ORIGINAL RESEARCH

Blood pressure levels post mechanical thrombectomy and outcomes in non-recanalized large vessel occlusion patients

Nitin Goyal,[1] Georgios Tsivgoulis,[1,2] Abhi Pandhi,[1] Kira Dillard,[1] Diana Alsbrook,[1] Jason J Chang,[3] Balaji Krishnaiah,[1] Christopher Nickele,[4] Daniel Hoit,[4] Khalid Alsherbini,[1] Andrei V Alexandrov,[1] Adam S Arthur,[4] Lucas Elijovich[1,4]

[1]Department of Neurology, University of Tennessee Health Science Center, Memphis, Tennessee, USA
[2]Second Department of Neurology, Attikon University Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece
[3]Medstar Washington Hospital Medical Center, Washington, District of Columbia, USA
[4]Department of Neurosurgery, University of Tennessee Health Science Center, Semmes-Murphey Neurologic and Spine Clinic, Memphis, Tennessee, USA

Correspondence to
Dr Nitin Goyal, Department of Neurology, University of Tennessee Health Science Center, Memphis, TN 38163, USA; ngoyal@uthsc.edu

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ABSTRACT

Objective Permissive hypertension may benefit patients with non-recanalized large vessel occlusion (nrLVO) post mechanical thrombectomy (MT) by maintaining brain perfusion. Data evaluating the impact of post-MT blood pressure (BP) levels on outcomes in nrLVO patients are scarce. We investigated the association of the post-MT BP course with safety and efficacy outcomes in nrLVO.
Methods Hourly systolic BP (SBP) and diastolic BP (DBP) values were prospectively recorded for 24 hours following MT in consecutive nrLVO patients. Maximum, minimum, and mean BP levels were documented. Three-month functional independence (FI) was defined as modified Rankin Scale (mRS) scores of 0–2.
Results A total of 88 nrLVO patients were evaluated post MT. Patients with FI had lower maximum SBP (160±19 mmHg vs 179±23 mmHg; P=0.001) and higher minimum SBP levels (119±12 mmHg vs 108±25 mmHg; P=0.008). Maximum SBP (183±20 mmHg vs 169±23 mmHg; P=0.008) and DBP levels (105±20 mmHg vs 89±18 mmHg; P=0.001) were higher in patients who died at 3 months while minimum SBP values were lower (102±28 mmHg vs 115±16 mmHg; P=0.007). On multivariable analyses, both maximum SBP (OR per 10 mmHg increase: 0.55, 95% CI 0.39 to 0.79; P=0.001) and minimum SBP (OR per 10 mmHg increase: 1.64, 95% CI 1.04 to 2.60; P=0.033) levels were independently associated with the odds of FI. Maximum DBP (OR per 10 mmHg increase: 1.61; 95% CI 1.10 to 2.36; P=0.014) and minimum SBP (OR per 10 mmHg increase: 0.65, 95% CI 0.47 to 0.90; P=0.009) values were independent predictors of 3-month mortality.
Conclusions Our study demonstrates that wide BP excursions from the mean during the first 24 hours post MT are associated with worse outcomes in patients with nrLVO.

INTRODUCTION

Recent landmark randomized controlled clinical trials (RCTs) with successful recanalization (SR) rates ranging from 66% to 88% have provided unequivocal evidence that endovascular reperfusion with mechanical thrombectomy (MT) in patients with large vessel occlusion (LVO) is safe and improves functional outcomes.[1–5] MT has become the new standard of care for acute ischemic stroke (AIS) due to LVO and health systems are reorganizing in order to implement this new therapy as quickly and as widely as possible.[6]

Current international recommendations on MT for AIS inadequately address blood pressure (BP) management before, during and after MT, given the lack of RCT data.[7 8] In the absence of specific guidelines, endovascular centers usually target BP to remain below 180/105 mmHg according to current American Heart Association (AHA) recommendations for BP management following intravenous thrombolysis (IVT) for AIS.[9] Preliminary data have indicated that higher maximum values of systolic blood pressure (SBP) during the first 24 hours following MT are independently associated with worse functional outcomes, higher mortality, and a higher rate of hemorrhagic complications in patients with LVO.[10 11]

Theoretically, BP control may be beneficial in LVO patients with SR following MT, since they are at risk of reperfusion hemorrhage following effective clot removal.[12–14] Our recent single-center study has provided preliminary data in support of this hypothesis, since it showed that moderate BP control in the first 24 hours following MT was related to lower odds of 3-month mortality compared with permissive hypertension in successfully recanalized LVO patients.[11]

Conversely, permissive hypertension may be beneficial in patients with non-recanalized LVO (nrLVO) by maintaining adequate brain perfusion pressure.[12] Additionally, aggressive BP reduction in the first 24 hours of ictus has been associated with poor outcomes.[15] Moreover, it may be argued that allowing the BP to spontaneously rise to optimize collateral blood flow may also assist in clearing emboli from distal vessels.[16] However, the data evaluating the impact of permissive hypertension in the post-MT period on outcomes in nrLVO patients are scarce. In view of these considerations, we sought to evaluate the association of BP course in the first 24 hours following MT with safety and efficacy outcomes of patients with nrLVO.

METHODS

Study population

Data from consecutive LVO patients who underwent MT at a tertiary care stroke center from July 2013 to December 2016 were prospectively collected as previously described.[17–19] At our comprehensive stroke center, the protocol-based practice is to perform MT for patients with CT angiography (CTA)-confirmed LVOs presenting within 6 hours of symptom onset. For the patients presenting 6–12 hours from symptom onset, additional imaging selection criteria are used such as Alberta Stroke Program Early CT Score (ASPECTS) ≥6 on brain CT and/or good collaterals on CTA. LVO was diagnosed on pretreatment CTA using standard criteria.[20] Brain CT head and CTA were performed on a 64-slice scanner. CT slice thickness was 1.25 mm with acquisitions in axial, sagittal, and coronal planes with 3D reformatting. A blinded neuroradiologistcalculated ASPECTS and CTA collateral scores as previously described.[17] Collateral scores were reported in a dichotomized fashion (good vs poor collaterals) for anterior circulation LVO using a methodology that has been shown to predict clinical outcome.[17]

Recanalization at the end of the endovascular procedure was defined by modified Thrombolysis in Cerebral Infarction (mTICI) grades,[21] which were obtained from the reports of endovascular specialists (LE, AA, DH). For the purpose of this study, successfully recanalized (mTICI grades 2b or 3) LVO patients were excluded from the analyses and only nrLVO patients (mTICI grades 0, 1, 2a) were further evaluated. At our center, AIS patients with emergent LVO are treated according to the AHA guidelines advocating IVT for all eligible patients and subsequent MT in cases with confirmed LVO by CTA. Some of the common reasons for not delivering IVT were delayed time window on presentation, pretreatment with oral anticoagulation therapy, and uncontrolled hypertension. In these situations, patients underwent direct MT without IVT pretreatment. Cerebral edema was determined to be present if both of the following criteria were met on two or more axial diffusion-weighted imaging (DWI) slices of the brain MRI which all patients underwent within 24–48 hours from symptom onset: (1) direct evidence of mass effect of affected gyri; or (2) indirect evidence based on new distortion of adjacent tissue, new midline shift, or new effacement of sulci or lateral ventricle. This two-by-two method was employed to reduce the chance of misclassifying infarct growth as swelling.[22]

Baseline characteristics

Stroke severity at hospital admission was documented using the National Institute of Health Stroke Scale (NIHSS) score by certified vascular neurologists. Baseline characteristics including demographics, vascular risk factors, admission NIHSS scores, admission ASPECTS, pretreatment with IVT, admission serum glucose, admission serum low density lipoprotein (LDL), admission systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels were recorded as previously described.[11 20 23]

BP management post MT

Hourly SBP and DBP recordings were obtained in all LVO patients during the first 24 hours following MT using oscillometric non-invasive BP monitoring devices as previously described.[9] We documented minimum, mean, and maximum SBP and DBP levels for each individual patient during the BP monitoring period. Standard of care at our tertiary care center is to allow permissive hypertension in nrLVO patients post MT with BP goal of <220/120 mmHg for patients without pretreatment with IVT according to AHA recommendations for AIS management.[24] For patients pretreated with IVT, permissive hypertension was set at <180/105 mmHg as advocated by AHA recommendations.[24] Intravenous nicardipine was the first-line BP-lowering medication that we used for treating patients with BP levels exceeding the former prespecified cut-offs. Second-line antihypertensive agents were intravenous labetalol or intravenous enalapril. If nrLVO patients developed symptomatic intracranial hemorrhage (sICH) post MT, BP goals were modified according to the treating physician's preference (<140/90 mmHg or <160/90 mmHg). Institutional Investigation Review Board approval for this study was granted based on the prospectively maintained Acute Ischemic Stroke Database. The Board waived the need for patient consent.

Definition of outcomes

sICH was defined as the presence of a parenchymal hematoma type 2 on brain CT and/or MRI gradient recall echo sequence accounting for deterioration with an increase in NIHSS score of ≥4 points within 36 hours from treatment.[25] Functional outcome was evaluated at 3 months using the modified Rankin Scale (mRS) scores by certified vascular neurologists. Functional status was evaluated in person either from a post hospital discharge clinic follow-up or from a hospital visit in all patients. Functional independence (FI) was defined as mRS scores of 0–2.[23] Endovascular specialists grading the degree of reperfusion at the end of MT and vascular neurologists assessing NIHSS and mRS scores were unaware of the purposes of the study and performed treatments and assessments as part of their clinical duties. The primary outcome included 3-month FI, while sICH and 3-month mortality represented secondary outcomes. Final infarct volume (FIV) was also calculated by the simplification of the ellipsoid rule A×B×C/2 on delayed (7–14 days) brain MRI using Fluid Averted Inversion Recovery (FLAIR) sequences.[20] Delayed brain CT was used in a small number of patients with contraindications to brain MRI.[20]

Statistical analyses

Continuous variables are presented as mean±SD (normal distribution) and as median with interquartile range (skewed distribution). Categorical variables are presented as percentages with their corresponding 95% CIs. Statistical comparisons for categorical variables between two or three groups were performed using a χ^2 test, or in case of small expected frequencies, Fisher's exact test. Continuous variables were compared using the unpaired t-test, Mann–Whitney U test, one-way analysis of variance or Kruskal–Wallis test as indicated. The correlation of BP measurements with FIV was evaluated using Spearman's correlation coefficient (r). Univariable and multivariable logistic regression models were used to evaluate associations between BP measurements during the first 24 hours following MT (mean, minimum, and maximum SBP and DBP post MT) with 3-month FI, 3-month mortality and sICH before and after adjustment for the following potential confounders: age, gender, race, vascular risk factors (hypertension, diabetes mellitus, hypercholesterolemia, atrial fibrillation, coronary artery disease, congestive heart failure and current smoking), admission SBP and DBP levels, admission stroke severity, admission serum glucose and LDL levels, pretreatment with IVT, baseline ASPECTS, onset to groin puncture time, type of anesthesia (general anesthesia vs conscious sedation), brain edema, and good collaterals. Associations are presented as OR with corresponding 95% CI. In the initial univariable analyses a P value <0.1 was set as the threshold for inclusion in the multivariable models. Statistical significance was achieved for P<0.05 in the final multivariable analyses. The Statistical Package for Social Science (SPSS Version 22.0 for Windows) was used for statistical analyses.

RESULTS

Our study population consisted of 88 nrLVO patients (mean age 62±15 years, 48% median NIHSS score 16 points (IQR 12–21),

Table 1 Baseline characteristics of the study population

Variable	n=88
Mean (SD) age, years	62 (15)
Male gender, n (%)	42 (48)
Caucasians, n (%)	36 (41)
Black race, n (%)	52 (59)
Hypertension, n (%)	69 (78)
Diabetes mellitus, n (%)	28 (32)
Hypercholesterolemia, n (%)	32 (37)
Atrial fibrillation, n (%)	27 (31)
Smoking, n (%)	23 (26)
Coronary artery disease, n (%)	16 (18)
Congestive heart failure, n (%)	15 (17)
Median baseline NIHSS score, points (IQR)	16 (12–21)
Pretreatment with intravenous thrombolysis, n (%)	56 (64)
Mean (SD) admission systolic blood pressure, mmHg	157 (32)
Mean (SD) admission diastolic blood pressure, mmHg	89 (20)
Mean (SD) systolic blood pressure post MT*, mmHg	141 (15)
Mean (SD) diastolic blood pressure post MT*, mmHg	72 (12)
Minimum (SD) systolic blood pressure post MT*, mmHg	110 (22)
Minimum (SD) diastolic blood pressure post MT*, mmHg	55 (12)
Maximum (SD) systolic blood pressure post MT*, mmHg	174 (23)
Maximum diastolic blood pressure post MT*, mmHg (SD)	94 (20)
Mean (SD) admission serum glucose, mg/dL	153 (82)
Mean (SD) admission low density lipoprotein, mg/dL	99 (40)
General anesthesia, n (%)	33 (38%)
Good collaterals, n (%)	31 (52%)†
Median (IQR) ASPECTS, points	9 (8–10)
Median (IQR) onset to tPA bolus time, min	130 (105–172)
Median (IQR) onset to arterial puncture time, min	226 (171–290)

*During the first 24 hours following the end of mechanical thrombectomy.
†Collateral score was available in 60 patients.
ASPECTS, Alberta Stroke Program Early CT score; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; MT, mechanical thrombectomy.

median onset to groin puncture time 226 min (IQR 171–290)). The baseline characteristics of our study population are shown in table 1. The location of LVO was the following: 31 in the M1 middle cerebral artery (MCA; 35%), 16 in the intracranial internal carotid artery (ICA; 18%), 12 in the posterior circulation (14%), 10 in M2 MCA (11%). The remaining 19 patients had tandem occlusions (22%). A total of 33 patients underwent MT under general anesthesia (38%), while the remaining 55 patients (62%) received conscious sedation.

In our cohort, a combination of distal aspiration and stent-retriever was used as the most common technique in 47 cases (53%). The second most commonly employed technique was the ADAPT (A Direct Aspiration First Pass Technique), and this was used in 22 cases (25%). Stent-retrievers without distal aspiration were used in 15 cases (17%). The remaining cases were mostly cervical or intracranial carotid occlusions in which acute angioplasty and/or stenting was employed. Systemic thrombolysis prior to MT was administered in 56 patients (64%). The rate of sICH was 9%. Cerebral edema occurred in 32 patients (37%). A total of 27% of patients achieved FI at 3 months, while the 3-month mortality rate was 37%.

The univariable associations of maximal SBP and DBP levels post MT with primary (FI) and secondary (sICH and 3 month mortality) outcomes are summarized in table 2. Patients with FI had lower maximal SBP (160±19 mmHg vs 179±23 mmHg; P=0.001), while maximal DBP did not differ between the two groups (88±14 mmHg vs 96±22 mmHg; P=0.157). Maximal SBP levels (183±20 mmHg vs 169±23 mmHg; P=0.008) and DBP levels (105±20 mmHg vs 89±18 mmHg; P=0.001) post MT were higher in patients who died at 3 months, while no difference was noted in maximal SBP (183±31 mmHg vs 173±22 mmHg; P=0.279) and DBP (97±25 mmHg vs 94±20 mmHg; P=0.692) levels in patients with and without sICH. Increasing maximal SBP measurements strongly correlated to larger FIV (Spearman's r: 0.534; P<0.001). There was no correlation (P>0.080) between any of the remaining BP measurements and FIV.

Table 2 also depicts the associations of minimum SBP and DBP levels post MT with primary and secondary outcomes. Patients with FI had higher minimum SBP levels (119±12 mmHg vs 108±25 mmHg; P=0.009), while minimal SBP values were lower in patients who died at 3 months (102±28 mmHg vs

Table 2 Maximum and minimum systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels during the first 24 hours following the end of mechanical thrombectomy (MT) in relation to primary (3-month functional independence) and secondary (symptomatic intracranial hemorrhage and 3-month mortality) outcomes

Outcome	Maximum SBP post MT (mean±SD), mmHg		P value	Maximum DBP post MT (mean±SD), mmHg		P value
Primary	Yes	No		Yes	No	
Three-month functional independence*	160±19	179±23	0.001	88±22	96±22	0.157
Secondary	Yes	No		Yes	No	
Symptomatic intracranial hemorrhage	183±31	173±22	0.279	97±25	94±20	0.692
Three-month mortality	183±20	169±23	0.008	105±20	89±18	0.001
	Minimum SBP post MT (mean±SD), mmHg		**P value**	**Minimum DBP post MT (mean±SD), mmHg**		**P value**
Primary	Yes	No		Yes	No	
Three-month functional independence*	119±12	108±25	0.008	54±11	55±12	0.757
Secondary	Yes	No		Yes	No	
Symptomatic intracranial hemorrhage	105±18	111±22	0.430	51±9	55±12	0.384
Three-month mortality	102±28	115±16	0.007	55±14	55±10	0.825

*Three-month functional independence: mRS scores of 0–2.

Table 3 Mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels during the first 24 hours following the end of mechanical thrombectomy (MT) in relation to primary (3-month functional independence) and secondary (symptomatic intracranial hemorrhage, and 3-month mortality) outcomes

Outcome	Mean SBP post MT (mean±SD), mmHg		P value	Mean DBP post MT (mean±SD), mmHg		P value
Primary	Yes	No		Yes	No	
Three-month functional independence*	140±13	141±17	0.798	71±11	72±12	0.579
Secondary	Yes	No		Yes	No	
Symptomatic intracranial hemorrhage	139±18	141±15	0.698	74±12	72±12	0.710
Three-month mortality	142±17	140±15	0.568	74±14	71±10	0.221

*Three-month functional independence: mRS scores of 0–2.

115±16 mmHg; P=0.007). No other association was detected between minimal SBP and DBP values post MT with the outcomes of interest. We also failed to document any association between mean SBP and DBP levels post MT and primary or secondary outcomes (table 3). Moreover, all post MT BP measurements did not differ (P>0.2) between patients with good and bad collateral status.

Table 4 shows the univariable and multivariable associations of BP measurements post MT and other baseline characteristics with 3-month FI. In the initial univariable analyses the following variables were related (P<0.1) to FI: admission SBP, admission NIHSS score, maximum SBP post MT and minimum SBP post MT. In the final multivariable models both minimum and maximum SBP were independently associated with FI. More specifically, a 10 mmHg increment in maximum SBP reduced the odds of FI (OR 0.55, 95% CI 0.39 to 0.79; P=0.001), while a 10 mmHg increment in minimum SBP increased the likelihood of FI (OR 1.64, 95% CI 1.04 to 2.60; P=0.033).

Table 5 summarizes the univariable and multivariable associations of BP measurements post MT and other baseline characteristics with 3-month mortality. In the initial univariable analyses the following variables were related (P<0.1) to mortality: admission SBP, admission NIHSS score, general anesthesia (vs conscious sedation), maximum SBP post MT, minimum SBP post MT, and maximum DBP post MT. In the final multivariable models both minimum SBP and maximum DBP were independently associated with mortality. More specifically, a 10 mmHg increment in maximum DBP increased the odds of mortality (OR 1.62; 95% CI 1.10 to 2.38; P=0.014), while a 10 mmHg increment in minimum SBP decreased the likelihood of mortality (OR 0.68, 95% CI 0.49 to 0.95; P=0.022).

We also performed sensitivity analyses (table 6) evaluating the association of post-MT BP measurements with outcomes in the subgroup of nrLVO patients without IVT pretreatment (n=32). Our sensitivity analyses reproduced the significant associations that were documented in the total study sample. Patients with 3-month FI had lower maximal SBP (160±19 mmHg vs 177±17 mmHg; P=0.040), while maximal SBP levels (181±8 mmHg vs 167±22 mmHg; P=0.025) post MT were higher in patients who died at 3 months. In addition, lower minimal SBP levels were also related to 3-month mortality (101±18 mmHg vs 115±18 mmHg; P=0.038).

Table 4 Univariable and multivariable logistic regression analyses depicting the associations of blood pressure measurements and other baseline characteristics with 3-month functional independence (mRS score of 0–2)

Variable	Univariable logistic regression analysis: OR (95% CI)	P value*	Multivariable logistic regression analysis*: OR (95% CI)	P value
Age (per 10 year increase)	0.82 (0.59 to 1.14)	0.239		
Male gender	0.86 (0.32 to 2.30)	0.767		
Black race	0.88 (0.33 to 2.36)	0.803		
NIHSS score at admission (per 1 point increase)	0.85 (0.77 to 0.94)	0.001	0.86 (0.76 to 0.97)	0.017
ASPECTS at baseline (per 1 point increase)	1.14 (0.78 to 1.67)	0.486		
Good collaterals	1.01 (0.29 to 3.52)	0.991		
Hypertension	0.96 (0.30 to 3.10)	0.947		
Diabetes mellitus	0.80 (0.30 to 2.17)	0.665		
Hyperlipidemia	0.85 (0.34 to 2.11)	0.721		
Atrial fibrillation	0.79 (0.27 to 2.34)	0.670		
Coronary artery disease	0.97 (0.27 to 3.44)	0.962		
Congestive heart failure	2.14 (0.60 to 7.65)	0.240		
Smoking	0.67 (0.21 to 2.10)	0.491		
Intravenous thrombolysis	1.96 (0.67 to 5.72)	0.218		
Onset to arterial puncture time (per 10 min increase)	0.98 (0.95 to 1.02)	0.311		
General anesthesia (vs conscious sedation)	0.59 (0.20 to 1.72)	0.331		
Serum glucose at admission (per 10 mg/dL increase)	1.00 (0.95 to 1.06)	0.895		
Serum LDL (per 10 mg/dL increase)	1.02 (0.90 to 1.15)	0.810		
SBP at admission (per 10 mmHg increase)	0.83 (0.70 to 1.00)	0.044	0.89 (0.69 to 1.14)	0.357
Mean SBP post MT (per 10 mmHg increase)†	0.96 (0.70 to 1.31)	0.795		
Minimum SBP post MT (per 10 mmHg increase)†	1.31 (1.00 to 1.72)	0.048	1.64 (1.04 to 2.60)	0.033
Maximum SBP post MT per 10 mmHg increase)†	0.67 (0.51 to 0.87)	0.003	0.55 (0.39 to 0.79)	0.001
DBP at admission (per 10 mmHg increase)	0.87 (0.67 to 1.13)	0.299		
Mean DBP post MT (per 10 mmHg increase)†	0.89 (0.58 to 1.35)	0.574		
Minimum DBP post MT per 10 mmHg increase)†	0.94 (0.61 to 1.43)	0.753		
Maximum DBP post MT per 10 mmHg increase)†	0.83 (0.64 to 1.08)	0.160		
Cerebral edema	0.43 (0.14 to 1.32)	0.140		

*Cut-off of P<0.1 was used for selection of candidate variables for inclusion in multivariable logistic regression models.
†During the first 24 hours following the end of mechanical thrombectomy.
ASPECTS, Alberta Stroke Program Early CT score; DBP, diastolic blood pressure; LDL, low density lipoprotein; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure.

Table 5 Univariable and multivariable logistic regression analyses depicting the associations of blood pressure measurements and other baseline characteristics with 3-month mortality

	Univariable logistic regression analysis		Multivariable logistic regression analysis*	
Variable	OR (95% CI)	P value*	OR (95% CI)	P value
Age (per 10 year increase)	1.12 (0.83 to 1.50)	0.460		
Male gender	0.94 (0.39 to 2.27)	0.886		
Black race	1.18 (0.48 to 2.90)	0.726		
NIHSS score at admission (per 1 point increase)	1.13 (1.04 to 1.22)	0.003	1.11 (1.00 to 1.23)	0.049
ASPECTS at baseline (per 1 point increase)	0.87 (0.65 to 1.17)	0.362		
Good collaterals	0.71 (0.25 to 2.04)	0.523		
Hypertension	1.82 (0.59 to 5.66)	0.301		
Diabetes mellitus	1.63 (0.68 to 3.91)	0.276		
Hyperlipidemia	0.68 (0.29 to 1.59)	0.376		
Atrial fibrillation	1.43 (0.56 to 3.69)	0.459		
Coronary artery disease	1.06 (0.34 to 3.25)	0.962		
Congestive heart failure	0.60 (0.17 to 2.09)	0.423		
Smoking	1.50 (0.57 to 3.99)	0.415		
Intravenous thrombolysis	0.75 (0.30 to 1.86)	0.537		
Onset to arterial puncture time (per 10 min increase)	1.00 (0.98 to 1.03)	0.975		
General anesthesia (vs conscious sedation)	2.88 (1.15 to 7.22)	0.024	2.73 (0.83 to 8.92)	0.097
Serum glucose at admission (per 10 mg/dL increase)	1.01 (0.96 to 1.06)	0.810		
Serum LDL (per 10 mg/dL increase)	0.94 (0.83 to 1.06)	0.285		
SBP at admission (per 10 mmHg increase)	1.19 (1.03 to 1.38)	0.019	1.21 (0.98 to 1.48)	0.072
Mean SBP post MT (per 10 mmHg increase)†	1.09 (0.81 to 1.46)	0.564		
Minimum SBP post MT (per 10 mmHg increase)†	0.72 (0.56 to 0.94)	0.015	0.68 (0.49 to 0.95)	0.022
Maximum SBP post MT (per 10 mmHg increase)†	1.25 (1.01 to 1.55)	0.042	1.12 (0.83 to 1.50)	0.464
DBP at admission (per 10 mmHg increase)	1.17 (0.93 to 1.47)	0.177		
Mean DBP post MT (per 10 mmHg increase)†	1.28 (0.86 to 1.88)	0.220		
Minimum DBP post MT (per 10 mmHg increase)†	0.96 (0.65 to 1.41)	0.823		
Maximum DBP post MT (per 10 mmHg increase)†	1.55 (1.14 to 2.10)	0.005	1.62 (1.10 to 2.38)	0.014
Brain edema	1.79 (0.72 to 4.46)	0.209		

*Cut-off of P<0.1 was used for selection of candidate variables for inclusion in multivariable logistic regression models.
†During the first 24 hours following the end of mechanical thrombectomy.
ASPECTS, Alberta Stroke Program Early CT score; DBP, diastolic blood pressure; LDL, low density lipoprotein; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure.

DISCUSSION

Our study demonstrates that wide BP excursions from the mean during the first 24 hours post MT are associated with worse outcomes in patients with nrLVO. This association was independent of demographics, vascular risk factors, baseline stroke severity, onset to groin puncture time, admission BP, serum glucose and LDL levels, early hypodensity on brain CT quantified by ASPECTS, type of anesthesia, collateral status, and early brain edema.

Successful reperfusion rates post MT have improved from 40–50% with first-generation devices to 70–90% with third-generation devices like stent-retrievers or aspiration catheters during the past 15 years.[26 27] Considering the fact that 10–30% of LVO patients still remain non-recanalized post MT carrying a dismal prognosis, it is important to identify other modifiable variables that might improve functional outcomes in this subgroup. Effective post-procedural BP management may be one of these factors. Theoretically, permissive hypertension may be beneficial in patients with nrLVO to maintain brain perfusion pressure. In our cohort of nrLVO patients, we documented that increasing maximum SBP and DBP levels during the first 24 hours following MT were associated with a higher likelihood of 3-month mortality and lower odds of 3-month FI. This finding is partly in line with a recent retrospective observational study that also reported an independent relationship between peak SBP levels during the first 24 hours following MT and worse functional outcomes at 3 months in a broader patient population (both recanalized and non-recanalized LVO patients).[10] On the other hand, minimum post-MT BP levels did not affect outcomes in the study by Mistry *et al*.[10] Nevertheless, there are important methodological considerations when comparing the two studies. First, the study population of patients with non-recanalized emergent LVO in our study (n=88) is almost double that in the study by Mistry *et al* (n=45).[10] Second, in the earlier study by Mistry and colleagues only 34 nrLVO patients had 90-day mRS evaluations available.[10] Therefore, their analysis was underpowered to reveal independent associations between post-MT BP measurements and 90-day functional outcomes. On the other hand, our study evaluated the association of post-MT BP levels with safety and efficacy outcomes using comprehensive univariable and multivariable logistic regression models.

The association of elevated maximum BP post MT with adverse functional outcomes cannot be attributed to the potential impairment of collateral circulation with extremely elevated BP levels in patients with LVO, since patients with good and bad collaterals in our cohort did not differ in any BP parameter post MT.[28] The association of increasing BP levels with increasing final infarct volume seen in the present study, detected both by our group[20] and other investigators in previous studies,[29] may account for the detrimental effect of higher maximum SBP and DBP post MT on functional outcomes. Alternative explanations may suggest that patients with exceptionally high BP are unhealthier due to coexisting comorbidities (diabetes mellitus, renal failure) or that acutely raised BP levels are a marker of extensive cerebral ischemia and early brain swelling. However, it is noteworthy that brain edema was included as a potential confounder in all analyses without modifying any of the reported associations.

In addition, we detected that lower minimum SBP levels post MT correlated to higher odds of mortality and functional dependence at 3 months. A U-shaped association between acute BP values and outcomes in AIS has been firmly established by multiple observational studies, indicating that extremely low BP levels during the first hours of acute cerebral ischemia are equally as harmful as markedly elevated BP values.[29–31] A similar U-shaped relationship between baseline SBP and functional outcome in LVO patients treated with MT has recently been reported by the MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands) investigators.[32] The detrimental effect of extremely low BP values following MT in patients with nrLVO may be attributed to impaired cerebral perfusion due to autoregulatory failure leading to infarct expansion and further neurological deterioration.[14 33]

Nevertheless, the fact that maximum and minimum and not mean BP levels were associated with adverse outcomes indirectly

Table 6 Maximum and minimum systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels during the first 24 hours following the end of mechanical thrombectomy (MT) in relation to primary (3-month functional independence) and secondary (symptomatic intracranial hemorrhage and 3-month mortality) outcomes in the subgroup of patients with emergent large vessel occlusion without intravenous thrombolysis pretreatment (n=32)

Outcome	Maximum SBP post MT (mean±SD), mmHg		P value	Maximum DBP post MT (mean±SD), mmHg		P value
Primary	Yes	No		Yes	No	
Three-month functional independence*	160±19	177±17	0.040	93±11	94±20	0.923
Secondary	Yes	No		Yes	No	
Symptomatic intracranial hemorrhage	169±57	173±15	0.925	99±22	94±19	0.638
Three-month mortality	181±8	167±22	0.025	97±14	92±22	0.500
	Minimum SBP post MT (mean±SD), mmHg		**P value**	**Minimum DBP post MT (mean±SD), mmHg**		**P value**
Primary	Yes	No		Yes	No	
Three-month functional independence*	121±15	107±19	0.104	57±11	54±11	0.528
Secondary	Yes	No		Yes	No	
Symptomatic intracranial hemorrhage	98±8	110±20	0.274	53±5	55±12	0.761
Three-month mortality	101±18	115±18	0.038	53±15	56±8	0.343

*Three months functional independence: mRS scores of 0–2.

supports the potential detrimental effect of extreme BP fluctuations during the immediate post-procedural period. The findings of our study are corroborated by a recent retrospective study which demonstrated worse clinical outcomes in non-recanalized AIS patients with the highest and the lowest BP values following reperfusion with IVT or endovascular procedures.[33] Additional well-designed multicenter studies are required to independently validate our initial observations and to determine the cut-off values above and below which BP should not fluctuate during the first critical hours following MT.

It is plausible to hypothesize that, among patients with nrLVO, those with viable penumbra are most likely to benefit from permissive hypertension. Although there is no easy way to quantify penumbra, high ASPECTS and good collaterals can be used as surrogates for viable hypoperfused cerebral tissue. In the present study, we included in our analyses both ASPECTS and collateral score as potential confounders that may moderate the association of BP measurements with 3-month FI (mRS score of 0–2) and 3-month mortality (tables 4 and 5). However, we failed to detect any significant interaction. Nevertheless, this lack of association may be attributed to a type II error due to the limited sample size (n=88). Future multicenter larger studies should evaluate the potential beneficial effect of permissive hypertension following MT in the subgroup of patients with emergent LVO with adequate collaterals and high ASPECTS.

It is also possible that permissive hypertension may have resulted in small improvements in hand or language functions in nrLVO patients. However, these improvements could not be quantified by the mRS score, which is a course outcome. Unfortunately, the activities of daily living at 3 months were not prospectively evaluated in this dataset. We plan to implement Barthel Index as a standard outcome measure of activities of daily living at 3 months in our future studies. Furthermore, we failed to assess volume status, a potentially essential variable for patients with pressure dependent examination that may benefit the most with permissive hypertension. Nevertheless, it should be acknowledged that the common practice in our center is to maintain euvolemia using fluid administration.

Several other limitations of the present report need to be addressed. First, the modest sample size and retrospective analysis of prospectively collected data are important methodological shortcomings. Second, our methods included primary and secondary outcomes lacking central adjudication. Third, we did not collect data on fluctuation of BP levels during MT and BP variability post MT and could not evaluate their impact on different outcomes. Fourth, the limited sample size prevented us from differentiating between mTICI 0, 1 and 2a recanalization grades when investigating the impact of BP levels post MT on outcomes. We realize that this is an important limitation, however we feel that stratifying the present cohort according to different non-recanalized grades (mTICI 0, 1 and 2a) will further significantly decrease the sample size in each group. This would make it difficult to draw any meaningful results/conclusions from the present study because of type II error. Future studies with a larger number of patients should stratify these groups. Fifth, patients with nrLVO pretreated with IVT had different post-MT BP goals (<180/105 mmHg) from patients treated with direct MT (<220/120 mmHg). Consequently, it would be important to differentiate these two groups in future larger studies, although it is important to note that IVT pretreatment was included as one of the potential confounders in our analyses and did not moderate the association of BP parameters with early functional outcomes and mortality. Sixth, follow-up vascular imaging after the termination of MT is not common practice at our center unless there is unexpected clinical worsening. Thus, we were unable to record the rates of spontaneous subsequent recanalization in the present dataset. Finally, the observational study design did not allow us to establish a cause–effect relationship between BP levels and outcomes in patients with nrLVO treated with MT. The strong correlation that we identified between increasing maximal SBP measurements and more extensive infarct volumes indicates that excessively high BP levels post MT may worsen functional outcome by increasing FIV.

In conclusion, our study demonstrates that nrLVO patients who do poorly are more likely to have had excursions of BP from the mean in the first 24 hours following MT. In the absence of RCT data, the majority of endovascular centers usually allow permissive hypertension for patients with nrLVO. Our preliminary findings indicate that extreme BP variations during the first 24 hours following MT are likely to be harmful and should be avoided. Additional well-designed multicenter studies are required to independently validate our initial observations and determine the actual cut-offs above and below which BP should not fluctuate during the first critical hours following MT. Future research is also necessary to identify the subgroup among nrLVO patients who are most likely to benefit from permissive hypertension (eg, patients with good collaterals and high ASPECTS).

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