

Systemic arterial blood pressure and intracerebral hemorrhage after mechanical thrombectomy in anterior cerebral circulation

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ABSTRACT

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The relationship between systemic arterial blood pressure (BP) and intracerebral hemorrhage (ICH) after mechanical thrombectomy (MT) of the cerebral artery remains unclear. This study aimed to determine the effect of BP variables on ICH after MT in patients with acute occlusions of the anterior cerebral circulation. Patients undergoing MT due to acute occlusions of the anterior cerebral circulation were enrolled in this singlecenter study. Non-invasive BP data following MT were obtained within the first 24 hours, including mean, maximum, minimum, difference between maximum and minimum, SD and coefficient of variation for systolic BP (SBP) and diastolic BP (DBP) and mean arterial pressure. ICH was defined and classified according to the European Cooperative Acute Stroke Study-II. In 164 enrolled patients (median age 65 (IQR 56-75) years; 31.7% female), higher maximum (89.5 mm Hg vs 98.5 mm Hg, p=0.001) and SD (9.8 mm Hg vs 10.9 mm Hg, p=0.038) of DBP were associated with higher risk of ICH. The optimal cut-off values associated with ICH for maximum SBP were 155 mm Hg and for maximum DBP 92.5 mm Hq, respectively. Higher BP within 24 hours after MT in acute occlusions of the anterior cerebral circulation is associated with a greater risk of ICH. More studies are needed to further determine optimal BP goals in the acute phase after MT.

INTRODUCTION

Endovascular thrombectomy (EVT) has been proven beneficial to patients who had acute ischemic stroke (AIS) due to large vessel occlusion (LVO).^{1–5} The DAWN and DEFUSE-3 trials, designed to show the efficacy of thrombectomy in selected patients with occlusion of proximal vessels in the anterior cerebral circulation up to 24 hours after suspected onset of symptoms, promote further development of EVT.⁶ However, intracerebral hemorrhage (ICH), as one of the common and potentially more serious complications after mechanical thrombectomy (MT), usually causes an increase in disability and mortality. Systemic arterial hypertension is an important risk factor for

Significance of this study

What is already known about this subject?

- The association between blood pressure (BP) and intracerebral hemorrhage (ICH) after endovascular thrombectomy (EVT) in patients who had acute ischemic stroke (AIS) has been controversial.
- Previous studies found higher maximum systolic BP (SBP) and SBP fluctuation after EVT to be associated with worse outcomes and higher rates of ICH in patients who had AIS, but only few studies reported the association between diastolic BP (DBP) and outcomes in patients who had AIS after EVT.

What are the new findings?

- Higher maximum DBP within 24 hours after mechanical thrombectomy (MT) was associated with higher odds of ICH (OR 1.03, 95% CI 1.01 to 1.05, adjusted p=0.028) when adjusted for age, baseline National Institutes of Health Stroke Scale (NIHSS) score, baseline Glasgow Coma Scale score, recanalization status (successful defined as modified Thrombolysis in Cerebral Ischemia (mTICI) 2b–3 vs unsuccessful defined as mTICI 0–2a) and procedure time.
- A maximum SBP of >155 mm Hg yielded an unadjusted OR of 2.53 (1.31–4.89) (p=0.006) and an adjusted OR of 2.42 (1.20– 4.87) (p=0.013) for suffering ICH, and patients with a peak DBP >92.5 mm Hg had 4.56 times higher odds of ICH.
- For maximum DBP, an ideal cut-off value of 92.5 mm Hg was identified (80% sensitivity, 57% specificity, area under the curve 0.65, 95% CI 0.57 to 0.74, p=0.001).

ischemic stroke and ICH.^{7–9} Although proper blood pressure (BP) management is associated with a reduced risk of ICH and mortality,¹⁰ the optimal target of BP management during and after MT remains unclear.

Current American Heart Association/American Stroke Association guidelines recommend maintaining BP at $\leq 180/105$ mm Hg for 24–48 hours after MT¹¹; however, it is



How might these results change the focus of research or clinical practice?

- Higher systemic arterial BP, especially maximal DBP, within 24 hours after MT in acute occlusions of the anterior cerebral circulation is associated with a greater risk of ICH, regardless of age, admission NIHSS score, recanalization time and recanalization status.
- In order to prevent ICH, doctors should pay more attention to both SBP and DBP after MT.

recommended indiscriminately to all patients receiving MT. Intensive BP control, theoretically, could be beneficial to patients with successful MT in terms of risk of ischemic/ reperfusion hemorrhage.¹² On the other hand, for patients with incomplete recanalization, permissive hypertension may be beneficial to maintain brain perfusion pressure.

Reasonable BP management after MT is considered helpful in preventing ICH; however, there are no consistent recommendations on specific BP management after MT. Some studies have found a correlation between hypertension and ICH after MT,¹³ while others reported no such association.^{10 14} This study therefore aimed to investigate the association between per interventional BP and hemorrhagic transformation after MT in patients who had ischemic stroke.

MATERIALS AND METHODS

Patient population

This is a retrospective, observational study of patients who had AIS¹⁵ with LVO of the anterior cerebral circulation undergoing MT. All consecutive unselected patients who were treated with MT between June 2015 and December 2019 in the stroke center of the First Affiliated Hospital of Xi'an Jiaotong University were enrolled in this study. Medical history, demographic information, baseline characteristics, initial imaging, and angiographic results of each case were obtained.

The protocol for selecting patients for MT and other stroke management decisions were made by the attending medical providers and the stroke care team according to current guidelines. Patients with premorbid modified Rankin Scale (mRS) score >2, severe systemic diseases such as terminal cancer, dementia, and end-stage heart or liver failure, and without a repeat head CT scan within 24 hours after MT were excluded. MT procedures were conducted using both stent retrievers and aspiration catheters. All patients were admitted to an intensive stroke unit for postprocedural care.

Baseline demographic and treatment parameters

Baseline parameters included age, sex, comorbidities, baseline mRS score, admission National Institutes of Health Stroke Scale (NIHSS) score, admission Glasgow Coma Scale (GCS) score, symptom onset-to-groin puncture time (minutes), pretreatment with intravenous tissue-type plasminogen activator (tPA) and admission systemic arterial BP levels. Procedural parameters included use of intra-arterial tPA or tirofiban, modified Thrombolysis in Cerebral Ischemia (mTICI) score and procedure time.

Successful reperfusion was defined as mTICI $\geq 2b$ at the end of intervention. If MT of the targeting artery was not successful, rescue therapies, such as balloon angioplasty, stent implantation, intra-arterial thrombolysis, or intracatheter tirofiban administration, were performed. Head CT scans were regularly performed 24 hours after the procedure or whenever an ICH was suspected by clinical symptoms.

BP parameters

Non-invasive BP values before and after the procedure were recorded in the intervention report. Hourly BP during the first 24 hours was measured by a non-invasive BP cuff of appropriate size. All BP data were reviewed by trained clinicians based on guidelines for every patient after the MT procedure. BP parameters included mean, coefficient of variation, maximum and minimum systolic BP (SBP), maximum and minimum diastolic BP (DBP), and mean arterial pressure during the first 24 hours after MT. In addition, we included SBP and DBP ranges (maximum-minimum) and SD as parameters for BP variation.

Definition of ICH after MT

ICH was defined and classified as one of the following subtypes according to the European Cooperative Acute Stroke Study-II (ECASS-II)¹⁶: hemorrhagic infarction (HI)-1: small petechiae along the margins of the infarct; HI-2: more confluent petechiae within the infarcted area, but without space-occupying effect; parenchymal hematoma (PH)-1: blood clot not exceeding 30% of the infarcted area with some mild space-occupying effect; and PH-2: dense blood clot(s) exceeding 30% of the infarct volume with significant space-occupying effect.

Statistical analysis

All statistical analyses were performed using SPSS V.24.0 software. Discrete variables are presented as counts (with percentages) and continuous variables as mean (SD) or median (IQR), as appropriate. Normal distribution of data was tested using the Shapiro-Wilk test. A Kruskal-Wallis test was used for non-parametric tests. Student's t-test and Kruskal-Wallis test were used to compare BP parameters at the univariate level, and multivariable logistic regression analyses were used to evaluate parameters of SBP and DBP as possible predictors of ICH. Variables with p < 0.05 on univariate analysis were included in the logistic regression models. Each BP variable that was significant at the univariate level or that was considered clinically relevant was entered into the multivariable logistics regression model. The area under the receiver operating characteristic curve has been used to determine the optimal cut-off BP values, which were defined as values with maximal Youden index. All tests used a two-sided α level of 0.05 for significance. All effect sizes are reported with 95% CI in addition to p values.

RESULTS

A total of 217 patients who had AIS undergoing MT met the inclusion criteria, 164 (76.6%, 164 of 217) of whom suffered from LVO in the anterior cerebral circulation and

Table 1	Baseline characteristics of the study cohort

	Total, N=164	ICH, n=60	No ICH, n=104
Age (years)	65 (56–75)	67 (56–75)	64 (55–75)
Female sex	52 (31.7)	22 (36.7)	30 (28.8)
Comorbidities			
Hypertension	100 (61.0)	34 (56.7)	66 (63.5)
Diabetes mellitus	69 (42.1)	30 (50)	39 (37.5)
Atrial fibrillation	62 (37.8)	32 (53.3)	30 (28.8)
Current smoking	71 (43.3)	24 (40)	47 (45.2)
Antiplatelet drug use	20 (12.2)	8 (13.3)	12 (11.5)
Anticoagulant use	12 (7.3)	5 (8.3)	7 (6.7)
Baseline laboratory values			
Glucose, mg/dL	6.9 (5.5–9.8)	7.8 (6.1–10.2)	6.6 (5.1–8.6)
Platelet count, ×109/L	191 (158–232)	186 (151–218)	192 (164–234)
INR	1.1 (0.9–1.3)	1.1 (1.0–1.4)	1.1 (0.9–1.3)
Stroke characteristics			
Baseline NIHSS score	13 (10–17)	14 (12–18)	12 (9–16)
Baseline GCS score	13 (9–15)	12 (9–14)	13 (10–15)
ICA occlusion	62 (37.8)	20 (33.3)	42 (40.4)
M1 occlusion	96 (58.5)	59 (98.3)	37 (35.6)
M2 occlusion	10 (6.1)	4 (6.7)	6 (5.8)
Left circulation	84 (51.2)	30 (50)	54 (51.9)
Stroke treatment			
Intravenous thrombolysis	40 (24.4)	15 (25)	25 (24)
Onset-to-groin (min)	327.5 (229.3–437.8)	312.5 (237.5–421.5)	332.5 (214.3–475.0)
Procedure time (min)	119.5 (84–150)	124 (92.3–174.5)	116 (81.5–141.5)
General anesthesia	18 (11.0)	7 (11.7)	11 (10.6)
Conscious sedation	146 (89.0)	53 (88.3)	93 (89.4)
mTICI 0	15 (9.1)	8 (13.3)	7 (6.7)
mTICI 1	4 (2.4)	2 (3.3)	2 (1.9)
mTICI 2a	26 (15.9)	12 (20)	14 (13.5)
mTICI 2b	25 (15.2)	7 (11.7)	18 (17.3)
mTICI 3	94 (57.3)	31 (51.7)	63 (60.6)
Blood pressure variables, mm Hg			
Admission SBP	146±24.3	145±3.3	147±2.5
Admission DBP	80±13.7	81±1.8	79±1.4
Admission MAP	102.0 (92.7–109.6)	102.3±2.0	101.4±1.5
Outcomes			
Any ICH	60 (36.6)		
HI-1	14 (8.5)		
HI-2	17 (10.4)		
PH-1	14 (8.5)		
PH-2	15 (9.1)		

Variables are shown as mean \pm SD, n (%), or median and IQR.

DBP, diastolic blood pressure; GCS, Glasgow Coma Scale; HI, hemorrhagic infarction; ICA, internal carotid artery; ICH, intracerebral hemorrhage; INR, international normalized ratio; MAP, mean arterial pressure; mTICI, modified Thrombolysis in Cerebral Ischemia; NIHSS, National Institutes of Health Stroke Scale; PH, parenchymal hematoma; SBP, systolic blood pressure.

were included in this study. Among the enrolled subjects, 60 (36.6%, 60 of 164) patients suffered from ICH during the first 24 hours after MT; HI-2 was the most common (10.4%, 17 of 164), followed by PH-2 (9.1%, 15 of 164), HI-1 (8.5%, 14 of 164), and PH-1 (8.5%, 14 of 164). Successful recanalization was achieved in 119 patients (72.6%, 119 of 164) (mTICI 2b–3), with a complete (mTICI 3) recanalization rate of 57.3% (94 of 164). The median age was 65 (56–75) years and 31.7% (52 of 164) were female. The mean admission BP was $146\pm 24/80\pm 14$ mm Hg. The

baseline characteristics of the study cohort are detailed in table 1.

As shown in table 2, BP parameters were compared between patients with and without ICH. The maximum (89.5 mm Hg vs 98.5 mm Hg, p=0.001) and SD (9.8 mm Hg vs 10.9 mm Hg, p=0.038) of DBP during the first 24 hours of monitoring were higher in the group with ICH. Admission, mean, and range of BP did not significantly differ between groups with and without ICH. Multivariable logistic regression revealed that higher maximum DBP

 Table 2
 Blood pressure variables during 24 hours following mechanical thrombectomy between patients with and without ICH

		ICH, n=60			
Variable	No ICH, n=104		P value	Adjusted OR* (95% CI)	Adjusted p value
Admission SBP	147 (24)	145 (24)	0.554	-	-
Admission DBP	79 (14)	81 (13)	0.457	-	-
24-hour SBP mean	129 (17)	131 (14)	0.412	-	-
24-hour DBP mean	70 (10)	73 (10)	0.166	-	-
24-hour MAP mean	90 (12)	92 (12)	0.485	-	-
24-hour SBP SD	11.9 (10–15)	12.5 (10–17)	0.144	-	-
24-hour DBP SD	9.8 (3.1)	10.9 (3.4)	0.038	1.06 (0.95 to 1.18)	0.34
24-hour SBP CV	9.8 (3.0)	10.6 (3.9)	0.223	-	-
24-hour DBP CV	13.9 (4.3)	15.1 (5.3)	0.122	-	-
24-hour SBP max	154 (22)	160 (19)	0.071	1.01 (0.99 to 1.03)	0.19
24-hour SBP min	104 (14)	107 (13)	0.153	-	-
24-hour DBP max	89.5 (83–100)	98.5 (93–107)	0.001	1.03 (1.01 to 1.05)	0.028
24-hour DBP min	53 (10)	55 (11)	0.257	-	-
24-hour SBP range	47 (39–59.5)	48 (40–63)	0.330	-	-
24-hour DBP range	39 (14)	43 (15)	0.055	1.02 (0.99 to 1.04)	0.14

Variables are mean \pm SD or median and IQR.

*Adjusted for age, baseline NIHSS score, baseline GCS score, recanalization status (successful defined as mTICI 2b–3 vs unsuccessful defined as mTICI 0–2a) and procedure time. CV, coefficient of variance; DBP, diastolic blood pressure; GCS, Glasgow Coma Scale; ICH, intracerebral hemorrhage; MAP, mean arterial pressure; max, maximum; min, minimum; mTICI, modified Thrombolysis in Cerebral Ischemia; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure.

within 24 hours after MT was associated with higher odds of ICH (OR 1.03, 95% CI 1.01 to 1.05, p=0.028) when adjusted for age, baseline NIHSS score, baseline GCS score, recanalization status (successful defined as mTICI 2b–3 vs unsuccessful defined as mTICI 0–2a) and procedure time.

Table 3 shows the optimal cut-off BP values to differentiate patients with versus without ICH. The optimal cut-off for maximum SBP was 155 mm Hg (65% sensitivity, 58% specificity, area under the curve 0.59, 95% CI 0.50 to 0.68, p=0.048; figure 1). A maximum SBP of >155 mm Hg yielded an unadjusted OR of 2.53 (1.31–4.89) (p=0.006) and an adjusted OR of 2.42 (1.20–4.87) (p=0.013) for suffering ICH. For maximum DBP, an ideal cut-off value of 92.5 mm Hg was identified (80% sensitivity, 57% specificity, area under the curve 0.65, 95% CI 0.57 to 0.74, p=0.001; figure 1). A total of 93 patients had a maximum DBP >92.5 mm Hg, of whom 48 (80%) had ICH as compared with 12 (17%) of 71 patients with maximum DBP \leq 92.5 mm Hg. Patients with a maximum DBP \geq 92.5 mm Hg had 4.56 times higher odds of ICH.

To explore the potential of recanalization status on the relationship between BP and ICH after MT, patients were divided into two subgroups of successful reperfusion (defined as mTICI 2b–3) and incomplete reperfusion (defined as mTICI 0–2a). Compared with the successful reperfusion group, the proportion of patients without ICH in the incomplete reperfusion group was lower (51% vs 68%). In the subgroup of successful reperfusion, patients who had higher maximum SBP or maximum DBP within the first 24 hours after MT were more likely to experience ICH (mean for maximal SBP, 160 vs 152, p=0.037; mean for maximal DBP, 98 vs 91, p=0.024; table 4). However, there was no significant difference in maximal SBP and DBP in patients with incomplete reperfusion after MT. Of the 119 patients with successful reperfusion, a maximal SBP >158.5 mm Hg was associated with a higher rate of ICH in both unadjusted (OR 3.07 (1.38–6.84); p=0.006) and adjusted (OR 2.89 (1.28–6.53); p=0.011) analyses (online supplemental table 1 and figure 2). Similar outcomes were also found for maximal DBP >91.5 mm Hg (unadjusted OR 5.18 (2.12–12.7), p<0.001; adjusted OR 4.94 (1.99–12.24), p=0.001; online supplemental table 1).

DISCUSSION

In this study, we showed that higher maximal systemic arterial BP within the first 24 hours after MT was independently associated with a higher risk of ICH. In addition, patients with a maximal post-MT SBP >155 mm Hg or post-MT DBP >92.5 mm Hg have a higher likelihood of suffering ICH within 24 hours after MT. Subgroup analysis of patients with successful reperfusion (defined as mTICI 2b–3) also showed similar effects of higher BP on ICH. Therefore, the optimal management of both SBP and DBP

Table 3 Association of blood pressure with ICH				
Outcome	OR	P value	Adjusted OR* (95% CI)	Adjusted p value
Any ICH (maximal SBP dichotomized >155 mm Hg)	2.53 (1.31–4.89)	0.006	2.42 (1.20 to 4.87)	0.013
Any ICH (maximal SBP as continuous variable per 1 mm Hg increase)	1.01 (1.00–1.03)	0.073	1.01 (1.00 to 1.03)	0.19
Any ICH (maximal DBP dichotomized >92.5 mm Hg)	5.24 (2.50–11.0)	< 0.001	4.56 (2.13 to 9.76)	<0.001
Any ICH (maximal DBP as continuous variable per 1 mm Hg increase)	1.03 (1.01–1.06)	0.009	1.03 (1.01 to 1.05)	0.028
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*Adjusted for age, baseline NIHSS score, baseline GCS score, recanalization status (successful defined as mTICI 2b–3 vs unsuccessful defined as mTICI 0–2a) and procedure time. DBP, diastolic blood pressure; GCS, Glasgow Coma Scale; ICH, intracerebral hemorrhage; mTICI, modified Thrombolysis in Cerebral Ischemia; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure.

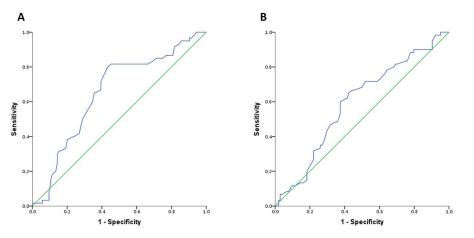


Figure 1 Receiver operating characteristic curves with corresponding AUC for maximum DBP (A) and SBP (B). The AUC of maximum DBP is 0.654 (95% CI 0.567 to 0.740, p=0.001) and of maximum SBP 0.593 (95% CI 0.504 to 0.682, p=0.048). AUC, area under the curve; DBP, diastolic blood pressure; SBP, systolic blood pressure.

should be taken seriously in patients who had AIS after MT to avoid ICH.

Previous studies found higher maximum SBP and SBP fluctuation after EVT to be associated with worse outcomes and higher rates of ICH in patients who had AIS.^{10 13 17-19} The results of our study are in accordance with these prior studies. Moreover, maximal DBP within 24 hours after MT expressed a more significant effect on ICH, but only few studies reported the association between DBP and outcomes in patients who had AIS after EVT. The resistance generated by peripheral arteries and arterioles forms the main part of DBP, and long-term hypertension can lead to progressive endothelial dysfunction, arterial stiffness and vasoconstriction of the arterioles until BP exceeds the upper limit of autoregulation,^{20 21} and which in turn causes vasodilation breakthrough, an increase in cerebral blood flow and blood-brain barrier dysfunction.²² Higher DBP indicates a decrease in large artery compliance.^{20 23} All the factors mentioned above can induce oxidative stress, inflammatory responses and other pathophysiological processes, causing ischemia-reperfusion injury in cerebral vessels. In this study, a peak DBP of 92.5 mm Hg within 24 hours after MT best dichotomized ICH and no ICH. Patients with a peak DBP >92.5 mm Hg had 4.56 times higher odds of ICH. In our study, the stronger relationship between higher DBP and

ICH is an important finding, since many stroke physicians pay more attention to SBP to maintain it within safe ranges. The mean SBP was 131 mm Hg in patients with ICH and 129 mm Hg in patients without ICH in our study, whereas other studies reported a mean SBP of 159 mm Hg in patients without ICH.¹³

Unlike DBP variables, there are vast data on the association between SBP in the first 24 hours post EVT and outcome, but there are less consistent results among these studies. A study of 228 patients with LVO in the anterior circulation demonstrated that both mean SBP and maximal SBP correlated with ICH, including asymptomatic and symptomatic ICH,¹³ while other studies found no association between BP parameters and hemorrhagic complications.^{10 24} The differences may be attributed to heterogeneity in inclusion criteria and the definition of hemorrhagic complications. Our study upheld that a maximal SBP of 155 mm Hg and a maximal DBP of 92.5 mm Hg in the 24 hours after MT best dichotomize ICH and no ICH. Patients in the maximal SBP >155 mm Hg group had 2.5 times higher odds of ICH as compared with patients whose maximal SBP was lower than 155 mm Hg.

A recent study in patients with successful revascularization after MT demonstrated that the course of elevated SBP and DBP was positively correlated with the rate of ICH.¹²

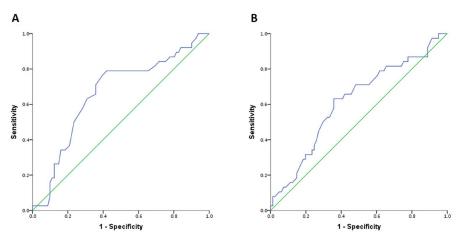
incomplete recanalization Outcome with incomplete recanalization (mTICI 0-2a)					
Maximal SBP as continuous	160 (17)	162 (26)	0.788	1.00 (0.97 to 1.03)	0.730
Maximal DBP as continuous	100 (11)	96 (16)	0.326	1.03 (0.98 to 1.08)	0.303
Outcome with successful recanaliza	tion (mTICI 2b–3)				
Variables, mean (SD)	Any ICH n=38 (32%)	No ICH n=81 (68%)	P value	Adjusted OR* (95% CI)	Adjusted p value
Maximal SBP as continuous	160 (20)	152 (21)	0.037	1.02 (1.00 to 1.04)	0.054
Maximal DBP as continuous	98 (14)	91 (14)	0.024	1.03 (1.01 to 1.06)	0.045

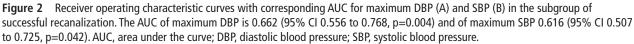
Table 4 Association of maximal blood pressure as a continuous variable with ICH in the two subgroups of successful recanalization and

Variables are mean±SD or n (%).

*Adjusted for age, baseline NIHSS score, baseline GCS score and procedure time.

DBP, diastolic blood pressure; GCS, Glasgow Coma Scale; ICH, intracerebral hemorrhage; mTICI, modified Thrombolysis in Cerebral Ischemia; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure.





Another study in patients with non-recanalized LVO showed no relationship between the level of BP and symptomatic ICH.¹⁷ Given the different results by recanalization status, patients in our study were divided into two subgroups of successful reperfusion (mTICI 2b–3) and incomplete reperfusion (mTICI 0–2a). Interestingly, a similar result was also found in our study. Increased maximal SBP and maximal DBP yielded a significantly higher odds of ICH in the subgroup of successful reperfusion, but there was no such association in the subgroup of incomplete reperfusion. This may indicate that maximal BP within 24 hours after MT has a larger effect on patients with successful reperfusion.

Limitations

The presented study has some limitations. First, this was a retrospective study. Therefore, this study is associated with adherent bias and did not include long-term follow-up information. Second, due to the fact that the Heidelberg Bleeding Classification²⁵ was not widely used in 2015, the classification of ICH was based on ECASS-II. Finally, the relatively small sample size limits the power for multivariable analysis.

CONCLUSIONS

Higher systemic arterial BP, especially maximal DBP, within 24 hours after MT in acute occlusions of the anterior cerebral circulation is associated with a greater risk of ICH, regardless of age, admission NIHSS score, recanalization time and recanalization status.

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Original research

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