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ORIGINAL RESEARCH

Delayed Intracranial Hemorrhage after Endovascular Thrombectomy Is Associated With Poor Functional Outcomes and Elevated Systolic Blood Pressure

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BACKGROUND: Hemorrhagic transformation after endovascular thrombectomy can occur either immediately (early intracranial hemorrhage [ICH]) or on follow-up imaging (delayed ICH), possibly reflecting distinct mechanisms and outcomes. This study aim to investigate the incidence and prognosis of early and delayed ICH and to examine how postprocedural blood pressure (BP) relates to delayed ICH.

METHODS: We analyzed consecutive patients undergoing endovascular thrombectomy (May 2019 through December 2024) who underwent post–endovascular thrombectomy dual energy computed tomography and follow-up imaging. Early ICH was defined as high attenuation on virtual noncontrast of dual energy computed tomography; delayed ICH was defined as new hemorrhage on follow-up after a negative virtual noncontrast. Hourly BP between dual energy computed tomography and follow-up was collected. Outcomes were 90-day functional independence (modified Rankin Scale score of 0–2) and 90-day death.

RESULTS: Among 268 patients, early ICH occurred in 32 (11.9%) patients, delayed ICH in 99 (36.9%), and no ICH in 137 (51.1%). Versus no ICH, delayed ICH was associated with lower odds of functional independence (adjusted odds ratio, 0.49 [95% CI, 0.25–0.94]) without a higher mortality rate (adjusted odds ratio, 1.48 [95% CI, 0.70–3.18]). Within delayed ICH, type of hemorrhagic infarction related to less functional independence, whereas type of parenchymal hematoma related to both functional dependence and death. Higher postprocedural systolic BP was associated with delayed ICH, with thresholds at mean >150 mm Hg and peak >166 mm Hg.

CONCLUSIONS: Delayed ICH was more common than early ICH and independently associated with worse outcomes. Dual energy computed tomography facilitated temporal distinction of hemorrhage and revealed BP-related risks for delayed ICH, suggesting that delayed ICH may be preventable through optimized BP management.

Key Words: acute ischemic stroke ■ blood pressure ■ cerebral infarct ■ endovascular thrombectomy ■ hemorrhagic transformation ■ intracranial hemorrhage

Hemorrhagic transformation is a frequent complication encountered after endovascular thrombectomy (EVT) in patients with acute ischemic stroke due to large-vessel occlusion.[1] Among the various forms of hemorrhagic transformation, symptomatic intracranial hemorrhage (ICH) typically occurs within the

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CLINICAL PERSPECTIVE

What Is New?

- Using immediate post–endovascular thrombectomy dual-energy computed tomography, we temporally distinguished early from delayed intracranial hemorrhage and found that delayed hemorrhage occurred in more than one third of patients and was independently associated with worse 3-month functional outcomes.

What Are the Clinical Implications?

- Delayed intracranial hemorrhage after thrombectomy is a common, clinically important complication rather than a benign imaging finding and should be systematically assessed in poststroke care.
- Among patients without early intracranial hemorrhage, higher mean and peak systolic blood pressure between the procedure and follow-up imaging were linked to delayed hemorrhage, suggesting that maintaining peak systolic blood pressure below 165 mm Hg during this window may help reduce hemorrhagic complications and warrants prospective evaluation.

Nonstandard Abbreviations and Acronyms

EVT	endovascular thrombectomy
HI	hemorrhagic infarction
ICH	intracranial hemorrhage
IVH	intraventricular hemorrhage
mRS	modified Rankin Scale
NIHSS	National Institutes of Health Stroke Scale
PH	parenchymal hematoma
VNC	virtual noncontrast

first few hours after EVT, with a lower incidence reported beyond the initial 24 hours.[2] However, the exact timing of ICH occurrence remains unclear. The emergence of dual-energy computed tomography (DECT), which can differentiate between iodinated contrast and hemorrhage on the basis of differential attenuation at 2 x-ray energy levels, has enhanced early detection of ICH.[3] Nonetheless, ICH not evident on immediate postprocedural DECT is often newly identified on subsequent follow-up imaging.[4–6] These 2 forms of ICH, those detected immediately after EVT (early ICH) and those evident only on follow-up imaging (delayed ICH), may reflect distinct pathophysiologic processes and carry different prognostic implications, although this distinction has not been previously studied.

In clinical practice, immediate post-EVT DECT is commonly used to exclude early ICH, whereas follow-up imaging at 24 hours is routinely performed to assess delayed hemorrhagic transformation and infarct burden, thereby informing risk–benefit decisions on initiation or resumption of antithrombotic therapy.[7] Blood pressure (BP) control is a central element of post-EVT management during the period between EVT and follow-up imaging.[8] Currently, guidelines recommend maintaining BP below 180/105 mm Hg during the first 24 hours after EVT.[9–12] Recent randomized clinical trials showed that lowering systolic BP to a target range of 120 to 140 mm Hg after EVT has not been shown to reduce the incidence of symptomatic ICH.[13–18] However, in these trials, even conventionally managed groups maintained mean systolic BP around 140 mm Hg, which was lower than the upper threshold of 180 mm Hg.[13–18] These findings highlight ongoing uncertainty about the relationship between elevated systolic BP and the development of ICH. Moreover, existing trials did not report the timing of hemorrhagic events.

Therefore, this study aimed to determine the incidence and prognostic significance of early versus delayed ICH after EVT and to evaluate the association between postprocedural BP levels during the interval from immediate DECT to follow-up imaging and the occurrence of delayed ICH.

METHODS

Data Availability

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

Study Populations and Endovascular Thrombectomy

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. We included patients who were admitted between May 2019 and December 2024, limited to those who underwent DECT after EVT. Patients with the isolated anterior cerebral artery occlusion or occlusion in posterior circulation were excluded. Additionally, patients with in-hospital stroke were excluded. EVT was performed in eligible patients with large-vessel occlusion who met the current clinical guidelines.[9,19] For the EVT procedure, device selection was determined at the discretion of the neurointerventionalist on the basis of the occlusion site and vascular tortuosity. Intravenous alteplase was administered within 4.5 hours of stroke onset unless contraindicated according to current clinical guidelines. The study was approved by the Institutional Review Board at Severance Hospital (Approval No. 4-2025-1054).

The Institutional Review Board at Severance Hospital waived the need for patient-informed consent due to the retrospective design and observational nature. Strengthening the Reporting of Observational Studies in Epidemiology guidelines were used to report the findings of this study.[20]

Imaging Protocol

DECT was typically performed during the transition from the angiography suite to the stroke unit after the completion of EVT. Imaging was performed using a 64-channel dual-source multidetector computed tomography (CT) scanner (SOMATOM Force, Siemens), equipped with 2 independently optimized x-ray tubes and dual stellar detectors housed within a single gantry. The scanning protocol enabled simultaneous image acquisition at 80 and 150 kV using 192×0.66-mm collimation, 1.0-second rotation time, and 0.7 pitch.[6] Postprocessing was performed to generate 2 distinct image sets: an iodine map, which selectively visualizes iodine-containing regions, and a virtual noncontrast (VNC) image, which displays brain parenchyma and hemorrhage with iodine effectively subtracted. These maps were used to differentiate regions of high attenuation caused solely by contrast staining from those indicative of true ICH. During the COVID-19 pandemic, due to restrictions on patient transport, patients were directly admitted to the stroke unit following EVT, and DECT was performed as soon as feasible thereafter. Follow-up imaging was primarily performed within 36 hours using magnetic resonance imaging (MRI), including diffusion-weighted imaging and susceptibility-weighted imaging or T2-weighted gradient recalled echocardiographic sequences. For patients who were unable to undergo MRI, noncontrast brain CT was used as an alternative.

Study Groups

We classified patients into 3 study groups. The no-ICH group included patients without any evidence of ICH on either VNC images from DECT or follow-up imaging, regardless of the presence of contrast staining on DECT (Figure 1A and 1B). The early-ICH group comprised patients with high-density lesions suggestive of hemorrhage identified on VNC images (Figure 1C). Subarachnoid hemorrhage (SAH) or intraventricular hemorrhage (IVH) detected on VNC image was also classified as early ICH. The delayed-ICH group included patients without high-density lesions on VNC image of DECT but with new ICH confirmed on follow-up imaging (Figure 1D).

Clinical and Radiological Variables

We collected patient data on demographics and vascular risk factors. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) score. The occlusion site, Alberta Stroke Program Early Computed Tomography Score on pre-EVT noncontrast CT, and collateral status based on the Tan scale were determined by consensus of at least 2 stroke neurologists who were blinded to outcome data. The modified Thrombolysis in Cerebral Infarction 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.). Two stroke neurologists (J.W.J. and B.K.) independently reviewed the immediate post-EVT DECT images for the presence of contrast staining, ICH, SAH, or IVH, while blinded to clinical outcomes. Any discrepancies between the 2 reviewers were resolved by consensus with a third reviewer (H.S.N.). The Heidelberg Bleeding Classification on follow-up brain imaging was determined through adjudication by ≥2 stroke neurologists or neurointerventionalists during a structured data workshop. The symptomatic ICH 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 ≥4 points in the NIHSS score or resulting in death.[21]

Outcome Measures

The outcomes included a functional independence defined as modified Rankin Scale (mRS) 0 to 2 at 3 months, shift analysis of the distribution of mRS scores at 3 months, and death within 3 months. Certified medical staff collected mRS scores at 3 months in person or via telephone using a structured interview guide based on the validated Korean version of the mRS (https://k-stroke-academy.co.kr).

Blood Pressure and Delayed ICH

To evaluate the association between BP parameters and the development of delayed ICH, systolic and diastolic BP values were collected hourly from the time of DECT acquisition to immediately before follow-up brain imaging, starting with the first BP measurement recorded upon admission to the stroke unit. During this period, use of antihypertensive medications was also collected. For each patient, the initial, highest, lowest, and mean systolic and diastolic BP values were obtained. If an hourly BP value was missing, it was replaced with the closest available value measured at 15- or 30-minute intervals; if no such value was available, the data point was left as missing without imputation.

Statistical Analysis

This retrospective cohort study was conducted within a prospectively maintained registry framework. The

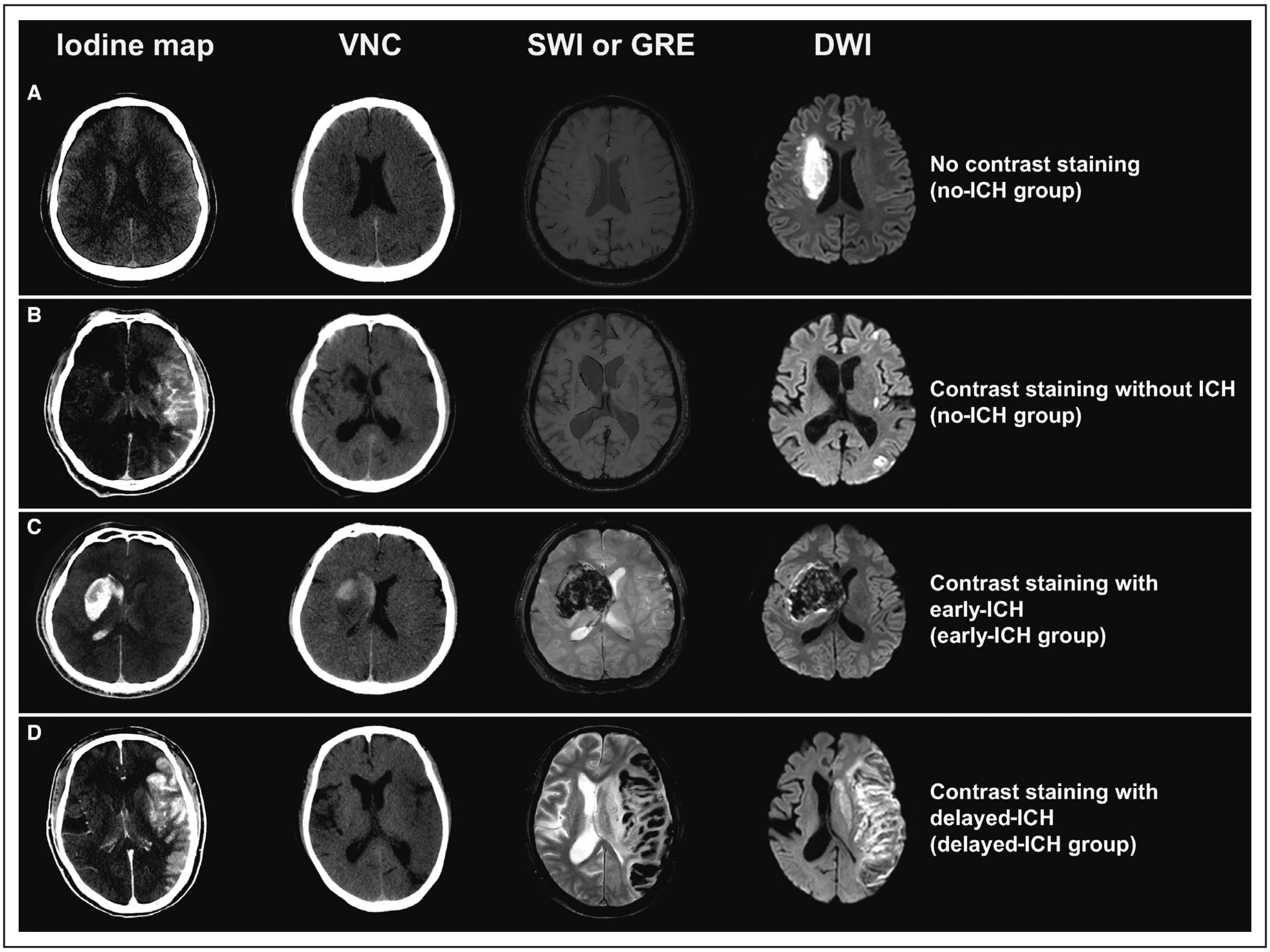

Figure 1. Imaging workflow and group definitions.
Representative cases after EVT showing the DECT iodine map and VNC images obtained immediately after the procedure, and the follow-up MRI (SWI or GRE) with DWI. **A**, No contrast staining on DECT and no hemorrhage on follow-up imaging (no-ICH group). **B**, Marked contrast staining on the iodine map without hyperdensity on the VNC image and no hemorrhage on follow-up MRI (no-ICH group). **C**, Hyperdensity compatible with hemorrhage on the VNC image with corresponding susceptibility on follow-up MRI (early-ICH group). **D**, No hyperdensity on the VNC image but new susceptibility on follow-up MRI indicating hemorrhage (delayed-ICH group). DECT indicates dual-energy computed tomography; DWI, diffusion-weighted image; EVT, endovascular thrombectomy; GRE, T2-weighted gradient echo; ICH, intracranial hemorrhage; MRI, magnetic resonance imaging; SWI, susceptibility-weighted imaging; and VNC, virtual noncontrast.

study objectives, exposure and outcome definitions, and statistical analysis plan were specified before data extraction for the present analysis on the basis of predefined registry variables and clinical considerations. Continuous variables were presented as median (interquartile range [IQR]), and categorical variables as numbers (percentages). The comparisons of clinical and radiological characteristics were performed using the Kruskal–Wallis rank-sum test, χ^2 test, or Fisher exact test as appropriate. Using the no-ICH group as the reference, the associations of the early-ICH and delayed-ICH groups with outcomes were analyzed. The mRS, used as the study outcome, is a 7-level ordinal scale ranging from 0 to 6, with higher scores indicating worse functional outcomes. For dichotomous outcome analyses, functional independence was defined as an mRS score of 0 to 2, whereas functional dependency or death was defined as an mRS score of 3 to 6. This binary outcome was analyzed using a binary logistic regression model. Separately, a shift analysis, defined as an analysis of the full ordinal distribution of mRS scores, was performed using a proportional odds (cumulative logit) regression model applied to all 7 levels of the mRS (0–6). Thus, the term *shift analysis* in this study specifically refers to the ordinal proportional odds model evaluating the full mRS distribution. The proportional odds assumption was evaluated using a likelihood ratio–based nominal test implemented in the ordinal regression framework, and no significant violation of the assumption was observed. For each regression analysis, results from the univariable model were first presented, followed by a model adjusted for demographic variables (age and sex), and finally by a fully adjusted model controlling for age, sex, hypertension, diabetes, atrial fibrillation, prestroke mRS score, NIHSS score at admission, use of intravenous tissue plasminogen activator, and the achievement of successful recanalization.[22] The adjusted odds ratios (ORs) with 95% CIs were reported. In the delayed-ICH group, associations between radiological (Heidelberg Bleeding Classification) and clinical (symptomatic or asymptomatic delayed ICH) classifications of hemorrhagic transformation and outcomes were assessed using ordinal and binary logistic regression models, adjusted for the same covariates as in the previous fully adjusted model.

To evaluate the influence of BP on delayed ICH, we conducted a subgroup analysis for the patients without early ICH. The association was analyzed using a multivariable binary logistic regression model, with covariates identical to those in the previously described fully adjusted model. Finally, to identify thresholds of mean systolic BP or highest systolic BP associated with delayed ICH, a 3-knot cubic spline analysis was performed, calculating the minimum BP threshold for each parameter that showed a significant association with delayed ICH. The spline analyses were adjusted for age, sex, hypertension, diabetes, atrial fibrillation, prestroke mRS score, NIHSS score at admission, Alberta Stroke Program Early Computed Tomography Score, presence of a good collateral state, and the achievement of successful recanalization. A 2-sided *P* value <0.05 was considered statistically significant, and all statistical analyses were conducted using R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Between May 2019 and December 2024, a total of 438 patients with acute ischemic stroke due to large-vessel occlusion underwent EVT. Of these, 84 patients were excluded due to in-hospital stroke. An additional 54 patients were excluded due to isolated anterior cerebral artery occlusion or occlusion in posterior circulation. Two patients underwent EVT twice due to recurrent stroke; for these cases, only the hospitalization data related to the first EVT were included. Among the remaining 298 patients with anterior circulation large-vessel occlusion who underwent EVT, 268 (89.9%) underwent DECT imaging and were finally included in the analysis (Figure S1).

The median age was 77.0 (IQR, 65.8–84.0) years, and 130 (44.8%) patients were women. The median NIHSS score was 13.5 (IQR, 9.0–18.0). The median time from final recanalization to DECT acquisition was 39.0 (IQR, 25.0–55.0) minutes, and the median time from DECT to follow-up imaging was 20.0 (IQR, 13.2–33.0) hours. Follow-up brain imaging was performed using MRI in 250 (93.3%) patients and CT in 18 (6.7%) patients.

Among the 268 patients included in the analysis, 32 (11.9%) had hemorrhage detected on immediate post-EVT DECT, defined as ICH, SAH, or IVH, and were assigned to the early-ICH group. Among the remaining 236 patients without hemorrhage on DECT, 99 (36.9%) demonstrated new hemorrhage on follow-up imaging and were categorized as the delayed-ICH group. The remaining 137 patients (51.1%) had no evidence of ICH on either DECT or follow-up imaging and were categorized as the no-ICH group. The no-ICH group had a lower prevalence of hypertension and higher Alberta Stroke Program Early Computed Tomography Score compared with the other study groups. In the early-ICH group, 59.4% of patients exhibited hemorrhagic transformation of parenchymal hematoma (PH), whereas in the delayed-ICH group, 65.6% showed hemorrhagic transformation of the hemorrhagic infarction (HI) type. All patients in the early-ICH group demonstrated contrast staining, and 98.0% of patients in the delayed-ICH group also showed contrast staining on DECT (Table 1). The interrater agreement between 2 raters of detecting contrast staining on the iodine map of DECT was good, with a κ score of 0.850. For identifying early ICH on VNC images, the interrater κ score was 0.850.

Early and Delayed ICH and Clinical Outcomes

Patients in the early-ICH group were significantly less likely to achieve functional independence than those in the no-ICH group (adjusted OR, 0.36 [95% CI, 0.13–0.98]; *P*=0.050). There were no significant differences between the early-ICH and no-ICH groups in the shift analysis of mRS scores at 3 months (adjusted common OR, 0.50 [95% CI, 0.25–1.00]; *P*=0.050) or in the 3-month mortality rate (adjusted OR, 0.88 [95% CI, 0.23–2.81]; *P*=0.844; Table 2 and Figure 2).

The delayed-ICH group had a significantly lower rate of achieving functional independence compared with the no-ICH group (adjusted OR, 0.49 [95% CI, 0.25–0.94]; *P*=0.034). In addition, the delayed-ICH group showed a significantly greater shift toward higher mRS scores at 3 months (adjusted common OR, 0.45 [95% CI, 0.28–0.72]; *P*=0.001). However, there was no significant difference in the 3-month mortality rate between the delayed-ICH and no-ICH groups (adjusted OR, 1.48 [95% CI, 0.70–3.18]; *P*=0.307; Table 3 and Figure 2).

To address the possibility that isolated SAH or IVH identified on DECT may subsequently progress to

Table 1. Baseline Characteristics

Variable	No ICH (n=137)	Early ICH (n=32)	Delayed ICH (n=99)	*P* value[†]
Age, median, y	76.0 (62.0–84.0)	76.0 (65.8–83.0)	80.0 (71.5–84.0)	0.108
Sex				0.361
Men	79 (57.7)	14 (43.8)	55 (55.6)	
Women	58 (42.3)	18 (56.3)	44 (44.4)	
Hypertension	95 (69.3)	29 (90.6)	81 (81.8)	0.011
Diabetes	50 (36.5)	11 (34.4)	42 (42.4)	0.575
Hyperlipidemia	52 (38.0)	12 (37.5)	39 (39.4)	0.969
Coronary artery obstructive disease	26 (19.0)	5 (15.6)	29 (29.3)	0.107
Atrial fibrillation	63 (46.0)	18 (56.3)	60 (60.6)	0.077
Congestive heart disease	6 (4.4)	2 (6.3)	3 (3.0)	0.682
Previous stroke history (n=265)	32 (23.7)	9 (29.0)	25 (25.3)	0.822
Prestroke mRS	0 (0.0–1.0)	0 (0.0–0.0)	0 (0.0–1.0)	0.424
Smoking (n=263)	19 (14.2)	4 (12.5)	16 (16.5)	0.855
Intravenous tissue plasminogen activator	50 (36.5)	14 (43.8)	30 (30.3)	0.338
NIHSS score at admission	12.0 (7.0–17.0)	15.0 (9.0–17.0)	14.0 (10.0–19.0)	0.096
Radiologic and procedural variables				
Occlusion site				0.044
M1	58 (42.3)	16 (50.0)	49 (49.5)	
M2	44 (32.1)	10 (31.3)	20 (20.2)	
Intracranial internal carotid artery	17 (12.4)	1 (3.1)	11 (11.1)	
Extracranial internal carotid artery	13 (9.5)	1 (3.1)	8 (8.1)	
Tandem occlusion	5 (3.6)	4 (12.5)	11 (11.1)	
ASPECTS	9.0 (7.0–10.0)	8.0 (6.0–9.0)	7.0 (6.0–9.0)	<0.001
Good collateral (Tan scale: 2–3)	99 (72.3)	20 (62.5)	62 (62.6)	0.240
mTICI score (immediate reperfusion)				0.842
0	9 (6.6)	1 (3.1)	4 (4.0)	
1	4 (2.9)	1 (3.1)	2 (2.0)	
2a	7 (5.1)	2 (6.3)	7 (7.1)	
2b	37 (27.0)	13 (40.6)	31 (31.3)	
2c	5 (3.6)	1 (3.1)	7 (7.1)	
3	75 (54.7)	14 (43.8)	48 (48.5)	
Successful recanalization (mTICI ≥2b)	117 (85.4)	28 (87.5)	86 (86.9)	0.968
Contrast staining on DECT	86 (62.8)	32 (100.0)	97 (98.0)	<0.001
Type of hemorrhagic transformation				<0.001
HI-1	0 (0.0)	3 (9.4)	34 (34.3)	
HI-2	0 (0.0)	2 (6.3)	31 (31.3)	
PH-1	0 (0.0)	9 (28.1)	26 (26.3)	
PH-2	0 (0.0)	10 (31.3)	8 (8.1)	
Subarachnoid hemorrhage	0 (0.0)	15 (46.9)	0 (0.0)	<0.001
Intraventricular hemorrhage	0 (0.0)	8 (25.0)	0 (0.0)	<0.001
Symptomatic ICH	0 (0.0)	12 (37.5)	12 (12.1)	<0.001
Time parameters				
Onset to puncture time, min	315.0 (175.0–615.0)	283.5 (199.3–717.0)	380.0 (220.5–706.0)	0.316
Onset to final recanalization time, min	351.0 (217.3–629.0)	370.0 (252.8–949.0)	420.0 (270.5–797.5)	0.059
Puncture to DECT time, min	89.0 (69.0–136.5)	98.5 (90.7–164.8)	83.5 (67.3–127.8)	0.071
Final recanalization to DECT time, min	40.0 (23.0–54.0)	48.0 (33.0–59.0)	32.0 (25.0–48.8)	0.088
DECT to follow-up imaging time, h	20.6 (13.4–33.7)	16.5 (12.5–34.1)	21.7 (13.3–31.6)	0.733

Values are median (IQR) or n (%). ASPECTS indicates Alberta Stroke Program Early Computed Tomography Score; DECT, dual-energy computed tomography; HI, hemorrhagic infarction; ICH, intracranial hemorrhage; IQR, interquartile range; M1, first segment of the middle cerebral artery; M2, second segment of the middle cerebral artery; mTICI, modified Treatment In Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale; and PH, parenchymal hematoma.

[†]*P* value <0.05 was considered of statistical significance.

Table 2. Comparison of Clinical Outcomes Between Early ICH and No ICH

	Early ICH (n=32)	No ICH (n=137)	Unadjusted effect size (95% CI)	*P* value	Adjusted effect size (95% CI) (model 1)*	*P* value	Adjusted effect size (95% CI) (model 2)†	*P* value
Functional independence at 3 mo (mRS score 0–2), No./total (%)	10/32 (31.3)	71/137 (51.8)	0.42 (0.18–0.94)	0.039	0.44 (0.18–1.00)	0.056	0.36 (0.13–0.98)	0.050
Shift of mRS score at 3 mo, median (IQR)	4.0 (2.0–5.0)	2.0 (1.0–5.0)	0.54 (0.28–1.05)	0.069	0.59 (0.30–1.14)	0.118	0.50 (0.25–1.00)	0.050
Mortality within 3 mo, No./total (%)	4/32 (12.5)	22/137 (16.1)	0.75 (0.21–2.15)	0.616	0.71 (0.20–2.06)	0.562	0.88 (0.23–2.81)	0.844

ICH indicates intracranial hemorrhage; IQR, interquartile range; mRS, modified Rankin Scale; and NIHSS, National Institutes of Health Stroke Scale.
*Model 1: adjusted for age and sex.
†Model 2: adjusted for age, sex, hypertension, diabetes, atrial fibrillation, prestroke mRS score, NIHSS score at admission, use of intravenous tissue plasminogen activator, and the achievement of successful recanalization.

delayed hemorrhagic transformation, we performed a sensitivity analysis in which 12 patients initially classified as early ICH with isolated SAH or IVH were reclassified. The results remained consistent with the primary analysis, with no meaningful changes in the direction or statistical significance of associations (Table S1).

Subtype of Delayed ICH and Clinical Outcomes

Among patients in the delayed-ICH group, the radiological subtype of hemorrhagic transformation was differentially associated with clinical outcomes. Patients with the HI type of delayed ICH showed a significant association with increased mRS scores (adjusted common OR, 0.52 [95% CI, 0.31–0.88]; *P*=0.017) and reduced functional independence at 3 months (adjusted OR, 0.44 [95% CI, 0.20–0.93]; *P*=0.035) compared with the no-ICH group but no significant association with the 3-month mortality rate (adjusted OR, 1.09 [95% CI, 0.42–2.70]; *P*=0.847), whereas patients with the PH type of delayed ICH demonstrated a significant association with both increased mRS scores (adjusted common OR, 0.33 [95% CI, 0.15–0.68]; *P*=0.003) and a higher 3-month mortality rate (adjusted OR, 2.66 [95% CI, 1.01–6.99]; *P*=0.046; Table 4 and Figure 3).

In an additional analysis stratifying delayed ICH by symptomatic status, asymptomatic delayed ICH was associated with reduced functional independence compared with no ICH (adjusted OR, 0.48 [95% CI, 0.24–0.94]; *P*=0.034) but was not associated with an increased 3-month mortality rate (adjusted OR, 0.92 [95% CI, 0.39–2.10]; *P*=0.841). In contrast, symptomatic delayed ICH showed a strong association with markedly worse functional outcomes (adjusted common OR, 0.09 [95% CI, 0.02–0.34]; *P*=0.001) and a

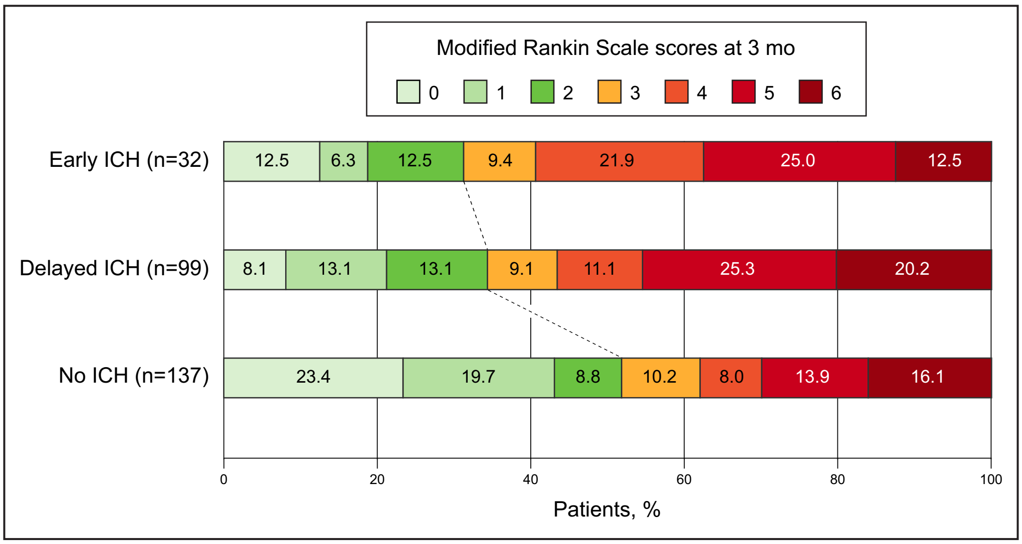

Figure 2. Distribution of mRS score according to study groups.
The mRS score ranges from 0 to 6, in which 0 denotes no symptoms (best outcome) and 6 represents death (worst outcome). This figure shows the distribution of mRS scores across the no-ICH, early-ICH, and delayed-ICH groups. ICH indicates intracranial hemorrhage; and mRS, modified Rankin Scale.

Table 3. Comparison of Clinical Outcomes Between Delayed ICH and No ICH

	Delayed ICH (n=99)	No ICH (n=137)	Unadjusted effect size (95% CI)	*P* value	Adjusted effect size (95% CI) (model 1)*	*P* value	Adjusted effect size (95% CI) (model 2)†	*P* value
Functional independence at 3 mo (mRS score 0–2), No./total (%)	34/99 (34.3)	71/137 (51.8)	0.49 (0.28–0.82)	0.008	0.53 (0.31–0.92)	0.025	0.49 (0.25–0.94)	0.034
Shift of mRS score at 3 mo, median (IQR)	4.0 (2.0–5.0)	2.0 (1.0–5.0)	0.47 (0.29–0.74)	0.001	0.49 (0.31–0.78)	0.003	0.45 (0.28–0.72)	0.001
Mortality within 3 mo, No./total (%)	20/99 (20.2)	22/137 (16.1)	1.32 (0.67–2.59)	0.412	1.36 (0.69–2.70)	0.371	1.48 (0.70–3.18)	0.307

ICH indicates intracranial hemorrhage; IQR, interquartile range; mRS, modified Rankin Scale; and NIHSS, National Institutes of Health Stroke Scale.
*Model 1: adjusted for age and sex.
†Model 2: adjusted for age, sex, hypertension, diabetes, atrial fibrillation, prestroke mRS score, NIHSS score at admission, use of intravenous tissue plasminogen activator, and the achievement of successful recanalization.

substantially higher 3-month mortality rate compared with no ICH (adjusted OR, 12.5 [95% CI, 2.93–69.1]; *P*=0.001; Table S2).

Blood Pressure and Delayed ICH

A total of 6447 time-stamped BP recordings were analyzed from the time of DECT acquisition to follow-up brain imaging. There was no significant difference in the number of BP measurements between the delayed-ICH and no-ICH groups during the observation period (delayed-ICH group: median, 20.0 [IQR, 14.0–33.0] versus no-ICH group: median, 19.0 [IQR, 14.0–32.0]; *P*=0.490); however, intravenous antihypertensives were used more frequently in the delayed-ICH group (delayed-ICH group, 54.5% versus no-ICH group, 34.3%; *P*=0.003). There were no significant differences in systolic or diastolic BP at the time of stroke unit admission between the groups. However, during the observation period, patients in the delayed ICH group had significantly higher systolic BP values, both for the highest systolic BP (median, 173.0 [IQR, 157.0–188.0] mm Hg versus 162.0 [IQR, 142.0–179.0] mm Hg; *P*=0.001) and the mean systolic BP (median, 143.8 [IQR, 129.2–152.5] mm Hg versus 135.2 [IQR, 121.0–145.9] mm Hg; *P*=0.003), compared with the no-ICH group (Table S3).

In the regression analysis evaluating the association between systolic BP during the interval between DECT and follow-up brain imaging and the occurrence of delayed ICH, systolic BP at stroke unit admission was not significantly associated with delayed ICH. However, higher highest systolic BP (per 10-mm Hg increase, adjusted OR, 1.20; 95% CI, 1.04–1.39; *P*=0.014) and higher mean systolic BP during the observation period (per 10-mm Hg increase: adjusted OR, 1.22 [95% CI, 1.02–1.48]; *P*=0.033) were significantly associated with an increased risk of

Table 4. Outcomes According to the Type of Hemorrhagic Transformation

				No ICH vs HI type			No ICH vs PH type		
Outcomes	No ICH (n=137)	HI type of delayed ICH (n=65)	PH type of delayed ICH (n=34)	Unadjusted effect size (95% CI)	Adjusted effect size (95% CI)*	*P* value	Unadjusted effect size (95% CI)	Adjusted effect size (95% CI)*	*P* value
Functional independence at 3 mo (mRS score 0–2), No./total (%)	71/137 (51.8)	25/65 (38.5)	9/34 (26.5)	0.58 (0.32–1.05)	0.44 (0.20–0.93)	0.035	0.33 (0.14–0.75)	0.65 (0.23–1.77)	0.406
Shift of mRS score at 3 mo, median (IQR)	2.0 (1.0–5.0)	3.0 (1.0–5.0)	5.0 (2.5–6.0)	0.65 (0.39–1.08)	0.52 (0.31–0.88)	0.017	0.24 (0.12–0.47)	0.33 (0.15–0.68)	0.003
Mortality within 3 mo, No./total (%)	22/137 (16.1)	9/65 (13.8)	11/34 (32.4)	0.84 (0.35–1.89)	1.09 (0.42–2.70)	0.847	2.50 (1.04–5.80)	2.66 (1.01–6.99)	0.046

HI indicates hemorrhagic infarction; ICH, intracranial hemorrhage; IQR, interquartile range; mRS, modified Rankin Scale; and PH, parenchymal hematoma.
*Multivariable analyses were adjusted for age, sex, hypertension, diabetes, atrial fibrillation, prestroke mRS score, NIHSS score at admission, use of intravenous tissue plasminogen activator, and the achievement of successful recanalization.

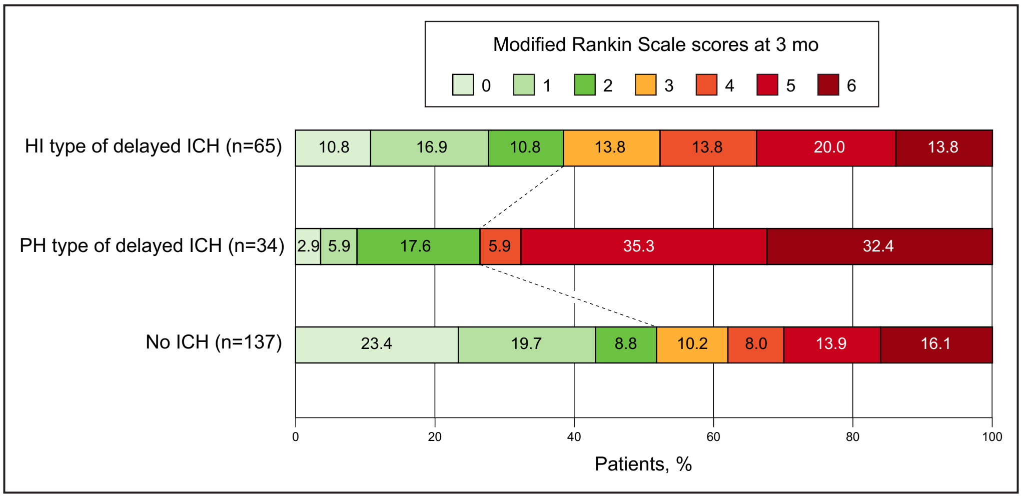

Figure 3. Distribution of mRS score according to the type of hemorrhagic transformation in delayed ICH.

The mRS score ranges from 0 to 6, in which 0 denotes no symptoms (best outcome) and 6 represents death (worst outcome). This figure shows the mRS score distribution across the no-ICH group and the delayed-ICH subtypes (HI and PH). HI indicates hemorrhagic infarction; ICH, intracranial hemorrhage; mRS, modified Rankin Scale; and PH, parenchymal hematoma.

delayed ICH (Table 5). Spline analysis demonstrated that the risk of delayed ICH increased progressively with higher systolic BP levels. The mean systolic BP measured from DECT to follow-up imaging showed a significant association with delayed ICH at values exceeding ≈150 mm Hg, while the highest systolic BP during this period became significantly associated at values >166 mm Hg (Figure S2).

DISCUSSION

In this restrospective cohort study, we demonstrated that delayed ICH, defined as new hemorrhage on follow-up imaging after a negative immediate post-EVT DECT, occurred in more than one third of patients and was >3 times more frequent than early ICH. Delayed ICH was independently associated with worse functional outcomes at 3 months, with the HI type specifically linked to a lower likelihood of functional independence and the PH type associated with poorer functional outcome and a higher mortality rate. By excluding early ICH with DECT, we identified a temporal association between postprocedural BP and delayed ICH, with both higher mean and peak systolic BP related to increased risk of delayed ICH. Notably, a mean systolic BP >150 mm Hg and a peak systolic BP >166 mm Hg were identified as thresholds associated with delayed ICH. These findings suggest that delayed ICH is a clinically meaningful complication after EVT, and delayed ICH risk can be modifiable through BP management.

In our study, delayed ICH was observed more frequently than early ICH. Considering that 37.5% (12/32) of patients in the early-ICH group had isolated SAH or IVH without hemorrhagic transformation, only 20 patients exhibited hemorrhagic transformation alone. Notably, all cases of SAH were identified exclusively in the early-ICH group, and no patients without SAH on DECT were found to have SAH on follow-up imaging. The markedly higher proportion of delayed ICH compared with early ICH may partly result from the predominant use of MRI (93.3%) as the follow-up imaging modality, which is more sensitive for detecting ICH. Nonetheless, it is also possible that this difference reflects distinct pathophysiologic mechanisms between delayed and early hemorrhagic transformation.[23]

Following ischemic stroke, injury to these tight junctions initiates blood–brain barrier breakdown, with the timing of blood product leakage varying according to the extent of damage.[24] Brain ischemia induces a time-dependent, progressive increase in microvascular permeability, allowing leakage of molecules and cellular components from the microvasculature into the extracellular space.[25] Thus, early ICH likely reflects procedure-related hemorrhage or abrupt, severe blood–brain barrier disruption, whereas delayed ICH may result from vasogenic edema secondary to progressive endothelial damage, which increases blood–brain barrier permeability and facilitates the extravasation of macromolecules and water into the interstitium.[26,27]

Table 5. Association Between Systolic BP–Related Variables and Delayed ICH

	Unadjusted effect size (95% CI)	*P* value	Adjusted effect size* (95% CI)	*P* value
Systolic BP at stroke unit admission, per 10 mm Hg	1.04 (0.94–1.15)	0.433	0.99 (0.88–1.11)	0.872
Highest systolic BP from stroke unit to follow-up imaging, per 10 mm Hg	1.21 (1.07–1.36)	0.002	1.20 (1.04–1.39)	0.014
Lowest systolic BP from stroke unit to follow-up imaging, per 10 mm Hg	1.16 (1.00–1.36)	0.062	1.10 (0.92–1.31)	0.300
Mean systolic BP from stroke unit to follow-up imaging, per 10 mm Hg	1.25 (1.08–1.46)	0.003	1.22 (1.02–1.48)	0.033

BP indicates blood pressure; and ICH, intracranial hemorrhage; and NIHSS, National Institutes of Health Stroke Scale.
*Multivariable analyses were adjusted for age, sex, hypertension, diabetes, atrial fibrillation, prestroke mRS score, NIHSS score at admission, Alberta Stroke Program Early Computed Tomography Score; presence of a good collateral state, and the achievement of successful recanalization.

We found that a large proportion of delayed ICH consisted of the HI type of hemorrhagic transformation, and the associations with functional independence and death differed between the HI and PH types. The clinical significance of HI-type hemorrhagic transformation has been debated, with some earlier studies suggesting a benign course.[28,29] However, a recent multicenter study investigating post-alteplase hemorrhages found that HI-type hemorrhage was also associated with poor functional outcomes.[30] Other multicenter studies similarly reported that, among hemorrhagic transformation after EVT, the HI-type was associated with poor functional outcomes.[31,32] In line with these findings, our study demonstrated that HI-type hemorrhagic transformation in the delayed-ICH group was associated with poor functional outcomes, suggesting that caution is warranted against considering HI-type hemorrhagic transformation clinically insignificant. In contrast, PH-type hemorrhagic transformation was more strongly associated with both mRS score at 3 months and death, which is consistent with its definition including mass effect. Similarly, not only symptomatic delayed ICH but also asymptomatic delayed ICH was associated with poor functional outcomes. Given the observed association between delayed ICH and poor functional outcomes, further research is warranted to identify therapeutic strategies that could reduce the incidence of delayed ICH after EVT.

Even when early post-EVT CT imaging excludes ICH, the initiation of antithrombotic agents is generally delayed until follow-up brain imaging at ≈24 hours. Although not explicitly recommended in current guidelines, this is a common clinical practice.[7] During this interval, BP management becomes the primary focus of post-EVT care, and 6 recent randomized controlled trials have addressed this issue.[13–18] However, intensive BP lowering to systolic BP targets of <140 mm Hg or <120 mm Hg was associated with poorer functional outcomes and showed no significant relationship with symptomatic ICH.[13,15] Because the participating centers in these trials used different imaging protocols and varied in whether DECT was performed immediately after EVT, it is difficult to determine whether the ICH identified in these trials corresponds to early ICH or delayed ICH as defined in our study. In other words, while ICH occurring immediately after EVT is unlikely to be influenced by postprocedural BP management, delayed ICH may be more closely related to post-EVT BP levels. In our study, early ICH was excluded in each patient by DECT immediately after EVT, and BP management was assessed individually for the interval until follow-up brain imaging, during which the occurrence of delayed ICH was determined. This design enabled us to demonstrate a clear temporal association between BP levels and delayed ICH. Higher BP values were associated with an increased risk of delayed ICH, with a particularly significant association observed for peak systolic BP >166 mm Hg. This finding indicates that a systolic BP threshold of 166 mm Hg may serve as a clinically meaningful safety margin in preventing delayed ICH. Further prospective clinical trials that include DECT may clearly show the influence of BP management on outcome.

Across 6 randomized clinical trials of post-EVT BP management, no significant difference in symptomatic ICH was observed between intensive and conventional BP strategies.[13–18] However, in these trials, the conventional BP management groups generally targeted systolic BP between 180 and 185 mm Hg, while the actual mean systolic BP during the first 24 hours was around 140 mm Hg, with only about a 10-mm Hg difference compared with intensive BP management groups. This narrow separation raises the possibility that at higher systolic BP levels, an increased risk of ICH, as suggested by our findings, may become evident. This interpretation is further supported by an individual patient data meta-analysis of 5874 patients, which demonstrated a linear increase in the risk of symptomatic ICH with higher mean systolic BP during the first 24 hours after EVT.[33]

Apart from the inherent limitations of being a single-center retrospective study, there are several limitations. First, although DECT can distinguish contrast staining from hemorrhage and improves early ICH detection compared with routine CT, its sensitivity remains lower than MRI with susceptibility-weighted imaging or T2-weighted gradient echocardiographic sequences; thus, false negatives are possible. MRI, however, is rarely feasible immediately after EVT due to the longer acquisition time and the need for continuous monitoring. Second, restricting the study population to patients who underwent DECT may have introduced selection bias. Nevertheless, as 90% of consecutive patients underwent DECT according to our protocol, the likelihood of substantial selection bias was minimized. Third, the timing of follow-up MRI varied, potentially increasing ICH detection in patients imaged later, and the exact onset of hemorrhage could not be determined. To maintain temporal validity, BP data were analyzed only up to the last pre-ICH measurement, but precise hemorrhage timing remains difficult to establish without serial imaging. Fourth, we did not assess individualized BP targets or BP variability, and hourly BP recordings may have missed interim fluctuations. Fifth, because delayed ICH events were relatively infrequent in the spline analysis, the wide CIs limit model stability, and the findings should be interpreted as exploratory. Finally, the small size of the early-ICH group reduced statistical power, limiting the ability to detect significant associations despite a similar mRS distribution to that of the delayed-ICH group.

CONCLUSIONS

Among patients who underwent EVT for acute ischemic stroke, delayed ICH was a common and clinically significant complication independently linked to poor functional outcomes. The temporal link between elevated postprocedural systolic BP and delayed ICH suggests that delayed ICH is not merely an imaging finding but a potentially preventable event through tailored BP management.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Tables S1–S3
Figures S1–S2
STROBE Checklist

REFERENCES

1. Hao Y, Zhang Z, Zhang H, Xu L, Ye Z, Dai Q, Liu X, Xu G. Risk of intracranial hemorrhage after endovascular treatment for acute ischemic stroke: systematic review and meta-analysis. *Interv Neurol*. 2017;6:57–64. doi: 10.1159/000454721
2. van der Steen W, van der Ende NA, van Kranendonk KR, Chalos V, Brouwer J, van Oostenbrugge RJ, van Zwam WH, van Doormaal PJ, van Es AC, Majoie CB, et al. Timing of symptomatic intracranial hemorrhage after endovascular stroke treatment. *Eur Stroke J*. 2022;7:393–401. doi: 10.1177/23969873221112279
3. Chen H, Bodanapally UK, Colasurdo M, Malhotra A, Gandhi D. Clinical applications of dual-energy computed tomography for acute ischemic stroke. *Stroke Vasc Interv Neurol*. 2024;4:e001193. doi: 10.1161/SVIN.123.001193
4. Baik M, Cha J, Ahn SS, Lee S-K, Kim YD, Nam HS, Jeon S, Lee HS, Heo JH. Dual-energy computed tomography quantification of extravasated iodine and hemorrhagic transformation after thrombectomy. *J Stroke*. 2022;24:152–155. doi: 10.5853/jos.2021.03391
5. Bonatti M, Lombardo F, Zamboni GA, Vittadello F, Currò Dossi R, Bonetti B, Pozzi Mucelli R, Bonatti G. Iodine extravasation quantification on dual-energy CT of the brain performed after mechanical thrombectomy for acute ischemic stroke can predict hemorrhagic complications. *Am J Neuroradiol*. 2018;39:441–447. doi: 10.3174/ajnr.A5513
6. Heo J, Yoon Y, Han HJ, Kim JJ, Park KY, Kim BM, Kim DJ, Kim YD, Nam HS, Lee SK, et al. Prediction of cerebral hemorrhagic transformation after thrombectomy using a deep learning of dual-energy CT. *Eur Radiol*. 2024;34:3840–3848. doi: 10.1007/s00330-023-10432-6
7. Jadhav AP, Molyneaux BJ, Hill MD, Jovin TG. Care of the post-thrombectomy patient. *Stroke*. 2018;49:2801–2807. doi: 10.1161/STROKEAHA.118.021640
8. Liu F, Anderson CS. Blood pressure management pre- and post-reperfusion in acute ischemic stroke: evidence and insights from recent studies. *Curr Neurol Neurosci Rep*. 2025;25:52. doi: 10.1007/s11910-025-01443-5
9. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, et al. Guidelines for the early Management of Patients with Acute Ischemic Stroke: 2019 update to the 2018 guidelines for the early Management of Acute Ischemic Stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2019;50:e344–e418. doi: 10.1161/STR.0000000000000211
10. Sandset EC, Anderson CS, Bath PM, Christensen H, Fischer U, Gąsecki D, Lal A, Manning LS, Sacco S, Steiner T, et al. European stroke organisation (ESO) guidelines on blood pressure management in acute ischaemic stroke and intracerebral haemorrhage. *Eur Stroke J*. 2021;6:li. doi: 10.1177/23969873211026998
11. Writing Committee M, Jones DW, Ferdinand KC, Taler SJ, Johnson HM, Shimbo D, Abdalla M, Altieri MM, Bansal N, Bello NA, et al. 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM guideline for the prevention, detection, evaluation and Management of High Blood Pressure in adults: a report of the American College of Cardiology/American Heart Association joint Committee on clinical practice guidelines. *Hypertension*. 2025;82:e212–e316. doi: 10.1161/HYP.0000000000000249
12. Jeong HS, Park H-K, Park J-M, Ko S-B, Seo W-K, Heo SH, Oh MS, Kim J-T, Lee H-Y, Park S, et al. Update of the Korean clinical practice

guidelines for stroke: blood pressure management. *J Clin Neurol*. 2025;21:370–383. doi: 10.3988/jcn.2025.0177
13. Nam HS, Kim YD, Heo J, Lee H, Jung JW, Choi JK, Lee IH, Lim IH, Hong SH, Baik M, et al. Intensive vs conventional blood pressure lowering after endovascular thrombectomy in acute ischemic stroke: the OPTIMAL-BP randomized clinical trial. *JAMA*. 2023;330:832–842. doi: 10.1001/jama.2023.14590
14. Mistry EA, Hart KW, Davis LT, Gao Y, Prestigiacomo CJ, Mittal S, Mehta T, LaFever H, Harker P, Wilson-Perez HE, et al. Blood pressure management after endovascular therapy for acute ischemic stroke: the BEST-II randomized clinical trial. *JAMA*. 2023;330:821–831. doi: 10.1001/jama.2023.14330
15. Yang P, Song L, Zhang Y, Zhang X, Chen X, Li Y, Sun L, Wan Y, Billot L, Li Q, et al. Intensive blood pressure control after endovascular thrombectomy for acute ischaemic stroke (ENCHANTED2/MT): a multicentre, open-label, blinded-endpoint, randomised controlled trial. *Lancet*. 2022;400:1585–1596. doi: 10.1016/S0140-6736(22)01882-7
16. Mazighi M, Richard S, Lapergue B, Sibon I, Gory B, Berge J, Consoli A, Labreuche J, Olivot JM, Broderick J, et al. Safety and efficacy of intensive blood pressure lowering after successful endovascular therapy in acute ischaemic stroke (BP-TARGET): a multicentre, open-label, randomised controlled trial. *Lancet Neurol*. 2021;20:265–274. doi: 10.1016/S1474-4422(20)30483-X
17. Zhang X, Cao L, Wu S, Wang D, Wang H, Zhang D, Wang J, Chen L, Lin X, Qian D, et al. Early intensive blood pressure management after endovascular treatment in ischaemic stroke (IDENTIFY): a multicentre, open-label, blinded-endpoint, randomised controlled trial. *Lancet Reg Health West Pac*. 2025;59:101589. doi: 10.1016/j.lanwpc.2025.101589
18. Katsanos AH, Catanese L, Sahlas DJ, Srivastava A, Veroniki AA, Perera K, Ng KKH, Joundi R, Van Adel B, Larrazabal R, et al. Blood pressure management following endovascular stroke treatment: a feasibility trial and meta-analysis of outcomes. *Stroke Vasc Interv Neurol*. 2024;4:e001287. doi: 10.1161/SVIN.123.001287
19. Ko S-B, Park H-K, Kim BM, Heo JH, Rha J-H, Kwon SU, Kim JS, Lee B-C, Suh SH, Jung C, et al. 2019 update of the Korean clinical practice guidelines of stroke for endovascular recanalization therapy in patients with acute ischemic stroke. *J Korean Neurol Assoc*. 2020;38:77–87. doi: 10.17340/jkna.2020.2.1
20. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ*. 2007;335:806–808. doi: 10.1136/bmj.39335.541782.AD
21. Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, Larrue V, Lees KR, Medeghri Z, Machnig T, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med*. 2008;359:1317–1329. doi: 10.1056/NEJMoa0804656
22. Chen, J-H, Su, I-C, Lu, Y-H, Hsieh, Y-C, Chen, C-H, Lin, C-J, Chen, Y-W, Lin, K-H, Sung, P-S, Tang, C-W, et al. Predictive modeling of symptomatic intracranial hemorrhage following endovascular thrombectomy: insights from the nationwide TREAT-AIS registry. *J Stroke*. 2025;27:85–94. doi: 10.5853/jos.2024.04119
23. Álvarez-Sabín J, Maisterra O, Santamarina E, Kase CS. Factors influencing haemorrhagic transformation in ischaemic stroke. *Lancet Neurol*. 2013;12:689–705. doi: 10.1016/S1474-4422(13)70055-3
24. Renú A, Amaro S, Laredo C, Román LS, Llull L, Lopez A, Urra X, Blasco J, Oleaga L, Chamorro Á. Relevance of blood–brain barrier disruption after endovascular treatment of ischemic stroke. *Stroke*. 2015;46:673–679. doi: 10.1161/STROKEAHA.114.008147
25. Hamann GF, Okada Y, del Zoppo GJ. Hemorrhagic transformation and microvascular integrity during focal cerebral ischemia/reperfusion. *J Cereb Blood Flow Metab*. 1996;16:1373–1378. doi: 10.1097/00004647-199611000-00036
26. Khatri R, McKinney AM, Swenson B, Janardhan V. Blood–brain barrier, reperfusion injury, and hemorrhagic transformation in acute ischemic stroke. *Neurology*. 2012;79:S52–S57. doi: 10.1212/WNL.0b013e3182697e70
27. Heo JH, Han SW, Lee SK. Free radicals as triggers of brain edema formation after stroke. *Free Radic Biol Med*. 2005;39:51–70. doi: 10.1016/j.freeradbiomed.2005.03.035
28. Paciaroni M, Agnelli G, Corea F, Ageno W, Alberti A, Lanari A, Caso V, Micheli S, Bertolani L, Venti M, et al. Early hemorrhagic transformation of brain infarction: rate, predictive factors, and influence on clinical outcome. *Stroke*. 2008;39:2249–2256. doi: 10.1161/STROKEAHA.107.510321
29. Lei C, Wu B, Liu M, Chen Y. Asymptomatic hemorrhagic transformation after acute ischemic stroke: is it clinically innocuous? *J Stroke Cerebrovasc Dis*. 2014;23:2767–2772. doi: 10.1016/j.jstrokecerebrovasdis.2014.06.024
30. Wang Y, Maeda T, You S, Chen C, Liu L, Zhou Z, Robinson TG, Lindley RI, Delcourt C, Mair G, et al. Patterns and clinical implications of hemorrhagic transformation after thrombolysis in acute ischemic stroke. *Neurology*. 2024;103:e210020. doi: 10.1212/WNL.0000000000210020
31. van Kranendonk KR, Treurniet KM, Boers AMM, Berkhemer OA, van den Berg LA, Chalos V, Lingsma HF, van Zwam WH, van der Lugt A, van Oostenbrugge RJ, et al. Hemorrhagic transformation is associated with poor functional outcome in patients with acute ischemic stroke due to a large vessel occlusion. *J Neurointerv Surg*. 2019;11:464–468. doi: 10.1136/neurintsurg-2018-014141
32. Zhou Y, Zhang L, Cavalcante F, Suzuki K, Treurniet KM, Yan B, Mitchell P, Bush S, Fischer U, Kaesmacher J, et al. Intracranial hemorrhage in patients with stroke after endovascular treatment with or without IV Alteplase: an individual participant data meta-analysis. *JAMA Neurol*. 2025;82:1031–1039. doi: 10.1001/jamaneurol.2025.2610
33. Katsanos AH, Malhotra K, Ahmed N, Seitidis G, Mistry EA, Mavridis D, Kim JT, Veroniki AA, Maier I, Matusevicius M, et al. Blood pressure after endovascular thrombectomy and outcomes in patients with acute ischemic stroke: an individual patient data meta-analysis. *Neurology*. 2022;98:e291–e301. doi: 10.1212/wnl.0000000000013049