



# Blood pressure fluctuation pattern and stroke outcomes in acute ischemic stroke

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## Abstract

Blood pressure (BP) fluctuates widely during the acute phase of stroke. Compared to single BP assessment, patterns of BP over time may have greater power in predicting stroke outcome. This study aims to investigate the effect of BP fluctuation patterns on stroke outcomes in acute ischemic stroke (IS) patients. IS patients within 24 h of onset registered in the BOSS registry between 2012 and 2014 were analyzed. Fluctuation of BP was predefined as the change trend in systolic BP (SBP) from Day 1 to Day 7 after onset and was used to divide patients into groups with sustained high SBP ( $\geq 160$  mmHg) during the first 7 days (C1); rapid (C2: within the first 2 days) or delayed (C3: after 2 days) decline from high ( $\geq 160$  mmHg) to low ( $< 160$  mmHg); consistently low SBP (C4); and elevation from low to high (C5). The primary stroke outcome was defined as a modified Rankin Scale score  $\geq 3$  at 3 months after onset. Of 1,095 IS patients, C1 ( $n = 90$ ) had the highest risk of poor outcome (23.3%), while C2 ( $n = 198$ , risk = 11.6%) and C4 ( $n = 650$ , risk = 12.2%) had the lowest risk. C2 and C4 had a significant reduction in poor outcome risk when compared to C1, even after adjustment for average BP and BP variability (BPV) during the first 7 days (adjusted odds ratio [OR]<sub>C2</sub> = 0.32, 95% CI: 0.12–0.80; OR<sub>C4</sub> = 0.37, 95% CI: 0.14–0.97). The BP fluctuation pattern in the acute phase of IS might be a useful predictive parameter for functional outcome independent of average BP and BPV.

**Keywords** Acute stroke · Blood pressure · Ischemic stroke · Outcome

## Introduction

The relationship between acute-phase blood pressure (BP) and stroke outcomes in patients with acute ischemic stroke

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(IS) is still controversial. Most previous studies showed a detrimental effect of increased levels of BP [1–4]; however, other studies found improved outcomes for high BP [5–7] or failed to identify any association at all [8]. Notably, most studies focus only on single-time-point BP or average BP during the acute phase, but recently, several studies have found that stroke outcome in acute IS was determined not only by initial BP levels but also by the direction and magnitude of associated BP change over the first 2 days after onset [9–11]. Most patients have high BP after stroke, and subsequently, BP settles over a period of approximately a week [12]. For patients with acute hypertensive response, there are three common BP fluctuation patterns during the first week after stroke: rapid decline within 48 h, delayed decline after 48 h, or maintenance of a sustained high level. Among patients with low BP at onset, some patients may have a delayed BP elevation afterwards or maintain consistent low or even reduce BP during the acute phase. It is not clear whether BP fluctuation patterns in the acute phase of IS could predict stroke outcomes and which BP pattern is better. In this study, we will investigate the effect of the above predefined BP fluctuation patterns during the acute phase on stroke outcomes in IS patients.

## Methods

### Study design and population

This study examined data from the BOSS (Blood Pressure and Clinical Outcome in TIA or Ischemic Stroke) registry [13]. Briefly, BOSS was a nationwide, hospital-based, prospective cohort study aiming to assess blood pressure parameters and clinical outcomes in 2608 IS/TIA patients consecutively enrolled from October 2012 to February 2014 conducted at 61 hospitals in China. The study was approved by the Central Institutional Review Board at Beijing Tiantan Hospital, and all patients or their designated relatives provided informed consent. The BOSS registry inclusion criteria were as follows: age 18 years or older; diagnosis of an acute IS or TIA; and recruited within 7 days of symptom onset. Baseline information about risk factors included the following: heavy drinking (two or more standard alcoholic beverages consumed per day), hypertension (a reported history of hypertension or antihypertensive medication use), diabetes mellitus (self-reported physician diagnosis of diabetes mellitus or use of antidiabetic drugs), and dyslipidemia (self-reported physician diagnosis of dyslipidemia or use of lipid-lowering agents). In this study, 1291 IS patients within 24 h of onset registered in the BOSS registry were chosen as the study population. A detailed patient-recruitment flowchart is illustrated in Supplementary Fig. 1.

### BP measurement

BP was measured by doctors or trained nurses at admission, discharge and the 3-month follow-up visit, according to a standard measurement protocol recommended by the American Heart Association (AHA) [14]. During hospitalization, BP was measured twice daily (6AM-9AM in the morning, 6PM-9PM in the evening) in the nonparetic arm, in the supine position, with a semiautomatic upper-arm BP monitor (HEM-4030, OMRON Life Science Co. Ltd, Kyoto, Japan), which was assigned to each patient after enrollment in the BOSS registry. Three blood pressure measurements were conducted at each time point, and six BP readings were recorded in the BP diary.

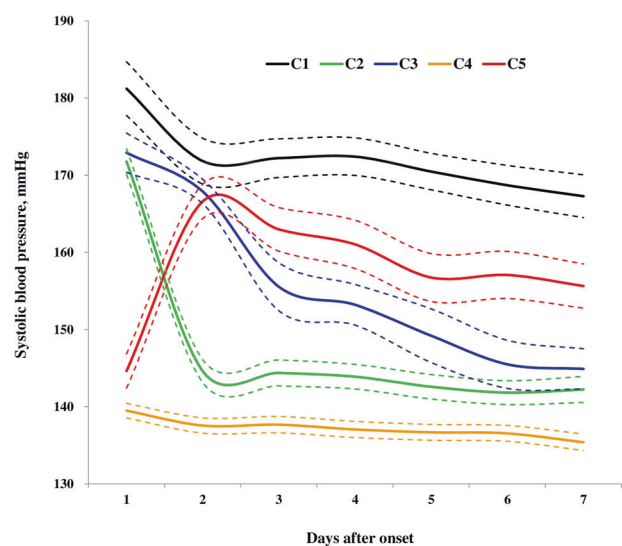
### BP fluctuation pattern classification

In this study, BP fluctuation patterns were defined in three time periods (day 1, day 2, and days 3–7). The BP on day 1 was calculated as the average of 3 BP readings at admission; the BP on day 2 was calculated as the average of 6 BP readings; and the BP on days 3–7 was calculated as the average of the BP over 5 days. High BP in each time period was defined as SBP  $\geq 160$  mmHg. All of the patients were divided into five classes (C1–C5) according to predefined

criteria: C1, consistent high BP during the acute phase (day 1:  $\geq 160$  mmHg; day 2:  $\geq 160$  mmHg; days 3–7:  $\geq 160$  mmHg); C2, rapid (within the first 2 days after onset) decline from high to low BP (day 1:  $\geq 160$  mmHg; day 2:  $< 160$  mmHg); C3, delayed (after 2 days) decline from high to low BP (day 1:  $\geq 160$  mmHg; day 2:  $\geq 160$  mmHg, days 3–7:  $< 160$  mmHg); C4, consistent low BP for the entire 7-day period (day 1:  $< 160$  mmHg; day 2:  $< 160$  mmHg, days 3–7:  $< 160$  mmHg); and C5, elevation from low to high over the 7-day time frame (day 1:  $< 160$  mmHg, [day 2:  $\geq 160$  mmHg, or days 3–7:  $\geq 160$  mmHg]). For example, if a patient's BP was 170 mmHg on admission, 165 mmHg on day 2, and 150 mmHg on days 3–7, he/she was classified as C3; if another patient's BP was 155 mmHg on admission, 155 mmHg on day 2, and 150 mmHg on days 3–7, he/she was classified as C4. The BP curves during the first 7 days for the five classes are shown in Fig. 1.

### Outcome assessment

Patients were examined for stroke outcomes at 3 months through face-to-face visits by trained neurologists. The primary outcome of this study was major disability or death at 3 months, defined as a modified Rankin scale score of 3–6. The secondary outcomes included stroke recurrence within 3 months and neurological deterioration at discharge compared to admission. Stroke recurrence was defined as a



**Fig. 1** SBP fluctuation patterns during the acute phase of ischemic stroke. The solid line represents the average SBP in a class. Dotted lines represent 95% confidence intervals. C1 consistently high SBP ( $\geq 160$  mmHg) for all 7 days, C2 rapid (within the first 2 days after onset) decline from high ( $\geq 160$  mmHg) to low ( $< 160$  mmHg), C3 delayed (after 2 days) decline from high ( $\geq 160$  mmHg) to low ( $< 160$  mmHg), C4 consistently low SBP ( $< 160$  mmHg) for the entire 7-day period, C5 SBP increasing from low ( $< 160$  mmHg) to high ( $\geq 160$  mmHg) over the 7-day time frame, SBP systolic blood pressure

new stroke event (ischemic or hemorrhagic) accompanied by evidence of a stroke on magnetic resonance imaging or computed tomography of the brain. Neurological deterioration was defined as an increase of at least 2 points in the total National Institutes of Health Stroke Scale [NIHSS] score at discharge compared with admission score [15].

## Statistical Analysis

Continuous variables were reported as the mean  $\pm$  standard deviation or median and interquartile range. Categorical variables were described using percentages. The Kolmogorov–Smirnov test was used to assess the normality of continuous variables. Baseline characteristics were compared using Student's *t* test or analysis of variance for nonpaired samples with normally distributed parameters, the Wilcoxon or Kruskal–Wallis rank test for nonparametric variables, and the  $\chi^2$  test or Fisher's exact test for categorical variables. All statistical analyses were performed using SAS software (version 9.4; SAS Institute Inc., Cary, NC, USA), and two-sided *p* values  $<0.05$  were considered statistically significant.

Univariate and multivariate logistic regression models were used to estimate the odds ratios (OR) and 95% confidence intervals (CI) for each BP fluctuation pattern and functional outcome at 3 months. Moreover, we applied a multivariate logistic regression model to evaluate predictors of poor outcome (mRS  $\geq 3$ ) at 3 months. A variable was included in the multivariate model if associated with BP pattern with a *P* value of  $<0.20$ . We created four multivariate-adjusted models. Model 1 was adjusted for age and sex; Model 2 was adjusted for age, sex, risk factors (history of hypertension, diabetes and hyperlipidemia), NIHSS on admission, IS subtype, antihypertensive medication history, and discharge with antihypertensive medication. Model 3 was adjusted for all variables in model 2 plus average SBP and BP variability (BPV, defined as the standard deviation) during the 7 days after onset. Moreover, to evaluate predictors of poor outcome (mRS  $\geq 3$ ) at 3 months, we applied a multivariate logistic regression model including all variables in model 3. Model 4 adjusted for all variables in model 2 plus average SBP and BPV (defined as the coefficient of variation) during the 7 days after onset.

## Sensitivity analyses

To eliminate the effect of antihypertensive treatment on BP fluctuation patterns, we conducted a sensitivity analysis in patients who did not receive antihypertensive treatment during the acute phase. Moreover, to eliminate the potential impact of recurrent stroke during the first 7 days on the BP

profile, we also conducted a sensitivity analysis in patients who did not have stroke recurrence during the acute phase.

## Results

### Baseline Characteristics of the study population

Of 1291 IS patients within 24 h of onset, 1095 patients were included in the final analysis after 196 patients were excluded (Supplementary Fig. 1). Compared with the study population, the excluded population was more likely to be female and was less likely to have a history of stroke or discharge with lipid-lowering agents (Supplementary Table 1).

A total of 1095 patients were divided into five groups based on BP patterns. The baseline characteristics are shown in Table 1. Compared with other groups, patients in the C1 group and C5 group seem more likely to have a history of hypertension, history of antihypertensive medication, and discharge with antihypertensive medication. It is worth noting that C1 had the highest average BP but had the second lowest BPV, while C4 had the lowest average BP and lowest BPV (Table 1).

### Associations between BP patterns and stroke outcomes

Table 2 shows the primary and secondary outcomes in each BP pattern group. C1 and C5 had the highest risk of death and major disability (mRS  $\geq 3$ ) at 3 months, neurological deterioration at discharge and stroke recurrence within 3 months. Table 3 shows that, compared with C1, patients in C2 and C4 had significantly lower risks for death and major disability (unadjusted odds ratio [OR]<sub>C2</sub> = 0.43, 95% confidence interval [CI]: 0.23–0.83; OR<sub>C4</sub> = 0.46, 95% CI: 0.26–0.78). A decreased risk of poor functional outcome was still apparent in C2 and C4 after adjusting for confounders and average blood pressure and BPV in model 1 and model 2.

Although patients in C4, who maintained low BP ( $<160$  mmHg) for all 7 days, had a better prognosis than those in C1, we further examined the prognosis of subcategories of the patients within C4. We divided patients in C4 into 3 groups based on their average systolic BP over the 7 days:  $<120$  mmHg, 120–140 mmHg, and 140–160 mmHg. The risk of death and major disability in those with BP  $<120$  mmHg group was 18.4%, and these patients experienced similarly detrimental outcomes to patients in C1 (23.3%), who maintained BP  $\geq 160$  mmHg during the acute phase, while patients in C4 with BP in the 120–140 mmHg and 140–160 mmHg ranges showed better outcomes (Supplementary Table 2).

**Table 1** Characteristics of the study participants according to the blood pressure fluctuation patterns

	Total N = 1095	Blood pressure fluctuation pattern					P Value
		C1 n = 90	C2 n = 198	C3 n = 69	C4 n = 650	C5 n = 88	
Age, mean $\pm$ SD, y	63.3 $\pm$ 11.2	66.2 $\pm$ 11.5	62.4 $\pm$ 10.8	61.9 $\pm$ 11.4	63.3 $\pm$ 11.2	63.7 $\pm$ 11.1	0.06
Female, n (%)	315 (28.8)	24 (26.7)	60 (30.3)	20 (29.0)	176 (27.1)	35 (39.8)	0.16
Previous or current smoking, n (%)	485 (44.3)	35 (38.9)	90 (45.5)	31 (44.9)	292 (44.9)	37 (42.1)	0.83
Drinking, n (%)							0.96
No drinking	701 (64.0)	59 (65.6)	125 (63.1)	49 (71.0)	414 (63.7)	54 (61.4)	
Light drinking	219 (20.0)	16 (17.8)	42 (21.2)	10 (14.5)	131 (20.2)	20 (22.7)	
Moderate to heavy drinking	175 (16.0)	15 (16.7)	31 (15.7)	10 (14.5)	105 (16.2)	14 (15.9)	
mRS prior to stroke >1, n (%)	91 (8.31)	12 (13.33)	18 (9.09)	5 (7.25)	50 (7.69)	6 (6.82)	0.43
Medical history, n (%)							
Stroke	258 (23.6)	26 (28.9)	47 (23.7)	13 (18.8)	150 (23.1)	22 (25.0)	0.65
Coronary heart disease	118 (10.8)	4 (4.4)	20 (10.1)	8 (11.6)	79 (12.2)	7 (8.0)	0.21
Hypertension	757 (69.1)	76 (84.4)	145 (73.2)	44 (63.8)	419 (64.5)	73 (83.0)	<0.001
Diabetes	251 (22.9)	21 (23.3)	38 (19.2)	19 (27.5)	139 (21.4)	34 (38.6)	<0.01
Hyperlipidemia	93 (8.5)	9 (10.0)	13 (6.6)	11 (15.9)	49 (7.5)	11 (12.5)	0.07
NIHSS on admission, median(IQR)	3 (1–5)	3 (2–6)	3 (2–5)	4 (2–6)	3 (1–5)	2.5 (1–5)	0.03
Ischemic stroke subtype, n (%)							0.15
Large-artery atherosclerosis	657 (60.0)	62 (68.9)	120 (60.6)	39 (56.5)	382 (58.8)	54 (61.4)	
Cardioembolism	60 (5.5)	2 (2.2)	8 (4.0)	1 (1.5)	47 (7.2)	2 (2.3)	
Small-artery occlusion	344 (31.4)	24 (26.7)	62 (31.3)	28 (40.6)	199 (30.6)	31 (35.2)	
Others	34 (3.1)	2 (2.2)	8 (4.0)	1 (1.5)	22 (3.4)	1 (1.1)	
History of antihypertensive medication, n (%)	586 (53.5)	64 (71.1)	104 (52.5)	34 (49.3)	324 (49.9)	60 (68.2)	<0.001
Discharge with medication, n (%)							
Antiplatelet agents	1055 (96.4)	84 (93.3)	192 (97.0)	67 (97.1)	625 (96.2)	87 (98.9)	0.37
Antihypertensive agents	749 (68.4)	79 (87.8)	154 (77.8)	57 (82.6)	383 (58.9)	76 (86.4)	<0.001
Lipid-lowering agents	977 (89.2)	77 (85.6)	183 (92.4)	61 (88.4)	582 (89.5)	74 (84.1)	0.21
Average systolic BP level during 7 days after onset, mean $\pm$ SD, mmHg	144.7 $\pm$ 14.7	172.0 $\pm$ 8.9	147.5 $\pm$ 7.7	155.7 $\pm$ 6.9	137.1 $\pm$ 10.9	157.8 $\pm$ 9.1	<0.001
BPV during 7 days after onset, mean $\pm$ SD							
CV-SBP	6.5 $\pm$ 3.5	5.9 $\pm$ 2.7	9.1 $\pm$ 3.7	8.7 $\pm$ 4.5	5.5 $\pm$ 2.9	7.3 $\pm$ 3.0	<0.001
SD-SBP	9.4 $\pm$ 4.9	10.3 $\pm$ 4.8	13.2 $\pm$ 5.3	13.4 $\pm$ 6.2	7.4 $\pm$ 3.4	11.6 $\pm$ 4.8	<0.001

C1 consistently high SBP ( $\geq 160$  mm Hg) for all 7 days, C2 rapid (within the first 2 days after onset) decline from high ( $\geq 160$  mm Hg) to low ( $< 160$  mm Hg), C3 delayed (after 2 days) decline from high ( $\geq 160$  mm Hg) to low ( $< 160$  mm Hg), C4 consistently low SBP ( $< 160$  mm Hg) for the entire 7 day period, C5 SBP increasing from low ( $< 160$  mm Hg) to high ( $\geq 160$  mm Hg) over the 7 day time frame, BP blood pressure, BPV blood pressure variability, CV-SBP coefficient of variation of systolic blood pressure, IQR interquartile range, mRS modified ranking scale, NIHSS National Institutes of Health Stroke Scale, SD standard deviation, SD-SBP standard deviation of systolic blood pressure

**Table 2** Primary and secondary outcomes in each blood pressure fluctuation pattern

	Total N = 1095	Blood pressure fluctuation pattern					P Value
		C1 n = 90	C2 n = 198	C3 n = 69	C4 n = 650	C5 n = 88	
Primary outcomes, n (%)							
mRS $\geq 3$ at 3 months	149 (13.6)	21 (23.3)	23 (11.6)	9 (13.0)	79 (12.2)	17 (19.3)	0.02
Secondary outcomes, n (%)							
Neurological deterioration <sup>a</sup> at discharge	44 (4.1)	8 (9.0)	5 (2.6)	3 (4.4)	22 (3.5)	6 (7.3)	0.06
Stroke recurrence during 7 days after onset	21 (1.9)	3 (3.3)	4 (2.0)	0 (0.0)	13 (2.0)	1 (1.1)	0.62
Stroke recurrence during 3 months after onset	55 (5.0)	7 (7.8)	7 (3.5)	3 (4.4)	30 (4.6)	8 (9.1)	0.22

C1 consistently high SBP ( $\geq 160$  mm Hg) for all 7 days, C2 rapid (within the first 2 days after onset) decline from high ( $\geq 160$  mm Hg) to low ( $< 160$  mm Hg), C3 delayed (after 2 days) decline from high ( $\geq 160$  mm Hg) to low ( $< 160$  mm Hg), C4 consistently low SBP ( $< 160$  mm Hg) for the entire 7 day period, C5 SBP increasing from low ( $< 160$  mm Hg) to high ( $\geq 160$  mm Hg) over the 7 day time frame, mRS modified ranking scale

<sup>a</sup>Increase of at least 2 points in the total NIHSS score at discharge compared with baseline score

## Predictors of poor functional outcome

Multivariate logistic regression analysis showed that, in addition to BP fluctuation patterns, age, history of diabetes, NIHSS on admission and IS subtype were predictors of poor functional outcome (mRS  $\geq 3$ ) at 3 months. Notably,

**Table 3** Association of blood pressure fluctuation patterns with functional outcome (mRS  $\geq 3$ ) at 3 months in univariate and multivariate analysis

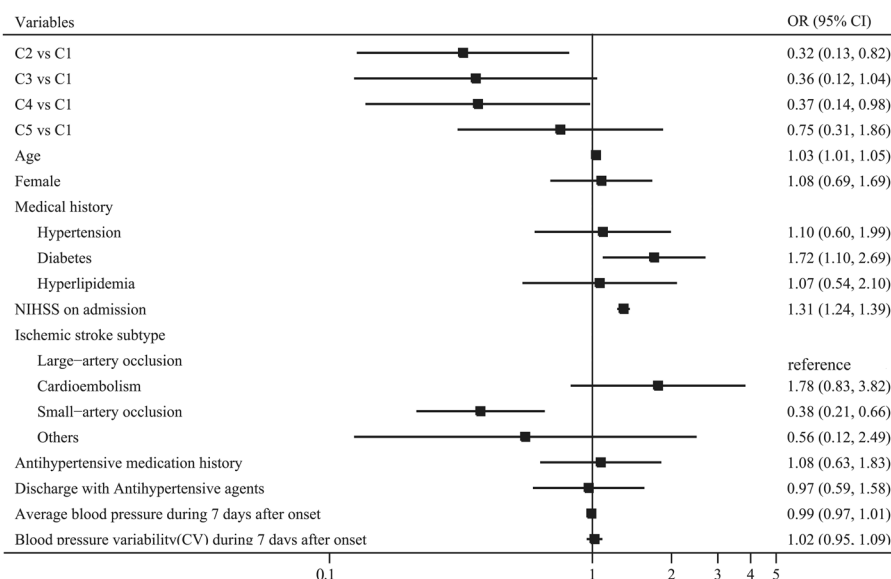
	Odds Ratios (95% Confidence Interval)		
	Unadjusted	Model 1 <sup>a</sup>	Model 2 <sup>b</sup>
<b>C1</b>	Reference	Reference	Reference
<b>C2</b>	0.43 (0.23–0.83)	0.32 (0.12–0.80)	0.32 (0.12–0.80)
<b>C3</b>	0.49 (0.21–1.16)	0.36 (0.13–1.05)	0.36 (0.13–1.05)
<b>C4</b>	0.46 (0.26–0.78)	0.37 (0.14–0.97)	0.37 (0.14–0.97)
<b>C5</b>	0.79 (0.38–1.62)	0.74 (0.30–1.82)	0.76 (0.31–1.86)

*C1* consistently high SBP ( $\geq 160$  mm Hg) for all 7 days, *C2* rapid (within the first 2 days after onset) decline from high ( $\geq 160$  mm Hg) to low ( $< 160$  mm Hg), *C3* delayed (after 2 days) decline from high ( $\geq 160$  mm Hg) to low ( $< 160$  mm Hg), *C4* consistently low SBP ( $< 160$  mm Hg) for the entire 7 day period, *C5* SBP increasing from low ( $< 160$  mm Hg) to high ( $\geq 160$  mm Hg) over the 7 day time frame

<sup>a</sup>Adjusted for age, gender, risk factors (history of hypertension, diabetes and hyperlipidemia), national institutes of health stroke scale on admission, ischemic stroke subtype, antihypertensive medication history, and discharge with antihypertensive medication. plus average blood pressure and blood pressure variability (SD-SBP) during 7 days after onset

<sup>b</sup>Adjusted for age, gender, risk factors (history of hypertension, diabetes and hyperlipidemia), national institutes of health stroke scale on admission, ischemic stroke subtype, antihypertensive medication history, and discharge with antihypertensive medication. plus average blood pressure and blood pressure variability (CV-SBP) during 7 days after onset

**Fig. 2** Risk factors for poor outcome (mRS  $\geq 3$ ) at 3 months among ischemic stroke patients. C1 consistently high SBP ( $\geq 160$  mmHg) for all 7 days, C2 rapid (within the first 2 days after onset) decline from high ( $\geq 160$  mmHg) to low ( $< 160$  mmHg), C3 delayed (after 2 days) decline from high ( $\geq 160$  mmHg) to low ( $< 160$  mmHg), C4 consistently low SBP ( $< 160$  mmHg) for the entire 7-day period, C5 SBP increasing from low ( $< 160$  mmHg) to high ( $\geq 160$  mmHg) over the 7-day time frame, mRS modified rankin scale, NIHSS National Institutes of Health Stroke Scale, CV coefficient of variation



average BP and BPV did not predict poor outcome independently (Fig. 2).

## Sensitivity analyses

A sensitivity analysis of patients without antihypertensive medication during the first 7 days was performed, and the results showed that, compared with the C1 group, C2 and C4 still showed a significant reduction in poor functional outcome in univariable and multivariable analyses (Supplementary Table 3). Moreover, 21 (1.9%) patients had stroke recurrence 7 days after onset in this study. To eliminate the influence of stroke recurrence events on BP pattern and functional outcome, we conducted a sensitivity analysis, and a similar result was found when these 21 patients were excluded (Supplementary Table 4).

## Discussion

In this prospective cohort study, BP fluctuation patterns, rather than single-timepoint BP or average BP, were used to investigate the association between acute-phase BP and IS outcome. Our results showed that patients with consistently high BP ( $\geq 160$  mmHg) during the acute phase of IS had the highest risk of poor functional outcome at 3 months, while patients with consistently low BP ( $< 160$  mmHg) and patients whose BP decreased over the first 48 h had the lowest risk.

Compared with traditional BP parameters, the BP fluctuation patterns could represent more comprehensive post-stroke BP information, including initial BP, the direction of BP fluctuation, and the amplitude of BP fluctuation. Although acute phase BPV describes the amplitude of BP fluctuation [15–17], it does not account for initial BP or



direction of fluctuation. For example, if there are two BP curves, one that decreases from 180 mmHg to 160 mmHg to 140 mmHg over the first three days of the acute phase, and the other that increases from 140 mmHg to 160 mmHg to 180 mmHg, average BP and BPV are identical, but the initial BP and direction of BP fluctuation are completely different. The prognosis of patients with these differing BP curves should be different from a clinical perspective. Hence, the BP fluctuation pattern seems likely to be more reliable than BPV when investigating the association between BP and stroke outcome. This study found that patients with different BP fluctuation patterns had different prognoses but that acute phase BPV alone could not predict stroke outcome. Moreover, after adjustment for average BP and BPV, the BP fluctuation pattern was still able to distinguish stroke outcomes, which implies that the BP fluctuation pattern is independent of average BP and BPV in predicting stroke outcome.

In this study, the highest risk of poor outcome was observed in the patients who had consistently high BP ( $\geq 160$  mmHg) or elevation from low to high BP during the acute phase, which implies that increased BP was detrimental. Our result was consistent with most previous studies. The International Stroke Trial (IST) [1] found that a high SBP ( $\geq 140$  mmHg) was independently related to an increased risk of early death and combined death or dependency in 17 398 patients with acute IS. A meta-analysis [12] including 32 studies and 10 892 patients also showed that high BP in acute IS was associated with subsequent death, death or dependency, and death or deterioration. Although some studies [5, 6] found improved outcomes for high BP, when analyzed with other studies, there was no evidence of a protective effect for high BP [12]. In addition, in this study, we further examined the prognosis of patients whose average BP was below 120 mmHg. We found that the risk of death and major disability was much higher in patients with an average BP  $< 120$  mmHg than in those within the 120–140 or 140–160 mmHg BP ranges. Those with BP  $< 120$  mmHg experienced almost similarly detrimental outcomes to patients who maintained BP  $\geq 160$  mmHg during the acute phase. This result confirmed a J-shaped association between acute phase BP and stroke outcome, which is consistent with recently reported studies [18, 19].

It is well known that increases in BP in the acute phase may be a result of vessel reocclusion or intracerebral hemorrhage [20, 21]. To eliminate the influence of stroke recurrence events during the acute phase on BP pattern and functional outcome, a sensitivity analysis was conducted in this study, and a similar result was found when patients with recurrence events during the acute phase were excluded. Moreover, to investigate the natural BP fluctuation pattern during the acute phase after IS, in this study, we also excluded patients with antihypertensive medication during

the first 7 days. A similar BP pattern was found, and an association between BP pattern and stroke outcome still existed. The consistency of the above sensitivity analysis with our primary results increased the credibility of our findings.

This study also has several limitations. First, the sample size allowed for only relatively small numbers of patients to be assigned to each BP pattern group, which may have influenced statistical power. Second, in this study, an SBP of 160 mmHg rather than 140 mmHg was designed as the cutoff for low BP because 140 to 160 mmHg was considered to have a protective effect for acute IS patients [1]. Studies including a significant proportion of patients with an SBP of 140 to 160 mmHg in the high BP group might be expected to miss a relation between high BP and poor outcome [12]. Third, the stroke severity of the study patients was relatively mild, with low NIHSS scores, indicating that our results may not generalize to more severe stroke patients. Fourth, the time window of inclusion was 24 h in this study, so we could not further evaluate the BP fluctuation within 24 h. Fifth, we have measurements of BP only twice daily; it would better describe the trajectory of blood pressure fluctuations if more frequent BP readings were obtained. In conclusion, we found that the BP fluctuation pattern might be a useful predictive parameter for stroke outcome in acute IS patients. However, our results need to be validated in larger sample studies.

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**Author contributors** Draft writing: JX and AXW. Study conception and design: YLW and YJW. Acquisition of laboratory data: LY and YG. Acquisition of clinical data: YL. Data analysis and interpretation: AXW and JX. Study supervision: YLW and YJW.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethics approval** The trial was approved by the Ethics Committee of Beijing Tiantan Hospital. Written informed consent was obtained from all participants or their legal proxies.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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