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ORIGINAL RESEARCH

The Relationship Between Cerebral Perfusion, Blood Pressure Variability and 90-Day Prognosis in Patients with Acute Posterior Circulation Cerebral Infarction: An Observational Study

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Background and Purpose: Research is still underway to determine the effect of blood pressure variability (BPV) on the prognosis of acute ischaemic stroke (AIS). The posterior circulation is vulnerable to BPV due to its unique anatomy. Our study systematically evaluated the effects of daily BPV and cerebral perfusion on 90-day prognosis of patients with acute posterior circulation cerebral infarction (PCCI) and further investigated their association.

Methods: The study included 462 patients diagnosed with PCCI. Cerebral perfusion was assessed by F.MTT (focus mean transit time), rCBV (relative cerebral blood volume) and rCBF (relative cerebral blood flow). Blood pressure (BP) was recorded twice daily and the daily BPV was calculated with standard deviation (SD) and coefficient of variation (CV). Subsequently, the correlation between daily BPV, cerebral perfusion and 90-day prognosis was examined using logistic regression modelling. Potential non-linear relationships were assessed through the use of smooth curve fitting. Assessment to explore the relationship between cerebral perfusion levels and daily BPV using stepwise logistic regression analysis. Finally, mediation analysis was performed to test the relationship between CT perfusion (CTP) mediated BPV and 90-day adverse prognosis.

Results: The study included 363 participants. Multivariate logistic regression analysis revealed that higher daily BPV and poorer cerebral perfusion were negatively associated with 90-day adverse prognosis in patients with PCCI ($P < 0.05$). In addition, poor cerebral perfusion was associated with higher daily BPV (MAP-SD: OR 1.15, 95% CI [1.03–1.27], $P = 0.011$; MAP-CV: OR 1.17, 95% CI [1.05 ~ 1.3], $P = 0.004$). Meanwhile, mediation analysis showed that rCBF mediated the association between daily BPV and 90-day adverse prognosis (indirect effect estimate = 0.918, direct effect estimate = 0.0621).

Conclusion: Our study demonstrated that daily BPV and cerebral perfusion were positively associated with 90-day adverse prognosis in patients with PCCI, which was partly mediated by rCBF.

Keywords: blood pressure variability, stroke, posterior circulation infarction, CT perfusion

Introduction

Stroke ranks as the second leading cause of mortality worldwide,[1] characterized by high rates of recurrence, disability, and mortality.[2,3] China has experienced the biggest increase in stroke prevalence in recent years.[4] Acute posterior circulation infarction (PCCI), accounting for approximately 20% of acute ischemic stroke (AIS), presents more severe prognosis.[5] This is because the posterior circulation (vertebrobasilar system) is mainly responsible for supplying blood to

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vital areas such as the brainstem and cerebellum (respiratory and cardiac centres), which have a higher demand for blood flow. However, the vessels of the vertebrobasilar system are more susceptible to blood pressure (BP) fluctuations due to their tortuous nature and slow blood flow.[6,7] Additionally, compared to the anterior circulation, the posterior circulation not only has less collateral circulation, but also has a sparse distribution of sympathetic fibres, which contributes to its lack of an effective blood flow compensation mechanism.[3] In the early stages of AIS, reactive hypertension and inadequate cerebral perfusion, as well as imbalances in central sympathetic and vagal tone, lead to high blood pressure variability (BPV) and impaired cerebral self-regulation. Small fluctuations in BP lead to inadequate or excessive cerebral perfusion, resulting in secondary brain damage.[8] However, there is limited data on the relationship between posterior circulation cerebral perfusion and BP and BPV. Most studies have focused on the relationship between short-term BPV and prognosis of neurological function.[9–11] Therefore, we conducted a retrospective study to investigate the relationship between 7-day BPV and cerebral perfusion and 90-day prognosis in patients with PCCI.

Methods

Participants

The ethics committee of Jiangsu Province Hospital of Traditional Chinese Medicine approved the experiments. From 1 January 2021 to 30 April 2024, a total of 462 patients with PCCI were admitted to the Department of Neurology, Jiangsu Province Hospital of Traditional Chinese Medicine. Inclusion criteria included: (1) age ≥18 years, managed according to Chinese guidelines for diagnosing and treating PCCI; (2) arrived at hospital within 72 hours of symptom onset, exceeded the time window for intravenous thrombolysis or endovascular therapy, or refused intravenous thrombolysis or endovascular therapy; and (3) stayed in hospital longer than 7 days. Exclusion criteria were: (1) previous stroke resulting in a modified Rankin Scale (mRS) ≥ 3; (2) incomplete follow-up data; (3) severe systemic disorders or a life expectancy of less than 90-day, such as advanced heart failure or cancer; (4) inadequate BP measurements or extreme systolic blood pressure (SBP) values >260 mmHg or <70 mmHg, and diastolic blood pressure (DBP) values >150 mmHg or <40 mmHg; and (5) No CTP examination was performed (shown in Figure 1).

Demographic and Clinical Assessment

At the time of registration, patient profiles such as age, sex and body mass index (BMI), risk factors such as hypertension (HT), diabetes mellitus (DM), atrial fibrillation (AF), smoking, and alcohol drinking were noted. The patients' medical history records on hyperlipidemia (HLP), coronary artery disease (CHD), stroke were analyzed. Laboratory results, including, total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) were recorded. HT was categorized into two classes: those not using antihypertensive medications with a BP of 140/90 mm Hg on repeated measurements, and those on antihypertensive medication.[12] DM was defined as FPG ≥ 126 mg/dL, a positive result in the ≥ 75 g oral glucose tolerance testing, or present therapy with oral hypoglycemic treatment or insulin to control blood glucose. Smoking was defined as ≥1 cigarette per day for more than 6 months. Alcohol consumption was defined as ≥1 alcoholic drink per week with ≥50 mL of alcohol for more than 6 months. Hyperlipidemia includes one or more of the following: total cholesterol (TC) ≥5.2 mmol/L, triglyceride (TG) ≥1.7 mmol/L, low-density lipoprotein cholesterol (LDL-C) ≥3.4 mmol/L, and high-density lipoprotein cholesterol (HDL-C) <1.0 mmol/L. The NIHSS was employed to assess neurological deficits upon enrollment.[13] PCCI was described as an acute ischemic stroke caused by occlusion of the vertebrobasilar artery and its branches, confirmed by computed tomography or magnetic resonance imaging of the brain. Individuals with PCCI were admitted to the hospital within 3 days following the onset of symptoms. The subtypes of stroke were classified according to the criteria of the Trial of ORG 10172 in Acute Stroke Treatment (TOAST).

Assessment of Cerebral Perfusion

All patients underwent CT angiography (CTA) and CT perfusion (CTP) examinations after admission. Scanning was conducted using a Philip Brilliance 128-slice spiral CT scanner. Scanning was performed, and 50 mL contrast agent (infusion rate of 5 mL/s) was infused into the elbow vein of the subject. The scan covered from the lower edge of the aortic arch to the top of the skull. Scan parameters included a layer thickness and spacing of 0.625 mm, current 250 mA,

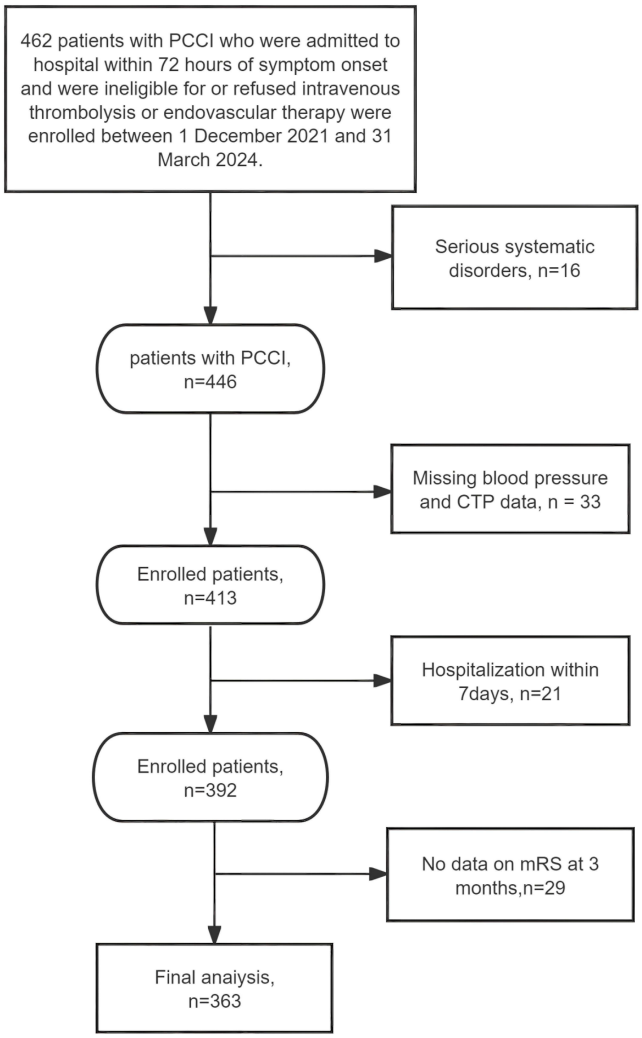

Figure 1 Flowchart demonstrating patient selection.

voltage 120 kV, pitch 0.927, speed 360 °/s, and a scanning threshold of 150 hu. After the scanning, the perfusion data were uploaded to the workstation. CTP yields quantitative cerebral perfusion data, effectively reflecting changes in local tissue blood perfusion.[14] CTP parameters in this study included Mean Transit Time (MTT): the time required for the contrast agent to pass from the intracranial arterial side to the venous side, and the mean value of all passing time (s). F. MTT means transit time of the ischemic area. Time to peak (TTP): Starting from the time when the contrast agent reaches the main artery of the imaging brain region, to the time when the contrast agent reaches the maximum amount (s). Cerebral blood flow (CBF): the number of blood flow per minute per 100g brain tissue [mL/ (100g.min)]. Cerebral blood volume (CBV): blood volume per 100g brain tissue [mL/100g]. The relationship is CBV = CBF × MTT, rCBF = focus CBF / contrast CBF, rCBV = focus CBV / contrast CBV.[15,16] A decrease in CBF values by more than 60% compared to non-ischemic brain regions accurately identifies cerebral ischemic areas. A decrease in CBV by more than 60% is diagnostic of cerebral ischemia. Decreased perfusion area was defined as MTT > 6s. The average MTT of normal MCA was 3.6s.[17] All information on parameters was collected via the image system recording approach by a well-trained neurologist from the Stroke Center of Jiangsu Province Hospital of Chinese Medicine.

BP Measurement and BPV

BP readings were taken twice daily for seven consecutive days, between 6:00 and 8:00 a.m., and again between 5:00 and 7:00 p.m. Each measurement was taken three times to calculate the average. We recorded the BP in the right arm or non-

paretic arm with the patient in supine using an automated electronic sphygmomanometer or non-invasive BP monitoring equipment (each patient's blood pressure was measured using the same sphygmomanometer throughout the hospitalization) and recorded the results manually into the patient's medical data according to the clinical regime. The same set of sphygmomanometers was used for all BP measurements. Mean arterial pressure (MAP) was calculated from the single recorded systolic blood pressure (SBP) and diastolic blood pressure (DBP) of each patient, and the standard deviation (SD) and coefficient of variation (CV = SD/mean × 100%) of SBP, DBP and MAP were used to analyze daily BPV within the first week post-stroke.[18]

Definition of Prognosis

The primary prognosis was the score on the modified Rankin Scale (mRS) at 90 days. Functional prognosis were classified using mRS scores: 0–2 indicating functional independence and ≥3 indicating moderate to severe disability or death, including recurrence of AIS or cerebral hemorrhage.[19]

Statistical Analyses

Baseline characteristics and outcomes of the study population were compared in two groups based on cerebral perfusion levels at admission. Categorical variables are expressed as number (percentage) and continuous variables as median (interquartile range [IQR]). Logistic regression models were used to test the correlation between daily BPV, cerebral perfusion and 90-day adverse prognosis. The chi-square test was used for categorical variables and the Mann–Whitney *U*-test for continuous variables. Results were presented as odds ratios (OR) and 95% confidence intervals (CI). Smooth curve fitting was applied to determine the non-linear relationship between daily BPV and adverse prognosis. To further explore the relationship between cerebral perfusion levels and daily BPV, we performed stepwise logistic regression analyses to assess the OR and corresponding 95% CI. Hazard variables on the basis of clinical significance and $P < 0.05$ in the univariate analysis were included in the multivariate analysis. Model 1 included adjustments for age and gender, while Model 2 also adjusted for BMI, smoking, drinking, HT, DM, HLP, AF, CHD, TC, TG, LDL, TOAST classification, NIHSS score at enrollment, mRS score at enrollment. Model 3 further incorporates mean MAP on top of the adjustments in Model 2. To correct for variations in cerebral perfusion (CTP), F.MTT, rCBF, and rCBV were categorized for trend analysis. Finally, the hypothesis that rCBF mediates the relationship between MAP-SD and adverse prognosis was tested in 363 samples using a bias-corrected bootstrap method. Dummy variables were used to represent missing covariate values. The percentage of missing values did not exceed 10% for any variable. All statistical analyses were conducted using R statistical software (http://www. R-project.org, the R Foundation) and the Free Statistics analysis platform.

Results

Baseline Characteristics

The study enrolled 363 subjects meeting the inclusion criteria. All were admitted to the hospital within 72 hours of symptom onset, outside the eligibility window for intravenous thrombolysis, and were either ineligible for or declined intravascular mechanical thrombectomy. Table 1 summarizes the comparison of baseline characteristics. The average age of the participants was 66.4 ± 11.6 years, and 25.1% of the participants were female. HP was present in 268 cases (73.8%), DM in 157 cases (43.3%), HLP in 86 cases (23.7%), AF in 24 cases (6.6%), CHD in 31 cases (8.5%), smoking in 125 cases (34.4%), and drinking in 86 cases (23.7%). According to F.MTT, the patients were divided into relatively good cerebral perfusion group (176 cases, 48.5%) and poor cerebral perfusion group (187 cases, 51.5%). Patients with poor cerebral perfusion were older, had a larger percentage of HT, AF, or CHD, had more serious neurological deficits at enrollment. 82 patients with PCCI (22.6%) had an adverse prognosis within 90 days. Of these, 11 patients died, 32 experienced recurrent strokes, and the rest remained disabled (Table 1).

Daily BPV and 90-Day Adverse Prognosis

Table 2 depicts the link between MAP variability and 90-day adverse prognosis in patients with PCCI, adjusting for age, gender, BMI, smoking, drinking, HP, DM, HLP, AF, CHD, LDL, TOAST classification, initial NIHSS and mRS scores,

Table 1 The Basic Characteristics in PCCI According to F.MTT

Variables	Total (n = 363)	Good Cerebral Perfusion (n = 176)	Poor Cerebral Perfusion (n = 187)	p
Gender, n (%)				0.237
Male	272 (74.9)	67 (72)	145 (77.5)	
Female	91 (25.1)	49 (27.8)	42 (22.5)	
Age, Mean ± SD	66.4 ± 11.6	65.2 ± 11.9	67.6 ± 11.1	0.05
BMI.kg.m^2, Mean ± SD	24.7 ± 2.7	24.6 ± 2.3	24.7 ± 3.0	0.816
Smoking, n (%)				0.309
NO	238 (65.6)	120 (68.2)	118 (63.1)	
YES	125 (34.4)	56 (31.8)	69 (36.9)	
Drinking, n (%)				0.057
NO	277 (76.3)	142 (80.7)	135 (72.2)	
YES	86 (23.7)	34 (19.3)	52 (27.8)	
Hypertension, n (%)				0.004
NO	95 (26.2)	58 (33)	37 (19.8)	
YES	268 (73.8)	118 (67)	150 (80.2)	
DM, n (%)				0.812
NO	206 (56.7)	101 (57.4)	105 (56.1)	
YES	157 (43.3)	75 (42.6)	82 (43.9)	
Stroke history, n (%)				0.943
NO	259(71.3)	125 (71)	134 (71.7)	
YES	104 (28.7)	51 (29)	53(28.3)	
HLP, n (%)				0.011
NO	277 (76.3)	124 (70.5)	153 (81.8)	
YES	86 (23.7)	52 (29.5)	34 (18.2)	
AF, n (%)				0.005
NO	337 (93.4)	170 (97.1)	167 (89.8)	
YES	24 (6.6)	5 (2.9)	19 (10.2)	
CHD, n (%)				0.003
NO	332 (91.5)	169 (96)	163 (87.2)	
YES	31 (8.5)	7 (4)	24 (12.8)	
Medical history				
Antiplatelet use, n (%)				0.156
NO	301 (82.8)	138 (78.5)	163 (86.9)	
YES	62 (17.2)	38 (21.5)	24 (13.1)	
Statin use, n (%)				0.069
NO	310 (85.4)	142 (80.6)	168 (89.9)	
YES	53 (14.6)	34 (19.4)	19 (10.1)	
Antihypertensive treatment, n (%)				0.2
NO	142 (39.1)	61 (34.4)	81 (43.4)	
YES	221 (60.9)	115 (65.6)	106 (56.6)	
Antidiabetic treatment, n (%)				0.868
NO	236 (65.1)	114 (64.5)	123 (65.7)	
YES	127 (34.9)	62 (35.5)	64 (34.3)	
TOAST classification, n (%)				0.004
LAA	216 (59.5)	95 (54)	121 (64.7)	
SVO	19 (5.2)	5 (2.8)	14 (7.5)	
CE	125 (34.4)	75 (42.6)	50 (26.7)	
OE and UD	3 (0.8)	1 (0.6)	2 (1.1)	

(*Continued*)

Table 1 (Continued).

Variables	Total (n = 363)	Good Cerebral Perfusion (n = 176)	Poor Cerebral Perfusion (n = 187)	p
Medications during hospitalization				
Antihypertensive treatment, n (%)				0.862
NO	153 (42.1)	75 (42.6)	78 (41.7)	
YES	210 (57.9)	101 (57.4)	109 (58.3)	
Antidiabetic treatment, n (%)				0.648
NO	208 (57.3)	103 (58.5)	105 (56.1)	
YES	155 (42.7)	73 (41.5)	82 (43.9)	
Median (IQR)				
NIHSS score at enrollment, Mean ± SD	3.5 ± 3.8	2.8 ± 2.5	4.1 ± 4.6	0.001
mRS score at enrollment, Mean ± SD	2.3 ± 1.3	2.2 ± 1.3	2.5 ± 1.3	0.02
Median (IQR)				
TC, Mean ± SD	4.4 ± 1.3	4.4 ± 1.2	4.4 ± 1.4	0.924
TG, Mean ± SD	3.1 ± 16.8	4.7 ± 24.1	1.7 ± 1.2	0.092
HDL.C, Mean ± SD	1.2 ± 0.3	1.2 ± 0.3	1.2 ± 0.3	0.682
LDL.C, Mean ± SD	2.6 ± 0.9	2.6 ± 0.8	2.6 ± 1.0	0.758
SBP.mean, Mean ± SD	142.0 ± 14.2	142.± 14.4	141.8 ± 14.0	0.72
SBP.SD, Mean ± SD	11.9 ± 4.6	11.3 ± 3.8	12.5 ± 5.2	0.01
SBP.CV, Mean ± SD	8.4 ± 3.4	8.0 ± 2.8	8.9 ± 3.8	0.012
DBP.mean, Mean ± SD	83.7 ± 9.2	83.7 ± 8.9	83.7 ± 9.5	0.99
DBP.SD, Mean ± SD	8.4 ± 4.9	8.2 ± 6.0	8.6 ± 3.8	0.536
DBP.CV, Mean ± SD	10.1 ± 6.3	9.9 ± 7.9	10.2 ± 4.3	0.65
MAP.mean, Mean ± SD	103.6 ± 9.8	103.3± 9.9	103.1 ± 9.7	0.856
MAP-SD, Mean ± SD	9.0 ± 3.7	8.6 ± 3.8	9.4 ± 3.5	0.033
MAP-CV, Mean ± SD	8.8 ± 3.6	8.4 ± 4.0	9.1 ± 3.2	0.053

Note: MAP=1/3SBP+2/3DBP.

Abbreviations: BMI, body mass index; DM, diabetes mellitus; HLP, hyperlipidemia; AF, atrial fibrillation; CHD, coronary artery disease; TOAST, the Trial of ORG 10172 in Acute Stroke Treatment; LAA, large-artery atherosclerosis; SVO, small-vessel occlusion; CE, cardioembolism; OE, stroke of other determined etiology; UD, stroke of undetermined etiology; TC, total cholesterol; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin scale; BP, blood pressure; BPV, blood pressure variability; CV, coefficient of variation; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure.

Table 2 Relationship Between Daily Blood Pressure Variability and 90-Day Adverse Prognosis in Patients with PCCI

Variable	n. total	n.event_%	crude.(OR 95CI)	P_value	adj.(OR 95CI)	P_value
MAP-SD	363	82 (22.6)	1.1 (1.01~1.18)	0.02	1.15 (1.03~1.27)	0.011
MAP-CV	363	82 (22.6)	1.11 (1.02~1.21)	0.016	1.17 (1.05~1.3)	0.004

Notes: Adjust for age, gender, BMI, smoking, drinking, hypertension, diabetes, hyperlipidemia, atrial fibrillation, coronary heart disease, LDL, TOAST classification, initial NIHSS and mRS scores, and mean arterial pressure.

Abbreviations: MAP, mean arterial pressure; SD, standard deviation; CV, coefficient of variation; OR, odds ratio; CI, confidence interval.

and mean MAP. The analysis revealed that the likelihood of 90-day adverse prognosis escalates with an increase in MAP variability. (OR for MAP-SD: 1.15, 95% CI [1.03–1.27], P=0.011; OR for MAP-CV: 1.17, 95% CI [1.05–1.3], P=0.004). We used the smooth curve fitting to identify whether there was a non-linear association between daily BPV and 90-day adverse prognosis. The results of the study showed that an elevated risk of adverse prognosis was associated with increased MAP-SD and MAP-CV over a 7-day time period (shown in Figure 2).

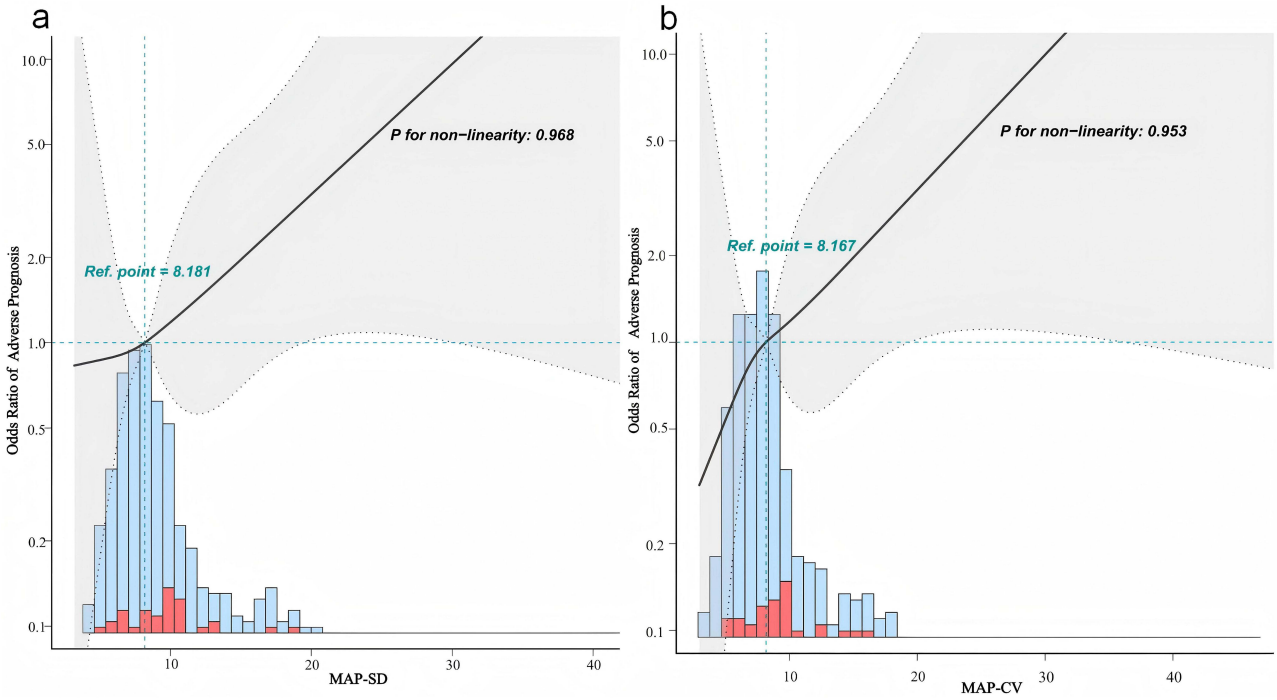

Figure 2 Restricted Cubic Spline(RCS) plot of daily blood pressure variability (BPV) and 90-day adverse prognosis outcome in patients with PCCI. (**a**) RCS plot of MAP-SD and 90-day unfavorable outcome; (**b**) RCS plot of MAP-CV and 90-day unfavorable outcome. Adjusted variables: age, sex, bmi, smoking, drinking, hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, coronary artery disease, total cholesterol, triglyceride, low-density lipoprotein, TOAST classification, NIHSS score at enrollment, mRS score at enrollment and mean arterial pressure. BPV, blood pressure variability.

Cerebral Perfusion and 90-Day Adverse Prognosis

Table 3 gives the OR and 95% CI for cerebral perfusion and 90-day adverse prognosis. Based on the clinical significance and Table 1, we incorporated multiple variables into the multivariate logistic regression analysis, including age, sex, BMI, smoking, drinking, HP, DM, HLP, AF, CHD, LDL, TOAST classification, NIHSS score at enrollment, mRS score at enrollment and mean MAP. The analysis revealed that the likelihood of 90-day adverse prognosis escalates with an increase in F.MTT (OR: 1.34, 95% CI [1.11–1.62], P=0.003), while it diminishes with heightened rCBF and rCBV (OR for rCBF: 0.05, 95% CI [0–0.45], P=0.008; OR for rCBV: 0.22, 95% CI [0.05–0.92], P=0.038).

The Relationship Between Cerebral Perfusion and Daily BPV

Univariate and multivariate logistic regression analyses were employed to assess the association between daily BPV and cerebral perfusion in patients with PCCI. Incorporating factors such as age, sex, BMI, smoking, drinking, HP, DM, HLP, AF, CHD, TC, TG, LDL, TOAST classification, NIHSS score at enrollment, mRS score at enrollment and mean MAP. In

Table 3 Relationship Between Cerebral Perfusion and 90-Day Adverse Prognosis in Patients with PCCI. F.MTT, rCBF and rCBV Were Cerebral Perfusion Parameters

Variable	n. total	n.event_%	crude.(OR 95CI)	P_value	adj.(OR 95CI)	P_value
F.MTT	363	82 (22.6)	1.35(1.12~1.62)	0.001	1.34(1.11~1.62)	0.003
rCBF	363	82 (22.6)	0.04(0~0.35)	0.004	0.05 (0~0.45)	0.008
rCBV	363	82 (22.6)	0.24 (0.06~0.92)	0.037	0.22 (0.05~0.92)	0.038

Notes: Adjust for age, sex, BMI, smoking, drinking, hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, coronary artery disease, low-density lipoprotein, TOAST classification, NIHSS score at enrollment, mRS score at enrollment and mean arterial pressure.

Abbreviations: MAP, mean arterial pressure; SD, standard deviation; CV, coefficient of variation; F.MTT, focus mean transit time; rCBF, relative blood flow (rCBF = focus CBF / contrast CBF); rCBV, relative blood volume (rCBV = focus CBV / contrast CBV); OR, odds ratio; CI, confidence interval.

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the initial models, MAP-SD and MAP-CV demonstrated associations with cerebral perfusion. Further multivariate logistic regression models revealed a positive correlation between MAP-SD and MAP-CV with F.MTT, and a negative correlation with rCBF, although no significant associations were found with rCBV. Specifically, in the adjusted Model 1, MAP-SD and MAP-CV showed positive correlations with F.MTT and negative correlations with rCBF (OR for MAP-SD :0.1, 95% CI [0.01–0.81], P=0.031; OR for MAP-CV: 0.09, 95% CI [0.01–0.75], P=0.027). Model 2 confirmed significant relationships between MAP-SD and MAP-CV with both F.MTT and rCBF. Adjustments in Model 3, including mean MAP, confirmed the significant positive correlations between MAP-SD and MAP-CV with F.MTT (OR for MAP-SD: 1.26, 95% CI [1.05–1.51], P=0.011; OR for MAP-CV: 1.28, 95% CI [1.07–1.54], P=0.008). However, negative correlations were observed between MAP-SD and rCBF (OR: 0.04, 95% CI [0–0.43], p=0.008), with similar findings for MAP-CV (OR: 0.06, 95% CI [0.01–0.56], p=0.014), although no significant relationships were found with rCBV (shown in Figure 3).

Patients were divided equally into 2 groups (Q1, Q2) according to the level of cerebral perfusion. Subsequent analyses adjusting for confounders showed an increase in MAP-SD associated with increasing F.MTT (OR: 2.53, 95% CI [1.38–4.64], P trend=0.003). Similarly, MAP-CV increased with increasing F.MTT. (OR: 2.33, 95% CI [1.28–4.26], P trend=0.006). A decrease in MAP-SD and MAP-CV was observed with higher rCBF and rCBV (shown in Figure 4).

Figure 5 illustrates significant differences in MAP variability between patients with different levels of cerebral perfusion. Patients with poor cerebral perfusion exhibited significantly higher daily MAP variability (MAP-SD, MAP-CV) (shown in Figure 5).

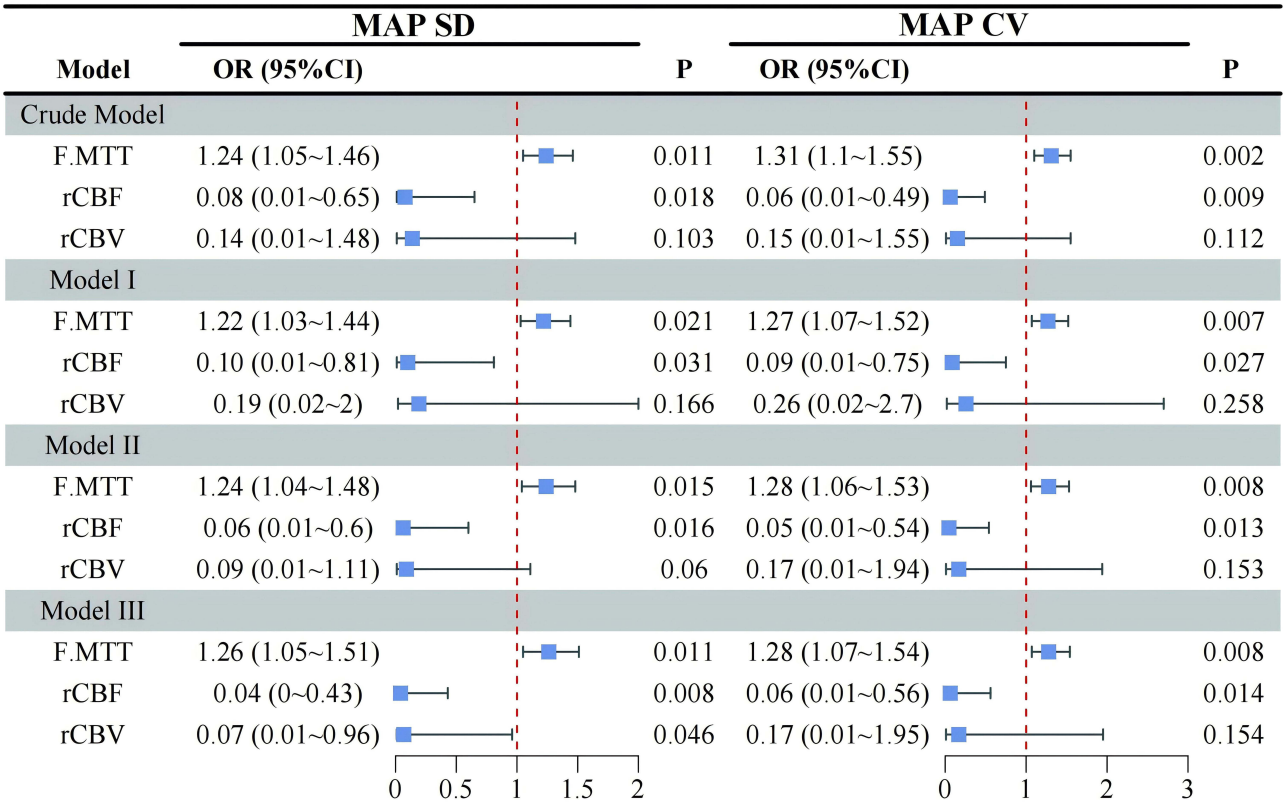

Figure 3 Forest plot of the relationship between cerebral perfusion (continuous) and daily blood pressure variability in different models of posterior circulation infarction. Model 1 was adjusted for age and gender. Model 2 was adjusted for Model 1 plus variables including BMI, smoking, drinking, hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, coronary artery disease, total cholesterol, triglyceride, low-density lipoprotein, TOAST classification, NIHSS score at enrollment, mRS score at enrollment. Model 3 was adjusted for mean MAP on the basis of Model 2.

Abbreviations: MAP, mean arterial pressure; SD, standard deviation; CV, coefficient of variation; F.MTT, focus mean transit time; rCBF, relative blood flow (rCBF = focus CBF / contrast CBF); rCBV, relative blood volume (rCBV = focus CBV / contrast CBV); OR, odds ratio; CI, confidence interval.

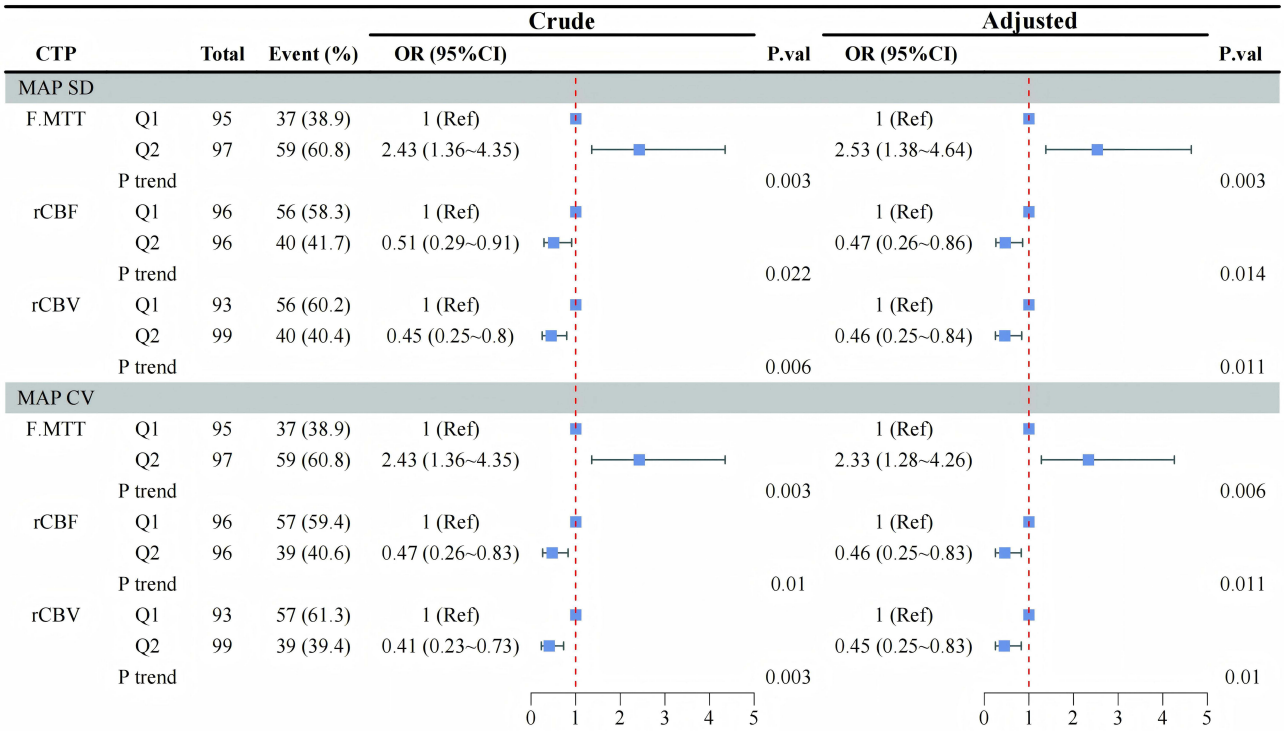

Figure 4 Forest plot of the relationship between different cerebral perfusion (quartile) and daily blood pressure variability. Adjusted for age, sex, bmi, smoking, drinking, hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, coronary artery disease, total cholesterol, triglyceride, low-density lipoprotein, TOAST classification, NIHSS score at enrollment, mRS score at enrollment and mean arterial pressure.

Abbreviations: MAP, mean arterial pressure; SD, standard deviation; CV, coefficient of variation; F.MTT, focus mean transit time; rCBF, relative blood flow (rCBF = focus CBF / contrast CBF); rCBV, relative blood volume (rCBV = focus CBV / contrast CBV); Q, quartile; Q1, first quartile; Q2, second quartile; OR, odds ratio; CI, confidence interval.

Mediation Analysis

Figure 6 shows the relative total, direct and indirect effects of cerebral perfusion on the relationship between daily BPV and 90-day adverse prognosis in the mediation model. Our mediation hypothesis was validated as bootstrapping revealed a significant relative indirect effect for adverse prognosis (indirect effect=0.918, direct effect=0.0621), suggesting that rCBF mediates the association between MAP-SD and adverse prognosis (shown in Figure 6).

Discussion

This study is a pioneering investigation of the relationship between mid-term BPV and cerebral perfusion in patients with PCCI. We analyzed data on BPV, cerebral perfusion and 90-day mRS score in patients with PCCI. Our results suggest that both high daily BPV and poor cerebral perfusion are significantly associated with poor 90-day prognosis in patients with PCCI. Furthermore, high daily BPV was associated with poor cerebral perfusion. Mediation analysis revealed that rCBF mediates the relationship between MAP-SD and poor prognosis (indirect effect=0.918, direct effect=0.0621). Under normal physiological conditions, BPV regulates neural reflexes (including central sympathetic, carotid sinus pressure and cardiopulmonary reflexes) as well as body fluids, the vascular system and hemorheology to maintain its own homeostasis.[20,21] AIS leads to high BPV and impaired brain self-regulation, especially in patients with pre-existing vascular dysfunction such as hypertension or atherosclerosis.[22] At this point, blood flow in the ischaemic brain region is mainly determined by MAP.[23–25] Therefore, even small fluctuations in BP can lead to under- or over-perfusion of the ischaemic brain.[26–30] However, the relationship between BPV and cerebral blood flow remains poorly understood. We calculated several daily BPV parameters such as SBP, DBP, MAP and their respective SD and CV, including SBP-SD, SBP-CV, DBP-SD, DBP-CV, MAP-SD, MAP-CV. The results showed that these parameters were significantly correlated with the level of cerebral perfusion. Notably, patients with PCCI have greater BPV compared to patients with anterior circulation infarcts, largely due to the greater impact of BP fluctuations on the posterior circulation, including the

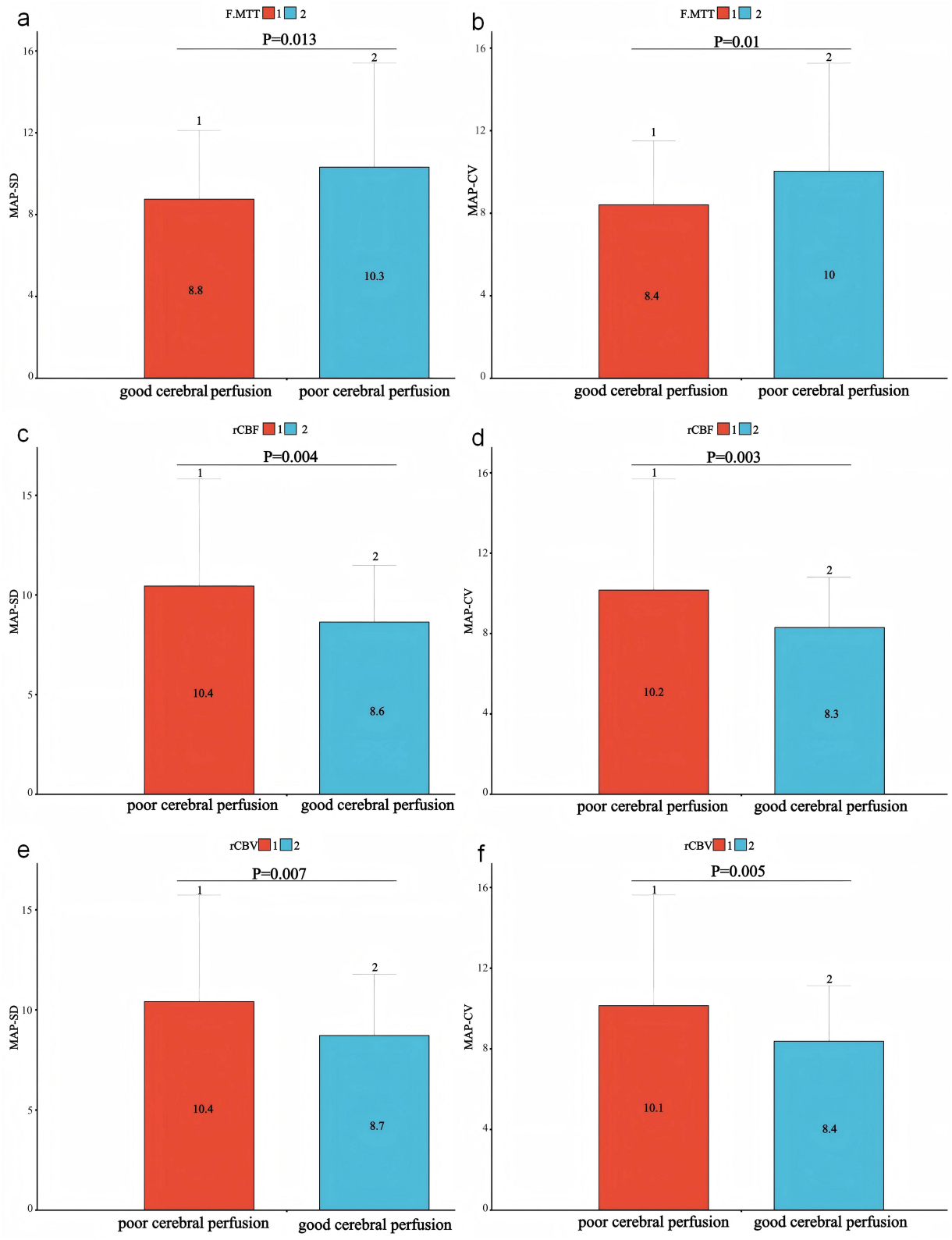

Figure 5 Barplot of blood pressure variability between patients with different levels of cerebral perfusion. (**a**) Barplot of MAP-SD and F.MTT in different levels of cerebral perfusion; (**b**) Barplot of MAP-CV and F.MTT in different cerebral perfusion; (**c**) Barplot of MAP-SD and rCBF in different cerebral perfusion; (**d**) Barplot of MAP-CV and rCBF in different cerebral perfusion; € Barplot of MAP-SD and rCBV in different cerebral perfusion; (**f**) Barplot of MAP-CV and rCBV in different cerebral perfusion.
Abbreviations: MAP, mean arterial pressure, SD, standard deviation, CV, coefficient of variation, 1, poor cerebral perfusion, 2, good cerebral perfusion.

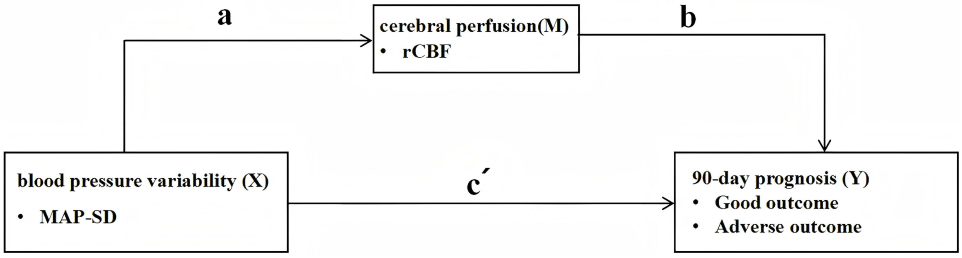

Figure 6 Model of the hypothetical causal pathway in patients with acute posterior circulation cerebral infarction. Total effect (c)=natural direct effect (c')+natural indirect effect (ab). MAP-SD represents the mean arterial pressure standard deviation, and rCBF denotes the relative cerebral blood flow.

vertebrobasilar arterial system. Ay, DROR and Kimura have observed differences in lateral regulation and site-specificity of BPV in patients with AIS.[31,32] However, there is no consensus on the differences in BPV characteristics between infarct sites. Some studies have shown that patients with PCCI also have significantly increased BPV and abnormal BP rhythms.[33]

Current research is mainly concerned with the relationship between short-term BPV and AIS prognosis, and there is also a lack of detailed analysis differentiating between anterior and posterior circulation infarcts.[9–11] There are few studies on the relationship between BPV and prognosis in the middle stage of AIS. Our study further explored the relationship between cerebral perfusion and mid-term blood pressure variability in patients with PCCI. Our study further explored the relationship between cerebral perfusion and mid-term BPV in patients with PCCI.

We found that MAP-SD and MAP-CV were associated with cerebral perfusion, and were more sensitive to F.MTT and rCBF. Cerebral perfusion levels significantly influenced the 90-day prognosis of patients with PCCI. We posit that high daily BPV could lead to cerebral hemodynamic instability, mainly in the form of prolonged increased F.MTT and reduced rCBF, which in turn leads to adverse prognosis. In particular, the vertebrobasilar system is particularly sensitive to BP fluctuations. And high daily BPV can exacerbate the above. In addition, high daily BPV may exacerbate brain injury by inducing oxidative stress and neuroinflammatory responses in AIS.[7,29,30,34] This speculation was confirmed in the mediation analysis. Isabel J.'s study found that BPV caused a decrease in cerebral perfusion despite normal mean BP.[35] Thus, high daily BPV, by impairing cerebral perfusion and cerebral self-regulation, may be an important mechanism for the adverse prognosis of patients with PCCI.

Limitations of our study: First, this is a retrospective study conducted in one hospital. Selection bias may be present. Second, we did not fully account for variations in antihypertensive medication during hospitalisation, which may influence the mean and variability of BP measurements. However, it should be noted that antihypertensive therapy did not contribute to stroke severity in the baseline characteristics of the study participants. The influence of antihypertensive medication is likely to be captured in the reported blood pressure levels, as these medications are typically administered empirically around hospital discharge, limiting their effect on the acute phase of stroke. Finally, the results of cerebral perfusion processing software on different devices may differ, but our research data are collected on the same device. In addition, the relationship between cerebral perfusion, BPV and 90-day prognosis requires further research.

Conclusion

In patients with PCCI, both poor cerebral perfusion and high daily BPV were linked to a heightened risk of adverse prognosis within 90-day. Additionally, daily BPV and cerebral perfusion levels are closely interrelated and interact significantly, exhibiting a causal relationship that is independent of overall BP. High daily BPV maybe lead to a decrease in rCBF, which can lead to adverse prognosis.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Statement of Ethics

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. The study protocol was approved by the Ethics Review Committee of the Jiangsu Provincial Hospital of Traditional Chinese Medicine (Approval No. 2017NL-012-01) before the start of the study. All participants or their legal representatives gave informed consent after receiving a detailed explanation of the purpose, procedure, potential risks and benefits of the study. The verbal informed consent procedure was acceptable in this study and was recognized and approved by the Ethics Committee of the Jiangsu Provincial Hospital of Traditional Chinese Medicine. Confidentiality of participant data was strictly maintained through anonymisation and secure storage. Throughout the study, special consideration was given to protecting vulnerable groups and ensuring their autonomy and well-being. This publication was supported by the Department of Neurology, Jiangsu Provincial Hospital of Traditional Chinese Medicine.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no conflicts of interest to declare in this work.

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