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Original Article

Association Between Hyperacute Blood Pressure Lowering and Outcomes in Patients With Endovascular Thrombectomy

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Background and Purpose Although blood pressure (BP) elevation is common in acute ischemic stroke, and guidelines recommend reducing systolic BP to <185 mm Hg prior to reperfusion therapy, the safety and efficacy of active BP lowering in the hyperacute phase before endovascular thrombectomy (EVT) remain uncertain.

Methods We conducted a retrospective analysis of a prospective hospital-based registry that included consecutive patients with anterior circulation large-vessel occlusion who underwent EVT between 2016 and 2024. Patients were categorized into the active BP lowering in the emergency department (ED) group or the absence of BP lowering in the ED group based on whether they received intravenous antihypertensive treatment prior to EVT. The primary outcome was the distribution of the modified Rankin Scale (mRS) scores at 3 months. Propensity score matching and multivariable regression analyses were also performed.

Results Of the 492 included patients, 53 (10.8%) received active BP lowering in the ED. After propensity score matching, patients who underwent active BP lowering showed a worse distribution of 3-month mRS scores compared with those who did not receive BP lowering (adjusted odds ratio, 0.38; 95% confidence interval [CI], 0.18 to 0.80; *P*=0.013). The active BP lowering group exhibited greater infarct volume growth (adjusted β coefficient, 33.4; 95% CI, 18.2 to 48.7; *P*<0.001), whereas the incidence of symptomatic intracerebral hemorrhage did not differ between groups.

Conclusions Active BP lowering in the ED before EVT was associated with worse functional outcomes and increased infarct growth without a corresponding reduction in the occurrence of symptomatic intracerebral hemorrhage. These findings highlight the need for caution in initiating antihypertensive therapy before reperfusion and support further investigations to define optimal pre-EVT BP management.

Keywords Antihypertensive agent; Blood pressure; Endovascular thrombectomy; Acute ischemic stroke; Cerebral infarct; Emergency department

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Introduction

Endovascular thrombectomy (EVT) has become the standard of care for patients with acute ischemic stroke due to large-vessel occlusion (LVO), offering significant improvements in functional outcomes.[1] However, optimal blood pressure (BP) management in the hyperacute phase is not well established. Elevated BP is common following stroke onset and may help maintain perfusion in the ischemic penumbra.[2] Conversely, excessive BP elevation may increase the risk of hemorrhagic transformation and reperfusion injury.[3] Aggressive BP lowering may worsen ischemia, especially in patients with impaired autoregulation or incomplete collateral flow.[4] Six randomized clinical trials have investigated BP management after successful EVT,[5-10] and meta-analyses of these trials have shown that intensive post-EVT BP lowering does not reduce the incidence of symptomatic intracerebral hemorrhage (sICH) but is associated with worse functional outcomes.[11-14] One proposed explanation for this association is that excessive BP reduction may further decrease blood flow to the oligemic area, thereby exacerbating ischemic injury.[5] Despite these findings, the effect of BP lowering performed during the hyperacute period prior to EVT in the emergency department (ED) has been rarely studied.[15,16]

The American Heart Association/American Stroke Association (AHA/ASA) and the European Stroke Organisation (ESO) guidelines for acute ischemic stroke recommend maintaining BP below 185/110 mm Hg prior to initiating reperfusion therapy.[17,18] The recommended BP thresholds are primarily based on the inclusion criteria of randomized clinical trials evaluating the effect of intravenous tissue plasminogen activator (tPA).[19,20] The BP threshold of 185/110 mm Hg, originally used as an exclusion criterion in tPA-related trials, was subsequently adopted without modification in trials evaluating the efficacy of EVT in the extended time window.[21,22] The Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke Trials Collaboration meta-analysis demonstrated an association between high admission systolic BP and worse functional outcomes after stroke.[23] However, this finding does not necessarily imply that active BP lowering in patients with elevated admission systolic BP improves prognosis. Nevertheless, the clinical consequences of early BP reduction in the ED before EVT remain unclear.

Using a prospective stroke registry, we investigated the clinical and radiological associations between active intravenous BP lowering in the ED prior to EVT. This study provides important real-world insights into the management of hyperacute BP in patients undergoing EVT.

Methods

Study population and EVT

This retrospective study used data from a prospective hospital-based registry (Yonsei Stroke Cohort; https://www.clinicaltrials.gov; NCT03510312) and included consecutive patients with stroke who underwent EVT. EVT was performed in eligible patients with LVO who met the prevailing clinical guidelines at the time of treatment.[18,24] To evaluate active BP lowering in the ED, patients with in-hospital stroke were excluded. Patients with LVO in the posterior circulation were also excluded. Patients with a pre-stroke modified Rankin Scale (mRS) score >2 were also excluded. Regarding the EVT procedure, a stent retriever and/or a direct aspiration device was selected according to the location of the occluded vessel, vascular tortuosity, and the neurointerventionalist's preference. Intravenous tPA was administered within 4.5 hours of stroke onset unless contraindicated according to the current clinical guidelines. Follow-up brain imaging was conducted 24±12 hours after EVT. At the study hospital, EVT was primarily performed without sedation; however, if the patient exhibited irritability, procedural sedation rather than general anesthesia was administered. After EVT, patients received optimal care in the stroke unit or intensive care unit.[25] The study was approved by the Institutional Review Board of Severance Hospital (approval number: 2025-1391-001).

BP monitoring and lowering

All BP measurements were obtained using noninvasive BP cuffs. We investigated systolic and diastolic BP values at five predefined time points for each patient. The five time points included (1) triage BP measurement upon arrival at the ED, (2) follow-up BP measurement during the ED stay, (3) initial BP measurement upon entry into the angiosuite, (4) BP measurement immediately after the first recanalization, and (5) final BP measurement before exiting the angiosuite. If the triage BP value was missing, it was substituted with the earliest BP measurement recorded after arrival at the ED. For follow-up BP measurements in the ED, the post-antihypertensive value was used if treatment was administered; otherwise, the highest value was selected. The same approach was applied in the angiosuite for patients without first recanalization.

For each time point, the exact time at which BP was measured was recorded. Additionally, we assessed whether intravenous antihypertensive or sedative agents were administered between the time points at the corresponding dosages. All BP lowering with intravenous antihypertensives was initiated at the discretion of the neurologist managing the patient in the ED. Each neurologist independently decided whether to initiate active BP

lowering when the systolic BP exceeded 185 mm Hg. However, active BP lowering is generally not recommended for patients with systolic BP <185 mm Hg. All active BP lowering was achieved using intravenous antihypertensives rather than oral medications, and intravenous antihypertensive agents were administered via bolus injection rather than continuous infusion. The choice of agent and dosage was determined at the discretion of the neurologist. Information regarding the specific drug, dosage, and time of initial administration was collected by a stroke coordinator (E.L.K.) with 15 years of experience who was blinded to the outcome data of each patient. We did not impute any missing data.

Study groups

Patients were categorized into active BP lowering and no BP lowering groups based on whether intravenous antihypertensive agents were administered at least once in the ED. This classification was limited to intravenous antihypertensive use within the ED and did not account for administration in other settings such as the angiosuite or stroke unit. In Korean clinical practice, prehospital BP lowering is not performed by emergency medical services; thus, active BP lowering in the ED can be regarded as the first instance of BP control following stroke onset.

Clinical and radiological variables

Demographic and vascular risk factor data were also collected. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS). The occlusion site, Alberta Stroke Program Early Computed Tomography Score (ASPECTS) on noncontrast computed tomography (CT), and collateral status based on the Tan scale were determined by consensus among at least two stroke neurologists who were blinded to the outcome data. All patients underwent a standardized prethrombectomy imaging protocol consisting of noncontrast CT, CT angiography, and CT perfusion, with perfusion mismatch assessed using RAPID AI software (iSchemaView, San Mateo, CA, USA). A tissue volume with cerebral blood flow (CBF) <30% was considered the infarct core. The mismatch volume was defined as the volume of time-to-maximum (Tmax) >6 seconds, excluding the volume with CBF <30%. Cases with errors in the values measured using the RAPID AI software were excluded from the imaging analysis. The modified Thrombolysis in Cerebral Infarction (mTICI) grade after EVT was adjudicated by consensus between stroke neurologists and neurointerventionalists (Y.D.K., B.M.K., D.J.K., and H.S.N.). Final infarct volume was primarily determined using RAPID AI software by measuring the volume of tissue with an apparent diffusion coefficient value $<620\times10^{-6}$ mm^2/s. In cases where overestimation or underestimation by RAPID was identified on magnetic resonance imaging (MRI), the infarct volume was manually calculated by delineating the infarct area on each 3-mm diffusion-weighted image slice, summing the areas, and multiplying by 3 mm. Patients without follow-up MRI (i.e., those with only follow-up CT) were excluded from the final infarct volume analysis because accurate infarct volume measurement was not feasible on CT.

Outcome measures

The primary outcome was a shift analysis of the distribution of mRS scores at 3 months. Secondary outcomes included a binary analysis of the mRS score at 3 months, categorizing scores as 0–2 for functional independence and 3–6 for functional dependence or mortality. Additional outcomes included a shift analysis of the distribution of the mRS score at discharge, change in the NIHSS score from admission to discharge, sICH within 36 hours, in-hospital mortality, and mortality within 3 months. Certified medical staff collected mRS scores at 3 months in person or via telephone using the Korean version of the mRS. The sICH was defined according to the European Cooperative Acute Stroke Study III criteria as any extravascular blood in the brain or cranium associated with clinical worsening, evidenced by an increase of four or more points in the NIHSS score or resulting in death.[26] Successful recanalization was defined as an mTICI grade of 2b or higher. Infarct growth volume from initial CT imaging in the ED to post-EVT was defined as the difference between the volume with CBF <30% on initial CT perfusion and the volume of tissue with an apparent diffusion coefficient $<620\times10^{-6}$ mm^2/s on follow-up MRI.

Statistical analysis

Continuous variables were presented as the mean±standard deviation (SD) or median (interquartile range [IQR]), and categorical variables as numbers (%). Comparisons of clinical and radiological characteristics were performed using the Wilcoxon rank-sum test, χ^2 test, or Fisher exact test as appropriate. To compare BP trends between active and no BP lowering in the ED groups over time, a linear mixed-effects model was used. An interaction term between time point and BP reduction in the ED was included to assess differential temporal trends by study group. The estimated marginal means of BP were calculated for each group at each time point, and pairwise group comparisons were performed at each time point. No adjustments were made for multiple comparisons. The primary outcome was tested using ordinal logistic regression adjusted for age, sex, hypertension, intravenous tPA use, NIHSS score at admission, time from stroke onset to ED admission, occlusion site, and pre-stroke mRS score. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs)

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were reported. Ordinal, binary logistic, and linear regression analyses were conducted for secondary outcomes, with adjustments using the same variables as for the primary outcome.

We used propensity score matching (PSM) to minimize potential selection bias and confounding factors. Propensity scores were estimated for each patient using a logistic regression model that included age, sex, intravenous tPA use, NIHSS score at admission, initial systolic BP at ED triage, and occlusion site. Patients who received BP lowering agents in the ED were matched 1:1 to those who did not, using the nearest-neighbor method, with a caliper width of 0.2. To evaluate covariate balance, standardized mean differences were calculated before and after matching, with a threshold of 20% used to identify meaningful imbalances between groups. After PSM, the primary and secondary outcomes were analyzed using appropriate regression models, depending on the type of variable. To avoid model overfitting, the adjusted analyses included age, sex, and NIHSS score at admission as covariates. Causal mediation analysis was performed using the PSM cohort to evaluate whether the effect of active BP lowering in the ED on 3-month functional independence was mediated by a drop in BP. The mediator model (early BP drop as the dependent variable) was fitted using linear regression with active BP reduction as the exposure, adjusting for age, sex, and NIHSS score at admission. The outcome model (3-month functional independence as the dependent variable) was fitted using logistic regression, including both active and early BP drop as predictors, with the same covariate adjustment. The average causal mediation effect (indirect effect), average direct effect, total effect, and mediated proportion were estimated using a non-parametric bootstrap method with 10,000 simulations.

For sensitivity analysis, inverse probability of treatment weighting (IPTW) was applied, targeting the average treatment effect. We estimated propensity scores for active BP lowering in the ED using a logistic regression model that included the following pretreatment covariates: age, sex, NIHSS score at admission, hypertension, diabetes, hyperlipidemia, congestive heart failure, atrial fibrillation, intravenous tPA use, and initial systolic BP at ED triage. To limit the influence of extreme propensity scores, we trimmed scores at the 1st and 99th percentiles (0.01–0.99). Post-weighting covariate balance was assessed using standardized mean differences, with <0.10 considered acceptable. All outcome analyses were performed on the IPTW-weighted sample using survey-weighted regression. Because the initial SBP at ED triage remained imbalanced after weighting, it was included as an additional covariate in the outcome model.

A multivariable linear regression model was used to compare infarct growth volume between the study groups. The model was adjusted for variables associated with infarct growth, including age, sex, hypertension, intravenous tPA use, NIHSS score at admission, collateral status, ASPECTS, immediate mTICI grade, Tmax >6 seconds volume, CBF <30% volume, and CT-to-first recanalization time. A two-sided *P*-value <0.05 was considered statistically significant. All statistical analyses were conducted using R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

Data availability

The anonymized dataset will be available on reasonable request to the corresponding author.

Results

Between January 2016 and December 2024, 1,226 patients underwent reperfusion therapy. After excluding 462 patients who received only intravenous tPA, 764 underwent EVT. Among them, 121 patients with in-hospital stroke, 118 with posterior circulation stroke, and 33 with a pre-stroke mRS score >2 were excluded, resulting in a final cohort of 492 patients (Supplementary Figure 1). The median age was 75 years (IQR, 63–83 years), 53.0% were males, and 53 patients (10.8%) received active BP lowering with intravenous antihypertensives in the ED. In the original dataset, patients in the active BP lowering group were older, had a higher proportion of females, had a higher prevalence of hypertension, had more frequent intravenous tPA use, and had higher admission NIHSS scores than those in the no BP lowering group (Table 1). After PSM, the demographics and baseline characteristics were well balanced between the groups, with 47 patients in both the active and non-active BP-lowering groups in the ED (Supplementary Figure 2 and Table 1).

BP trend and lowering

In the original dataset, the active BP lowering in the ED group showed significantly higher systolic BP across all five time points compared with the no BP lowering group. At ED triage, the initial systolic BP difference between the two groups was 32.9 mm Hg (95% CI: 25.7 to 40.1). This difference decreased to 7.2 mm Hg (95% CI: 0.0 to 14.4) at the follow-up systolic BP measurement in the ED, depending on the use of intravenous antihypertensives (Figure 1A). The time interval between the initial BP measurement at ED triage and follow-up BP measurement in the ED was significantly longer in the active BP lowering in the ED group than in the no BP lowering group (active BP lowering in the ED, median 54 min vs. no BP lowering in the ED, median 44 min; *P*=0.017) (Table 2). Detailed BP values measured in the ED are presented in Supplementary Table 1. Among patients who received active BP lowering in the ED, 96.2% were treated

Table 1. Baseline characteristics

Variable	Original dataset			1:1 Propensity score matched dataset		
	Active BP lowering in the ED (n=53)	No BP lowering in the ED (n=439)	*P*	Active BP lowering in the ED (n=47)	No BP lowering in the ED (n=47)	*P*
Demographics						
Age (yr)	80.0 (73.0–86.0)	75.0 (63.0–82.0)	0.003	80.0 (73.5–85.5)	80.0 (70.5–85.0)	0.901
Male sex	19 (35.8)	242 (55.1)	0.008	18 (38.3)	19 (40.4)	0.833
Medical history						
Hypertension	48 (90.6)	315 (71.8)	0.003	42 (89.4)	39 (83.0)	0.370
Diabetes	22 (41.5)	136 (31.0)	0.121	19 (40.4)	15 (31.9)	0.391
Hyperlipidemia	19 (35.8)	139 (31.7)	0.538	18 (38.3)	17 (36.2)	0.831
Atrial fibrillation	30 (56.6)	229 (52.2)	0.541	27 (57.4)	25 (53.2)	0.678
Congestive heart disease	2 (3.8)	21 (4.8)	>0.999	2 (4.3)	2 (4.3)	>0.999
Previous stroke history (n=490)	9 (17.0)	98 (22.4)	0.365	9 (19.1)	10 (21.3)	0.797
Current smoker (n=486)	8 (15.1)	73 (16.9)	0.745	7 (14.9)	5 (10.6)	0.536
IV-tPA	31 (58.5)	170 (38.7)	0.006	26 (55.3)	25 (53.2)	0.836
NIHSS score at admission	17.0 (10.0–20.0)	13.0 (9.0–18.0)	0.003	18.0 (10.0–21.0)	16.0 (12.0–20.0)	0.699
Radiologic variables						
Occlusion site			0.083			0.949
M1	17 (32.1)	198 (45.1)		17 (36.2)	15 (31.9)	
M2	11 (20.8)	108 (24.6)		8 (17.0)	10 (21.3)	
Distal ICA	11 (20.8)	59 (13.4)		9 (19.1)	11 (23.4)	
Proximal ICA	7 (13.2)	49 (11.2)		7 (14.9)	6 (12.8)	
Tandem	7 (13.2)	25 (5.7)		6 (12.8)	5 (10.6)	
ASPECTS (n=491)	9.0 (6.0–10.0)	8.0 (7.0–10.0)	0.991	9.0 (6.0–10.0)	8.0 (7.0–10.0)	0.511
Collateral state (Tan scale) (n=490)	2.0 (1.0–2.0)	2.0 (1.0–2.0)	0.280	2.0 (1.0–2.0)	1.5 (1.0–2.0)	0.548
Good collateral state (Tan scale of 2–3) (n=490)	28 (52.8)	285 (65.2)	0.076	25 (53.2)	23 (50.0)	0.758
Tmax >6 seconds volume (mL) (n=438)	148.0 (106.0–203.0)	120.0 (77.0–178.0)	0.141	145.5 (87.0–204.5)	125.0 (74.0–199.0)	0.573
CBF <30% volume (mL) (n=438)	10.0 (0.0–41.0)	6.0 (0.0–31.0)	0.401	9.0 (0.0–29.0)	10.0 (0.0–45.5)	0.717
Mismatch volume (mL) (n=438)	122.0 (59.0–149.0)	100.0 (62.0–145.0)	0.277	114.5 (58.3–149.3)	91.0 (67.5–133.0)	0.372
mTICI score (immediate)			0.673			0.338
0	2 (3.8)	23 (5.2)		1 (2.1)	3 (6.4)	
1	1 (1.9)	12 (2.7)		1 (2.1)	1 (2.1)	
2a	4 (7.5)	22 (5.0)		4 (8.5)	1 (2.1)	
2b	15 (28.3)	151 (34.4)		13 (27.7)	19 (40.4)	
2c	0 (0.0)	13 (3.0)		0 (0.0)	0 (0.0)	
3	31 (58.5)	218 (49.7)		28 (59.6)	23 (48.9)	
Successful recanalization (mTICI 2b, 2c, or 3)	46 (86.8)	382 (87.0)	0.964	41 (87.2)	42 (89.4)	0.748
Time parameters (min)						
Onset to ED visit time	115.0 (57.0–360.0)	213.0 (67.5–513.5)	0.051	141.0 (66.0–410.5)	158.0 (42.0–398.0)	0.705
Onset to puncture time	246.0 (165.0–490.0)	320.0 (165.0–604.0)	0.248	260.0 (179.0–497.5)	245.0 (140.0–495.5)	0.473
Onset to first recanalization time	274.0 (209.0–554.0)	354.0 (209.0–642.0)	0.220	296.0 (218.0–559.0)	249.5 (172.5–466.3)	0.321
Onset to final recanalization time	281.0 (217.0–581.0)	378.0 (225.8–663.5)	0.175	317.5 (218.0–581.8)	277.0 (185.5–496.0)	0.533

Values are median (interquartile range) or number (%).
BP, blood pressure; ED, emergency department; IV, intravenous; tPA, tissue plasminogen activator; NIHSS, National Institutes of Health Stroke Scale; M1, first segment of the middle cerebral artery; M2, second segment of the middle cerebral artery; ICA, internal carotid artery; ASPECTS, Alberta Stroke Program Early CT Score; CBF, cerebral blood flow; mTICI, modified Treatment In Cerebral Infarction.

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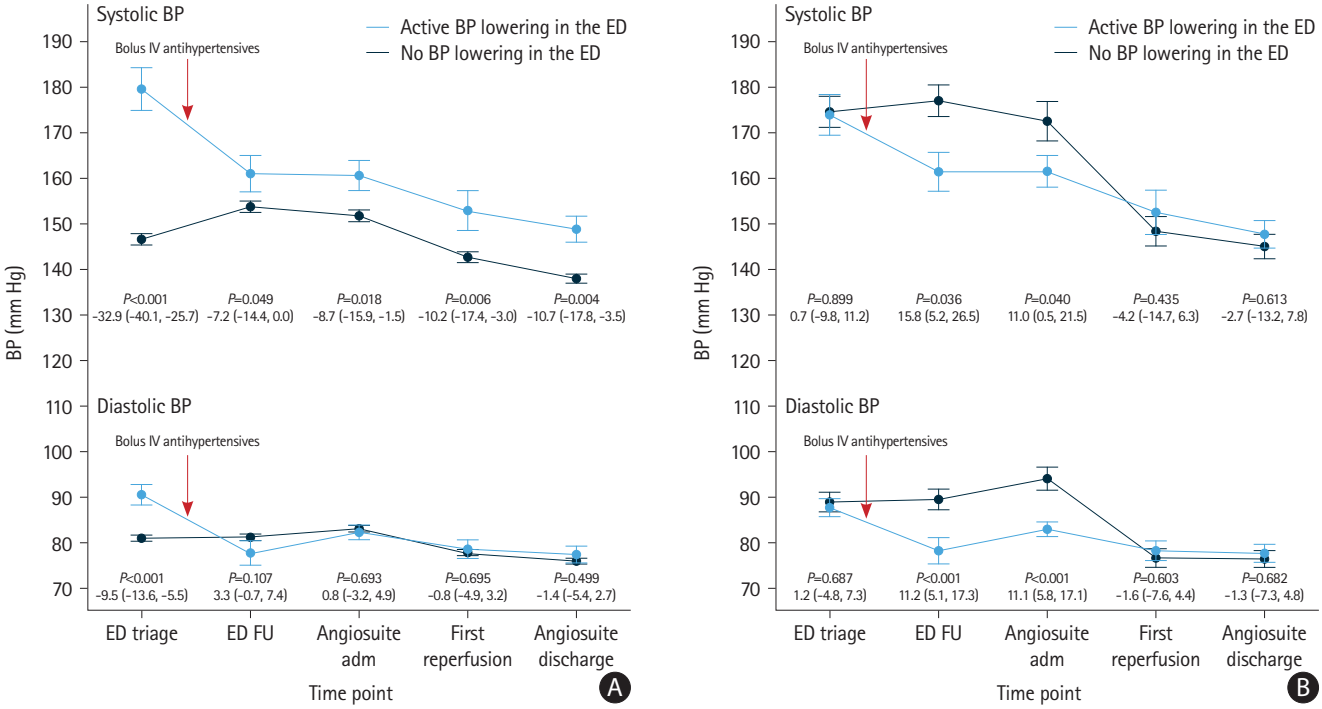

Figure 1. BP trend according to the presence of BP lowering in the ED. Systolic and diastolic BP values are shown at five time points: ED triage, ED FU, angiosuite admission, first reperfusion, and angiosuite discharge. Estimated marginal means and 95% confidence intervals are shown for each time point. Between-group comparisons at each time point were conducted using linear mixed-effects models with interaction terms. The red arrow indicates the administration of an IV bolus of antihypertensive agents. (A) BP trend from ED arrival to the end of EVT (orginal dataset). (B) BP trend from ED arrival to the end of EVT (matched dataset). *P*-values and mean differences with 95% confidence intervals are shown for each time point. BP, blood pressure; ED, emergency department; EVT, endovascular thrombectomy; FU, follow-up; IV, intravenous.

with nicardipine and 3.8% with labetalol, with a median dose of 2 mg (IQR: 1.0–2.0). The use of conscious sedation in the ED was numerically higher in the active BP lowering in the ED group (*P*=0.053). In the angiosuite, BP lowering was more frequent in the ED group, whereas the frequency of conscious sedation did not significantly differ between the two groups.

In the matched dataset, no difference was observed in initial systolic BP at ED triage between the two groups (systolic BP difference, 0.7 mm Hg [95% CI: -9.8 to 11.2]) (Figure 1B). However, following the administration of intravenous antihypertensives, the active BP lowering in the ED group demonstrated a significantly lower systolic BP than that in the no BP lowering group. Specifically, the follow-up systolic BP in the ED was lower by a median of 15.8 mm Hg (95% CI: 5.2 to 26.5), and BP at angiosuite entry was lower by a median of 11.0 mm Hg (95% CI: 0.5 to 21.5). No significant differences were observed in the systolic BP between the groups at later time points. Consistent with the original dataset, the time interval between the initial BP measurement at ED triage and the follow-up measurement in the ED remained significantly longer in the active BP lowering in the ED group. No significant differences were observed between the groups in the use of conscious sedation or the frequency of BP reduction in the angiosuite (Table 2).

Primary outcome

In the original dataset, the no BP lowering in the ED group had a median 3-month mRS of 3.0 (IQR: 1.0–5.0), while the active BP lowering in the ED group had a median of 5.0 (IQR: 3.0–5.0). In the 3-month mRS shift analysis, the active BP lowering group showed a significantly greater shift toward higher mRS scores (AOR, 0.44; 95% CI, 0.25 to 0.76; *P*=0.004) (Figure 2A). After PSM, the median 3-month mRS remained 3.0 (IQR: 1.0–5.0) in the no BP lowering group and was 4.0 (IQR: 2.5–6.0) in the active BP lowering group. The active BP lowering group continued to show a significantly worse mRS distribution compared with the no BP lowering group (AOR, 0.38; 95% CI, 0.18 to 0.80; *P*=0.013) (Table 3 and Figure 2B).

Secondary outcomes

The rate of functional independence at 3 months was significantly lower in the active BP lowering group compared with the no BP lowering group (AOR, 0.27; 95% CI, 0.11 to 0.60; *P*=0.002). The change in the NIHSS score from admission to discharge was also significantly lower in the active BP lowering group. Additionally, the mRS score at discharge (*P*=0.014) and mortality rate within 3 months (*P*=0.037) were significantly higher in the active BP lowering group than in the no BP lowering group. How-

Table 2. Timing and dose of IV antihypertensives and sedative agents

Variable	Original dataset			1:1 Propensity score matched dataset		
	Active BP lowering in the ED (n=53)	No BP lowering in the ED (n=439)	*P*	Active BP lowering in the ED (n=47)	No BP lowering in the ED (n=47)	*P*
BP variables (mm Hg)						
Initial SBP at ED triage	183.0 (163.0–197.0)	148.0 (126.0–165.0)	<0.001	181.0 (156.5–193.0)	176.0 (161.5–189.5)	0.742
Initial DBP at ED triage	87.0 (79.0–98.0)	79.0 (71.0–89.3)	<0.001	85.0 (77.5–94.0)	89.0 (78.5–98.0)	0.477
SBP immediately before BP lowering	194.0 (186.0–210.0)	-	-	194.0 (185.5–204.0)	-	-
DBP immediately before BP lowering	100.0 (85.0–108.0)	-	-	98.0 (84.5–108.0)	-	-
FU SBP in the ED	159.0 (140.0–185.0)	153.0 (137.0–170.8)	0.075	162.0 (142.0–187.0)	175.0 (161.0–196.5)	0.015
FU DBP in the ED	78.0 (64.0–90.0)	79.0 (72.0–89.0)	0.153	79.0 (66.0–89.5)	88.5 (77.8–98.3)	0.002
Initial SBP at angiosuite	164.0 (144.0–176.0)	149.0 (132.0–169.0)	0.007	164.0 (151.5–176.0)	175.0 (148.0–189.0)	0.062
Initial DBP at angiosuite	81.0 (75.0–91.0)	81.0 (73.0–92.0)	0.995	81.0 (76.0–91.5)	91.0 (80.5–103.0)	0.001
FU SBP at angiosuite after first recanalization	154.0 (132.0–173.0)	143.0 (123.0–152.0)	0.019	154.0 (125.0–172.5)	146.0 (135.5–160.5)	0.533
FU DBP at angiosuite after first recanalization	75.0 (69.0–89.0)	76.5 (68.0–86.0)	0.851	74.0 (68.5–88.5)	76.0 (67.0–85.5)	0.806
Final SBP at angiosuite	149.0 (135.0–158.0)	140.0 (123.0–152.0)	0.001	148.0 (135.0–157.5)	148.0 (135.0–156.5)	0.642
Final DBP at angiosuite	75.0 (65.0–90.0)	75.0 (66.3–85.0)	0.538	77.0 (65.0–90.0)	77.0 (66.5–84.0)	0.620
Time interval between time points (min)						
Stroke onset to initial BP at ED triage	118.0 (60.0–375.0)	214.5 (75.5–516.8)	0.052	146.0 (67.5–414.0)	178.0 (45.0–400.0)	0.736
Initial BP at ED triage to FU BP in the ED	54.0 (38.0–63.0)	44.0 (30.0–64.0)	0.017	54.0 (41.0–63.0)	44.0 (33.0–58.0)	0.049
FU BP in the ED to initial BP at angiosuite	33.0 (15.0–52.0)	31.0 (15.0–55.0)	0.959	32.0 (12.5–47.5)	29.0 (16.5–43.5)	0.913
Initial BP at angiosuite to FU SBP at angiosuite	58.0 (40.0–73.0)	52.0 (40.0–73.0)	0.437	58.0 (41.0–72.5)	52.0 (38.5–76.5)	0.465
FU SBP at angiosuite to final BP at angiosuite	40.0 (29.0–55.0)	33.0 (20.0–50.8)	0.079	40.0 (29.0–56.0)	30.5 (20.0–43.3)	0.071
BP lowering to FU BP in the ED	5.0 (2.0–10.0)	-		5.0 (2.0–9.5)	-	
BP lowering or sedative agent in the ED						
Classes of IV antihypertensives						
Calcium channel blocker	51 (96.2)	0 (0.0)	-	45 (95.7)	0 (0.0)	-
Alpha/beta-adrenergic antagonist	2 (3.8)	0 (0.0)	-	2 (4.3)	0 (0.0)	-
Both	0 (0.0)	0 (0.0)	-	0 (0.0)	0 (0.0)	-
Dose of BP lowering agent* (mg)	2.0 (1.0–2.0)	0.0 (0.0–0.0)	<0.001	2.0 (1.0–2.0)	0.0 (0.0–0.0)	<0.001
Conscious sedation	5 (9.4)	15 (3.4)	0.053	5 (10.6)	3 (6.4)	0.714
BP lowering or sedative agent at angiosuite						
BP lowering at angiosuite	24 (45.3)	106 (24.1)	0.001	23 (48.9)	25 (53.2)	0.680
Classes of IV antihypertensives						
Calcium channel blocker	22 (41.5)	91 (20.7)		21 (44.7)	22 (46.8)	
Alpha/beta-adrenergic antagonist	2 (3.8)	5 (1.1)		2 (4.3)	2 (4.3)	
Both	1 (1.9)	10 (2.3)		1 (2.1)	1 (2.1)	
Dose of BP lowering agent* (mg)	0.0 (0.0–2.0)	0.0 (0.0–0.0)	<0.001	0.5 (0.0–2.0)	1.0 (0.0–2.0)	0.936
Conscious sedation	20 (37.7)	180 (41.0)	0.647	18 (38.3)	20 (42.6)	0.674
Timing of BP lowering (min)						
Onset to first BP lowering	182.0 (103.0–400.0)	-	-	188.0 (109.5–456.0)	-	-
ED arrival to first BP lowering	52.0 (39.0–58.0)			52.0 (40.0–60.0)		-
First BP lowering to first recanalization	94.0 (68.0–127.5)	-	-	92.5 (68.0–122.8)	-	-
First BP lowering to final recanalization	106.0 (94.0–145.0)	-	-	104.5 (93.3–146.5)	-	-

Values are median (interquartile range) or number (%). Hyphen (-) denotes data that were not available.
IV, intravenous; BP, blood pressure; ED, emergency department; SBP, systolic BP; DBP, diastolic BP; FU, follow-up.
*For statistical analysis, the dose of alpha/beta-adrenergic antagonist (labetalol) divided by 10 was equal to the dose of a calcium channel blocker (nicardipine) and then summed.

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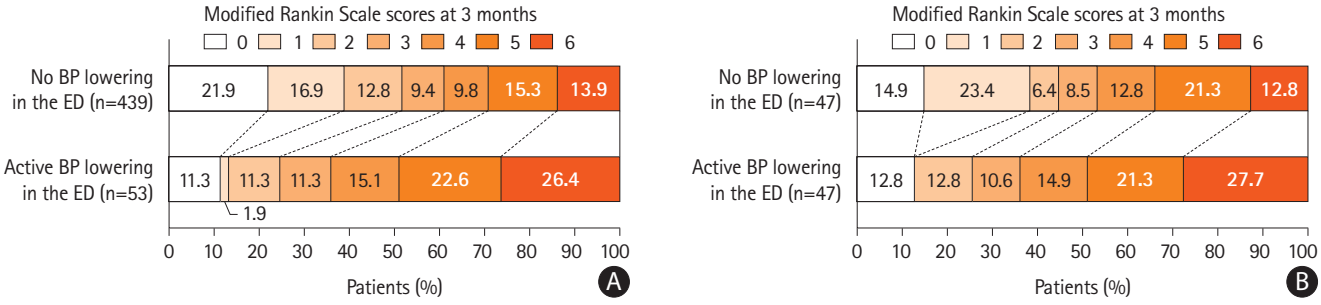

Figure 2. Distribution of modified Rankin Scale score at 3 months. The mRS score ranged from 0 to 6, where 0 denoted no symptoms (best outcome) and 6 represented death (worst outcome). Figure 2A shows a comparison of the mRS scores between the study groups in the original dataset, whereas Figure 2B presents a comparison of the mRS scores between the study groups in the matched dataset. BP, blood pressure; ED, emergency department.

Table 3. Clinical outcomes according to active BP lowering in the ED

Outcomes	Original dataset					1:1 Propensity score matched dataset				
	Active BP lowering in the ED (n=53)	No BP lowering in the ED (n=439)	Unadjusted effect size* (95% CI)	Adjusted effect size* (95% CI)	$P^{\dagger}$	Active BP lowering in the ED (n=47)	No BP lowering in the ED (n=47)	Unadjusted effect size* (95% CI)	Adjusted effect size* (95% CI)	$P^{\dagger}$
Primary outcome										
Shift of mRS score at 3 months (n=491)	5.0 (3.0–5.0)	3.0 (1.0–5.0)	0.39 (0.23 to 0.63)	0.44 (0.25 to 0.76)	0.004	4.0 (2.5–6.0)	3.0 (1.0–5.0)	0.45 (0.22 to 0.93)	0.38 (0.18 to 0.80)	0.013
Secondary outcomes										
Functional independence at 3 months (mRS score 0–2) (n=491)	13/53 (24.5)	226/438 (51.6)	0.30 (0.15 to 0.57)	0.27 (0.11 to 0.60)	0.002	12/47 (25.5)	21/47 (44.7)	0.42 (0.17 to 1.00)	0.33 (0.11 to 0.88)	0.031
Change in NIHSS score (NIHSS at discharge – NIHSS at admission)	2.0 (-5.0–9.0)	6.0 (1.0–10.0)	-3.53 (-6.46 to -0.60)	-3.28 (-6.35 to -0.21)	0.037	2.0 (-5.0–8.0)	6.0 (2.5–11.0)	-3.77 (-8.62 to 1.09)	-3.91 (-8.8 to 0.99)	0.122
mRS score at discharge	5.0 (3.0–5.0)	3.0 (1.0–5.0)	0.36 (0.21 to 0.61)	0.48 (0.26 to 0.86)	0.014	5.0 (3.0–5.0)	4.0 (1.0–5.0)	0.54 (0.25 to 1.13)	0.48 (0.22 to 1.02)	0.062
Symptomatic intracerebral hemorrhage (n=480)	6/52 (11.5)	30/428 (7.0)	1.73 (0.62 to 4.12)	0.86 (0.26 to 2.46)	0.788	6/46 (13.0)	5/45 (11.1)	1.20 (0.34 to 4.47)	1.14 (0.31 to 4.34)	0.844
In-hospital mortality	8/53 (15.1)	25/439 (5.7)	2.92 (1.18 to 6.62)	1.84 (0.70 to 4.42)	0.191	8/47 (17.0)	3/47 (6.4)	3.01 (0.81 to 14.5)	2.96 (0.75 to 14.9)	0.142
Mortality within 3 months (n=491)	14/53 (26.4)	61/438 (13.9)	2.22 (1.11 to 4.25)	2.41 (1.03 to 5.47)	0.037	13/47 (27.7)	6/47 (12.8)	2.61 (0.93 to 8.12)	2.67 (0.86 to 9.18)	0.099

Values are median (interquartile range) or number/total (%).
BP, blood pressure; ED, emergency department; CI, confidence interval; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.
*The effect size is reported for mRS score shift at 3 months and discharge, as a common odds ratio with the 95% CI; for change in NIHSS score, as β coefficient with 95% CI; and for other outcomes, as the odds ratio with the 95% CIs; †*P*-values correspond to adjusted effect sizes.

ever, no significant differences were observed between the groups in terms of the incidence of sICH or in-hospital mortality. In the PSM dataset, the active BP lowering group still showed a significantly lower rate of functional independence at 3 months compared with the no BP lowering group (AOR, 0.33; 95% CI, 0.11 to 0.88; *P*=0.031). However, no significant differences were observed between the groups in the change in NIHSS score during hospitalization, mRS score at discharge, in-hospital mortality, mortality rate within 3 months, or incidence of sICH (Table 3).

Mediation analysis

Active BP lowering in the ED was strongly associated with a greater early BP drop (adjusted β coefficient, -23.46; 95% CI, -34.15 to -12.77; *P*<0.001; path A). A larger BP drop was significantly associated with a lower proportion of functional independence at 3 months (AOR, 1.03; 95% CI, 1.00 to 1.05; *P*=0.024; path B). Active BP lowering was also associated with poor functional outcome (AOR, 0.33; 95% CI, 0.11 to 0.88; *P*=0.031; path C), but this direct effect was attenuated and became non-significant after accounting for BP drop (AOR, 0.50; 95% CI, 0.16 to 1.44; *P*=0.203; path C'). The indirect effect of BP lowering

through BP drop was significant, and the proportion of the total effect mediated by BP drop was 46.60% (95% CI, 4.45 to 168.10; *P*=0.032) (Table 4 and Supplementary Figure 3).

Infarct growth comparison between study groups

Among the 492 patients, 428 (87.0%) achieved mTICI ≥2b. Of these, 30 were excluded owing to unavailable RAPID AI software processing, 12 owing to RAPID processing errors, and 30 owing to a lack of post-EVT MRI. A total of 356 patients were included in this analysis: 40 in the active BP lowering group and 316 in the no BP lowering group. The active BP lowering group had a higher proportion of females, more patients with hypertension, higher intravenous tPA use, and higher admission NIHSS scores (Supplementary Table 2). The mean infarct growth volume was significantly higher in the active BP lowering group compared with the no BP lowering group (45.8±83.3 mL vs. 13.1±40.5 mL, *P*=0.023). In multivariable linear regression, active BP lowering in the ED was associated with an increased infarct growth volume (β coefficient, 33.4; 95% CI, 18.2 to 48.7; *P*<0.001) (Supplementary Table 3 and Figure 3).

Sensitivity analysis

We performed three sensitivity analyses to examine the association between active BP reduction in the ED and clinical outcomes: (1) among patients with successful recanalization; (2) among those who received intravenous tPA; and (3) after applying IPTW to balance the baseline covariates. In the analysis limited to patients with successful recanalization, the active BP lowering in the ED group demonstrated significantly worse outcomes, which was consistent with the findings of the main analysis. However, the difference in the mortality rate within 3 months between the groups was not statistically significant (Supplementary Tables 4 and 5). In the analysis limited to patients who received tPA treatment, the active BP lowering in the ED group showed worse functional outcomes in the original dataset; however, after 1:1 PSM, statistical significance was not reached for the shift analysis of mRS scores (AOR, 0.36; 95% CI, 0.12 to 1.06; *P*=0.074) or achievement of functional independence (AOR, 0.25; 95% CI, 0.05 to 0.98; *P*=0.057), although similar trends were observed (Supplementary Tables 6 and 7). Finally, in the IPTW analysis, the initial systolic BP at ED triage showed a mild deviation with a standardized mean difference of 0.141 (median, 182.5 mm Hg [IQR, 160.0–197.0] vs. 176.0 mm Hg [IQR, 160.0–192.0]), while all other covariates were well balanced (Supplementary Table 8 and Supplementary Figure 4). Following IPTW, the treatment effect remained statistically significant, and these results were consistent with the analyses of the original and PSM datasets (Supplementary Table 9).

Discussion

In this cohort study, we investigated the clinical and radiological associations between active BP lowering in the ED and outcomes in patients undergoing EVT for anterior circulation LVO over a 9-year period. The active BP lowering group exhibited a persistently higher systolic BP from admission to angiosuite discharge and received more intravenous antihypertensives than the no BP lowering group. Patients with active BP lowering showed worse 3-month functional outcomes, less improvement in NIHSS scores, and greater infarct growth volume, although the incidence of sICH was similar between the groups. Notably, after adjusting for baseline systolic BP through PSM, the active BP lowering group showed significantly lower BP in the ED following antihypertensive medication administration and continued to exhibit worse functional outcomes and larger infarct growth. These findings suggest a harmful effect of early BP lowering before reperfusion, even after accounting for differences in initial stroke severity, demographics, and BP levels.

The AHA/ASA and ESO guidelines recommend maintaining BP below 185/110 mm Hg before intravenous thrombolysis or EVT.[17,18] This threshold was originally established as an exclusion criterion in the National Institute of Neurological Disorders and Stroke-tissue plasminogen activator trial and was subsequently adopted in major EVT trials for LVO, which generally excluded patients with BP ≥185/110 mm Hg.[27-31] These recommendations have since been incorporated into current guidelines. However, it remains unclear how active BP reduction to achieve these targets affects the ischemic penumbra during autoregulatory failure. In this study, active BP lowering in the ED using intravenous antihypertensives resulted in a systolic BP reduction of approximately 20 mm Hg, and this early BP lowering was associated with worse functional outcomes and less improvement in NIHSS scores. Notably, patients who did not receive BP lowering therapy in the ED often exhibited stable or even increasing BP trends until reperfusion, suggesting that in a state of autoregulatory failure, the ischemic penumbra may be particularly vulnerable to hypoperfusion induced by antihypertensive-related BP reduction. These findings imply that the decision to initiate active BP lowering prior to reperfusion should be approached with caution, as it may inadvertently compromise collateral perfusion to salvageable brain tissue.

The recent Fourth Intensive Ambulance-Delivered Blood Pressure Reduction in HyperAcute Stroke Trial (INTERACT-4) investigated the impact of BP lowering during the hyperacute phase of ischemic or hemorrhagic stroke, initiated in an ambulance. While the trial did not show a significant effect on the primary outcome in the overall population, subgroup analysis revealed

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Table 4. Mediation analysis of active BP lowering, BP drop, and functional independence at 3 months in the propensity score matching dataset

	Unadjusted analysis			Adjusted analysis		
	Measure	Effect size (95% CI)	*P*	Measure	Effect size (95% CI)	*P*
A (X→M)*	β coefficient	-23.17 (-33.80 to -12.54)	<0.001	Adjusted β coefficient	-23.46 (-34.15 to -12.77)	<0.001
B (M→Y)	OR	1.02 (1.00 to 1.04)	0.022	AOR	1.03 (1.00 to 1.05)	0.024
C (X→Y)	OR	0.42 (0.17 to 1.00)	0.054	AOR	0.33 (0.11 to 0.88)	0.031
C' (X+M→Y)	OR	0.66 (0.25 to 1.70)	0.385	AOR	0.50 (0.16 to 1.44)	0.203
Proportion of total effect mediated (%) (95% CI)†		55.90 (-0.40 to 327.00)	0.052		46.60 (4.45 to 168.10)	0.032
Indirect effect (95% CI)†		-0.11 (-0.22 to -0.02)	0.018		-0.10 (-0.20 to -0.01)	0.020

Adjusted for age, sex, and National Institutes of Health Stroke Scale score at admission, where X is the independent variable (active BP lowering in the ED), M is the mediator variable (early BP drop), and Y is the dependent variable (functional independence [modified Rankin Scale 0–2] at 3 months).
BP, blood pressure; CI, confidence interval; OR, odds ratio; AOR, adjusted OR; ED, emergency department; SBP, systolic BP.
*Early BP drop was defined as the difference between the initial SBP at ED triage and the follow-up SBP in the ED; if follow-up SBP in the ED was missing, it was defined as the difference between the initial SBP at triage and the initial SBP in the angiosuite. All measurements were expressed in millimeters of mercury (mm Hg); †Nonparametric bootstrap CIs with the percentile method (with 10,000 replications).

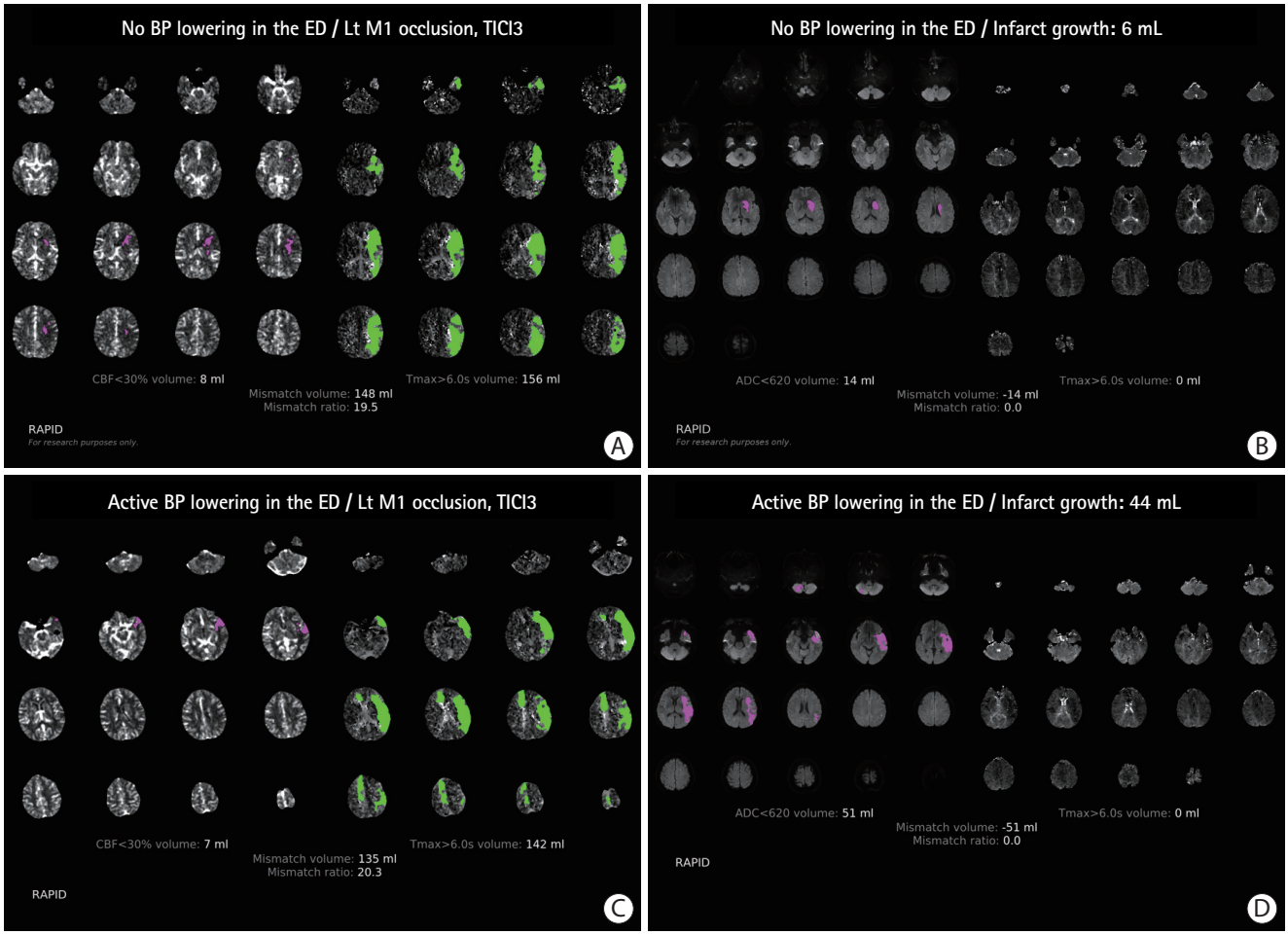

Figure 3. iSchemaView RAPID summary images for cases with active and no BP lowering in the ED. Figure 3A shows a patient who presented with an initial NIHSS score of 18 and left M1 occlusion. The image shows a RAPID summary of the initial CTP in the ED. Figure 3B shows a follow-up MRI RAPID summary after successful reperfusion with 3. This patient showed infarct volume growth from 8 mL (CBF <30%) to 14 mL (ADC <620×10^{-6} mm^2/s), resulting in a 6 mL increase. Figure 3C shows a patient who presented with an initial NIHSS score of 10 and left M1 occlusion. The image shows the RAPID summary of the initial CTP. Figure 3D shows a follow-up MRI RAPID summary after mTICI 3 reperfusion. This patient exhibited infarct volume growth from 7 mL (CBF <30%) to 51 mL (ADC <620×10^{-6} mm^2/s), corresponding to a 44 mL increase. BP, blood pressure; ED, emergency department; M1, first segment of the middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; CTP, computed tomography perfusion; MRI, magnetic resonance imaging; CBF, cerebral blood flow; ADC, apparent diffusion coefficient; mTICI, modified Treatment In Cerebral Infarction.

that early BP lowering with intravenous antihypertensives in patients with ischemic stroke was associated with worse functional outcomes (common OR, 1.30; 95% CI, 1.06 to 1.60).[32] In this subgroup, patients who received active BP lowering experienced an approximately 20 mm Hg reduction in systolic BP by the time of hospital arrival, compared with those who did not undergo BP lowering. This finding closely mirrors the approximately 20 mm Hg systolic BP reduction observed in our study following intravenous antihypertensive administration in the ED.

Similarly, the Thrombolysis in Uncontrolled Hypertension (TRUTH) study examined different strategies for managing elevated BP (>185/110 mm Hg) before intravenous alteplase administration. In the TRUTH study, patients with BP >185/110 mm Hg prior to intravenous thrombolysis were assigned to either a group that underwent active BP lowering to achieve a target of <185/110 mm Hg before alteplase administration or a group that was observed without active BP lowering, receiving alteplase only if their BP spontaneously decreased to <185/110 mm Hg.[33] Despite the active BP lowering group having a shorter onset-to-needle time and a higher rate of intravenous tPA administration, the 3-month functional outcome did not show a statistically significant difference; however, the trend suggested numerically worse outcomes in the active BP lowering group. Our study expands on the potential harm of active BP lowering within a focused, homogeneous cohort, specifically including patients with anterior circulation LVO who underwent EVT. Despite using PSM to balance the initial systolic BP at ED triage, NIHSS score, and baseline demographics, the active BP lowering group demonstrated significantly worse 3-month functional outcomes. These results suggest that beyond BP lowering before intravenous thrombolysis, active BP lowering in the pre-EVT phase also warrants careful evaluation. Further research, ideally through randomized clinical trials, is crucial to clarify the safety and efficacy of active BP lowering in the ED before EVT in acute ischemic stroke with LVO.

In patients with stroke due to LVO, six randomized clinical trials investigating BP management during the first 24 to 72 hours following successful reperfusion have demonstrated that intensive BP lowering after successful EVT does not prevent sICH and may worsen functional outcomes.[5-10] Meta-analyses confirm these findings, reinforcing the concern that active BP lowering in the hyperacute phase could impair perfusion to the ischemic penumbra.[11,12] Extrapolating from these post-EVT BP management trials, one can reasonably hypothesize that similar or even greater harm may occur if BP is aggressively reduced prior to reperfusion, when collateral circulation is the primary mechanism maintaining penumbral viability. *Post hoc* analyses of post-EVT BP management trials have shown that more intensive BP lowering was associated with worse functional outcomes in patients with poor collateral status,[34] and the use of intravenous antihypertensive agents was linked to poorer functional outcomes.[35] Additionally, the finding that medication-induced BP decrease rather than a spontaneous decrease within the first 24 hours after successful EVT was associated with poor outcomes also suggests a potential harmful effect of antihypertensive-induced BP lowering.[36] Our study supports this hypothesis by demonstrating an association between early BP lowering in the ED and unfavorable functional outcomes, even among patients with successful reperfusion.

In our study, patients who underwent BP lowering in the ED showed an infarct volume growth of approximately 32 mL greater than that of patients who did not undergo BP lowering. One study investigating optimal BP targets during EVT procedures demonstrated that a mean arterial pressure below 70 mm Hg sustained for more than 10 minutes was associated with poor functional outcomes.[37] In our study, the active BP lowering group primarily received bolus nicardipine with a median dose of 2 mg, and the effect of bolus nicardipine typically lasted for approximately 24 minutes.[38] Because of its short duration of action, the matched dataset showed significantly lower follow-up BP in the ED and lower BP at angiosuite admission in the active BP lowering group compared with the no BP lowering group, whereas no significant differences were observed at subsequent time points. Taken together with the findings of the previous study, the reduction in BP observed in our study may represent a sufficiently long duration to induce hypoperfusion-related ischemic changes. Additionally, the administration of intravenous antihypertensives may have caused abrupt BP fluctuations, which could have contributed to harmful effects.

This finding is clinically meaningful, as infarct growth of this magnitude has been associated with substantial increases in disability and mortality.[39] Our analysis revealed that early BP lowering was independently associated with increased infarct growth, even after accounting for collateral status, ASPECTS, and perfusion mismatch variables. These results suggest that lowering BP in the pre-reperfusion phase may compromise penumbral tissue and convert salvageable brain tissue into irreversible infarction. The lack of difference in sICH rates supports the hypothesis that early BP lowering may be harmful without reducing the risk of hemorrhage.

Our study has certain limitations. First, it was conducted using data from a single-center registry, which limits external validity and reproducibility. Therefore, our findings may reflect center-specific practice patterns rather than generalizable treatment effects. Second, this study did not specifically analyze the impact of post-EVT BP management on outcomes. Recent evidence

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has highlighted the critical role of optimal BP control in the post-reperfusion phase in influencing functional recovery and reducing complications. As our study primarily focused on the hyperacute pre-EVT period, the potential confounding or modifying effects of post-EVT BP dynamics on the observed associations remain unclear. Third, approximately 26% of the patients received additional BP lowering in the angiosuite, and approximately 40% underwent conscious sedation, which may have contributed to BP reduction. Although BP lowering in the angiosuite was not specifically accounted for in our analysis, these factors were balanced between the groups in the matched dataset, suggesting that their potential effects may have influenced both groups in a similar manner. Fourth, the number of BP measurements varied among patients, and our analysis was based on BP values at specific time points, which limited our ability to capture the overall BP trend for each individual. However, in the acute stroke setting, the clinical workflow from presentation to EVT is extremely rapid, making continuous and uniform BP monitoring across all patients practically challenging. More frequent BP timestamp data are needed to allow time-dependent quantification of BP exposure using an area under-the-curve approach. Fifth, the BP values in the ED were collected using an asymmetric method between groups, in which post-treatment BP was used for those who received active BP lowering, whereas the highest BP was used for those who did not; this may have introduced selection bias in between-group comparisons. Sixth, because an intravenous bolus of nicardipine was predominantly used for BP lowering, the effects of other classes of antihypertensive agents remain unknown. Seventh, the decision to initiate BP lowering was made at the discretion of individual neurologists, potentially introducing treatment selection bias. Finally, the relatively small sample size of the BP-lowering group, despite matching, may limit the statistical power of some secondary outcomes.

Conclusions

Our findings suggest that active BP reduction in the ED before EVT is associated with adverse clinical and radiological outcomes, including worse functional recovery and greater infarct growth without a corresponding reduction in sICH. These results underscore the need for caution regarding early intravenous antihypertensive use before reperfusion and support the need for randomized clinical trials to determine optimal BP targets in the pre-EVT phase.

Supplementary materials

Supplementary materials related to this article can be found online at https://doi.org/10.5853/jos.2025.04147.

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Conflicts of interest

The authors have no financial conflicts of interest.

Author contribution

Conceptualization: Jae Wook Jung, Hyo Suk Nam. Study design: Jae Wook Jung, Hyo Suk Nam. Methodology: Jae Wook Jung, Eun Lee Ko, Hyo Suk Nam. Data collection: Jae Wook Jung, Eun Lee Ko, JoonNyung Heo, Hyungwoo Lee, Byungjae Kim, Young Dae Kim, Haram Joo, Byung Moon Kim, Dong Joon Kim. Statistical analysis: Jae Wook Jung. Writing—original draft: Jae Wook Jung, Hyo Suk Nam. Writing—review & editing: Jae Wook Jung, Hyo Suk Nam. Funding acquisition: Hyo Suk Nam. Approval of final manuscript: all authors.

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Supplementary Table 1. BP values in the ED

Variable	Original dataset			1:1 Propensity score matched dataset		
	Active BP lowering in the ED (n=53)	No BP lowering in the ED (n=439)	*P*	Active BP lowering in the ED (n=47)	No BP lowering in the ED (n=47)	*P*
BP variables in the ED (mm Hg)						
Number of BP measure	3.0 (2.0–5.0)	2.0 (1.0–2.0)	0.007	3.0 (2.0–4.5)	2.0 (1.0–2.5)	<0.001
Mean SBP in the ED	173.5 (165.8–187.3)	149.5 (134.6–164.1)	<0.001	173.5 (165.5–187.1)	172.0 (157.8–185.6)	0.456
Mean DBP in the ED	84.3 (79.0–90.5)	78.0 (71.0–87.0)	<0.001	84.3 (79.0–90.2)	83.5 (76.8–97.9)	0.790
Highest SBP in the ED	198.0 (192.0–213.0)	153.0 (137.0–170.8)	<0.001	195.0 (190.0–212.0)	175.0 (161.0–196.5)	<0.001
Highest DBP in the ED	100.0 (89.0–110.0)	79.0 (72.0–89.0)	<0.001	100.0 (86.5–110.0)	88.5 (77.8–98.3)	0.001
Lowest SBP in the ED	144.0 (134.0–169.0)	143.0 (126.0–158.5)	0.267	146.0 (128.0–167.5)	165.0 (145.8–178.3)	0.002
Lowest DBP in the ED	72.0 (62.0–80.0)	74.0 (67.0–83.0)	0.037	72.0 (63.0–80.0)	80.0 (72.3–92.3)	0.001

Values are median (interquartile range).
BP, blood pressure; ED, emergency department; SBP, systolic BP; DBP, diastolic BP.

Supplementary Table 2. Baseline characteristics of patients with successful recanalization who were eligible for infarct growth analysis

Variables	Active BP lowering in the ED (n=40)	No BP lowering in the ED (n=316)	*P**
Demographics			
Age (yr)	80.0 (73.0–86.0)	75.5 (64.0–83.0)	0.856
Male sex	15 (37.5)	178 (56.3)	0.024
Medical history			
Hypertension	37 (92.5)	226 (71.5)	0.004
Diabetes	14 (35.0)	98 (31.0)	0.609
IV-tPA	24 (60.0)	119 (37.7)	0.007
NIHSS score at admission	17.5 (8.8–20.0)	13.0 (8.0–17.0)	0.009
Radiologic variables			
ASPECTS	9.0 (6.8–10.0)	9.0 (7.0–10.0)	0.553
Collateral state (Tan scale)	2.0 (1.0–2.0)	2.0 (1.0–2.0)	0.554
RAPID AI			
Tmax >6 seconds volume (mL)	149.5±78.3	134.6±82.8	0.094
CBF <30% volume (mL)	31.1±51.5	22.5±40.8	0.203
Mismatch volume (mL)	118.4±70.0	112.1±68.7	0.197
mTICI score (immediate)			0.627
2b	14 (35.0)	124 (39.2)	
2c	0 (0.0)	9 (2.8)	
3	26 (65.0)	183 (57.9)	
Time parameters (min)			
Brain imaging to first recanalization time	126.9±40.9	116.2±39.7	0.097
Brain imaging to final recanalization time	147.8±44.5	134.2±44.9	0.061
BP lowering in the ED to first recanalization time	94.5±40.2	-	-
BP lowering in the ED to final recanalization time	115.4±46.7	-	-

Values are median (interquartile range), number (%), or mean±standard deviation. Hyphen (-) denotes data that were not available.
BP, blood pressure; ED, emergency epartment; IV, intravenous; tPA, tissue plasminogen activator; NIHSS, National Institutes of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; Tmax, time-to-maximum; CBF, cerebral blood flow; mTICI, modified Treatment In Cerebral Infarction.
**P*-value <0.05 was considered of statistical significance.

Supplementary Table 3. Infarct growth in patients with successful recanalization

Outcomes	Active BP lowering in the ED (n=40)	No BP lowering in the ED (n=316)	*P*	Unadjusted effect size*	Adjusted effect size*	*P*†
Final infarct volume (mL)	76.9±104.8	35.6±59.9	0.007	41.3 (19.5–63.1)	33.4 (18.2–48.7)	<0.001
Infarct growth volume (mL)	45.8±83.3	13.1±40.5	0.023	32.7 (17.2–48.2)	33.4 (18.2–48.7)	<0.001

Values are mean±standard deviation or median (interquartile range).
BP, blood pressure; ED, emergency department.
*The effect size is reported for final infarct volume and infarct growth volume, as β coefficient with 95% confidence interval; †*P*-values correspond to adjusted effect sizes.

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Supplementary Table 4. Baseline characteristics of patients with successful recanalization

Variables	Active BP lowering at ED (n=46)	No BP lowering at ED (n=382)	*P*
Demographics			
Age (yr)	80.0 (73.0–85.8)	75.0 (64.0–82.0)	0.012
Male sex	17 (37.0)	218 (57.1)	0.010
Medical history			
Hypertension	41 (89.1)	273 (71.5)	0.010
Diabetes	17 (37.0)	119 (31.2)	0.424
Hyperlipidemia	17 (37.0)	121 (31.7)	0.469
Atrial fibrillation	27 (58.7)	204 (53.4)	0.496
Congestive heart disease	2 (4.3)	20 (5.2)	>0.999
Previous stroke history (n=426)	7 (15.2)	84 (22.1)	0.282
Current smoker (n=423)	7 (15.2)	62 (16.4)	0.831
IV-tPA	28 (60.9)	152 (39.8)	0.006
NIHSS score at admission	18.0 (9.3–20.0)	13.0 (9.0–18.0)	0.005
Radiologic variables			
Occlusion site			0.036
M1	12 (26.1)	175 (45.8)	
M2	11 (23.9)	91 (23.8)	
Distal ICA	10 (21.7)	45 (11.8)	
Proximal ICA	7 (15.2)	46 (12.0)	
Tandem occlusion	6 (13.0)	25 (6.5)	
ASPECTS (n=427)	9.0 (6.0–10.0)	9.0 (7.0–10.0)	0.637
Collateral state (Tan scale) (n=426)	2.0 (1.0–2.0)	2.0 (1.0–2.0)	0.391
Good collateral state (Tan scale of 2-3) (n=426)	25 (54.3)	254 (66.8)	0.092
Tmax >6 seconds volume (mL) (n=384)	149.0 (108.0–203.0)	120.0 (79.5–177.0)	0.114
CBF <30% volume (mL) (n=384)	11.0 (0.0–41.0)	6.0 (0.0–29.5)	0.267
Mismatch volume (mL) (n=384)	135.0 (69.0–150.0)	101.0 (64.0–145.0)	0.184
mTICI score (immediate)			0.333
2b	15 (32.6)	151 (39.5)	
2c	0 (0.0)	13 (3.4)	
3	31 (67.4)	218 (57.1)	
Time parameters (min)			
Onset to ED visit time	94.5 (51.3–358.8)	198.5 (67.3–497.5)	0.029
Onset to puncture time	218.0 (153.3–480.3)	309.0 (163.5–592.3)	0.162
Onset to first recanalization time (n=426)	254.5 (192.0–530.3)	350.0 (208.0–629.5)	0.124
Onset to final recanalization time (n=425)	270.5 (211.8–569.8)	378.0 (225.5–660.0)	0.103

Values are median (interquartile range) or number (%).
BP, blood pressure; ED, emergency epartment; IV, intravenous; tPA, tissue plasminogen activator; NIHSS, National Institutes of Health Stroke Scale; M1, first segment of the middle cerebral artery; M2, second segment of the middle cerebral artery; ASPECTS, Alberta Stroke Program Early CT Score; Tmax, time-to-maximum; CBF, cerebral blood flow; mTICI, modified Treatment In Cerebral Infarction.

Supplementary Table 5. Outcome in patients with successful recanalization

Outcomes	Active BP lowering in the ED (n=46)	No BP lowering in the ED (n=382)	Unadjusted effect size* (95% CI)	Adjusted effect size* (95% CI)	$P^{\dagger}$
Primary outcome					
Shift of mRS score at 3 months (shift analysis) (n=427)	4.0 (2.0–5.0)	2.0 (1.0–5.0)	0.39 (0.23 to 0.66)	0.40 (0.23 to 0.70)	0.001
Secondary outcomes					
Functional independence at 3 months (mRS score 0–2) (n=427)	13/46 (28.3)	214/381 (56.2)	0.31 (0.15 to 0.59)	0.26 (0.11 to 0.58)	0.001
NIHSS score improvement (NIHSS at discharge – NIHSS at admission)	3.0 (0.0–9.8)	7.0 (2.3–11.0)	-2.85 (-5.90 to 0.20)	-3.34 (-6.43 to -0.26)	0.034
mRS score at discharge	5.0 (3.0–5.0)	2.0 (1.0–5.0)	0.37 (0.21 to 0.64)	0.40 (0.22 to 0.74)	0.003
Symptomatic intracerebral hemorrhage (n=417)	4/45 (8.9)	22/372 (5.9)	1.55 (0.44 to 4.30)	1.34 (0.34 to 4.21)	0.641
Mortality within 3 months (n=427)	11/46 (23.9)	47/381 (12.3)	2.23 (1.02 to 4.58)	1.81 (0.73 to 4.20)	0.179

Values are median (interquartile range) or number/total (%).
BP, blood pressure; ED, emergency department; CI, confidence interval; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.
*The effect size is reported for mRS score shift at 3 months and discharge, as a common odds ratio with the 95% CI; for change in NIHSS score, as beta coefficient with 95% CI; and for other outcomes, as the odds ratio with the 95% CIs; $^{\dagger}P$-values correspond to adjusted effect sizes.

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Supplementary Table 6. Baseline characteristics in patients with tissue plasminogen activator

Variable	Original dataset			1:1 Propensity score matched dataset		
	Active BP lowering in the ED (n=31)	No BP lowering in the ED (n=170)	*P*	Active BP lowering in the ED (n=23)	No BP lowering in the ED (n=23)	*P*
Demographics						
Age (yr)	80.0 (75.0–86.0)	71.0 (62.0–80.0)	0.001	80.0 (69.5–85.5)	79.0 (72.5–83.0)	0.435
Male sex	14 (45.2)	97 (57.1)	0.221	11 (47.8)	13 (56.5)	0.555
Medical history						
Hypertension	26 (83.9)	116 (68.2)	0.079	19 (82.6)	18 (78.3)	>0.999
Diabetes	12 (38.7)	43 (25.3)	0.123	10 (43.5)	8 (34.8)	0.546
Hyperlipidemia	10 (32.3)	60 (35.3)	0.744	8 (34.8)	11 (47.8)	0.369
Atrial fibrillation	19 (61.3)	95 (55.9)	0.576	13 (56.5)	14 (60.9)	0.765
Congestive heart disease	0 (0.0)	6 (3.5)	0.593	0 (0.0)	0 (0.0)	>0.999
Previous stroke history	5 (16.1)	26 (15.4)	0.999	4 (17.4)	2 (9.1)	0.665
Current smoker	5 (16.1)	35 (20.8)	0.548	5 (21.7)	5 (21.7)	>0.999
NIHSS score at admission	17.0 (10.5–20.0)	14.0 (9.3–18.0)	0.081	15.0 (9.5–19.5)	15.0 (11.0–16.5)	0.860
Radiologic variables						
ASPECTS	9.0 (7.5–10.0)	9.0 (7.0–10.0)	0.771	9.0 (8.0–10.0)	9.0 (8.0–10.0)	0.891
Good collateral state (Tan scale of 2–3)	17 (54.8)	102 (60.7)	0.540	14 (60.9)	11 (47.8)	0.375
mTICI score (immediate)			0.638			0.422
0	2 (6.5)	5 (2.9)		2 (8.7)	1 (4.3)	
1	1 (3.2)	4 (2.4)		1 (4.3)	0 (0.0)	
2a	0 (0.0)	9 (5.3)		0 (0.0)	2 (8.7)	
2b	10 (32.3)	56 (32.9)		8 (34.8)	5 (21.7)	
2c	0 (0.0)	4 (2.4)		0 (0.0)	0 (0.0)	
3	18 (58.1)	92 (54.1)		12 (52.2)	15 (65.2)	
Successful recanalization (mTICI 2b, 2c, or 3)	28 (90.3)	152 (89.4)	>0.999	20 (87.0)	20 (87.0)	>0.999
BP parameters (min)						
Initial SBP at ED triage	187.0 (156.5–197.5)	148.0 (126.0–163.5)	<0.001	166.0 (150.0–193.0)	170.0 (153.0–186.0)	0.912
FU SBP in the ED	144.0 (132.0–181.0)	153.0 (135.0–165.0)	0.819	148.0 (135.0–181.0)	157.0 (152.0–181.0)	0.173
Initial SBP at angiosuite	162.0 (141.0–167.5)	146.0 (130.0–169.0)	0.163	160.0 (139.5–170.5)	171.0 (139.0–188.0)	0.297
FU SBP at angiosuite after first recanalization	151.0 (129.5–166.0)	140.0 (124.0–156.0)	0.095	139.0 (119.5–168.5)	140.0 (125.5–150.5)	0.455
Final SBP at angiosuite	146.0 (133.0–156.0)	137.0 (123.0–150.0)	0.024	139.0 (128.5–155.5)	137.0 (126.5–148.0)	0.510

Values are medians (interquartile range) or number (%).
BP, blood pressure; ED, emergency department; NIHSS, National Institutes of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; mTICI, modified Treatment In Cerebral Infarction; SBP, systolic BP; FU, follow-up.

Supplementary Table 7. Outcomes in patients with tissue plasminogen activator

Outcomes	Original dataset					1:1 Propensity score matched dataset				
	Active BP lowering in the ED (n=31)	No BP lowering in the ED (n=170)	Unadjusted effect size* (95% CI)	Adjusted effect size* (95% CI)	$P^{\dagger}$	Active BP lowering in the ED (n=23)	No BP lowering in the ED (n=23)	Unadjusted effect size* (95% CI)	Adjusted effect size* (95% CI)	$P^{\dagger}$
Primary outcome										
Shift of mRS score at 3 months	4.0 (2.0–5.5)	2.0 (0.0–4.0)	0.27 (0.13 to 0.55)	0.38 (0.18 to 0.80)	0.012	4.0 (2.0–5.5)	2.0 (0.5–4.5)	0.38 (0.13 to 1.06)	0.36 (0.12 to 1.06)	0.074
Secondary outcomes										
Functional independence at 3 months (mRS score 0–2)	10/31 (32.3)	106/170 (62.4)	0.29 (0.12 to 0.63)	0.29 (0.10 to 0.81)	0.021	8/23 (34.8)	14/23 (60.9)	0.34 (0.10 to 1.11)	0.25 (0.05 to 0.98)	0.057
mRS score at discharge	5.0 (2.5–5.0)	2.0 (1.0–5.0)	0.27 (0.13 to 0.56)	0.38 (0.17 to 0.81)	0.014	5.0 (2.0–5.0)	2.0 (1.0–5.0)	0.40 (0.14 to 1.15)	0.35 (0.11 to 1.05)	0.074
Symptomatic intracerebral hemorrhage	2/30 (6.7)	14/163 (8.6)	0.76 (0.12 to 2.92)	0.58 (0.07 to 3.19)	0.568	2/23 (8.7)	3/22 (13.6)	0.60 (0.07 to 4.02)	0.55 (0.06 to 3.88)	0.556
In-hospital mortality	5/31 (16.1)	6/170 (3.5)	5.26 (1.43 to 18.70)	3.22 (0.53 to 19.60)	0.196	4/23 (17.4)	1/23 (4.3)	4.63 (0.62 to 94.80)	4.28 (0.47 to 95.60)	0.239
Mortality within 3 months	8/31 (25.8)	14/170 (8.2)	3.88 (1.41 to 10.10)	2.26 (0.61 to 8.03)	0.211	6/23 (26.1)	1/23 (4.3)	7.76 (1.17 to 154.00)	9.42 (1.13 to 214.00)	0.069

Values are median (interquartile range) or number/total (%).
BP, blood pressure; ED, emergency department; CI, confidence interval; mRS, modified Rankin Scale.
*The effect size is reported for mRS score shift at 3 months and discharge, as a common odds ratio with the 95% CI; for change in NIHSS score, as beta coefficient with 95% CI; and for other outcomes, as the odds ratio with the 95% CIs; $^{\dagger}P$-values correspond to adjusted effect sizes.

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Supplementary Table 8. Baseline characteristics after IPTW

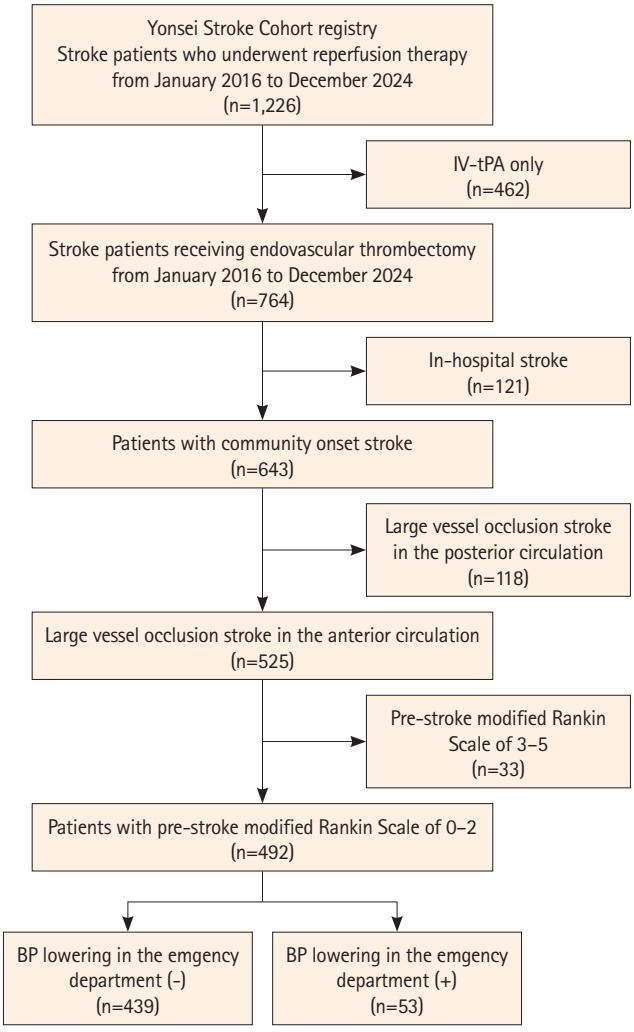
Variable	After IPTW		
	Active BP lowering in the ED (n=53)	No BP lowering in the ED (n=49.72)	*P**
Demographics			
Age (yr)	80.0 (73.0–85.8)	80.0 (71.0–84.0)	0.714
Male sex	19 (35.8)	16.8 (33.8)	0.798
Medical history			
Hypertension	48 (90.6)	45.2 (90.9)	0.947
Diabetes	22 (41.5)	19.3 (38.7)	0.742
Hyperlipidemia	19 (35.8)	19.1 (38.5)	0.756
Atrial fibrillation	30 (56.6)	26.7 (53.7)	0.739
Congestive heart disease	2 (3.8)	2.1 (4.2)	0.885
Previous stroke history	9 (17.0)	7.8 (15.8)	0.838
Current smoker	8 (15.1)	5.1 (10.3)	0.324
NIHSS score at admission	17.0 (9.3–20.0)	16.0 (12.0–20.0)	0.766
IV-tPA	31 (58.5)	29.2 (58.8)	0.975
Radiologic variables			
ASPECTS	9.0 (6.0–10.0)	8.7 (7.0–10.0)	0.690
Good collateral state (Tan scale of 2–3)	28 (52.8)	28.3 (57.3)	0.599
mTICI score (immediate)			0.485
0	2 (3.8)	1.6 (3.2)	
1	1 (1.9)	2.6 (5.2)	
2a	4 (7.5)	2.4 (4.9)	
2b	15 (28.3)	16.3 (32.7)	
2c	0 (0.0)	1.3 (2.6)	
3	31 (58.5)	25.6 (51.4)	
Successful recanalization (mTICI 2b, 2c, or 3)	46 (86.8)	43.1 (86.7)	0.991
Tmax >6 seconds volume (mL)	146.0 (91.8–200.3)	134.4 (81.0–202.8)	0.603
CBF <30% volume (mL)	9.5 (0.0–37.0)	13.0 (0.0–64.6)	0.780
BP parameters (mm Hg)			
Initial SBP at ED triage	182.5 (160.0–197.0)	176.0 (160.0–192.0)	0.248
FU SBP in the ED	157.5 (138.5–184.8)	173.0 (158.0–191.0)	0.025
Initial SBP at angiosuite	164.0 (142.5–176.0)	166.0 (145.5–188.6)	0.402
FU SBP at angiosuite after first recanalization	153.5 (128.3–172.8)	148.0 (130.0–160.0)	0.271
Final SBP at angiosuite	148.5 (135.0–158.0)	147.0 (134.0–156.0)	0.190

Values are median (interquartile range) or number (%).
IPTW, inverse probability of treatment weighting; BP, blood pressure; ED, emergency department; NIHSS, National Institutes of Health Stroke Scale; IV, intravenous; tPA, tissue plasminogen activator; ASPECTS, Alberta Stroke Program Early CT Score; mTICI, modified Treatment In Cerebral Infarction; Tmax, time-to-maximum; CBF, cerebral blood flow; SBP, systolic BP; FU, follow-up.
*Wilcoxon rank-sum test for complex survey samples; chi-squared test with Rao & Scott's second-order correction.

Supplementary Table 9. Outcomes after IPTW

Outcomes	Unadjusted effect size (95% CI)	Adjusted effect size (95% CI)	*P*
Primary outcome			
Shift of mRS score at 3 months	0.47 (0.25 to 0.86)	0.47 (0.25 to 0.90)	0.023
Secondary outcomes			
Functional independence at 3 months (mRS score 0–2)	0.37 (0.17 to 0.79)	0.38 (0.18 to 0.82)	0.014
mRS score at discharge	0.52 (0.28 to 0.97)	0.54 (0.28 to 1.04)	0.064
Symptomatic intracerebral hemorrhage	1.20 (0.42 to 3.41)	1.19 (0.42 to 3.38)	0.746
In-hospital mortality	1.94 (0.70 to 5.42)	1.96 (0.70 to 5.51)	0.201
Mortality within 3 months	1.92 (0.85 to 4.36)	1.95 (0.86 to 4.44)	0.111

IPTW, inverse probability of treatment weighting; CI, confidence interval; mRS, modified Rankin Scale.



Supplementary Figure 1. Study flowchart. IV, intravenous; tPA, tissue plasminogen activator; BP, blood pressure.

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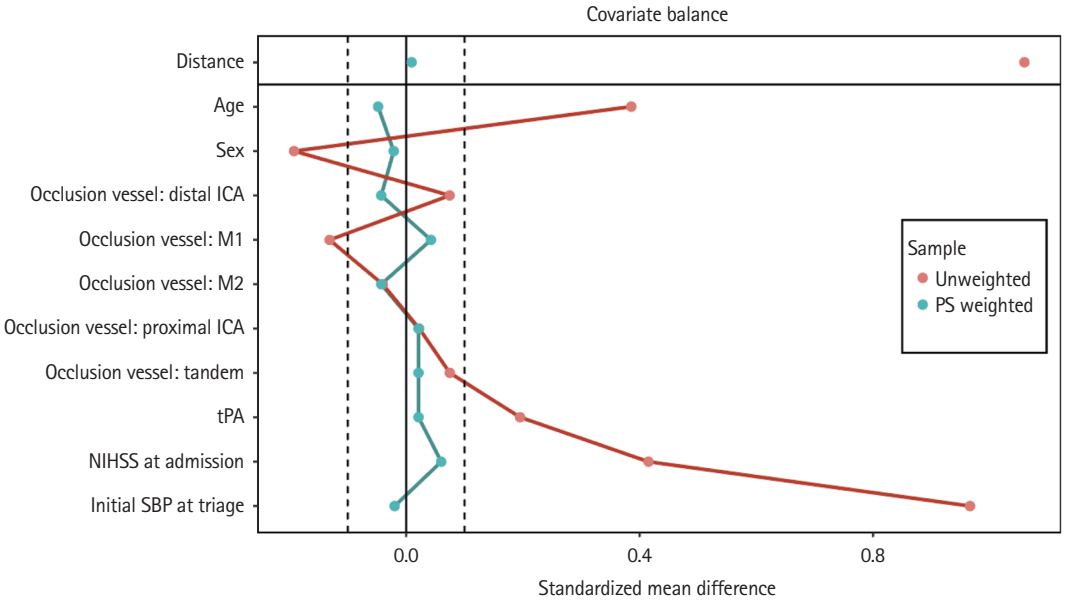
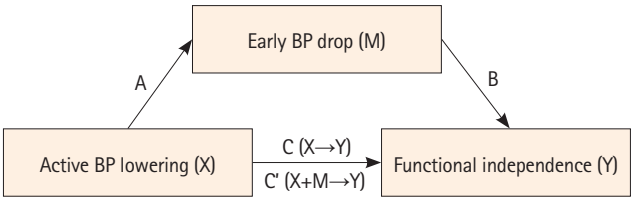
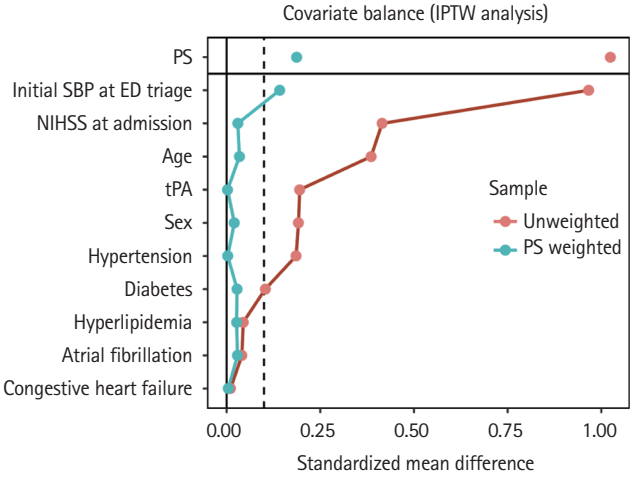


Supplementary Figure 2. Standardized mean differences before and after propensity score matching (PSM method). ICA, internal carotid artery; M1, first segment of the middle cerebral artery; M2, second segment of the middle cerebral artery; tPA, tissue plasminogen activator; NIHSS, National Institutes of Health Stroke Scale; PS, propensity score; SBP, systolic blood pressure.



Supplementary Figure 3. Mediation analysis of the association between active BP lowering in the ED, early BP drop, and 3-month functional outcome. The figure illustrates the hypothesized causal pathways linking active BP lowering in the ED, early BP drop, and 3-month functional outcome. Path A represents the association between active BP lowering and early BP drop; Path B represents the association between early BP drop and functional outcome; Path C represents the total effect of active BP lowering on outcome; and Path C' represents the direct effect after accounting for the mediator (BP drop). The indirect effect reflects the proportion of the total effect mediated through early BP drop. BP, blood pressure; ED, emergency department.



Supplementary Figure 4. Standardized mean differences before and after PS weighting (IPTW method). IPTW, inverse probability of treatment weighting; SBP, systolic blood pressure; ED, emergency department; NIHSS, National Institutes of Health Stroke Scale; tPA, tissue plasminogen activator; PS, propensity score.