of blood pressure in patients with vascular stenosis of intravenous thrombolytic stroke

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Abstract

The prognostic relationship between blood pressure (BP) and ischemic stroke remains controversial in patients receiving intravenous thrombolysis (IVT), and it is unclear whether vascular stenosis could influence this association. The systolic BP data within 24 hours of IVT in 465 ischemic stroke patients were obtained from the Soochow Stroke Registry System database and the mean BP measurements 24 hours after thrombolysis were stratified. Patients who received intravenous thrombolysis were divided into two groups: with or without vascular stenosis $\geq$70%. The study outcomes were death, major disability (modified Rankin Scale (mRS) 3–6) and intracranial hemorrhagic transformation 3 months after IVT. A "J"-shaped relationship was observed between mean systolic BP within 24 hours of IVT and 3-month clinical outcomes in patients with vessel stenosis $\geq$70%. Systolic BP between 130–140 mmHg was associated with lowest risk of poor clinical outcomes. Patients with the lowest mean systolic BP (<130 mmHg) had 4.94 times higher risk of poor prognosis compared to those with systolic blood pressure (SBP) between 130–140 mmHg (Odd ratio (OR) 4.94; 95% confidence interval (CI) 1.01 to 24.20; p = 0.049), and patients with highest mean systolic BP ($\geq$150 mmHg) had 22.12 times higher risk of poor prognosis than patients with mean systolic BP between 130–140 mmHg (OR 22.12; 95% CI 3.62–135.30, $p < 0.001$). However, we observed no relationship between BP within 24 hours of IVT and clinical outcome in patients without vascular stenosis $\geq$70% (P_{trend} = 0.780). A "J"-shaped relationship was observed between mean systolic BP and prognosis in patients with severe stenosis, and those with lowest mean systolic BP between 130–140 mmHg had least risk of poor prognosis.

Keywords

Stroke; Intravenous thrombolysis; Blood pressure; Vascular stenosis; Prognosis

1. Introduction

Stroke is the leading cause of death and disability worldwide, of which ischemic stroke is its most common type [1]. Reperfusion therapy in the hyper-acute phase of ischemic stroke, including intravenous thrombolysis and mechanical thrombectomy, is known to significantly reduce mortality and disability after stroke [2]. However, the therapeutic significance of blood pressure management after IVT remains unclear.

Blood pressure was shown to influence the short- and long-term prognosis of patients with ischemic stroke, which can be effectively improved by lifestyle changes and/or pharmacological interventions [3, 4]. Thus, studying the effects of blood pressure on the prognosis of ischemic stroke patients treated with intravenous thrombolysis can help reduce associated adverse clinical outcomes by actively monitoring and optimizing the blood pressure of patients with high risk of stroke and poor prognoses. It was reported that approximately 70% of patients with ischemic stroke had increased blood pressure. Among them, some had no previous history of hypertension, mainly in the acute phase, with pain, nausea, vomiting, increased intracranial pressure, confusion, anxiety, and post-stroke stress causing secondary blood pressure elevation [5].

Previous epidemiological studies reported conflicting results between blood pressure and ischemic stroke prognosis after intravenous thrombolysis [6–8]. A meta-analysis of 26 studies by Malhotra *et al.* [6] showed a positive association between blood pressure levels and the risk of poor clinical prognosis in 56,513 stroke patients treated with intravenous thrombolysis. However, a retrospective analysis comprising 11,080 stroke patients with safely performed thrombolysis showed that systolic blood pressure in the acute phase demonstrated a "U-shaped" relationship with mortality and functional outcomes. After a 3-month follow-up, it was observed that a systolic blood pressure of 141–150 mmHg was associated with the most favorable prognosis [7]. Similarly, another previous study based on 626 stroke patients treated with intravenous thrombolysis supported the benefits of intensive BP lowering in patients with a systolic blood pressure of 141–150 mmHg [8]. In contrast, a recent clinical trial of 2227 patients showed that intensive antihypertensive therapy did not significantly improve the 3-month prognosis of patients with ischemic stroke treated with intravenous thrombolysis [9]. We believe that these contrasting results might have occurred due to different study designs and participant characteristics, thus, indicating the importance of exploring the relationship between systolic blood pressure and ischemic stroke prognosis after intravenous thrombolysis.

In this study, we investigated the relationship between blood pressure and prognosis of patients with ischemic stroke after intravenous thrombolysis and the influence of vascular stenosis on this relationship using the data from the Suzhou Stroke Registry.

2. Materials and methods

2.1 Study participants

The data of a total of 620 consecutive ischemic stroke patients treated with intravenous thrombolysis from January 2012 to December 2018 at the Second Affiliated Hospital of Soochow University were retrieved and assessed. The study inclusion criteria were as follows: (i) met the diagnostic criteria of acute ischemic stroke; (ii) aged ≥18 years; within 4.5 hours from onset to injection; (iii) the patients' diagnosis was confirmed by cranial computed tomography (CT) or magnetic resonance imaging (MRI); (iv) provided signed informed consent. The exclusion criteria were: (i) diagnosed with pseudo-stroke based on clinical presentation and MRI; (ii) lacked blood pressure data in the acute phase; (iii) no continuous blood pressure monitoring within 24 hours. Based on these criteria, a total of 465 patients with ischemic stroke were found eligible for this study, among whom 439 had complete intracranial and extracranial vascular examinations (Fig. 1).

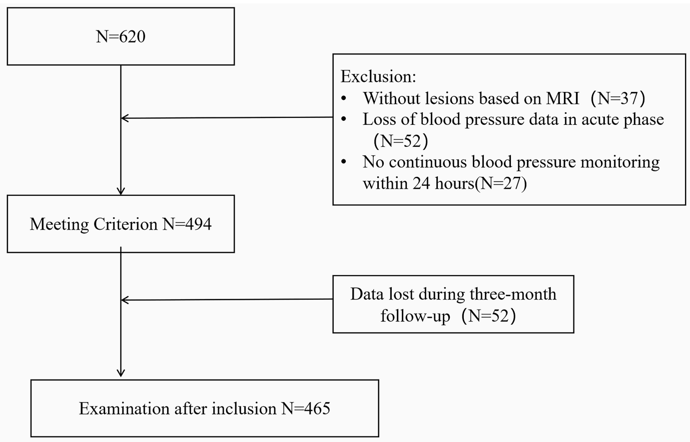

FIGURE 1. Flow chart of study patient selection. MRI: magnetic resonance imaging.

2.2 Study methods

2.2.1

Baseline characteristics collected from the patient's record included age, gender, smoking, alcohol consumption, baseline blood pressure, blood glucose, and weight. Smoking history was defined as ≥1 cigarette per day for any duration, and drinking history as at least 1 alcoholic drink per day for the past ≥1 year. Hypertension was defined as previous or post-admission stable systolic blood pressure ≥140 mmHg or/and diastolic blood pressure ≥90 mmHg, including a history of hypertensive medication and meeting the diagnosis of hypertension. Diabetes mellitus was defined as previous or post-admission fasting blood glucose ≥7.0 mmol/L or random blood glucose ≥11.1 mmol/L, or history of diabetic medication use and meeting corresponding diagnostic criteria. Atrial fibrillation (AF) was defined as a previous definite diagnosis of AF or a post-admission electrocardiograph (ECG), ECG monitoring or 24-hour ambulatory ECG indicating AF. Hyperlipidemia referred to previous or admission laboratory tests showing total cholesterol >5.2 mmol/L and/or low density lipoprotein (LDL) >2.58 mmol/L or current treatment with lipid-lowering drugs. Routine blood, coagulation, liver and kidney function, lipid panel, uric acid and ferritin tests were performed in emergency or within 24 hours of admission. A head CT examination was completed in emergency, and MRI and Magnetic Resonance Angiography (MRA) or computed tomography angiography (CTA) examination of the head and neck were completed during hospitalization without special circumstances, following which the infarct location and stenosis of blood vessels were recorded.

2.2.2

Blood pressure after intravenous thrombolytic therapy was monitored using a cardiac monitoring system and recorded once every hour. The emergency admission blood pressure was recorded as random blood pressure, recombinant tissue plasminogen activator (rt-PA) intravenous thrombolytic therapy was recorded once every hour for 6 hours and once every 3 hours for the following 18 hours. A total of 13 blood pressure recordings were made.

2.2.3

Severe stenosis was defined as more than one stenosis ≥70% or occlusion of the internal carotid artery, middle cerebral artery, vertebral artery and basilar artery on magnetic resonance angiography or computed tomographic angiography of head and neck, regardless of the patient with atrial fibrillation.

2.2.4

Study outcomes included death, major disability (modified Rankin Scale (mRS) 3–6) and intracranial hemorrhagic transformation at 3 months after IVT. Other outcomes included death within 3 months and intracranial hemorrhagic transformation. Death certificates were obtained for deceased patients, and hospital data were abstracted for intracranial hemorrhagic transformation.

2.3 Statistical analysis

Statistics analyses were performed using the SPSS v25.0 statistical software (IBM Corp, Armonk, NY, USA). Statistical tests were performed using a two-sided test with $p < 0.05$ used to indicate statistical significance. Continuous variables conforming to normal distribution were expressed as mean ± standard deviation (x ± s), *t*-test was used for comparison between two groups, and analysis of variance (ANOVA) was used for comparison between multiple groups. The data of continuous variables with skewed distribution are expressed as median (interquartile spacing), Wilcoxon rank sum test was used for comparison between two groups, and the Kruskal-Wallis test for comparison between multiple groups. Continuous data are described as frequency (%), and the chi-square test was used for comparison between groups. The mean systolic blood pressure and systolic blood pressure variability were used as grouping and continuous variables. The relationship between these variables and clinical outcomes was analyzed using logistic regression model to calculate the odds ratio (OR) and Cox proportional hazard regression model to calculate the hazard ratio (HR) and corresponding 95% confidence interval (CI) for the other quartile groups and the control group.

3. Results

3.1 Baseline characteristics

A total of 465 acute ischemic stroke patients, consisting of 294 males (63.2%), treated with intravenous thrombolysis were included in this study. The mean age of the entire cohort was 64.2 ± 10.1 years. There were 347 (74.6%) patients with a previous history of hypertension, 90 (19.4%) with a previous history of diabetes mellitus, 115 (24.7%) with a previous history of AF, and 78 with a previous history of stroke (16.8%). Of the included patients, 206 (44.3%) had hyperlipidemia, and 175 (37.6%) were smokers. Further, the patients had an National Institutes of Health Stroke Scale (NIHSS) score of 8 (4, 13), onset to treatment time (OTT) of 182 ± 142 minutes, door to needle time (DNT) of 77.9 ± 35.5 minutes, 164 patients (37.4%) had severe stenosis of the offending vessels, 121 (30.9%) had severe cerebral white matter hyperintensities. Their blood glucose level was 7.3 (6.4, 9.0) mmol/L, systolic blood pressure 151.3 ± 17.8 mmHg, diastolic blood pressure 83.7 ± 14.9 mmHg, 24-hour mean systolic blood pressure 135.1 ± 16.8 mmHg, 24-hour mean diastolic blood pressure 75.2 ± 10.8 mmHg, LDL 3.2 ± 0.9 mmol/L and total cholesterol 4.84 ± 1.1 mmol/L. In addition, 161 (34.6%) patients had a poor prognosis, 45 (9.7%) died within 3 months, and 45 (9.7%) had intracranial hemorrhagic transformation after thrombolysis (Table 1).

3.2 Association between mean systolic BP and clinical outcomes

The blood pressure within 24 hours of intravenous thrombolysis with rt-PA was recorded in all enrolled patients, and the data showed a decreasing trend of 24-hour blood pressure after IVT. The median systolic BP (interquartile interval) and diastolic BP during IVT therapy were 147 (134–161) mmHg and 80 (71–90) mmHg, respectively, while the 24-hour median systolic BP and diastolic BP after IVT therapy was 137 (interquartile interval: 122–152) mmHg and 75 (interquartile interval: 66–86) mmHg, respectively.

The mean 24-hour systolic blood pressure, after IVT was used as a categorical variable, was divided into three groups, namely, high (>145.23 mmHg), medium (131.23–145.23 mmHg) and low (<131.23 mmHg) based on trichotomization. In univariate analysis, the risk of poor outcome in the highest trichotomic group of mean systolic blood pressure was 2.64 times higher than in the lowest trichotomic group (OR 2.64; 95% CI 1.63–4.29; $P_{trend} < 0.001$) and had a 4.49 times higher risk of death (HR 4.49; 95% CI 1.90–10.62; $P_{trend} < 0.001$) in the lowest quartile group. Despite no difference was observed in the risk of intracranial hemorrhagic ($P_{trend} = 0.081$).

After adjustment of confounders, the adjusted HRs or ORs associated with the highest tertile of mean systolic BP within 24 hours after IVT were 2.92 (95% CI, 1.10–8.01; $P_{trend} = 0.006$) for death, 1.51 (95% CI, 0.80–2.86; $P_{trend} = 0.180$) for death or major disability, and 1.33 (95% CI, 0.57–3.11; $P_{trend} = 0.444$) for intracranial hemorrhagic transformation. On the continuous analyses showed that for every 10 mmHg increase in mean systolic blood pressure, the patients had a 44% increase in the risk of death (HR 1.44; 95% CI 1.13–1.83; p = 0.003) and an 18% increase in the risk of poor prognosis (OR 1.18; 95% CI 1.00–1.40; p = 0.049) within three months after stroke (Table 2).

3.3 Interaction of stenosis >70% and 24-hour mean systolic blood pressure after thrombolysis with prognosis

Intracranial and extracranial vascular examinations were performed in 439 of the included patients, of whom 164 (37.4%) had severe stenosis or occlusion of the affected vessel. Our data revealed an interaction between the stenosis degree of the affected vessel and the 24-hour systolic blood pressure level after thrombolysis on the patients' 3-month functional prognosis (p for interaction = 0.042). In patients with combined severe stenosis of the responsible vessel, univariate analysis showed that in the highest blood pressure group (>150 mmHg), the risk of adverse prognosis was 4.20 times that of the risk in the control group (130–140 mmHg) (OR 4.20; 95% CI 1.46–12.09; $p = 0.008$).

Moreover, both the lowest blood pressure group (<130 mmHg) and the control group (130–140 mmHg) showed no statistically significant difference with adverse prognosis ($p = 0.49$). After adjusting for confounders, the risk of adverse prognosis in the lowest blood pressure group (<130 mmHg) was 4.94 times higher than in the control group (130–140 mmHg) (OR 4.94; 95% CI 1.01–24.20, $p = 0.049$). In patients with combined severe stenosis of the responsible vessels, the risk of poor prognosis in the highest blood pressure group (>150 mmHg) was 22.12 times higher than in the control group (130–140 mmHg) (OR 22.12; 95% CI 3.62–135.30, $p < 0.001$). Therefore, in acute ischemic stroke patients with severe stenosis in the responsible vessel, a "J"-shaped relationship was observed between the mean systolic blood pressure

TABLE 1. Baseline characteristics of the study participants.

Baseline characteristic[a]	N = 465
Age	64.2 ± 10.1
Male (%)	294 (63.2)
Current smoker (%)	175 (37.6)
Current drinker (%)	101 (21.7)
Hypertension history (%)	347 (74.6)
Diabetes mellitus history (%)	90 (19.4)
AF history (%)	115 (24.7)
Stroke history (%)	78 (16.8)
Coronary disease history (%)	31 (6.7)
Hyperlipidemia (%)	206 (44.3)
Blood glucose, mmol/L	7.3 (6.4, 9.0)
Uric acid, μmol/L	319 ± 98.2
Inosine, μmol/L	62.0 (42.0, 77.0)
Homocysteine, μmol/L	13.0 (10.1, 18.0)
Low density lipoprotein, mmol/L	3.2 ± 0.9
High-density lipoprotein, mmol/L	1.1 (0.9, 1.4)
Triglyceride, mmol/L	1.3 (0.9, 2.8)
Total cholesterol, mmol/L	4.8 ± 1.1
C-reactive protein, mg/L	6.3 (5.5, 7.1)
Fibrinogen, g/L	3.0 ± 0.7
D-dimer, μg/mL	1.9 (0.8, 5.6)
Baseline NIHSS score	8.0 (4.0, 13.0)
Baseline systolic blood pressure, mmHg	147 (134, 161)
Baseline diastolic blood pressure, mmHg	80 (71, 90)
Mean systolic blood pressure for 24 h, mmHg	135.1 ± 16.8
Mean diastolic blood pressure for 24 h, mmHg	75.2 ± 10.8
rt-PA dose, mg	50.0 (46.8, 60.0)
DNT, minute	77.9 ± 35.5
OTT, minute	182.0 ± 142.0
Severe stenosis of offending vessels (%)[b]	164 (37.4)
Severe WMH (%)[c]	121 (30.9)
TOAST type	
LAA (%)	213 (45.8)
SA (%)	117 (25.2)
CE (%)	116 (25.0)
SOE (%)	9 (1.9)
SUE (%)	8 (1.7)
OCSP type	
TACI (%)	81 (17.5)
PACI (%)	196 (42.2)
LACI (%)	109 (23.5)
POCI (%)	78 (16.8)
NIHSS score discharged from hospital	2 .0 (0.0, 7.0)
Poor prognosis (%)	161 (34.6)
Death (%)	45 (9.7)
Hemorrhage transformation (%)	45 (9.7)

Abbreviations: CE, cardioembolism; DNT, door to needle time; LAA, large-artery atherosclerosis; LACI, lacunar infarcts; NIHSS: National Institutes of Health Stroke Scale; OCSP, Oxfordshire Community Stroke Project; OTT, onset to treatment time; PACI, partial anterior circulation infarcts; POCI, posterior circulation infarcts; rt-PA, recombinant tissue plasminogen activator; SA, small-artery occlusion lacunar; SOE, acute stroke of other determined etiology; SUE, stroke of other undetermined etiology; TACI, total anterior circulation infarcts; TOAST, Trial of Org 10172 in acute stroke treatment; WMH: white matter hypersignal.

[a] *Continuity variables were expressed by mean ± standard deviation or median (interquartile spacing). Categorical variables were expressed as frequency (%).*

[b] *439 patients completed intracranial and extracranial vascular examinations.*

[c] *381 patients were assessed for WMH.*

TABLE 2. Relationship between 24-hour mean systolic blood pressure after intravenous thrombolysis and 3-month prognosis of ischemic stroke.

Variables	24-hour mean systolic blood pressure (mmHg)			P_{trend}	Each 10-mmHg increase in mean systolic blood pressure	p
	<131.23	131.23–145.23	≥145.23			
Poor outcome (mRS 3–6)[a]						
Cases, n (%)	38 (24.68)	52 (32.91)	71 (46.41)			
Univariate model	1.00	1.50 (0.91–2.46)	2.64 (1.63–4.29)	<0.001	1.32 (1.16–1.50)	<0.001
Multivariate model	1.00	0.82 (0.43–1.55)	1.51 (0.80–2.86)	0.180	1.18 (1.00–1.40)	0.049
Death[b]						
Cases, n (%)	7 (4.55)	10 (6.21)	28 (17.61)			
Univariate model	1.00	1.39 (0.52–3.75)	4.49 (1.90–10.62)	<0.001	1.47 (1.21–1.80)	<0.001
Multivariate model	1.00	0.50 (0.15–1.68)	2.92 (1.10–8.01)	0.006	1.44 (1.13–1.83)	0.003
Intracranial hemorrhagic transformation[a]						
Cases, n (%)	11 (7.1)	14 (8.9)	20 (13.1)			
Univariate model	1.00	1.26 (0.56–2.88)	1.96 (0.90–4.23)	0.081	1.16 (0.96–1.40)	0.130
Multivariate model	1.00	0.87 (0.36–2.11)	1.33 (0.57–3.11)	0.444	1.09 (0.88–1.35)	0.438

Adjusted for age, sex, current smoking, alcohol drinking, blood glucose, dyslipidemia, baseline NIHSS score, history of hypertension, history of diabetes mellitus, history of atrial fibrillation, history of coronary heart disease, and ischemic stroke subtype. Abbreviations: mRS, modified Rankin Scale;

[a] *Logistic regression model was applied because of the non-eventive nature of major disability and intracranial hemorrhagic transformation.*

[b] *Cox proportional hazard models were performed.*

at 24 hours after intravenous thrombolysis and poor prognosis. However, for patients without distinct stenosis in the offending vessel, there was no statistically significant difference in prognosis in different blood pressure groups compared with the control group. After adjusting for relevant confounders, there was still no significant correlation between mean systolic blood pressure and prognosis after thrombolysis (P_{trend} = 0.780). Therefore, these results indicated that the degree of vascular stenosis significantly affected the relationship between mean systolic blood pressure and prognosis ($P_{interaction}$ = 0.046) (Table 3).

4. Discussion

In this study, we found that blood pressure tended to decrease after intravenous thrombolysis. The risk of death within 3 months was significantly associated with high systolic blood pressure within 24 hours after intravenous thrombolysis. For patients with vessel stenosis ≥70% on post-thrombolytic vascular imaging, a "J"-shaped relationship was observed between mean systolic blood pressure at 24 hours after thrombolysis and prognosis, and the proportion of poor outcomes was lowest when systolic blood pressure was between 130 and 140 mmHg. These results suggested that positive antihypertensive therapy and smooth blood pressure control could help improve the rehabilitation and care of patients with ischemic stroke treated with intravenous thrombolysis.

The relationship between blood pressure and prognosis of patients post-thrombolysis revascularization was also investigated. The result showed that in patients with severe stenosis on post-thrombolytic imaging angiography, there was a "J"-shaped relationship between post-thrombolytic 24-hour systolic blood pressure and clinical prognosis. However, there was no significant difference between blood pressure and stroke prognosis in patients with <70% post-thrombolytic large vascular stenosis, indicating that good revascularization after thrombolysis could alter the balance between hypoperfusion and hyperperfusion injury.

Blood pressure under the conditioned parameters was associated with a reduced risk of exacerbating stroke symptoms, whereas higher systemic blood pressure may directly contribute to cranial neurological deficits. We also found that elevated systolic blood pressure was associated with poor prognosis ($p < 0.001$), similar to the results of the stroke-

TABLE 3. Interaction between offending vascular stenosis ≥70% and 24-hour mean systolic blood pressure and outcome.

Poor prognosis (mRS >2)	Univariate OR (95% CI)	*p*	multivariate OR (95% CI)	*p*
Offending vascular stenosis ≥70%				
<130	1.40 (0.53–3.67)	0.490	4.94 (1.01–24.20)	0.049
130–140	Ref.		Ref.	
140–150	1.71 (0.68–4.33)	0.260	4.49 (1.00–20.29)	0.051
≥150	4.20 (1.46–12.09)	0.008	22.12 (3.62–135.30)	<0.001
p for trend = 0.041				
Offending stenosis <70%				
<130	0.32 (0.12–0.89)	0.032	0.50 (0.15–1.62)	0.252
130–140	Ref.		Ref.	
140–150	0.91 (0.38–2.23)	0.844	0.42 (0.13–1.33)	0.138
≥150	0.56 (0.19–1.66)	0.297	0.62 (0.17–2.30)	0.483
p for trend = 0.780				

p for interaction = 0.0422.
Adjusted for age, sex, current smoking, alcohol drinking, blood glucose, dyslipidemia, baseline NIHSS score, history of hypertension, history of diabetes mellitus, history of atrial fibrillation, history of coronary heart disease, and ischemic stroke subtype.
Abbreviations: mRS, modified Rankin Scale;
a Logistic regression model was applied because of the non-eventive nature of major disability and intracranial hemorrhagic transformation.

international stroke thrombolysis register study (SITS-ISTR). In addition, it was linearly associated with symptomatic intracranial hemorrhage and demonstrated a "U" shaped association with death and disability under optimal clinical outcomes occurring between a systolic blood pressure range of 141–150 mmHg [10]. A previous study reported that patients who were not revascularized or incompletely revascularized after intravenous thrombolytic therapy had significantly higher post-treatment systolic blood pressure than patients with adequate revascularization and that the higher blood pressure functioned to maintain perfusion pressure distal to the occluded stenotic vessel [11]. A recent analysis quantifying collateral circulation via multimodal imaging found that elevated blood pressure was detrimental in poorly reperfused stroke patients, whereas increasing blood flow in the collateral circulation improved prognosis in well-reperfused patients [12]. Therefore, lower blood pressure could increase the risk of loss of ischemic penumbra, thereby leading to poorer prognosis in patients with incomplete cerebral revascularization.

Higher systemic blood pressure can damage the blood-brain barrier, leading to increased brain tissue edema or hemorrhagic transformation, increasing the risk of poor prognosis. Patients with small vascular occlusion and relatively good perfusion have smaller infarct volumes, lesser severe clinical symptoms and smaller ischemic semidark zone volumes; thus, in such settings, blood pressure fluctuations have a lesser impact on the relationship between semidark zone volume and functional prognosis. Nevertheless, the risk of hemorrhagic transformation in patients with intravenous thrombolysis and mild stroke was shown to be significantly lower than average [13]. Patients with good recanalization after treatment generally do not have significant hypoperfused tissue, indicating that the blood pressure in such patients can return to its usual physiological at the early stage. Although some studies found prognostic benefits of lower blood pressure in patients with satisfactory degrees of revascularization, our study found no significant correlation between blood pressure levels and stroke patients' clinical prognosis despite good revascularization after thrombolysis. However, vascular examination after intravenous thrombolytic therapy is lagging compared with endovascular treatment. Besides, in regard to stroke, the incidence of large artery atherosclerosis and vascular occlusion are predominant in China, so early assessment of the degree of revascularization after intravenous thrombolytic therapy is important to adequately guide subsequent vascular management. Moreover, in the prospective data, no "J"-type relationship between blood pressure and poor prognosis was found in patients with severe stenosis of the combined responsible vessels. Only a positive association between blood pressure and poor prognosis was found in univariate analyses. Thus, a larger sample of prospective data is still needed to confirm these observations due to the possibility of significant statistical bias, given that the number of cases per group was relatively small.

This present study had several advantages. First, it comprised a large sample size, allowing us to perform a valid and powerful statistics analysis. Second, standardized protocol and strict quality control procedures were used for baseline data collection and outcome assessment during follow-up. However, there were still some limitations worth addressing. First, this was a single-center study based on the database of the Suzhou Stroke Registry. Therefore, the existence of selection bias might have been inevitable, limiting the generalizability of our findings. Second, although some important confounding factors were controlled in the multivariate adjustment model, residual confounding factors could not be eliminated. Third, considering that systolic blood pressure was measured within 24 hours after intravenous thrombolytic therapy, we could not study the effects of blood pressure from symptom onset to hospitalization on the prognosis of acute ischemic stroke. Lastly, all participants were from China, and the validity of these findings in other populations should be further clarified.

5. Conclusion

For patients with vessel stenosis $\geq$70% on post-thrombolytic vascular imaging, a "J"-shaped relationship was observed between mean systolic blood pressure at 24 hours after thrombolysis and prognosis, and the proportion of poor outcomes was lowest when systolic blood pressure was between 130 and 140 mmHg.

AUTHOR CONTRIBUTIONS

XM, JZ, YC—designed the research study. XM—performed the research. DW, SX and SW—analyzed the data. XM and ZL—wrote the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was granted an exemption from requiring ethics approval (The ethics committee of the Second Affiliated Hospital of Soochow University). This study was a retrospective medical record registry study, and all clinical data were obtained with the consent of the patients and their immediate family members.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the global burden of disease study 2019. The Lancet Neurology. 2021; 20: 795–820.

[2] Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, *et al*. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the american heart association/American stroke association. Stroke. 2018; 49: e46–e110.

[3] Yong M, Kaste M. Association of characteristics of blood pressure profiles and stroke outcomes in the ECASS-II trial. Stroke. 2008; 39: 366–372.

[4] He J, Zhang Y, Xu T, Zhao Q, Wang D, Chen CS, *et al*. Effects of immediate blood pressure reduction on death and major disability in patients with acute ischemic stroke: the CATIS randomized 302 clinical trial. JAMA. 2014; 311: 479–489.

[5] IST-3 collaborative group, Sandercock P, Wardlaw JM, Lindley RI, Dennis M, Cohen G, *et al*. The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST-3]): a randomised controlled trial. Lancet. 2012; 379: 2352–2363.

[6] Malhotra K, Ahmed N, Filippatou A, Katsanos AH, Goyal N, Tsioufis K, *et al*. Association of elevated blood pressure levels with outcomes in acute ischemic stroke patients treated with intravenous thrombolysis: a systematic review and meta-analysis. Journal of Stroke. 2019; 21: 78–90.

[7] Ahmed N, Wahlgren N, Brainin M, Castillo J, Ford GA, Kaste M, *et al*. Relationship of blood pressure, antihypertensive therapy, and outcome in ischemic stroke treated with intravenous thrombolysis: retrospective analysis from safe implementation of thrombolysis in stroke-international stroke thrombolysis register (SITS-ISTR). Stroke. 2009; 40: 2442–2449.

[8] Li C, Wang Y, Chen Y, Zhang C, Dong Z, Zhang S, *et al*. Optimal blood pressure levels in patients undergoing intravenous thrombolysis for AIS. Minerva Medica. 2015; 106: 255–258.

[9] Anderson CS, Huang Y, Lindley RI, Chen X, Arima H, Chen G, *et al*. Intensive blood pressure reduction with intravenous thrombolysis therapy for acute ischaemic stroke (ENCHANTED): an international, randomised, open-label, blinded-endpoint, phase 3 trial. The Lancet. 2019; 393: 877–888.

[10] Wahlgren N, Ahmed N, Dávalos A, Hacke W, Millán M, Muir K, *et al*. Thrombolysis with alteplase 3–4.5 h after acute ischaemic stroke (SITS-ISTR): an observational study. The Lancet. 2008; 372: 1303–1309.

[11] Kellert L, Hametner C, Ahmed N, Rauch G, MacLeod MJ, Perini F, *et al*. Reciprocal interaction of 24-hour blood pressure variability and systolic blood pressure on outcome in stroke thrombolysis. Stroke. 2017; 48: 1827–1834.

[12] Hong L, Cheng X, Lin L, Bivard A, Ling Y, Butcher K, *et al*. The blood pressure paradox in acute ischemic stroke. Annals of Neurology. 2019; 85: 331–339.

[13] Coutts SB, Dubuc V, Mandzia J, Kenney C, Demchuk AM, Smith EE, *et al*. Tenecteplase-tissue-type plasminogen activator evaluation for minor ischemic stroke with proven occlusion. Stroke. 2015; 46: 769–774.

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