Effect of short-term blood pressure variability on functional outcome after intra-arterial treatment in acute stroke patients with large-vessel occlusion

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Abstract
Background: Endovascular treatment (EVT) is advocated for acute ischemic stroke with large-vessel occlusion (LVO), but perioperative periods are challenging. This study investigated the relationship between post-EVT short-term blood pressure variability (BPV) and early outcomes in LVO patients.

Methods: We retrospectively reviewed 72 LVO patients undergoing EVT between June 2015 and June 2018. Hourly systolic and diastolic blood pressures (SBP and DBP, respectively) were recorded in the first 24 hours post-EVT. BPV were evaluated as standard deviation (SD), coefficient of variation (CV), and successive variation (SV) separately for SBP and DBP. Three-month functional independence was defined as a modified Rankin Scale (mRS) score of 0-2. Results: For 58.3% patients with favorable outcomes, median National Institutes of Health Stroke Scale and Alberta Stroke Program Early CT scores on admission were 14 and 8, respectively. The maximum SBP (154.3±16.8 vs. 163.5±15.6, P=0.02), systolic CV (8.8%±2.0% vs. 11.0%±1.8%, P<0.001), SV (11.4±2.3 vs. 14.6±2.0, P<0.001), and SD (10.5±2.4 vs. 13.8±3.9, P<0.001) were lower in patients with favorable outcomes. On multivariable logistic regression analysis, systolic SV (OR: 4.273, 95% CI: 1.030 to 17.727, P=0.045) independently predicted unfavorable prognosis. The area under the curve was 0.868 (95% CI: 0.781 to 0.955, P<0.001), and sensitivity and specificity were 93.3% and 73.8%, respectively, showing excellent value for 3-month poor-outcome predictions. Conclusions: Decreased systolic SV following intra-arterial therapies result in favorable 3-month outcomes. Systolic SV may be a novel predictor of functional prognosis in LVO patients.

Background
Early endovascular treatment (EVT) for patients who had acute ischemic stroke with large-vessel occlusion (AIS-LVO) is highly recommended based on the findings of six randomized controlled clinical trials [1-6]. However, several factors during the perioperative period of EVT, including blood pressure (BP) management, need urgent attention. The optimal range of BP following EVT remains unclear. The 2018 American Heart Association and American Stroke Association guidelines for the early management of patients with AIS recommends maintaining the BP at <180/105 mm Hg (IIb, B-NR) in patients who underwent mechanical thrombectomy (MT) with successful reperfusion [7].
Chinese guidelines also recommend a target BP of 140/90 or a BP of 20 mmHg lower than that at baseline, but it should also not be less than 100/60 mmHg (II, C) [8]. However, although the BP is maintained within the target range, reperfusion injury still occurs.

Blood pressure variability (BPV) is the fluctuation of BP in a certain period of time. In the acute stage of cerebrovascular disease, the fluctuation of cerebral perfusion pressure is aggravated by short-term BPV due to impaired automatic regulation of cerebral blood flow [9]. Hypertension during the perioperative period may lead to adverse events such as reperfusion syndrome and cardiovascular complications, while hypotension may lead to hypoperfusion and increases the risk of infarction. A recent systematic review reported that increased BPV after stroke is associated with higher rates of intracranial hemorrhage and disability [10]. However, there is limited epidemiological evidence to evaluate the relationship between BP level and early functional prognosis after EVT. Thus, this study aimed to explore the association of short-term BPV in the first 24 hours following EVT with functional outcomes in patients with AIS-LVO.

**Methods**

**Patient selection**

This is a retrospective study was approved by the Institutional Review Board of Taiyuan Central Hospital, Shanxi, People’s Republic of China. Consecutive AIS-LVO patients who underwent emergency EVT in the tertiary care stroke center of Taiyuan Central Hospital between June 2015 and June 2018 were enrolled. The inclusion criteria were as follows: (1) age of ≥18 years; (2) AIS confirmed via head computed tomography (CT) or magnetic resonance imaging at admission; (3) occlusion of the internal carotid artery or M1 of the middle cerebral artery diagnosed within 6 hours after onset by digital subtraction angiography; (4) preoperative Alberta Stroke Program Early CT Score (ASPECTS) of ≥6, prestroke modified Rankin Scale (mRS) score of <2, and National Institutes of Health Stroke Scale (NIHSS) score of ≥6; (5) treatment initiated (groin puncture) within 6 hours of symptom onset; (6) clinical features and BP recorded at baseline and hourly for at least 24 hours after EVT; and (7) follow up by phone or face-to-face consultations at 3 months with complete documentation. Patients were excluded if they had active bleeding or a bleeding tendency (including primary intracerebral
hemorrhage, and potential causes such as gastrointestinal malignancy, liver cirrhosis, renal failure, hematologic tumor, vitamin K deficiency, and sepsis, which could lead to bleeding events), serious heart failure or respiratory failure pre-admission, glucose <50 mg/dL or >400 mg/dL, severe hypertension beyond drug control, and severe non-cardiovascular events that occurred within 3 months of follow-up. The management of patients with AIS-LVO was based on the Chinese guidelines for diagnosis and treatment of AIS 2014 and Chinese guidelines for the endovascular treatment of acute ischemic stroke 2015 [11, 12].

Data collection
Baseline characteristics such as demographics, vascular risk factors, previous use of anti-platelet aggregation drugs, Trial of ORG 10172 in acute stroke treatment (TOAST) types on admission, NIHSS scores on admission, ASPECTS on admission, systolic BP (SBP) and diastolic BP (DBP) on admission, laboratory values, and type of treatment for the EVT were collected. The degree of recanalization at the end of EVT was measured using the Thrombolysis in Cerebral Infarction (TICI) score [13] as obtained from the reports of interventional specialists (C.W. and F.Z.). All patients were examined via brain CT in the first 24 hours after EVT to determine any changes in intracranial hemorrhage using the criteria developed by the European Cooperative Acute Stroke Study (ECASS) [14]: HI1, small petechiae with an indistinct border within the vascular territory; HI2, more confluent petechiae, no mass effect; PHI, hematoma within infarcted tissue, occupying <30% of the infarcted area, no substantive mass effect; and PH2, >30% of the infarcted area with significant space-occupying effect or parenchymal hematoma distant from the infarcted brain tissue.

BP monitoring and BPV presentation post EVT
The hourly SBP and DBP of all patients were recorded during the first 24 hours following EVT. Postoperative management of blood pressure depended on whether the responsible vessels were successful recanalized according to the Chinese guidelines for the endovascular treatment of acute ischemic stroke 2015 [12], which recommend a target BP of 20-30 mmHg lower than that at baseline, but it should not be less than 90/60 mmHg in patients with successful recanalization. For patients without successful recanalization, permissive hypertension was set at a systolic blood pressure more
than 150 but not exceeding 180 mmHg. For patients pretreated with intravenous thrombolysis, permissive hypertension was set at <180/105 mmHg. All patients with postoperative hypertension were treated with intravenous urapidil (first choice) or sodium nitroprusside (second choice) when BP levels exceeded the former prespecified cut-offs. We documented the maximum, minimum, and mean arterial BP (MAP, SBP + 2 × DBP)/3) levels for each individual. Based on previously published studies, BPV was calculated using the following equation:

(1) Standard deviation of mean BP (SD): [Due to technical limitations, Equation 1 is only available as a download in the supplemental files section],

(2) Coefficient of variability (CV [%]): SD/BP \_mean \times 100,

(3) Successive variation (SV): [Due to technical limitations, Equation 3 is only available as a download in the supplemental files section] [15].

**Evaluation of functional prognosis**

Functional outcome was evaluated at 3 months by certified neurologists using the mRS score. The patients were then divided into two groups based on the functional outcome score: the favorable and unfavorable outcome groups comprised patients with mRS 0-2 and mRS 3-5, respectively. The mRS scores were determined based on the follow-up findings.

**Statistical analysis**

All data analyses were performed using SPSS V. 25.0 software. Continuous variables were expressed as means±SD (normal distribution) or median with interquartile range (IQR) (skewed distribution).

Comparisons between groups were conducted using the Students t-test, Mann-Whitney U test, or \( \chi^2 \) test, or One-way ANOVA analysis as appropriate. Univariable and multivariable logistic regression models were used to explore the association between BPV indexes during the first 24 hours post EVT with 3-month functional outcome before and after adjustment for the following potential confounders: age, sex, hypertension, coronary heart disease, atrial fibrillation, diabetes mellitus, smoking, admission NIHSS scores, admission serum glucose and LDL-C levels, admission SBP and DBP levels, type of anesthesia (general anesthesia vs conscious sedation), baseline ASPECTS, onset to groin
puncture time, vascular lesion (M1 of the MCA vs ICA), frequency of MT, and type of EVT. In the initial univariable analyses, a P value < 0.05 was set as the threshold for inclusion in the multivariable models. Odds ratios (OR) and 95% confidence interval (CI) were calculated to determine any associations.

To determine the predictive capabilities according to SBP SV, the receiver operating characteristic (ROC) curves were generated, and the sensitivities, specificities, positive predictive values (PPV) and negative predictive values (NPV) of systolic SV were calculated. Because the interaction between SBPV and successful reperfusion or offending artery was significant, a subgroup analysis by BPV parameters with 3-month functional outcome were used. We also examined the impact of BPV on functional outcome by different systolic SV. Patients were stratified according to the quartile of their systolic SV during the first 24 hours post EVT and the distribution of the patients with favorable outcomes was calculated in each group.

Results

Patient demographics and clinical characteristics

Among 83 patients who underwent emergency EVT in our stroke unit, 11 (13.3%) patients were excluded due to the following causes: 2 (2.4%) died as a result of non-cardiovascular disease, 4 (4.8%) had inadequate BP during the first 24 hours, 3 (3.6%) exited the study during the 3-month follow-up, and 2 (2.4%) died as a result of cerebral hernia. As a result, 72 patients with AIS-LVO within the anterior circulation were enrolled in this study.

The baseline clinical demographic characteristics of the study population are summarized in Table 1. Of the 72 patients, including 42 (58.3%) with favorable outcomes and 30 (41.7%) with unfavorable outcomes at 3-months, the mean age was 64.8±10.9 years, and 27 (37.5%) were women. The median NIHSS score at admission was 14 points [IQR, 9-19], while the median ASPECTS was 8 points [IQR, 7-9]. Of the 72 patients, 86.1% patients achieved recanalization (TICI 2b or 3). In total, 26.4% patients received combined intravenous thrombolysis and thrombectomy, 13.9% of patients were treated with intra-arterial thrombolysis alone, and 59.7% of patients were treated with direct mechanical thrombectomy. Intracranial hemorrhagic transformation occurred in 13 patients (18.0%), while the
hemorrhagic transformation was no different between the patients with the three treatments of EVT (Supplemental Table 1).

**Table 1. Baseline characteristics of patients in the two outcome groups**

Compared to patients with an unfavorable outcome group, the NIHSS scores, admission SBP level, and frequency of MT were significantly lower in the favorable outcome group (all P<0.05). Patients with a 3-month favorable outcome were more likely to have M1 of middle cerebral artery offending, to have higher rates of successful recanalization, to have higher admission ASPECT scores, and to receive intra-arterial thrombolysis alone. The rates of vascular risk factors, time of symptom onset to groin puncture, and HI were not significantly different between the two groups.

Table 2 lists the baseline characteristics of patients in different groups, in which patients are divided quartile by systolic SV values. Compared to the high level (Q4) of systolic SV group, patients in the other three groups (Q1, Q2 and Q3) were had a higher frequency of MT, lower ASPECT score at admission and had a lower rates of successful recanalization post EVT.

**Table 2. Baseline characteristics of patients**

**BPV and 3-month functional outcome**

In this study (Fig. 1), we detected the difference in maximum SBP, systolic CV, SV, and SD between the two outcome groups. Patients with unfavorable prognosis had higher maximum SBP ([163.5±15.6] vs. [154.3±16.8], P=0.02), systolic CV ([11.0%±1.8%] vs. [8.8%±2.0%], P<0.001), SV ([14.6±2.0] vs. [11.4±2.3], P<0.001), and SD ([13.8±3.9] vs. [10.5±2.4], P<0.001). We found no significant difference in the level of MAP, mean SBP, minimum SBP, and dates of DBP variability between the two groups (P>0.05). In a subgroup analysis, we also found the maximum SBP, systolic SV, CV, SD were lower in patients with a favorable outcome in the successful recanalization group, but there was no significant different in the non-successful recanalization group. Lower systolic SV, CV, and SD were found in M1 of the MCA lesion group, according to vascular lesions. In the ICA lesion group, the systolic SV was lower amongst those patients with a favorable outcome; other BPV parameters were not found to be different (Table 3).

**Table 3. Comparison of SBP and DBP variability parameters between**
different subgroups

Influencing factors of 3-month functional independence

Table 4. summarizes the univariable and multivariable associations of BP measurements after EVT and other clinical characteristics with the 3-month functional prognosis. The following variables were significantly related (P<0.05) to 3-month functional independence in the initial univariable analyses: NIHSS score at admission; SBP at admission; ASPECTS at admission; M1of the MCA occlusion; frequency of mechanical thrombectomy; measurement of EVT; successful recanalization; maximum SBP and systolic SD, CV, and SV post MT. After adjusting for potential confounders, multivariable logistic regression revealed that systolic SV (OR: 4.273, 95% CI: 1.030 to 17.727, P=0.045) was an independent predictor of unfavorable outcome, and a high ASPECTS was independently associated with a better likelihood of a favorable outcome (OR: 0.200, 95% CI: 0.054 to 0.744, P=0.016).

Table 4 Univariate and multivariate analyses of the favorable outcomes after EVT

mRS score distribution according to quartiles of systolic SV

Patients were divided into quartiles by systolic SV values. mRS scores were statistically different in each group and the patients with lower systolic SV had lower mRS scores at 3-month. However, no difference in mRS scores was noted in patients with systolic SV 0-25% and 25-50% [P>0.05; Fig.2].

ROC analysis

ROC analysis demonstrated that the areas under the curve (AUC) of systolic SV for predicting unfavorable outcome was 0.868 (95% CI: 0.781 to 0.955, P<0.001; Fig. 3). The optimal cut-off value was 12.499, which resulted in 93.3% sensitivity, 73.8% specificity, 71.1% PPV, and 91.2% NPV (Table 5). This indicates that an systolic SV of 12.499 had an excellent predictive value for a poor 3-month functional outcome.

Table 5 Cut-off values of systolic SV

Discussion

The clinical outcome in patients with ischemic stroke is affected by many factors, including age,
severity of stroke, collateral compensation, time of successful reperfusion, and device selected for EVT. BP management and its effect on functional outcome is particularly controversial. A previous study showed that increased systolic BPV positively contributed to symptomatic intracerebral hemorrhage and death after intravenous thrombolysis [16]. However, less is known about the effect of short-term BPV after EVT on the early outcomes of AIS-LVO patients. Our study shows that lower maximum SBP and systolic CV, SV, and SD levels during the first 24 hours after EVT are related to a better 3-month functional outcome, which was consistent with the results reported by Bennett [17]. BPV is divided into physiological and pathological variability, which fluctuates with physiological regulation, environmental changes, pathological influence. The possible pathophysiological mechanisms regarding short-term BPV in AIS patients with EVT are not clear. In a previous study, increased BPV may promote shear force of blood vessels and produce vascular inflammation by increasing endothelial expression of cytokines, which affect the structure of the vascular wall and lead to the formation of atherosclerotic plaques [18-19]. Another hypothesis is that the effects of increased BPV on brain tissue may vary with the degree of impaired cerebral autoregulation [20], and the cerebral blood flow dependent on cerebral perfusion pressure and blood viscosity [21]. Endovascular therapy can not only stimulate endothelial cells, but also change the cerebral perfusion pressure and vascular resistance in LVO-AIS patients. Therefore, there is a potential correlation between blood pressure variability and outcome of LVO-AIS patients after intra-arterial treatment.

BPV are commonly quantified by calculating SD, CV, and SV [19]. Several studies have shown that higher systolic CV or SD is associated with poor prognosis after stroke [22-23]; however, systolic SV, an indicator of systolic blood pressure variability, is more commonly used in many studies, because it can better reflect the time-series variability of BP, while other parameters, such as SD and CV, ignore the temporal change of data, resulting in the same SD or CV in individuals with different clinical characteristics [24]. In our study, we confirmed that the systolic SV, rather than systolic CV and SD, was closely associated with 3-month functional outcome. Lower systolic SV levels may be beneficial to achieving 3-month functional independence. These findings suggest that keeping a stable BP may be more useful than just controlling the BP level after EVT.
A study of 217 patients who underwent MT showed that a higher maximum SBP was closely related to 3-month mortality and poor outcome. Each 10 mmHg increase in maximum SBP during the first 24 hours post MT was associated with a lower 3-month functional prognosis and a higher odds of 3-month mortality [25]. Although our study did not found the maximum SBP was an influential factor for functional outcome, this may related to our study subjects’ characteristics. Our research found that the rate of successful recanalization was higher in the favorable outcome group, which also had lower maximum SBP, indirectly suggesting that patients with successful reperfusion are more likely to benefit from lower SBP [26].

Some studies showed that BP within the first 48 hours after a stroke showed a U-shaped correlation with clinical outcome [17, 27], particularly in patients with non-recanalization. The authors argued that patients with unsuccessful recanalization had larger infarct size and ischemic penumbra, and impaired cerebral autoregulation led to further enlargement of the ischemic penumbra [17]. The effect of BPV on the ischemic penumbra is different from that on the infarct core [19]. In the hours after onset, potentially ischemic penumbra are particularly sensitive to blood pressure fluctuations, with sudden drops in blood pressure increasing the risk of tissue ischemia and reducing the chance of reperfusion, and sudden increases in blood pressure increasing the risk of bleeding. Patients who received EVT and had unsuccessful reperfusion enlarged the ischemic penumbra, which was sensitive to blood pressure variability, greatly increasing the risk of neurological deterioration caused by BPV.

In addition, cerebral ischemia and MT itself can lead to the destruction of blood-brain barrier, resulting in vasogenic edema and hemorrhagic transformation after infarction. Moreover, iatrogenic injury to endothelial cells during MT can cause a series of reperfusion-related injuries [28] that not only increase intracranial hemorrhage associated with SBP, but also lead to adverse functional prognosis.

In this study, due to the small number of cases of patients without recanalization, no significant difference was found between the two groups in terms of functional outcome. Future studies should focus on enlarging the sample size to be more adequately powered for these sorts of subanalyses. Another study also showed that the peak level of SBP was closely related to poor outcome regardless of whether LVO recanalization was achieved or not. The authors suggested that this is probably
because abnormally elevated BP may be associated with potential collateral circulation damage [29]. The impairment of cerebral autoregulation is influenced by infarct size [30]. Thus, BPV may exert a greater pathophysiological role in patients with severe stroke than in patients with mild stroke. In our study, patients with favorable prognosis were more likely to have M1 of the middle cerebral artery affected, which may, in theory, produce a smaller infarct volume. Our subgroup analysis also confirmed that in patients with M1 of MCA lesions, the systolic SV, CV, and SD were lower in the favorable outcome group.

Several limitations of the present study need to be acknowledged. First, this was a single-center retrospective study with a relatively small sample size. Thus, selection bias in baseline data could not be avoided. Second, a recent study demonstrated that BPV post MT may increase the rate of symptomatic intracranial hemorrhage (sICH) [10], but we did not evaluate the relationship between BPV and sICH because the patients who developed intracranial hemorrhage during follow-up were classified according to ECASS criteria without the clinical classification for sICH. Third, variable reasons such as the varying time from stroke onset to arrival at our hospital for first BP measurement and differences in time intervals between BP measurements may cause bias in our results. However, we exerted every effort to provide reliable dates to mitigate the inherent limitations. Fourth, SD, CV and SV are not suitable for the long-term evaluation of BPV after EVT; severe stroke with a poor prognosis may give rise to greater variability in BP. Therefore, additional well-designed and larger prospective randomized cohort studies are required to confirm the association of BPV and functional prognosis and to determine strategies to reduce the BPV.

Conclusions
Decreased systolic SV following intra-arterial therapies result in favorable 3-month outcomes. This shows that systolic SV may be a novel predictor of functional prognosis in LVO patients.

Abbreviations
EVT: Endovascular treatment; LVO: Large-vessel occlusion; BP: Blood pressure; BPV: Blood pressure variability; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; SD: Standard deviation; CV: Coefficient of variation; SV: Successive variation; mRS: Modified Rankin Scale; AIS: Acute ischemic
stroke; MT: Mechanical thrombectomy; ASPECTS: Alberta Stroke Program Early CT Score; NIHSS: National Institutes of Health Stroke Scale; TOAST: Trial of ORG 10172 in acute stroke treatment; TICI: Thrombolysis in Cerebral Infarction; ECASS: European Cooperative Acute Stroke Study; MCA: middle cerebral artery; LDL-C: Low-density lipoprotein cholesterol; IQR: Interquartile range; OR: Odds ratio; CI: confidence interval; ROC: Receiver operating characteristic; AUC: Area under the curve; HI: Petechial infarction without space-occupying effect; PH: Hemorrhage (coagulum) with mass effect; ICH: intracerebral hemorrhagic.

Declarations
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Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors’ contributions
WRL conceived the study and revised the manuscript. TLZ wrote the manuscript and analyzed the data. XLW, CW, FZ, and SWG performed intra-arterial treatment and collected the data and interpreted the analysis. SQL, XDZ and JS critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

Ethics approval and consent to participate
This study was approved by the ethic committee of the Taiyuan Central Hospital, ShanXi, China.
Patient’s consents were waived by the ethic committee of the ethic committee of the Taiyuan Central Hospital, due to the retrospective design of the study.

Consent for publication
Not applicable.
Competing interests

The authors declare that they have no competing interests.

Disclosures

The authors declare no conflicts of interest.

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Tables

Table 1. Baseline characteristics of patients in the two outcome groups

| Variable               | Total       | Favorable outcome group (n=42, 58.3%) | Unfavorable outcome group (n=30, 41.7%) | P value |
|------------------------|-------------|---------------------------------------|----------------------------------------|---------|
| Age (years), mean ± SD | 64.8±10.9   | 64.5±11.8                             | 65.1±9.8                               | 0.820   |
| Male, n (%)            | 45 (62.5)   | 27 (64.3)                             | 18 (60.0)                              | 0.711   |
| Condition                                        | n (%)     | n (%)     | n (%)     | p-value   |
|-------------------------------------------------|-----------|-----------|-----------|-----------|
| Hypertension, n (%)                             | 48 (66.7) | 28 (66.7) | 20 (66.7) | 1.000     |
| Diabetes mellitus, n (%)                        | 23 (31.9) | 17 (40.5) | 6 (20.0)  | 0.066     |
| Coronary heart disease, n (%)                   | 21 (29.2) | 12 (28.6) | 9 (30.0)  | 0.895     |
| Atrial fibrillation, n (%)                      | 24 (33.3) | 16 (31.8) | 8 (26.7)  | 0.310     |
| Previous history of cerebrovascular disease, n (%) | 10 (13.9) | 5 (11.9)  | 5 (16.7)  | 0.565     |
| Previous antiplatelet therapy, n (%)            | 14 (19.4) | 9 (21.4)  | 5 (16.7)  | 0.615     |
| Current smoker, n (%)                           | 34 (47.2) | 21 (50.0) | 13 (43.3) | 0.576     |
| NIHSS score at admission, median (IQR)          | 14 (9-19) | 13 (8-17) | 17 (12-20)| 0.015*    |
| Glucose level at admission (mg/dL), mean±SD     | 152.3±85.0| 163.8±108.0| 135.0±30.6| 0.157     |
| SBP level at admission (mmHg), mean±SD          | 153.8±23.5| 146.9±18.5| 163.5±25.5| 0.003*    |
| DBP level at admission (mmHg), mean±SD          | 85.2±13.4 | 83.4±12.8 | 87.6±14.0 | 0.189     |
| LDL-C at admission (mg/dL), median (IQR)        | 44.73 (34.97-55.71)| 45.18 (34.43-53.15)| 44.01 (35.19-57.60)| 0.541     |
| TOAST type, n (%)                                |           |           |           |           |
| Large artery atherosclerosis                     | 44 (61.1) | 23 (54.8) | 21 (70.0) | 0.442     |
| Cardioembolism                                   | 23 (31.9) | 16 (38.1) | 7 (23.3)  |           |
| Clear reason                                     | 4 (5.6)   | 2 (4.8)   | 2 (6.7)   |           |
| Unknown reason                                   | 1 (1.4)   | 1 (2.4)   | 0 (0.0)   |           |
| ASPECT at admission, median (IQR)                | 8 (7-9)   | 8 (8-9)   | 7 (6.75-8)| <0.001*   |
| Vascular lesion                                  |           |           |           |           |
| M1 of the middle cerebral artery                | 51 (70.8) | 35 (83.3) | 16 (53.3) | 0.006*    |
| Internal carotid artery                          | 21 (29.2) | 7 (16.7)  | 14 (46.7) |           |
| Type of anesthesia                               |           |           |           |           |
| General anesthesia, n (%)                       | 9 (12.5)  | 4 (9.5)   | 5 (16.7)  | 0.366     |
| Conscious sedation, n (%)                       | 63 (87.5) | 38 (90.5) | 25 (83.3) | 0.366     |
| Time from stroke                                 | 290.5±80.5| 297.0±72.5| 281.4±91.1| 0.421     |
onset to groin puncture (min), mean±SD

| Type of endovascular treatment                                      | Quartile 1 | Quartile 2 | Quartile 3 | Quartile 4 | P-value |
|---------------------------------------------------------------------|------------|------------|------------|------------|---------|
| Combined intravenous thrombolysis and thrombectomy, n (%)          | 19 (26.4%) | 8 (19.0)   | 11 (36.7)  |            | 0.094   |
| Intra-arterial thrombolysis, n (%)                                  | 10 (13.9)  | 9 (21.4)   | 1 (3.3)    |            | 0.029*  |
| Direct mechanical thrombectomy, n (%)                               | 43 (59.7)  | 25 (59.5)  | 18 (60.0)  |            | 0.968   |
| Frequency of mechanical thrombectomy, median (IQR)                  | 2 (2-3)    | 2 (1-3)    | 3 (2-3)    |            | 0.024*  |
| Rates of successful recanalization, n (%)                           | 62 (86.1)  | 40 (95.2)  | 22 (73.3)  |            | 0.008*  |
| Intracranial hemorrhagic transformation, n (%)                       |            |            |            |            |         |
| HI1                                                                 | 5 (6.9)    | 4 (9.5)    | 1 (3.3)    |            | 0.197   |
| HI2                                                                 | 5 (6.9)    | 2 (4.8)    | 3 (10.0)   |            |         |
| PH1                                                                 | 2 (2.8)    | 0 (0.0)    | 2 (6.7)    |            |         |
| PH2                                                                 | 1 (1.4)    | 0 (0.0)    | 1 (3.3)    |            |         |

*Statistically significant.

NIHSS National Institutes of Health Stroke Scale, SBP systolic blood pressure, DBP diastolic blood pressure, LDL-C low-density lipoprotein cholesterol, ASPECT Alberta Stroke Program Early CT Score, HI petechial infarction without space-occupying effect, PH hemorrhage (coagulum) with mass effect

Table 2. Baseline characteristics of patients

| Variable                        | Quartile 1 18 | Quartile 2 18 | Quartile 3 18 | Quartile 4 18 | P-value |
|---------------------------------|---------------|---------------|---------------|---------------|---------|
| Age (years), mean±SD            | 64.8±10.2     | 60.1±12.5     | 64.6±10.3     | 69.4±9.4      | 0.090   |
| Male, n (%)                     | 11 (61.1)     | 12 (66.7)     | 9 (50.0)      | 13 (72.2)     | 0.557   |
| Hypertension, n (%)             | 10 (55.6)     | 12 (66.7)     | 12 (66.7)     | 14 (77.8)     | 0.572   |
| Diabetes mellitus, n (%)        | 5 (27.8)      | 9 (50.0)      | 4 (22.2)      | 5 (27.8)      | 0.287   |
| Coronary heart                  | 3 (16.7)      | 7 (38.9)      | 7 (38.9)      | 4 (22.2)      | 0.330   |
| Condition                                      | Value 1     | Value 2     | Value 3     | Value 4     | p-value  |
|-----------------------------------------------|-------------|-------------|-------------|-------------|----------|
| **Atrial fibrillation, n (%)**                | 7 (38.9)    | 6 (33.3)    | 5 (27.8)    | 6 (33.3)    | 0.919    |
| **Previous history of cerebrovascular disease, n (%)** | 3 (16.7)    | 3 (16.7)    | 0 (0.0)     | 4 (22.2)    | 0.243    |
| **Current smoker, n (%)**                     | 8 (44.4)    | 12 (66.7)   | 5 (27.8)    | 9 (50.0)    | 0.134    |
| **NIHSS score at admission, median (IQR)**    | 9.5 (7.8-14.8) | 13 (9.0-16.3) | 18 (8.5-21.3) | 16.5(13.8-20.0) | 0.070    |
| **Glucose level at admission (mg/dL), mean ±SD** | 149.0±78.1 | 184.3±141.3 | 138.4±37.2 | 137.4±33.7 | 0.309    |
| **SBP level at admission (mmHg), mean ±SD**   | 143.4±23.9  | 156.7±17.3  | 158.7±27.0  | 156.4±23.4  | 0.189    |
| **DBP level at admission (mmHg), mean ±SD**   | 81.9±15.1   | 87.3±11.1   | 82.7±12.9   | 88.8±14.0   | 0.335    |
| **LDL-C at admission (mg/dL), median (IQR)**  | 43.5 (33.9-56.4) | 49.0 (36.2-56.0) | 36.8 (30.3-3.56.7) | 46.2 (41.5-56.4) | 0.384    |
| **TOAST type, n (%)**                         |             |             |             |             |          |
| Large artery atherosclerosis                  | 9 (50.0)    | 11 (61.1)   | 12 (66.7)   | 12 (66.7)   | 0.442    |
| Cardioembolism                                | 6 (33.3)    | 6 (33.3)    | 5 (27.8)    | 6 (33.3)    | 0.377    |
| Clear reason                                  | 3 (16.7)    | 0 (0.0)     | 1 (5.6)     | 0 (0.0)     |          |
| Unknown reason                                | 0 (0.0)     | 1 (5.6)     | 0 (0.0)     | 0 (0.0)     |          |
| **ASPECT at admission, median (IQR)**         | 7.8 (8-9)   | 8 (8-9)     | 7 (7-8.3)   | 7 (6-7.3)   | <0.001*  |
| **Vascular lesion**                           |             |             |             |             |          |
| M1 of the middle cerebral artery              | 14 (77.8)   | 16 (88.9)   | 10 (55.6)   | 11 (61.1)   | 0.106    |
| Internal carotid artery                       | 4 (22.2)    | 2 (11.1)    | 8(44.4)     | 7 (38.9)    |          |
| **Type of anesthesia**                        |             |             |             |             |          |
| Conscious sedation, n (%)                     | 17 (94.4)   | 14 (77.8)   | 16 (88.9)   | 16 (88.9)   | 0.491    |
| General anesthesia, n (%)                     | 1 (5.6)     | 4 (22.2)    | 2 (11.1)    | 2 (11.1)    |          |
| **Time from stroke onset to**                 | 284.6±60.7  | 300.1±75.8  | 308.7±84.6  | 268.7±97.4  | 0.467    |
| Type of endovascular treatment | Combined intravenous thrombolysis and thrombectomy, n (%) | Intra-arterial thrombolysis alone, n (%) | Direct mechanical thrombectomy, n (%) | Frequency of mechanical thrombectomy, median (IQR) | Rates of successful recanalization, n (%) |
|--------------------------------|----------------------------------------------------------|-----------------------------------------|--------------------------------------|----------------------------------|----------------------------------------|
|                                | 4 (22.2)                                                 | 4 (22.2)                                | 10 (55.6)                           | 1.5 (0-3)                       | 18 (100.0)                             |
|                                | 7 (38.9)                                                 | 2 (11.1)                                | 9 (50.0)                            | 1.5 (1-2.3)                     | 17 (94.4)                             |
|                                | 4 (22.2)                                                 | 2 (11.1)                                | 12 (66.7)                           | 2 (1.8-3)                       | 14 (77.8)                             |
|                                | 4 (22.2)                                                 | 2 (11.1)                                | 12 (66.7)                           | 2.5 (2-3.3)                     | 13 (72.2)                             |
|                                |                                                          |                                         |                                      | 0.777                            |                                         |
|                                |                                                          |                                         |                                      | 0.038*                           |                                         |
|                                |                                                          |                                         |                                      | 0.048*                           |                                         |
| Intracranial hemorrhagic transformation, n (%) |                                                          |                                         |                                      |                                  |                                         |
| HI1                            | 1 (5.6)                                                  | 1 (5.6)                                 | 1 (5.6)                             | 2 (11.1)                        |                                         |
| HI2                            | 2 (11.1)                                                 | 0 (0.0)                                 | 1 (5.6)                             | 2 (11.1)                        |                                         |
| PH1                            | 0 (0.0)                                                  | 0 (0.0)                                 | 1 (5.6)                             | 1 (5.6)                         |                                         |
| PH2                            | 0 (0.0)                                                  | 0 (0.0)                                 | 0 (0.0)                             | 1 (5.6)                         |                                         |
| *Statistically significant.                                          |                                         |                                      |                                      |                                  |                                         |

**NIHSS** National Institutes of Health Stroke Scale, **SBP** systolic blood pressure, **DBP** diastolic blood pressure, **LDL-C** low-density lipoprotein cholesterol, **ASPECT** Alberta Stroke Program Early CT Score, **HI** petechial infarction without space-occupying effect, **PH** hemorrhage (coagulum) with mass effect

Table 3. Comparison of SBP and DBP variability parameters between different subgroups
| Maximum SBP | 153.4±15 .9 | 165.4±16 .0 | 0.006 | Maximum SBP | 172.0±32 .5 | 158.1±13 .9 | 0.341 |
|-------------|-------------|-------------|-------|-------------|-------------|-------------|-------|
| Maximum DBP | 94.8±9.6    | 90.4±6.8    | 0.063 | Maximum DBP | 106.5±7.8  | 94.9±9.6    | 0.154 |
| Minimum SBP | 111.2±14 .8 | 110.0±13 .7 | 0.751 | Minimum SBP  | 131.0±38 .2 | 103.9±12 .8 | 0.496 |
| Minimum DBP | 60.0±10.3   | 58.3±9.3    | 0.498 | Minimum DBP | 64.5±30.4  | 59.4±8.5    | 0.851 |
| Mean SBP    | 130.9±15 .0 | 134.2±13 .7 | 0.395 | Mean SBP    | 151.7±33 .3 | 131.1±18 .0 | 0.239 |
| Mean DBP    | 76.1±8.9    | 73.7±8.0    | 0.296 | Mean DBP    | 77.4±25.5  | 77.1±7.5    | 0.987 |
| Systolic SV | 11.4±2.3    | 14.4±2.0    | <0.001 | Systolic SV | 12.8±1.8   | 15.0±1.9    | 0.174 |
| Systolic SD | 10.0±2.4    | 14.0±4.3    | <0.001 | Systolic SD | 8.7±1.6    | 13.2±2.6    | 0.052 |
| Systolic CV | (8.8±2.0)%  | (10.8±1.7)% | <0.001 | Systolic CV | (8.8±3.1)% | (11.7±2.2)% | 0.160 |
| Diastolic SV| 9.8±3.2     | 8.8±2.3     | 0.182 | Diastolic SV| 12.1±5.0   | 10.4±3.2    | 0.544 |
| Diastolic SD| 8.3±2.2     | 8.0±2.0     | 0.610 | Diastolic SD| 8.7±3.7    | 8.2±1.7     | 0.796 |
| Diastolic CV| (13.1±4.8)% | (12.1±3.6)% | 0.377 | Diastolic CV| (17.7±12.3)% | (13.8±5.0)% | 0.459 |
| M1 of MCA   |             |             |       | ICA         |             |             |       |

| BPV index | Favorable outcome | Unfavourable outcome | P value | BPV index | Favorable outcome | Unfavourable outcome | P value |
|-----------|-------------------|----------------------|---------|-----------|-------------------|----------------------|---------|
| Maximum SBP | 154.2±16 .6 | 159.5±14 .9 | 0.278 | Maximum SBP | 154.7±19 .5 | 168.0±15 .5 | 0.106 |
| Maximum DBP | 96.6±8.8 | 90.8±8.6 | 0.032 | Maximum DBP | 89.1±13.0 | 92.5±6.6 | 0.437 |
| Minimum SBP | 112.9±16 .1 | 109.1±15 .0 | 0.420 | Minimum SBP | 108.0±17 .3 | 107.5±12 .0 | 0.939 |
| Minimum DBP | 60.0±11.3 | 57.6±8.1 | 0.450 | Minimum DBP | 61.6±11.0 | 59.6±10.0 | 0.691 |
| Mean SBP | 132.1±16 .6 | 133.1±16 .6 | 0.847 | Mean SBP | 130.9±18 .5 | 133.8±12 .9 | 0.678 |
| Mean DBP | 76.1±9.4 | 74.4±7.4 | 0.512 | Mean DBP | 76.4±11.0 | 74.9±8.8 | 0.734 |
| Systolic SV | 11.5±1.9 | 14.5±1.9 | <0.001 | Systolic SV | 11.4±3.9 | 14.6±2.1 | 0.02 |
| Systolic SD | 10.1±2.0 | 12.6±2.6 | <0.001 | Systolic SD | 12.8±3.3 | 15.1±4.7 | 0.259 |
| Systolic CV | (8.8±1.9)% | (11.0±2.1)% | <0.001 | Systolic CV | (8.7±2.5)% | (11.0±1.6)% | 0.018 |
| Diastolic SV | 10.4±3.3 | 9.8±2.9 | 0.533 | Diastolic SV | 7.7±2.1 | 8.5±2.3 | 0.406 |
| Diastolic SD | 8.5±2.3 | 8.3±1.9 | 0.709 | Diastolic SD | 7.4±1.3 | 7.9±2.0 | 0.552 |
| Diastolic CV | (14.0±5.3)% | (13.3±4.2)% | 0.644 | Diastolic CV | (10.0±2.0)% | (11.6±3.8)% | 0.288 |
**SBP** Systolic blood pressure, **DBP** Diastolic blood pressure, **BPV** Blood pressure variability, **SD** Standard deviation, **CV** Coefficient of variation, **SV** Successive variation

### Table 4 Univariate and multivariate analyses of the favorable outcomes after EVT

| Variable                                      | Univariable logistic regression analysis | Multivariable logistic regression analysis* |
|-----------------------------------------------|------------------------------------------|--------------------------------------------|
|                                               | OR (95% CI)                              | OR (95% CI)                                |
|                                               | P value*                                 | P value                                    |
| Age                                           | 1.005 (0.963-1.050)                      | 0.931 (0.808-1.073)                       | 0.325                                    |
| Male                                          | 1.200 (0.457-3.151)                      | 1.045 (0.993-1.100)                       | 0.092                                    |
| Hypertension                                  | 1.000 (0.370-2.702)                      | 0.931 (0.808-1.073)                       | 0.325                                    |
| Coronary heart disease                        | 1.071 (0.383-2.997)                      | 0.931 (0.808-1.073)                       | 0.325                                    |
| Atrial fibrillation                           | 0.591 (0.213-1.641)                      | 0.200 (0.054-0.744)                       | 0.016                                    |
| Diabetes mellitus                             | 0.368 (0.124-1.089)                      | 0.076 (0.005-1.078)                       | 0.057                                    |
| Smoking                                       | 0.765 (0.298-1.962)                      | 0.098 (0.092-1.003)                       | 0.415                                    |
| Glucose level at admission                    | 0.893 (0.755-1.057)                      | 0.268 (0.138-0.522)                       | 0.008                                    |
| NIHSS at admission                            | 1.072 (1.002-1.148)                      | 0.268 (0.138-0.522)                       | 0.008                                    |
| SBP level at admission                        | 1.036 (1.010-1.063)                      | 0.268 (0.138-0.522)                       | 0.008                                    |
| DBP level at admission                        | 1.025 (0.988-1.063)                      | 0.268 (0.138-0.522)                       | 0.008                                    |
| LDL-C at admission                            | 1.170 (0.724-1.891)                      | 0.268 (0.138-0.522)                       | 0.008                                    |
| Conscious sedation                            | 1.900 (0.465-7.769)                      | 0.268 (0.138-0.522)                       | 0.008                                    |
| ASPECT at admission                           | 0.268 (0.138-0.522)                      | 0.268 (0.138-0.522)                       | 0.008                                    |
| Time from stroke onset to groin puncture      | 0.998 (0.992-1.003)                      | 0.268 (0.138-0.522)                       | 0.008                                    |
| M1 of the MCA occlusion                       | 0.229 (0.077-0.675)                      | 0.076 (0.005-1.078)                       | 0.057                                    |
| Frequency of mechanical thrombectomy          | 0.098 (0.011-0.860)                      | 1.499 (0.038-59.877)                       | 0.830                                    |
| Combined intravenous thrombolysis and thrombectomy | 2.461 (0.844-7.172)              |                                             |                                          |
| Intra-arterial thrombolysis                   | 0.097 (0.012-0.801)                      | 0.012 (0.000-1.457)                       | 0.071                                    |
| Successful recanalization                     | 0.138 (0.027-0.075)                      | 0.030 (0.001-1.842)                       | 0.095                                    |
| Maximum SBP post EVT**                        | 1.036 (1.004-1.069)                      | 0.894 (0.777-1.028)                       | 0.116                                    |
| Maximum DBP post EVT**                        | 0.953 (0.901-1.008)                      |                                             |                                          |
|                              | Minimum SBP post EVT** | 0.983 (0.952-1.015) | 0.297 |
|------------------------------|------------------------|---------------------|-------|
| Minimum DBP post EVT**       | 0.983 (0.939-1.030)    | 0.482               |       |
| Mean SBP post EVT**          | 1.006 (0.976-1.037)    | 0.686               |       |
| Mean DBP post EVT**          | 0.980 (0.929-1.034)    | 0.456               |       |
| Systolic SD post EVT**       | 1.531 (1.203-1.948)    | 0.001               | 1.217 (0.803-1.842) | 0.355 |
| Systolic CV post EVT**       | 2.732E+28 (8.024E+12-9.303E+43) | <0.001             | 0.000 (0.000-7.704E+24) | 0.221 |
| Systolic SV post EVT**       | 2.046 (1.444-2.898)    | <0.001              | 4.273 (1.030-17.727) | 0.045 |

*Cut-off of P<0.05 was used for selection of candidate variables for inclusion in multivariable logistic regression models.**During the 24 hours following the endovascular treatment

NIHSS National Institutes of Health Stroke Scale, SBP Systolic blood pressure, ASPECT Alberta Stroke Program Early CT Score, MCA Middle cerebral artery, EVT Endovascular treatment; LDL-C Low-density lipoprotein cholesterol; DBP Diastolic blood pressure; SD Standard deviation; CV Coefficient of variation; SV Successive variation

Table 5 Cut-off values of systolic SV

| Values     | Best cut-off | Sensitivity (%) | Specificity (%) | PPV*(%) | NPV*(%) |
|------------|--------------|-----------------|-----------------|---------|---------|
| Systolic SV| 12.499       | 93.3            | 73.8            | 71.1    | 91.2    |

SV Successive variation; PPV Positive predictive values; NPV Negative predictive values.

Figures
Figure 1

Comparison of maximum SBP and systolic SV, SD, CV in the 24 hours post-EVT between two groups. EVT endovascular treatment; SBP systolic blood pressure; SV successive variation; SD standard deviation; CV coefficient of variation
Score on Modified Rankin Scale

Modified Rankin Scale scores distribution according to quartiles of systolic SV.
Figure 3

Systolic SV and 3-month unfavorable outcomes. SBP systolic blood pressure; SV successive variation

Supplementary Files
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- diastolic blood pressure.sav
- eq 3.jpg
systolic blood pressure.sav
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