### **Original Article**

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## Compromised dynamic cerebral autoregulation is a hemodynamic marker for predicting poor prognosis even with good recanalization after endovascular thrombectomy

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#### Abstract:

**PURPOSE:** In patients undergoing endovascular thrombectomy (EVT) with acute ischemic stroke (AIS), dynamic cerebral autoregulation (dCA) may minimize neurological injury from blood pressure fluctuations. This study set out to investigate the function of dCA in predicting clinical outcomes following EVT.

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Submission: 13-09-2023 Revised: 30-11-2023 Accepted: 22-12-2023 Published: 21-03-2024 **METHODS:** 43 AIS of the middle cerebral or internal carotid artery patients underwent with EVT, and 43 healthy individuals (controls) were enrolled in this case control research. The dCA was evaluated using transcranial Doppler 12 h and five days after EVT. The transfer function analysis was used to derive the dCA parameters, such as phase, gain, and coherence. The modified Rankin scale (mRS) at 3 months after EVT was used to assess the clinical outcomes. Thefavorable outcome group was defined with mRS  $\leq 2$  and the unfavorable outcome group was defined with mRS score of 3–6. Logistic regression analysis was performed to determine the risk factors of clinical outcomes.

**RESULTS:** A significant impairment in dCA was observed on the ipsilateral side after EVT, particularly in patients with unfavorable outcomes. After 5 days, the ipsilateral phase was associated with poor functional outcomes (adjusted odds ratio [OR] = 0.911, 95% confidence interval [CI]: 0.854–0.972; P = 0.005) and the area under the curve (AUC) (AUC, 0.878, [95% CI: 0.756–1.000] P < 0.001) (optimal cutoff, 35.0°). Phase change was an independent predictor of clinical outcomes from 12 h to 5 days after EVT (adjusted OR = 1.061, 95% CI: 1.016–1.109, P = 0.008).

**CONCLUSIONS:** dCA is impaired in patients with AIS after EVT. Change in dCA could be an independent factor related to the clinical outcomes.

#### Keywords:

Head-and-neck imaging, neurology, stroke, ultrasound, vascular surgery

#### Introduction

The most beneficial therapy is endovascular thrombectomy (EVT) among patients with acute ischemic stroke (AIS) caused by large artery occlusion. However, almost 56% of patients have poor clinical outcomes despite the achievement of a sufficient recanalization.<sup>[1]</sup> This failure to derive clinical benefit from apparent treatment success is poorly understood and may relate to brain physiologic reserve, infarct growth preceding intervention, and posttreatment complications, such as re-occlusion, "no-reflow" phenomenon,<sup>[2-5]</sup> and "reperfusion injury" (increased edema and hemorrhage transformation).<sup>[6-8]</sup> Understanding the underlying mechanisms

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may help identify the novel approaches to optimize treatment efficacy.

Despite variations in cerebral perfusion pressure and arterial blood pressure, the brain is critically dependent on steady and stable cerebral blood flow because of its finite energy stores.<sup>[9,10]</sup> Dynamic cerebral autoregulation (dCA) can protect the brain from ischemic and hyperperfusion damage by adjusting to fluctuating blood pressures. dCA is essential to regulate cerebral hemodynamics, and its dysfunction contributes to the occurrence and progression of stroke<sup>[11]</sup> by increasing an individual's susceptibility to stroke and impairing micro-embolus clearance.<sup>[12]</sup>

Therefore, in the present study, we aimed to investigate dCA status after successful tissue reperfusion by mechanical thrombectomy and explore the relationship between dCA and clinical outcomes. Our findings may provide a novel prognostic tool for patients with AIS undergoing EVT.

#### Methods

#### **Ethics statements**

Study approval was obtained from the appropriate ethics committee, and the principles of the Declaration of Helsinki were followed. Upon admission to the hospital, patients who met the inclusion criteria provided written informed permission through their lawfully chosen representatives.

#### Study design and participants

Patients with AIS due to internal carotid artery or middle cerebral artery (MCA) obstruction who accepted EVT between March and September 2022 were enrolled. The following were the inclusion criteria for this study: (i) Age >18 years, (ii) completely recanalized (thrombolysis in cerebral infarction grade 2b or 3) MCA, and (iii) presence of enough temporal windows to perform a transcranial Doppler (TCD) evaluation. Exclusion criteria: (i) Inability to perform dCA after EVT due to restlessness, (ii) re-occlusion of the culprit MCA after EVT, and (iii) other issues, like serious heart disease-related reduced cerebral blood flow. Healthy controls (HCs) with no neurological conditions were enrolled based on age and sex matching. All patients' initial characteristics were noted.

#### **Endovascular thrombectomy**

This study was conducted as part of a prospective registry study conducted at a research center.<sup>[13]</sup> All the patients were evaluated using computed tomography (CT) after attending to the emergency department; CT perfusion (CTP) and CT angiography (CTA) were not compulsory. Patients received intravenous t-PA

treatment before EVT with the conditions of large vessel occlusion and the time window spanned <4.5 hours. All individuals were anesthetized, with local or general anesthesia dependent on the cooperation level of the patient. During the procedure, it was mandatory to administer intravenous heparin to maintain the activated clotting time between 250 and 300 s, except for subjects who received intravenous alteplase. The procedures were performed through the femoral artery. The selection of stent retriever type and size, along with any required devices, such as guide wires and catheters, as well as the intervention strategy, was at the interventionists' discretion. Within 12-24 h post EVT, all participants underwent a follow-up CT scan of the head to evaluate hemorrhage and the infarct volume. Transcranial color Doppler (TCCD) ultrasound or TCD was performed to evaluate the cerebral hemodynamics between 12 and 24 h.

#### Measurement of dynamic cerebral autoregulation

The dCA examination protocol followed the guidelines of the International Cerebral Autoregulation Research Network.<sup>[14]</sup> EMS-9D PRO (Delica Medical, Shenzhen, China) ultrasound equipment were used to assess dCA with 2.0 MHz probes <12 h and 5 days after EVT.

Examinations were conducted in a silent, distraction-free room, and the room temperature was maintained between 20°C and 24°C. A supine position was used for the patients' examinations. Over the bilateral temporal acoustic window, two 2.0 MHz probes were positioned and clamped with a head frame. A continuous measurement of noninvasive blood pressure (NIBP) and cerebral blood flow velocity (CBFV) was taken during a 10-min period with the participant in the supine position. At a depth of 50–60 mm, continuous CBFV was assessed in the bilateral MCAs. On a middle finger, a servo-controlled plethysmograph was used to measure the NIBP. The brachial blood pressure was measured using an Omron HBP-1300 sphygmomanometer from Omron in Kyoto, Japan, before each NIBP measurement to calibrate the baseline blood pressure signal. An EMS-9D PRO with a nasal cannula connected was used to measure the end-tidal CO2.

To determine the relationship between NIBP and CBF, transfer function analysis (TFA) was used to calculate cerebral autoregulation.<sup>[14]</sup> From the 10-min recording, the TFA approach entailed choosing the steady 5-min beat-to-beat NIBP as well as raw data of CBFV for dCA analysis. A Hanning window length of 100 s with a 50% superposition was used. Between 0.02-0.07 Hz (very low frequency [VLF]) and 0.07-0.20 Hz (low frequency), the phase of both hemispheres was estimated, as well as absolute gain (cm/s/mmHg), normalized gain (%/mmHg), and coherence. According to the recent

research, autoregulation is best efficient at frequencies around or below 0.03 Hz.<sup>[11]</sup> Phase shift is a measure of the CBFV response's temporal delay to NIBP; a higher phase shift denotes a more effective dCA. A lower gain suggests more successful autoregulation and it gauges the degree to which dCA dampens blood pressure (BP) oscillation intensity. In the case of highly linear TFA systems, coherence approaches one.<sup>[15]</sup> Usually, in the event when the coherence is over 0.5 between 0.02 and 0.07 Hz, we will estimate the dCA parameters. The mean hemispheres were used to examine the dCA data from HCs.

#### **Data collection**

At the time of hospital admission, information about the patient's demographics, medical history, AIS risk factors, previous stroke medications, and clinical laboratory findings was gathered. Neurologists evaluated the National Institutes of Health Stroke Scale (NIHSS) and Alberta Stroke Program Early CT Score (ASPECTS).

The clinical prognosis was assessed with the modified Rankin Scale (mRS), with mRS of 2 or less defined as a favorable outcome at 90 days. All mRS assessments at 90 days after stroke onset were performed by two investigators who were unaware of the study protocol.

The modified Rankin Scale (mRS) was performed to assess the clinical prognosis at 3 months after stroke onset.<sup>[16]</sup> A favorable outcome group (mRS  $\leq$  2) and an unfavorable outcome group (mRS 3–6) were created from among the patients. Two separate doctors who were not aware of any relevant clinical or dCA information simultaneously investigated each mRS score evaluation through telephonic follow-ups.

#### Statistical analysis

The one-sample Kolmogorov-Smirnov test was used to identify the distribution of continuous variables. The means and standard deviations are used to present the continuous variables with normal distribution, whereas medians (interquartile ranges) are used to present variables with nonnormal distribution. The frequencies (percentages) are the unit of expression for the categorical variables. To examine the variations between the two clinical outcome groups, two-sided Student's *t*-tests with normally distributed data, Wilcoxon tests with nonnormally distributed data, and Chi-squared tests were used. Logistic regression analysis was used to calculate odds ratios (ORs) between the two groups. Age, BMI, hypertension, atrial fibrillation, diabetes mellitus, hyperlipidemia, smoking, NIHSS score at admission, ASPECTS, intravenous thrombolysis, onset to recanalization time, infarct volume and symptomatic hemorrhage transformation were all taken into account while adjusting the models.

The phase on the affected side and the 3-month mRS score were correlated using the Spearman correlation analysis. To establish the dCA cutoff value on the afflicted side for the best prediction of inferior functional results (mRS score: 3–6), a receiver operating characteristic curve was constructed. The cutoff value to optimize sensitivity and specificity was determined based on the maximum Youden index. The confidence intervals (CIs) were set at 95%, and the level of statistical significance was set at P < 0.05. The IBM Corp., Armonk, NY, USA's SPSS software, version 24.0, was used for all statistical analyses.

#### Results

#### Demographics of study participants

During the period, a total of 73 patients accepted the EVT in anterior circulation (mean age:  $56.3 \pm 13.4$  years, 63 men). According to the exclusion criteria, 43 EVT patients (mean age of  $54.9 \pm 14.5$  years, 36 men and 7 women) were included [Figure 1]. Meantime, 43 healthy volunteers with a mean age of  $57.6 \pm 9.7$  years; 35 men and 8 women were included in the study. Systolic BP was higher in patients with AIS than in HCs (*P* < 0.001).

All participants were monitored at the MCA using TCD, and the beat-to-beat NIBP was recorded. The favorable and unfavorable outcome groups included 27 and 16 patients, respectively. Creatine kinase (CK) levels were lower in the favorable outcome group than in the unfavorable outcome group (P < 0.05). However, in the group with a poor outcome, the rate of symptomatic hemorrhage transformation was noticeably higher (P < 0.05). There were no significant differences in clinical characteristics and other demographics [Table 1].

# Dynamic cerebral autoregulation parameters in acute ischemic stroke and healthy controls

The phase of the VLF on the affected side among patients with AIS was significantly lower than the dCA parameters of HCs (P < 0.05) at both 12 h and 5 days after EVT. In patients with AIS, the phase of the VLF on the affected side was significantly lower than that on the unaffected side (P < 0.05) [Table 2].

#### Dynamic cerebral autoregulation parameters of the two groups with different clinical outcomes

The dCA parameters at 12 h and 5 days after EVT for the two clinical outcome groups are presented in Table 3. The VLF phase on the affected side was significantly lower (P < 0.001) in the unfavorable outcome group than that in the favorable outcome group at 5 days. In the favorable group, the VLF phase on the unaffected side after 5 days was higher than that at 12 h (P < 0.05). Figure 2 shows a trend in which the phase was lower at 5 days than at 12 h in the unfavorable group, although the difference was not statistically significant.



Figure 1: Flow chart of the study. EVT: endovascular thrombectomy, AIS: acute ischemic stroke, MCA: middle cerebral artery, TICI, thrombolysis in cerebral infarction score, dCA: dynamic cerebral autoregulation



**Figure 2:** VLF phase on affected side after EVT between groups. \*Phase of the favorable outcome group at five days was noticeably higher than unfavorable outcome group (*P*<0.001). #Phase at five days was significantly higher than at 12 hours in favorable outcome group (*P*<0.05). EVT: endovascular thrombectomy, VLF: very low frequency

An independent predictor of clinical outcomes in AIS patients was the phase value in the ipsilateral hemisphere 5 days after EVT, according to the results of the logistic regression analysis (adjusted OR=0.911, 95% CI: 0.854-0.972; *P*=0.005), when age, BMI, hypertension, atrial fibrillation, diabetes mellitus, hyperlipidemia, smoking, NIHSS score at admission, ASPECTS, intravenous thrombolysis, onset to recanalization time, infarct 80

volume, and symptomatic hemorrhage transformation are adjusted for confounding factors. In addition, the mRS score and the phase value at 5 days were associated (r = -0.590, P < 0.001). In order to accurately predict the negative outcomes, the best cutoff value for the VLF phase on the affected side at 5 days was predicted to be 35.0°, with this value yielding a sensitivity of 87.5%, specificity of 83.3%, and area under the curve of 0.878 (95% CI: 0.756–1.000; P = 0.001) [Figure 3].

Based on the optimal cutoff values, the mRS score at 3 months was predicted by the phase of VLF on the affected side after 5 days (adjusted OR = 0.317, 95% CI: 0.143–0.705, *P* = 0.005), with the baseline NIHSS score and age was adjusted.

We then compared symptomatic hemorrhage transformation and dCA parameters 12 h and 5 days after EVT. Five days after EVT, we discovered that patients with symptomatic hemorrhage transformation had significantly lower phase of the VLF on the affected side than patients without symptomatic hemorrhage (P = 0.002). Further, we excluded patients with hemorrhage and analyzed the dCA across the two various clinical outcome groups. We noticed that the phase of the VLF on the affected side remained lower in patients in the unfavorable group than in those with favorable clinical results after 5 days (P = 0.013).

Brain Circulation - Volume 10, Issue 1, January-March 2024



Figure 3: ROC curve of the phase at 5 days for clinical outcomes and at 3 months after thrombectomy. The ROC curve for the VLF phase on the affected side five days after EVT is shown by the dotted line. EVT: endovascular thrombectomy, ROC: receiver operating characteristic, VLF: very low frequency

Finally, we compared the changes in dCA between 12 h and 5 days and observed a substantial difference between the groups (P = 0.013), indicating that, in the unfavorable group, the phase decreased and, in the favorable group, dCA was increased [Figures 2 and 4]. Phase change in the ipsilateral hemisphere after EVT was an independent predictor of clinical outcome, according to logistic regression analysis, even after confounding variables such as age, BMI, intravenous thrombolysis, hypertension, diabetes mellitus, hyperlipidemia, smoking, CK level, onset-to-recanalization time, hypersensitive C-reactive protein levels, ASPECTS, NIHSS score on admission, and infarct volume were taken into account (adjusted OR=1.061, 95% CI: 1.016–1.109, P=0.008).

#### Discussion

Previous studies have investigated the correlation between the clinical outcomes and cerebral autoregulation

#### Table 1. Demographic and clinical characteristics of groups with different outcomes

	Total (n=43)	Favorable outcome	Unfavorable outcome	Р
		group ( <i>n</i> =27)	group ( <i>n</i> =16)	
Male Sex (%)	36 (83.7)	22 (81.5)	14 (87.5)	0.605
Age (years)	54.9±14.5	53.0±13.8	58.1±15.7	0.298
BMI	26.5±4.0	25.8±4.4	27.6±3.0	0.112
SBP (mmHg)	143.8±21.3	139.0±20.3	151.8±22.1	0.059
DBP (mmHg)	82.3±15.0	79.7±15.1	86.8±14.1	0.131
Hypertension	27 (62.8)	18 (66.7)	9 (56.3)	0.530
Hyperlipidemia	6 (14.0)	4 (14.8)	2 (12.5)	0.832
Diabetes	9 (20.9)	5 (18.5)	4 (25.0)	0.614
Smoking	26 (60.5)	16 (159.3)	10 (62.5)	0.547
Cardio artery disease	5 (11.6)	2 (7.4)	3 (18.8)	0.344
Atrial fibrillation	4 (9.3)	1 (3.7)	3 (18.8)	0.101
Prior stroke	12 (27.9)	7 (25.9)	5 (31.3)	0.737
Stroke mechanism				
Atherosclerotic mechanism	34 (79.1)	21 (77.8)	13 (81.3)	0.554
Cardiogenic embolism	8 (18.6)	5 (18.5)	3 (18.8)	0.985
LSW	420.6±254.6	429.3±263.1	406.0±247.4	0.773
onset to recanalization	475.0 (344.0, 681.0)	471.0 (344.0, 681.0)	486.5 (332.5, 710.0)	0.960
Glucose	6.3 (5.4, 7.1)	5.9 (5.4, 7.1)	6.6 (5.6, 7.5)	0.171
LDL	2.5±0.8	2.5±0.8	2.3±0.7	0.350
HDL	1.0±0.2	1.1±0.2	1.0±0.3	0.298
HSCRP	11.3 (5.0, 21.7)	8.3 (4.0, 17.4)	15.3 (7.7, 24.2)	0.083
СК	113.0 (62.0, 207.0)	84.0 (54.0, 179.0)	174.5 (114.3, 430.3)	0.012
Intravenous thrombolysis	17 (39.5)	9 (33.3)	8 (50.0)	0.343
infarct volume	23.1 (8.9, 59.4)	20.9 (11.0, 59.0)	34.0 (8.5, 60.9)	0.688
Symptomatic hemorrhage transformation	6 (14.0)	0 (0.00)	6 (37.5)	0.001
ASPECTS	8.0±5.3	7.8±1.7	8.3±1.6	0.352
mRS score >2 at admission	39 (92.9)	24 (92.3)	15 (93.8)	0.860
NIHSS at hospital admission	12.6±4.5	12.1±4.2	13.5±4.9	0.353
NIHSS at hospital discharge	6.0 (2.0, 9.3)	4.0 (1.0, 7.0)	10.5 (8.3, 15.0)	0.001

Values are presented as mean±standard deviation, median (interquartile range), or *n* (%), as appropriate. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LSW, last seen well time; LDL, low-density lipoprotein; HDL, high-density lipoprotein; HSCRP, hypersensitive C-reactive protein; CK, creatine kinase; NIHSS, The National Institutes of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; mRS, modified Rankin scale score

Table 2:	The dCA	parameters	comparison	in different	hemisphere at	12 h and 5 days
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	12 h ( <i>n</i> =43)			5 d ( <i>n</i> =36)			
	Affected side	Unaffected side	Р	Affected side	Unaffected side	Р	
VLF							
Gain (cm/s/mmHg)	0.89±0.54*	0.96±0.50*	0.417	0.90±0.44*	0.88±0.43*	0.605	
Gain (%/mmHg)	1.26±0.71	1.54±0.63*	0.002	1.29±0.50	1.38±0.52	0.619	
Phase	39.31±24.11*	61.33±30.62	0.001	44.81±24.64*	58.63±24.45	0.726	
LF							
Gain (cm/s/mmHg)	0.94±0.61	0.88±0.41	0.605	0.96±0.38	0.99±0.47	0.362	
Gain (%/mmHg)	1.35±0.80	1.30±0.52*	0.619	1.47±0.69	1.58±0.64	0.320	
Phase	34.42±25.81*	36.14±24.01*	0.726	27.64±33.67*	34.12±28.55*	0.385	
Et-CO <sub>2</sub>	36.4	3±2.80	-	36.3	3±2.58	-	

dCA, dynamic cerebral autoregulation; AIS, acute ischemic stroke; VLF, very low frequency with 0.02–0.07 Hz; LF, low frequency with 0.07–0.2 Hz; Et-CO<sub>2</sub>, end-tidal carbon dioxide. \*Significant difference between healthy controls and AIS patients. *P*-values: comparisons between the affected side and the unaffected side in AIS patients

	Affected side			Unaffected side			
	Favorable outcome group ( <i>n</i> =27)	Unfavorable outcome group ( <i>n</i> =16)	Р	Favorable outcome group ( <i>n</i> =27)	Unfavorable outcome group ( <i>n</i> =16)	Р	
		12 h					
VLF							
Gain (cm/s/mmHg)	0.86±0.49	0.94±0.64	0.669	0.98±0.55	0.93±0.44	0.730	
Gain (%/mmHg)	1.55±0.69	1.39±0.95	0.408	1.55±0.69	1.53±0.54	0.914	
Phase	38.74±22.33	40.27±27.60	0.852	58.77±30.63	65.65±31.13	0.487	
LF							
Gain (cm/s/mmHg)	0.90±0.35	0.95±0.89	0.835	0.86±0.34	0.91±0.51	0.703	
Gain (%/mmHg)	1.33±0.72	1.39±0.94	0.832	1.33±0.53	1.25±0.51	0.617	
Phase	33.88±20.63	35.32±33.55	0.863	41.65±26.95	26.83±14.43	0.024	
Et-CO <sub>2</sub>	36.04±2.85	36.56±2.78	0.557	36.04±2.85	36.56±2.78	0.557	
		5 d					
VLF							
Gain (cm/s/mmHg)	0.92±0.39	0.89±0.46	0.860	0.84±0.49	0.96±0.27	0.382	
Gain (%/mmHg)	1.26±0.47	1.36±0.57	0.618	1.32±0.55	1.49±0.46	0.346	
Phase	54.95±21.78	24.54±16.35	0.001	63.25±26.23	49.38±18.19	0.074	
LF							
Gain (cm/s/mmHg)	0.86±0.32	1.10±0.36	0.061	0.86±0.38	1.25±0.57	0.047	
Gain (%/mmHg)	1.23 (0.99, 1.66)	1.44 (1.08, 2.32)	0.177	1.37 (1.17, 1.59)	1.70 (1.30, 2.38)	0.097	
Phase	24.29 (19.77, 41.87)	17.82 (6.76, 43.64)	0.280	40.95 (22.41, 54.04)	34.61 (18.27, 43.74)	0.379	
Et-CO <sub>2</sub>	36.25±2.51	35.42±3.57	0.437	36.25±2.51	35.42±3.57	0.437	

Values are expressed as the median (95% confidence interval) or mean±standard deviation. dCA, dynamic cerebral autoregulation; VLF, very low frequency with 0.02–0.07 Hz; LF, low frequency with 0.07–0.2 Hz; Et-CO2, end-tidal carbon dioxide. P-values: comparisons between the favorable and unfavorable outcome groups

levels as well as the association between the extent of cerebral autoregulation dysfunction and clinical outcomes.<sup>[22,23]</sup> In our study, the dCA 5 days after EVT in the group with a favorable outcome was considerably superior than that in the group with a negative outcome. Recently, Tian *et al.*<sup>[20]</sup> found that a phase, which was obtained at the 0.06–0.12 Hz frequency range, exceeding 26.93° on the affected side at 24 h after EVT, indicated a good clinical prognosis. However, in our study, we evaluated the dCA parameters at a lower frequency domain range of 0.02–0.07 Hz, the optimal cutoff value for the phase was 35° at the VLF on the affected side at 5 days. Conventionally, cerebral edema and hemorrhage transformation manifest within 3 days following EVT,<sup>[24]</sup> which may affect the dCA results. By treating patients within 5 days, the majority of patients experienced stabilization of their conditions. Consequently, the phase of the VLF beyond 5 days may be associated with clinical outcomes.

Notably, in our research, we found that the dCA demonstrated improvement from 12 h to 5 days after EVT in the favorable outcome group, while it deteriorated in the unfavorable outcome group. However, most previous studies<sup>[11,20,22]</sup> only have focused on the dCA value rather than the change in dCA after EVT. Therefore, we hypothesized that the change in dCA may be a predictor of the clinical outcome in patients after EVT, and the importance of the change in dCA for remote clinical outcomes need to be further verified.





A global multicenter study conducted in 2017 in collaboration with multiple hospitals in Portugal and the United States<sup>[23]</sup> found that in the first few hours following an ischemic stroke, less effective dCA was linked to a higher risk of hemorrhagic transformation and cerebral edema, probably due to breakthrough hyperperfusion and microvascular damage.

In the current study, the VLF phase at 5 days was lower in patients who underwent symptomatic hemorrhage transformation than those without hemorrhage, and the rate of symptomatic hemorrhage transformation was considerably higher in the group with a poor outcome than in the group with a good outcome. Thus, we hypothesized that the impact of impaired dCA on clinical outcomes following EVT may be attributed to symptomatic hemorrhage transformation. Furthermore, when we excluded patients with hemorrhage, dCA remained an independent risk factor after EVT for patients' poor clinical outcomes.

Our study has some limitations. First, TCD measures blood flow rate but not volume. As long as the diameter of the insonated artery does not change, the former serves as a suitable substitute for the latter. The diameter of the observed artery has no changes because we collected the data while the subject was supine and relied on spontaneous assessments. Second, to avoid delaying the treatment of patients with AIS, no evaluation of dCA was performed before EVT; thus, baseline dCA data for patients were not available. However, this study looked at whether dCA could predict the clinical outcomes of postoperative patients rather than comparing dCA before and after surgery. Third, this case–control research only involved one center. In order to validate our findings, a bigger cohort study is required.

#### Conclusions

Patients with AIS who have EVT may have compromised dCA. The changes in dCA might be an independent risk factor for clinical outcomes, and impaired dCA might be a brand-new indicator of those outcomes in AIS patients who have received EVT.

#### **Author contributions**

1. RL and YX contributed to the study conception and design and drafting the manuscript; 2. RL, HC, NL and FZ contributed to the data acquisition, analysis, and interpretation; 3. RL, PW, and WZ drafted and critically revised the manuscript for important intellectual content; 4. YX and QM agree to be accountable for all aspects of the work by ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

#### **Ethics approval**

The study was approved by the Ethics Committee of Xuanwu Hospital (approval number: LYS [2022]137, dated on September 7<sup>th</sup> 2022) and conformed to the tenets of the Declaration of Helsinki.

#### Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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The funding agencies had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

#### **Conflicts of interest**

Dr. Wenbo Zhao is an Associate Editor of Brain Circulation. The article was subject to the journal's standard procedures, with peer review handled independently of this Editor and their research groups.

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