International Journal of Stroke
WSO

International Journal of Stroke
1–12

DOI: 10.1177/17474930251367867
journals.sagepub.com/home/wso
Sage

Clinical and safety outcomes following endovascular treatment for large ischemic core stroke with Alberta Stroke Program Early Computed Tomography Score 3–5 in the 12-to 24-h time window

Trung Quoc Nguyen[1,2], Khang Vinh Nguyen[3], Hang Thi Minh Tran[4], Binh Nguyen Pham[1], Anh Le Tuan Truong[1,4], Thien Quang Le[5], Hai Quang Duong[5], Trung Thanh Nguyen[5], Binh Thi Thanh Do[5], Lanh Chi Nguyen[6], Duc Tan Ha[6], Tran Tran Ngoc Nguyen[6], Dung Tri Bach[3], Nhi Thanh Nguyen[1], Vu Thanh Tran[7], Tra Vu Son Le[7], Huy Quoc Do[7], Huong Thi Bich Nguyen[1], Huy Quoc Huynh[1], Huy Quang Dang[1], Duc Nguyen Chiem[1], Thai Nguyen Thanh Pham[1], Hanh Thi My Doan[1], Dinh Chau Bao Hoang[8], Trinh Thi Kim Ngo[9], Hung Minh Dang[10], Bang Phan[11], Yimin Chen[12], Thanh N Nguyen[13], Thang Ba Nguyen[2,3*] and Thang Huy Nguyen[1,4*]

Abstract

Introduction: Although the efficacy and safety of endovascular treatment (EVT) for large-core ischemic stroke have been proven, most trials used perfusion imaging or included early-window patients, limiting generalizability to the late window, particularly in developing countries.

Aim: We aimed to evaluate the safety and functional outcomes of EVT in large-core stroke patients treated between 12 and 24 h (late window) from last known well (LKW).

Methods: We conducted a prospective, multicenter observational study across four comprehensive stroke centers in Vietnam, enrolling consecutive patients who underwent EVT within 24 h of symptom onset between August 2023 and September 2024. Large core was defined by an Alberta Stroke Program Early CT Score (ASPECTS) of 3 to 5 on non-contrast computerized tomography (NCCT) or diffusion-weighted magnetic resonance imaging (DWI-MRI). Patients who underwent EVT within 12–24 h after LKW were compared to those treated before 12 h (early window). Primary and safety outcomes were independent ambulation (90-day modified Rankin scale (mRS) = 0–3) and symptomatic intracranial hemorrhage (sICH). Secondary outcomes were 90-day mRS 0–2, ordinal mRS, successful reperfusion (modified Thrombolysis in Cerebral Infarction score ⩾2b, early neurological deterioration (END)), and 90-day mortality.

Results: Of 1872 patients receiving EVT, 343 with large ischemic cores (median age = 64.0 years, 33.8% female) were included, with 103 (30.0%) treated in the 12- to 24-h window. Compared to early-window patients, late-window patients had lower rates of intravenous thrombolysis (2.9% vs. 32.9%, $p < 0.001$), higher brain MRI use (51.5% vs. 16.2%, $p < 0.001$), and longer pre-treatment imaging-to-groin puncture times (106 vs. 77 min, $p < 0.001$). After adjusting for confounders, there were no significant differences in 90-day mRS 0–3 (56.3% vs. 55.0%, adjusted odds ratio (aOR) = 0.71, 95% confidence interval (CI) = 0.39–1.28, $p = 0.26$), ordinal mRS (aOR = 1.21, 95% CI = 0.78–1.90, $p = 0.39$), and sICH (aOR = 1.12, 95% CI = 0.32–3.50, $p = 0.85$). Other secondary outcomes were also similar.

Conclusion: In patients with anterior circulation large vessel occlusion stroke and low ASPECTS, EVT at 12–24 h versus <12 h from symptom onset showed no significant differences in clinical or safety outcomes. Larger trials are needed to confirm these findings, especially in developing regions.

Keywords
Stroke, large core, low ASPECTS, >12-h time window, late window, fast progression, endovascular treatment

Received: 2 January 2025; accepted: 12 July 2025

Introduction

Endovascular treatment (EVT) for acute stroke due to large vessel occlusion (LVO) is a highly effective therapy in select patients.[1] Through the years, the indications for EVT have progressively expanded.[2,3] Recent clinical trials demonstrated the efficacy and safety of EVT in treating patients with large ischemic core presenting within 24 h of symptom onset.[4–9]

The LArge Stroke Therapy Evaluation (LASTE) trial demonstrated the efficacy and safety of EVT for acute, unrestricted large ischemic core patients when performed within 6.5 h of symptom onset, predominantly (82.4%) using MRI for patient selection.[7] Similarly, the RESCUE-Japan LIMIT trial randomized patients either within 6 h of the last-known time of being well or within 6 to 24 h after the patient was last known to be normal, with no signal change on the fluid-attenuated inversion recovery (FLAIR) image, suggesting that patients were presenting within an early onset period. There were only 12 EVT cases who were beyond 12 h in RESCUE-Japan LIMIT.[4]

Other trials, such as SELECT 2 and ANGEL-ASPECT, employed computed tomography angiography (CTA) and computed tomography perfusion (CTP) to select patients within 24 h of onset, but these methods pose challenges for routine practice.[5,6,10] In addition, the SELECT 2 and ANGEL-ASPECT trials incorporated CTP in ASPECTS (Alberta Stroke Program Early CT Score) scoring, which may introduce bias when ASPECTS is assessed solely with non-contrast CT (NCCT).[5,6] On the contrary, the TENSION trial relied mainly on NCCT for ASPECTS scoring, focusing on patients for EVT within 12 h of symptom onset. TENSION provides strong evidence proving the clear benefit of EVT up to 12 h from symptom onset in large-core patients, although the median (interquartile range, IQR) time of onset of patients randomized in TENSION was 2 (1.2–3.6) h.[8] Inconsistent findings emerged from the TESLA trial, which used NCCT for ASPECTS scoring and selected patients within 24 h of onset.[10] The TESLA trial showed neutral results, raising uncertainties regarding the effectiveness of EVT in the 12- to 24-h time window for large-core stroke patients.[10] This suggests that while the benefit of EVT in the early window (up to 12 h) is well-supported, the evidence for EVT in the late window (12–24 h) remains inconclusive, with limited data.

For large-core stroke trials, only ANGEL-ASPECT was conducted in an upper-middle-income country, while the other trials were conducted in developed countries.[4–8,10] In addition, the stroke incidence in developing countries tends to occur at a younger age compared to developed regions.[11]

[1]Department of Cerebrovascular Disease, 115 People's Hospital, Ho Chi Minh City, Vietnam
[2]University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam
[3]Department of Neurology, University Medical Center HCMC, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam
[4]Pham Ngoc Thach University of Medicine, Ho Chi Minh City, Vietnam
[5]Stroke Department, Da Nang Hospital, Da Nang, Vietnam
[6]Stroke Center, Can Tho Central Hospital, Can Tho, Vietnam
[7]Department of Neurointervention, 115 People's Hospital, Ho Chi Minh City, Vietnam
[8]Department of Neurology, Tam Anh Hospital, Ho Chi Minh City, Vietnam
[9]Faculty of Medicine, Nguyen Tat Thanh University, Ho Chi Minh City, Vietnam
[10]Department of Neurology, Trung Vuong Hospital, Ho Chi Minh City, Vietnam
[11]Department of Internal Medicine, Buon Ma Thuot University Medical Hospital, Buon Ma Thuot, Vietnam
[12]Department of Neurology, Nanfang Hospital, Southern Medical University, Guangzhou, China
[13]Department of Neurology, Boston Medical Center, Boston University Chobanian and Avedisian School of Medicine, Boston, MA, USA

*Authors have made an equal contribution to this paper.

Corresponding author:
Thang Huy Nguyen, Department of Cerebrovascular Disease, 115 People's Hospital, 527 Su Van Hanh Street, District 10, Ho Chi Minh City 700000, Vietnam.
Email: nguyenhuythang115@gmail.com

Pre-hospital and in-hospital delays in stroke care are also common, further complicating clinical decision-making in resource-limited settings.[12] This raises critical questions regarding whether EVT should be offered to large-core patients beyond 12 h from symptom onset, particularly in developing countries where healthcare resources are constrained.[13]

To address these uncertainties, our study aimed to compare the clinical outcomes of large ischemic core stroke patients who underwent EVT within two distinct time windows: 12–24 h (late window) and <12 h (early window) post-symptom onset. Patients were selected based on an ASPECTS of 3–5, and the study was conducted across four comprehensive stroke centers in Vietnam.

Methods

Study design and patient enrollment

We conducted a prospective, multicenter, observational study in Vietnam involving four comprehensive stroke centers, screening consecutive patients who underwent EVT within 24 h of symptom onset from August 2023 to September 2024. Large ischemic core was defined by an ASPECTS of 3–5 on NCCT or diffusion-weighted magnetic resonance imaging (DWI-MRI) and was assessed by two ASPECTS-certified stroke neurologists (www.letsgetproof.com), with disagreements resolved by a senior reader. An ASPECTS region was considered abnormal if more than 30% of its area, or a confluent region, exhibited restricted diffusion or hypoattenuation on NCCT.[14] The RAPID AI software (iSchemaView, Menlo Park, CA, USA) was used to evaluate the core and penumbra of acute stroke patients when perfusion imaging was performed. The following inclusion criteria were applied, which are consistent with routine treatment criteria for EVT: presentation to our neuroangiography lab within 24 h after last-known well time; age ⩾18 years; pre-stroke mRS score of 0–2; National Institutes of Health Stroke Scale (NIHSS) ⩾6; had CTA/MRA (magnetic resonance angiography) evidence of a LVO (internal carotid artery (ICA), M1 or proximal M2 segments of middle cerebral artery, or tandem occlusion). The exclusion criteria were as follows: symptom onset beyond 24 h, multiple or bilateral ischemic strokes, anterior distal anterior cerebral artery occlusion or acute vertebrobasilar artery occlusion, severe or end-stage medical conditions, severe coagulation disorders, and inability to provide consent or follow-up. The decision for EVT was made by a treating physician according to the hospital protocol.

The primary outcome was the 90-day functional ambulation rate, defined as an mRS score of 0–3. Safety outcomes were defined as sICH (symptomatic intracerebral hemorrhage), PH2 (parenchymal hemorrhage type 2), any hemorrahge according to the safe implementation of thrombolysis in stroke-monitoring study (SITS-MOST) criteria, the mortality rate and early neurological deterioration (END). Secondary outcomes included functional independence (mRS of 0–2), mRS shift analysis, and rates of successful reperfusion (modified thrombolysis in cerebral infarction (mTICI 2b–3)). Stroke etiologies were defined based on the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria.[15]

END was specified as an increase in the NIHSS score by ⩾4 points within 24 h after EVT. Good collateral status was defined using the Tan et al.[16] score, which classifies collaterals as "good" if they are seen in ⩾50% of the middle cerebral artery territory based on CTA, or if the hypoperfusion index is <0.4 based on MRI perfusion.[17] In cases with MRI, collateral status was scored using the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) collateral scale based on DSA (Digital subtraction angiography). Grades 0–1, 2, and 3–4 are typically regarded as poor, moderate, and good collateral flow, respectively.[18] The follow-up assessment with the mRS at 90 days was conducted either via telephone or during outpatient visits.

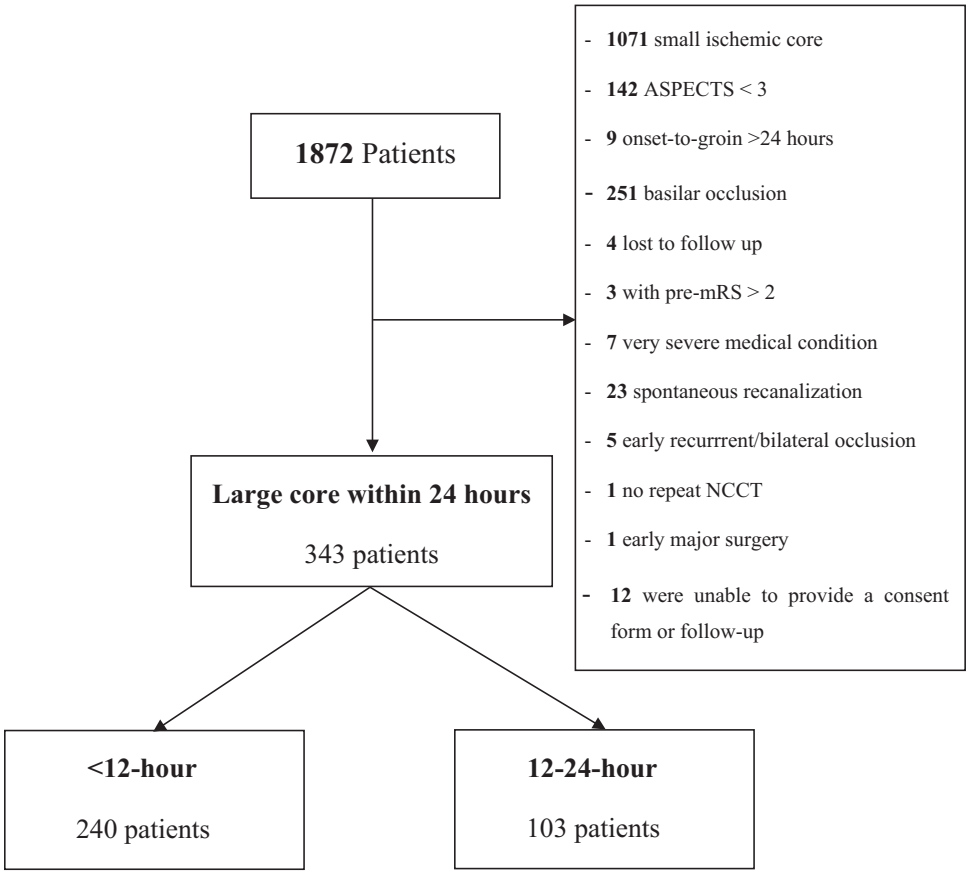
Our study was approved by the Research Ethics Committee of the University of Medicine and Pharmacy at Ho Chi Minh City (reference no. 939/HĐĐĐ-ĐHYD), and ethics approval was obtained from each participating site prior to patient enrollment. Informed consent was obtained from patients or their caregivers before inclusion in the study. This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines and was registered in clinicaltrials.gov under the identifier NCT06016348.

Statistical analysis

Descriptive statistics were used to analyze and compare baseline characteristics, treatment variables, and functional outcomes. Categorical variables were analyzed using the chi-square test or Fisher's exact test, as appropriate. Continuous variables were assessed using the Wilcoxon rank-sum test or the *t*-test, depending on the data distribution. Continuous data are presented as mean (standard deviation) or median (IQR), based on distribution characteristics.

We adjusted regression analyses for key baseline and potential pathophysiological covariates that could influence patient outcomes: age, sex, diabetes, hypertension, atrial fibrillation (AF), pre-stroke mRS, NIHSS, ASPECTS, occlusion site, pre-treatment imaging-to-groin time, and imaging modality (CT or MRI).[19,20] Binary logistic regression was used to compare the odds of achieving mRS 0–3 at 90 days, as well as safety and secondary outcomes. Ordinal logistic regression was used to assess shifts across

Figure 1. Flowchart of patients' selection.



ASPECTS: Alberta Stroke Program Early CT Score; pre-mRS: pre-stroke Modified Rankin Score; NCCT: Non-Contrast Computed Tomography.

the full mRS distribution between groups. Odds ratios, 95% confidence intervals, and corresponding p-values were calculated. In addition, we assessed the heterogeneity of the late-window effect size on independent ambulation (mRS = 0–3) at 90 days in pre-specified subgroups: age group, collateral status (good vs. bad),[21] imaging modalities (CT or MRI),[22] ASPECTS (4–5 and 3),[23] and sICH or PH2 to highlight differences in our population.

The Cochran–Armitage trend test was used to assess trends in mRS proportional distribution differences between the treatment window groups, as well as trends in independent ambulation at 90 days and mRS 5–6 at 90 days between age groups. The Fisher exact test was used to assess differences in functional ambulation across stroke center sites. The adjusted distribution of mRS by collateral status (good vs. poor) and ASPECTS (4–5 vs. 3) was compared using ordinal logistic regression. All analyses were conducted using RStudio (Version 2024.12.0.467), with a p-value of <0.05 considered statistically significant.

Results

Study population

From 1872 patients screened, 1071 patients were excluded due to small ischemic core, 251 due to acute vertebrobasilar artery occlusion. After removal of patients with other exclusion criteria, 343 patients with large ischemic core ASPECTS of 3–5 were included in this study, of whom 103 (30.03%) had symptom onset to groin puncture in the late window (12–24 h) (Figure 1). Both groups had similar age distributions, with median ages (64 [55.5–68] vs. 64 [54.8–70.2], $p=0.59$), mean ages (61.7 (standard deviation (SD): 11.7) vs. 62.8 (SD: 12.7), $p=0.43$), proportion of females (27.2% vs. 36.7%, $p=0.09$), NIHSS scores (16 [13–21] vs. 18 [14.0–22.0], $p=0.32$), pre-mRS scores, and comorbidity profiles, indicating a well-matched baseline. There was a higher frequency of MRI (51.5% vs. 16.2%, $p<0.001$) or perfusion MRI (42.7% vs. 8.75%, $p<0.001$) performed in the late-window group. In addition, significant differences were observed in time metrics. The median onset-to-arrival

Table 1. Baseline characteristics of ASPECTS 3–5 patients undergoing endovascular treatment by time to treatment: 12–24 h vs. <12 h.

	All (n = 343)	Symptom onset 12–24 h (n = 103)	Symptom onset <12 h (n = 240)	p
Age, median (IQR)	64.0 (55.0-70.0)	64.0 (55.5-68.0)	64.0 (54.8-70.2)	0.59
Female sex—no. (%)	116 (33.8)	28 (27.2)	88 (36.7)	0.09
Diabetes (%)	76 (22.2)	20 (19.4)	56 (23.3)	0.42
Hypertension (%)	297 (86.6)	93 (90.3)	204 (85.0)	0.19
AF (%)	95 (27.7)	23 (22.3)	72 (30.0)	0.15
Prior stroke (%)	58 (16.9)	16 (15.5)	42 (17.5)	0.66
Pre-stroke modified Rankin scale—no. (%)				
0 (%)	298 (86.9)	90 (87.4)	208 (86.7)	0.865
1 (%)	25 (7.29)	8 (7.77)	17 (7.08)	
2 (%)	20 (5.83)	5 (4.85)	15 (6.25)	
NIHSS				
Median (IQR)	17 (13.0-22.0)	16.0 (13.0-21.0)	18.0 (14.0-22.0)	0.32
Range	6-34	6-34	6-29	
Transfer status				
Transfer (%)	185 (53.9)	64 (62.1)	121 (50.4)	0.046
Direct admission (%)	158 (46.1)	39 (37.9)	119 (49.6)	
Prior intravenous alteplase (%)	82 (23.9)	3 (2.91)	79 (32.9)	<0.001
Mode of onset:				
Wake-up stroke, n (%)	88 (25.7)	62 (60.2)	26 (10.8)	
Unwitnessed onset, n (%)	33 (9.91)	13 (12.6)	21 (8.75)	<0.001
Witnessed onset, n (%)	221 (64.4)	28 (27.2)	193 (80.4)	
ASPECTS				
Median (IQR)	4.0 (4.0-5.0)	4.0 (4.0-5.0)	4.0 (3.0-5.0)	1.00
3	84 (24.5)	22 (21.4)	62 (25.8)	
4	113 (33.2)	40 (38.8)	74 (30.8)	0.34
5	145 (42.3)	41 (39.8)	104 (43.3)	
Glucose level (mmol/L) (IQR)	6.4 (5.4-8.0)	5.95 (5.19-6.99)	6.64 (5.53-8.18)	0.002
Imaging modality:				
NCCT-CTA, n (%)	251 (73.2)	50 (48.5)	201 (83.8)	<0.001
MRI, n (%)	92 (26.8)	53 (51.5)	39 (16.2)	
MRI perfusion, n (%)	65 (19.0)	44 (42.7)	21 (8.75)	<0.001
Core (mL) (IQR)	56.0 (42.0-75.0)	56.5 (42.8-77.5)	56.0 (40.0-70.0)	0.89

(Continued)

Table 1. (Continued)

	All (n = 343)	Symptom onset 12–24 h (n = 103)	Symptom onset < 12 h (n = 240)	p
Tmax > 6 s (mL)	144 (117-197)	144 (110-193)	143 (120-204)	0.73
Mismatch volume (mL)	82.0 (57.0-130)	82.0 (53.5-122)	86.5 (64.2-135)	0.67
Good collaterals, n (%) (n = 333)	152 (45.6)	45 (45.5)	107 (45.7)	0.96
Occlusion sites (%)				
ICA	60 (17.5)	20 (19.4)	40 (16.7)	
M1	205 (59.8)	67 (65.0)	138 (57.5)	0.21
Proximal M2	14 (4.08)	2 (1.94)	12 (5.0)	
Tandem	64 (18.7)	14 (13.6)	50 (20.8)	
TOAST				
Cardioembolic (%)	107 (31.2)	26 (25.2)	81 (33.8)	
Large vessel (%)	103 (30.0)	36 (35.0)	67 (27.9)	0.24
Other and undetermined (%)	133 (38.8)	41 (39.8)	92 (38.3)	
Onset to arrival (IQR) (h)	5.60 (3.00-9.98)	13.0 (10.3-15.6)	3.92 (2.47-5.97)	<0.001
Pre-treatment imaging to groin (IQR) (min)	90.5 (66.2-131)	106.0 (81.0-148.0)	77.5 (58.0-124.0)	<0.001
Door to groin (IQR) (min)	157 (111-223)	207 (160-279)	138 (103-197)	<0.001
Groin to revascularization (min)	60.0 (40.0-75.0)	60.0 (45.0-79.0)	60.0 (40.0-75.0)	0.14
Onset to groin (IQR) (h)	8.5 (5.54-12.9)	16.5 (13.6-19.2)	6.72 (4.98-8.69)	<0.001
Conscious sedation (%)	335 (97.7%)	101 (98.1%)	234 (97.5%)	0.99
ACA territory infarcts	29 (8.45)	10 (9.71)	19 (7.92)	0.58

AF: atrial fibrillation; NIHSS: National Institutes of Health Stroke Scale; tPA: tissue plasminogen activator; ASPECTS: Alberta Stroke Program early CT Score; NCCT-CTA: non-contrast computed tomography and computed tomographic angiography; MRI: magnetic resonance imaging; ICA: internal carotid artery; M1: Branch of M1 Segment of middle cerebral artery; M2: Branch of M1 Segment of middle cerebral artery; TOAST: Trial of ORG 10172 in Acute Stroke Treatment; ACA, anterior cerebral artery.

time was substantially longer in the late-window group compared to the early-window group (13.0 (10.3–15.6) vs. 3.92 (2.47–5.97) h, $p < 0.001$). Similarly, the median door-to-groin puncture time was significantly longer in the late-window group (207 [160–279] vs. 138 [103–197] min, $p < 0.001$), as was the median pre-treatment imaging-to-groin puncture time (106.0 [81.0–148.0] vs. 77.0 [58.0–124.0] min, $p < 0.001$) (Table 1).

The overall median onset-to-groin time was significantly longer in the late compared to the early group (16.5 (13.6–19.2) vs. 6.72 (5.0–8.7) h, $p < 0.001$).

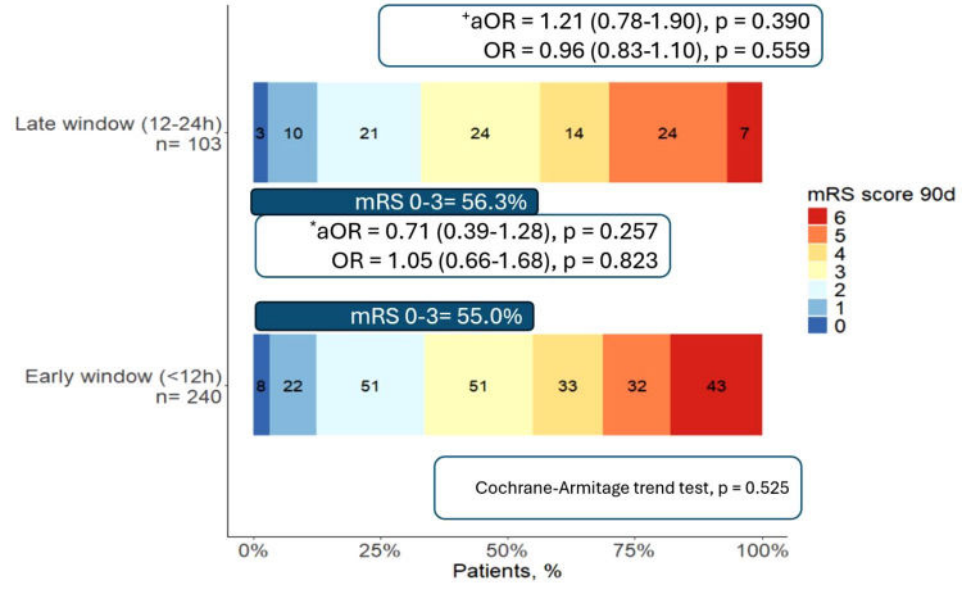
Clinical outcomes

We observed no significant difference in 90-day ambulation (mRS 0–3) between the late- and early-window groups, both before and after adjusting for confounders (56.3% vs. 55.0%, adjusted odds ratio (aOR) = 0.71, 95% CI = 0.39–1.28, $p = 0.257$) (Figure 2). Similarly, we did not find a significant difference in the odds of an ordinal shift in mRS between late- and early-window patients (aOR = 1.21, 95% CI = 0.78–1.90, $p = 0.390$) (Figure 2).

Safety outcome analysis

The safety outcomes, including symptomatic intracranial hemorrhage (sICH), PH2, any hemorrhage are detailed in Table 2. No statistically significant differences were observed between the late and early groups for the following outcomes: sICH (aOR = 1.12, 95% CI = (0.32–3.50), $p = 0.847$), PH2 (aOR = 1.11 (0.38–2.96), $p = 0.840$), and any hemorrhage (aOR = 0.70 (0.40–1.23), $p = 0.210$) (Table 2).

Figure 2. Grotta bar plot of mRS 0–3 in ASPECTS 3–5 post-EVT patients: 12- to 24-h vs. <12-h time window.



*Binomial model (mRS 0–3 vs. 4–6): adjusted for Age, Sex, Diabetes, Hypertension, AF, Pre-stroke mRS, NIHSS, ASPECTS, Occlusion site, Pre-treatment imaging to groin time, and CT-MRI imaging.
+Proportional odds model: adjusted for Age, Sex, Diabetes, Hypertension, AF, Pre-stroke mRS, NIHSS, ASPECTS, Occlusion site, Pre-treatment imaging to groin time, and CT-MRI imaging.
aOR: adjusted odds ratio; OR: odds ratio; mRS: modified Rankin score; ASPECTS: Alberta Stroke Program Early CT Score; EVT: endovascular treatment.

Secondary outcomes

We did not observe any significant differences between late- and early-window patients in successful reperfusion rates (89.3% vs. 91.7%, aOR = 0.64, 95% CI = 0.27–1.55, p=0.305) and 90-day mortality (6.8% vs. 17.9%, aOR = 0.67, 95% CI = 0.24–1.72, p=0.422). Similarly, secondary outcomes showed a similar proportion of patients achieving mRS 0–2 at 90 days (33.0% vs. 33.8%, aOR = 0.67, 95% CI = 0.35–1.24, p=0.209) and END (7.77% vs. 16.7%, aOR 0.50, 95% CI = 0.19–1.16, p=0.121) (Table 2).

Heterogeneity of treatment effect across subgroups

There was no heterogeneity in the effects of the late or early window on ambulation (mRS 0–3) at 90 days across the pre-specified subgroups—age, ASPECTS (4–5 vs. 3), imaging modality (CT or MRI), and collateral status (good vs. bad) (Figure 3). Similarly, there was no difference in the rates of sICH and PH2 between the late and early windows (Figure 3).

Subgroup analyses

The study showed a high rate of mRS 0–3 in both the late and early windows (Supplemental Figure S1). The rate of mRS 0–3 was consistent across the four stroke centers without statistical difference (p=0.762) (Supplemental Figure S1). In addition, we observed a clear age-dependent decline in functional outcomes. Functional ambulation decreased from 77.2% in patients aged ⩽55 years (61/79) to 28.6% in those aged >75 years (12/42) (p<0.001), while the rate of very severe disability (mRS 5–6) increased from 13.9% to 61.9% (p<0.001) (Figure 4). Our study included 45.6% (152/333) of patients with good collateral status, revealing a significant association between collateral status and mRS scores, with a shift toward lower mRS scores in the good collateral group (p=0.001) (Figure 5). There was also a trend toward lower mRS scores in patients with ASPECTS 4–5 compared to those with ASPECTS 3, although the difference was not statistically significant (p=0.052) (Supplemental Figure S2).

Discussion

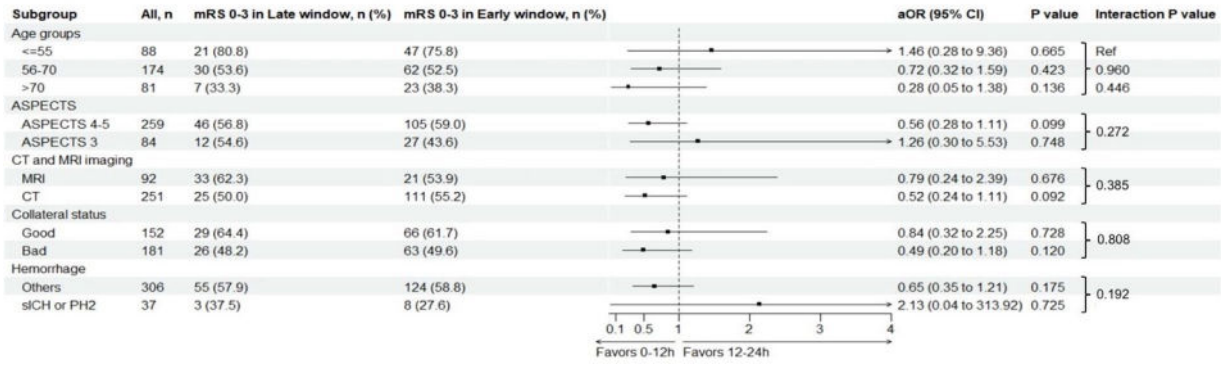
Our study observed that in patients with anterior circulation LVO and an ASPECTS of 3–5, late-window EVT (12–24 h) was associated with similar rates of independent ambulation (mRS 0–3) at 90 days and no increase in sICH compared to the early-window group (<12 h), with consistent results across subgroups.

Table 2. Multivariable regression analysis of late versus early window and clinical outcomes.

	Total	12–24 h (n = 103)	<12 h (n = 240)	Unadjusted analysis		Adjusted analysis*	
				OR (95% CI)	p	aOR (95% CI)	p
	Efficacy outcomes						
mRS 0-2, n (%)	115 (33.5)	34 (33.0)	81 (33.8)	0.97 (0.59-1.58)	0.894	0.67 (0.35-1.24)	0.209
mTICI 2b-3, n (%)	312 (91.0)	92 (89.3)	220 (91.7)	0.76 (0.35-1.71)	0.487	0.64 (0.27-1.55)	0.305
	Safety outcomes						
sICH, n (%)	24 (7.0)	5 (4.85)	19 (7.9)	0.61 (0.19-1.57)	0.308	1.12 (0.32-3.50)	0.847
PH2, n (%)	34 (9.9)	7 (6.8)	27 (11.2)	0.59 (0.23-1.33)	0.206	1.11 (0.38-2.96)	0.840
Any hemorrhage, n (%)	237 (69.1)	64 (62.1)	173 (72.1)	0.64 (0.39-1.04)	0.068	0.70 (0.40-1.23)	0.210
END, n (%)	48 (14.0)	8 (7.77)	40 (16.7)	0.43 (0.18-0.91)	0.029	0.50 (0.19-1.16)	0.121
Mortality at 90d, n (%)	50 (14.6)	7 (6.8)	43 (17.9)	0.34 (0.13-0.74)	0.007	0.67 (0.24-1.72)	0.422

*Adjusted for Age, Sex, Diabetes, Hypertension, AF, Pre-stroke mRS, NIHSS, ASPECTS, Occlusion site, Pre-treatment imaging to groin time, and CT-MRI imaging.
mRS: modified Rankin score; aOR: adjusted odds ratio; mTICI: modified treatment in cerebral infarction; sICH: symptomatic intracranial hemorrhage; PH2: parenchymal hemorrhage type 2; END: early neurological deterioration.

Figure 3. Forest plots for the late-window endovascular treatment adjusted effect for mRS 0–3 at 90 days across pre-specified subgroups.

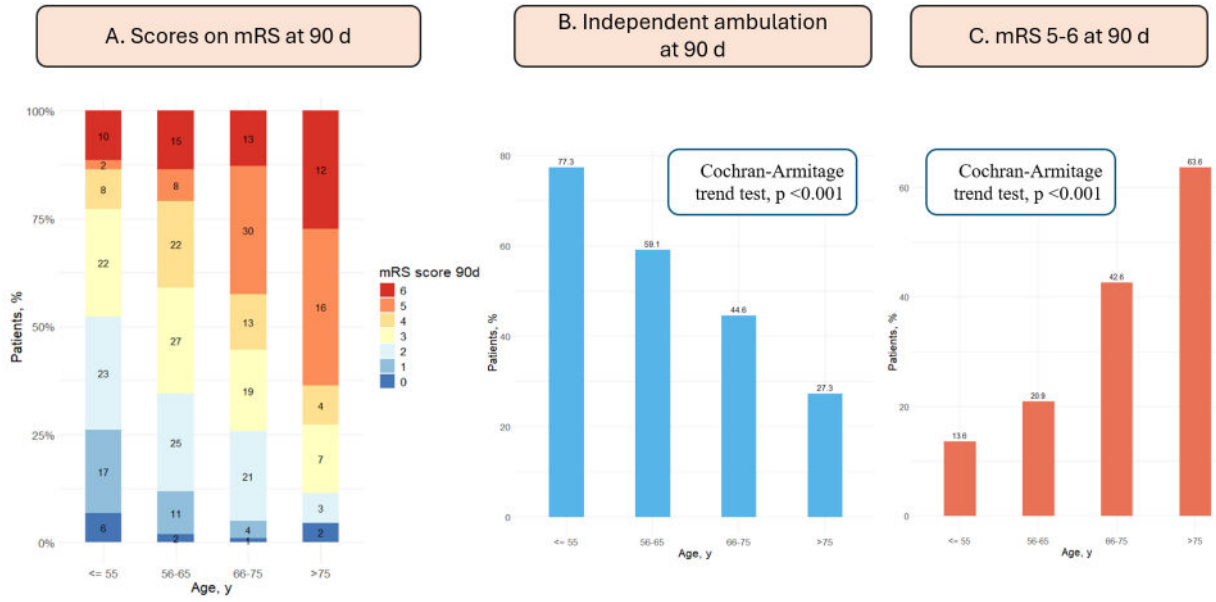


The adjusted odds ratio was calculated by using binary logistic regression of the following variables into account: Age, Sex, Diabetes, Hypertension, AF, Pre-stroke mRS, NIHSS, ASPECTS, Occlusion site, Pre-treatment imaging to groin time, and CT-MRI imaging.
aOR: adjusted odds ratio; ASPECTS: Alberta Stroke Program Early CT Score; CT: computed tomography; MRI: magnetic resonance imaging; sICH: symptomatic intracranial hemorrhage; PH2: parenchymal hemorrhage type 2.

These findings partially align with data from the STAR collaboration, which demonstrated comparable outcomes between <6 h and 6–24 h EVT groups with ASPECTS 2–5.[24] Similar to Elawady et al., our study found a non-significant trend toward higher sICH and END in the early-window group, possibly due to poor collateral circulation and rapid infarct progression in these patients, who might be excluded in the late window as the ischemic core enlarges over time.[24–27] Our study, however, focuses upon EVT between 12 and 24 h in large-core patients, a group underrepresented in randomized controlled trials (RCTs).[26] An ANGEL-ASPECT substudy supports EVT efficacy up to 13 h and 22 min,[28] consistent with our 12- to 24-h findings.

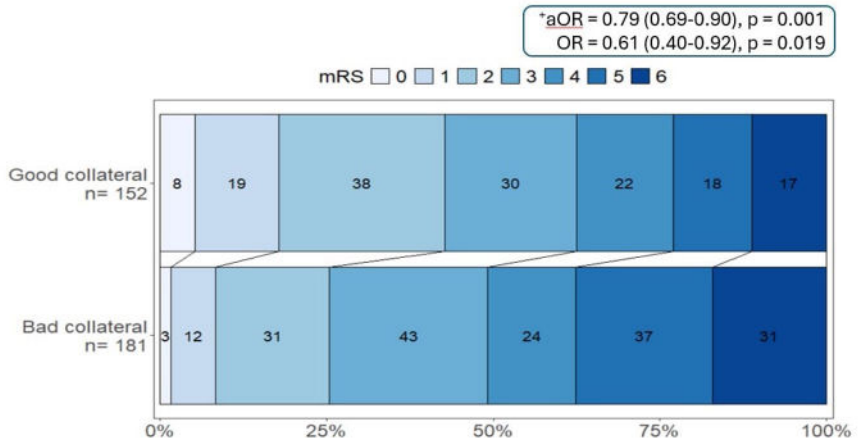
The study demonstrated a high functional ambulation rate (mRS 0–3) with consistent findings across four stroke centers (Supplemental Figure S1), driven by favorable clinical factors. First, the cohort had a younger median age (64.0 years), lower than in major trials, and younger age was significantly associated with better outcomes

Figure 4. Age-based subgroup analysis of functional outcomes in patients with ASPECTS 3–5 after endovascular treatment, assessing association with good (mRS 0–3) and poor (mRS 5–6) outcomes.



The Cochran–Armitage trend test was used to test for trend in proportion.
mRS: modified Rankin score; ASPECTS: Alberta Stroke Program Early CT Score.

Figure 5. Grotta bar plot of mRS in ASPECTS 3–5 post-EVT patients: good vs. poor collaterals.



+Proportional odds model: adjusted for Age, Sex, Diabetes, Hypertension, AF, Pre-stroke mRS, NIHSS, ASPECTS, Occlusion site, Pre-treatment imaging to groin time, and CT-MRI imaging.
aOR: adjusted odds ratio; OR: odds ratio; ASPECTS: Alberta Stroke Program Early CT Score; EVT: endovascular treatment.

($p < 0.001$) (Figure 4). Second, 45.6% of patients had good collaterals, higher than in TENSION (36.3%),[21] and strongly associated with favorable mRS shift ($p = 0.001$) (Figure 5). Third, 75.2% had ASPECTS 4–5, indicating smaller infarcts compared to 43.5% in the EVT arm of ANGEL-ASPECT,[5] with a trend toward better outcomes than ASPECTS 3 ($p = 0.052$) (Supplemental Figure S2), consistent with prior data.[23] While ASPECTS scoring is known for variability among stroke physicians, we addressed this by having each imaging study assessed by

two independent certified ASPECTS raters, with a senior rater resolving any disagreements. In addition, when comparing early- and late-window groups, potential ASPECTS scoring bias was likely similar between them. Furthermore, our study achieved a high successful reperfusion rate (91.0%), which likely contributed to good outcomes, supported by previous studies.[26,29] Younger age may have facilitated EVT, and our high-volume centers (>150 cases/year) likely enhanced procedural success.[30] Recent small-core EVT studies in Asian populations have shown similar trends.[31]

The intravenous thrombolysis (IVT) rate in our study was 23.9% (82/343), consistent with reported rates of 20.8–39%.[6,8,32] Current guidelines lack a definitive threshold for hypoattenuation severity to predict IVT response, except for contraindications like intracranial hemorrhage, extensive hypoattenuation, or frank hypodensity.[33] Among IVT recipients, 41.5% (34/82) with small ischemic cores received IVT at primary stroke units before transfer to a thrombectomy facility; repeat imaging at the stroke center showed rapid core progression to large infarcts. IVT decisions for others followed guideline-based physician discretion. END and mortality were lower in the late window (7.77% vs. 16.7%, p=0.029; 6.8% vs. 17.9%, p=0.007), but differences were non-significant after confounder adjustment (Table 2). A higher rate of perfusion or brain MRI use in the late-window group may have introduced selection bias by excluding patients with a poor prognosis from EVT.[34] Subgroup analyses from ANGEL-ASPECT and SELECT 2 trials showed no interaction between EVT effect and imaging mismatch.[35,36] At our centers, patients were selected for EVT using the DEFUSE-3 criteria, excluding those without sufficient mismatch (mismatch volume >15 mL, ratio >1.8), which may have contributed to the lower rates of deterioration and mortality observed in the late window. To ensure consistency, ASPECTS was scored using diffusion-weighted imaging in patients who underwent perfusion MRI. Although prior studies suggest DWI-ASPECTS outperforms NCCT-ASPECTS,[22] we found no outcome differences between these modalities (Figure 3).

Our findings support extending endovascular therapy (EVT) to the 12- to 24-h window for large-core ischemic stroke (ASPECTS 3–5) in developing countries like Vietnam, where younger patients and delayed presentations are prevalent.[11,12,37] Despite limited guideline support beyond 12 h in developing regions,[38] and inconclusive evidence from trials such as RESCUE-Japan LIMIT (n=12), ANGEL-ASPECT (n=56), SELECT 2 (n=70), and TESLA (n=68), our data demonstrate comparable outcomes to the <12-h window, confirming safety in resource-limited settings. Strategies such as direct-to-angiography transfer, as demonstrated in the ANGIO-CAT trial,[39] could improve reperfusion and outcomes by minimizing delays. Further RCTs and meta-analyses, utilizing minimal imaging protocols and exploring adjunctive therapies,[40] are needed to optimize 12- to 24-h EVT strategies and enhance patient outcomes.

Our study has several limitations. First, it relies on an indirect comparison, inferring the safety and efficacy of thrombectomy in the 12- to 24-h window by comparing it with <12-h treatment, without a direct comparison to best medical therapy. Second, the small sample size (n=343) from major stroke centers restricts applicability to diverse populations in developing and developed countries. Third, the absence of a standardized imaging protocol for late-window patients limits the generalizability of our findings. Fourth, the non-randomized observational design inherently introduces selection bias. Fifth, more frequent use of advanced imaging (MRI or perfusion MRI) in the late window may introduce selection bias by favoring EVT for patients with better prognoses. Sixth, ASPECTS scoring poses challenges, including inter-rater variability.[41] Seventh, quantifying early ischemic changes in ASPECTS regions is complex. Eighth, the clinical impact of ASPECTS regions varies by eloquence.[42] Ninth, diagnostic and treatment delays may reduce relevance to settings with established stroke care systems. Tenth, exclusion of very large infarct cores may skew results. Eleventh, we did not evaluate brain edema or malignant edema, which could affect outcomes. In addition, we did not re-assess recanalization status at 24–36 h, so we cannot exclude the possibility of re-occlusion in high-risk intracranial atherosclerotic disease cases, despite the high rate of successful reperfusion observed on the final angiogram.[43]

Conclusion

Our study suggests that EVT can be performed safely and without statistically significant differences in clinical outcomes in patients with LVO and large ischemic cores within the late (12–24 h) and early (<12 h) time windows from symptom onset, potentially expanding the indication strategy for the late window, particularly in resource-limited settings.

Acknowledgements

We would like to express our gratitude to the staff at the Department of Cerebrovascular Diseases and the Department of Neurointervention at 115 People's Hospital; the Stroke Department at Da Nang Hospital; the Stroke Center at Can Tho Central Hospital; and the Department of Neurology at the University Medical Center of Ho Chi Minh City, who treated the patients and provided the data for this study.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. Thanh N. Nguyen reports Associate Editor of Stroke;

Advisory board of Brainomix, Aruna Bio; Speaker for Genentech, Kaneka; and consulting for Medtronic.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: T.Q.N. was funded by the PhD Scholarship Program of Vingroup Innovation Foundation (VINIF), code VINIF.2023.TS.139.

Data availability

The data sets generated during and/or analyzed during the study are available from the corresponding author on reasonable request after ethics clearance and approval by all authors.

ORCID iDs

Trung Quoc Nguyen https://orcid.org/0000-0003-1091-9320
Khang Vinh Nguyen https://orcid.org/0000-0002-1183-388X
Hang Thi Minh Tran https://orcid.org/0009-0000-0321-8863
Huy Quoc Huynh https://orcid.org/0009-0009-8850-592X
Thanh N Nguyen https://orcid.org/0000-0002-2810-1685
Thang Huy Nguyen https://orcid.org/0000-0002-6057-8379

Supplemental material

Supplemental material for this article is available online.

References

1. Nguyen TN, Abdalkader M, Fischer U, et al. Endovascular management of acute stroke. *Lancet* 2024; 404: 1265–1278.
2. Sahoo A, Abdalkader M, Yamagami H, et al. Endovascular therapy for acute stroke: new evidence and indications. *J Neuroendovasc Ther* 2023; 17: 232–242.
3. Nguyen TN, Castonguay AC, Siegler JE, et al. Mechanical thrombectomy in the late presentation of anterior circulation large vessel occlusion stroke: a guideline from the Society of Vascular and Interventional Neurology Guidelines and Practice Standards Committee. *Stroke Vasc Interv Neurol* 2023; 3: e000512.
4. Yoshimura S, Sakai N, Yamagami H, et al. Endovascular therapy for acute stroke with a large ischemic region. *N Engl J Med* 2022; 386: 1303–1313.
5. Huo X, Ma G, Tong X, et al. Trial of endovascular therapy for acute ischemic stroke with large infarct. *N Engl J Med* 2023; 388: 1272–1283.
6. Sarraj A, Hassan AE, Abraham MG, et al. Trial of endovascular thrombectomy for large ischemic strokes. *N Engl J Med* 2023; 388: 1259–1271.
7. Costalat V, Jovin TG, Albucher JF, et al. Trial of thrombectomy for stroke with a large infarct of unrestricted size. *N Engl J Med* 2024; 390: 1677–1689.
8. Bendszus M, Fiehler J, Subtil F, et al. Endovascular thrombectomy for acute ischaemic stroke with established large infarct: multicentre, open-label, randomised trial. *Lancet* 2023; 402: 1753–1763.
9. Sarraj A, Abraham MG, Hassan AE, et al. Endovascular thrombectomy plus medical care versus medical care alone for large ischaemic stroke: 1-year outcomes of the SELECT2 trial. *Lancet* 2024; 403: 731–740.
10. Yoo AJ, Zaidat OO, Sheth SA, et al. Thrombectomy for stroke with large infarct on noncontrast CT: the TESLA randomized clinical trial. *JAMA* 2024; 332: 1355–1366.
11. Nguyen TH, Gall S, Cadilhac DA, et al. Processes of stroke unit care and outcomes at discharge in Vietnam: findings from the Registry of Stroke Care Quality (RES-Q) in a major public hospital. *J Stroke Med* 2019; 2: 119–127.
12. Nguyen TQ, Tran MH, Phung HN, et al. Endovascular treatment for acute ischemic stroke beyond the 24-h time window: selection by target mismatch profile. *Int J Stroke* 2024; 19: 305–313.
13. Nguyen TN, Klein P, Berberich A, et al. Late window imaging selection for endovascular therapy of large vessel occlusion stroke: an international survey. *Stroke* 2023; 3: e000595.
14. Derraz I, Moulin S, Gory B, et al. Endovascular thrombectomy outcomes with and without intravenous thrombolysis for large ischemic cores identified with CT or MRI. *Radiology* 2023; 309: e230440.
15. Adams HP, Jr, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke* 1993; 24: 35–41.
16. Tan JC, Dillon WP, Liu S, Adler F, Smith WS and Wintermark M. Systematic comparison of perfusion-CT and CT-angiography in acute stroke patients. *Ann Neurol* 2007; 61: 533–543.
17. Olivot JM, Mlynash M, Inoue M, et al. Hypoperfusion intensity ratio predicts infarct progression and functional outcome in the DEFUSE 2 Cohort. *Stroke* 2014; 45: 1018–1023.
18. Liebeskind DS, Tomsick TA, Foster LD, et al. Collaterals at angiography and outcomes in the Interventional Management of Stroke (IMS) III trial. *Stroke* 2014; 45: 759–764.
19. Nezu T, Koga M, Nakagawara J, et al. Early ischemic change on CT versus diffusion-weighted imaging for patients with stroke receiving intravenous recombinant tissue-type plasminogen activator therapy: stroke acute management with urgent risk-factor assessment and improvement (SAMURAI) rt-PA registry. *Stroke* 2011; 42: 2196–2200.
20. Mujanovic A, Strbian D, Demeestere J, et al. Safety and clinical outcomes of endovascular therapy versus medical management in late presentation of large ischemic stroke. *Eur Stroke J* 2024; 9: 907–917.
21. Winkelmeier L, Kniep H, Thomalla G, et al. Arterial collaterals and endovascular treatment effect in acute ischemic stroke with large infarct: a secondary analysis of the TENSION trial. *Radiology* 2025; 314: e242401.
22. Sakakibara F, Uchida K, Yoshimura S, et al. Mode of imaging study and endovascular therapy for a large ischemic core: insights from the RESCUE-Japan LIMIT. *J Stroke* 2023; 25: 388–398.
23. Uchida K, Shindo S, Yoshimura S, et al. Association between Alberta Stroke Program Early computed tomography score and efficacy and safety outcomes with endovascular therapy in patients with stroke from large-vessel occlusion: a secondary analysis of the Recovery by Endovascular Salvage for Cerebral Ultra-acute Embolism-Japan Large Ischemic Core Trial (RESCUE-Japan LIMIT). *JAMA Neurol* 2022; 79: 1260–1266.

24. Elawady SS, Cunningham C, Matsukawa H, et al. Outcomes of mechanical thrombectomy for patients with stroke presenting with low Alberta Stroke Program Early Computed Tomography Score in early and late time windows. *Neurosurgery* 2024; 95: 877–885.
25. Galecio-Castillo M, Farooqui M, Hassan AE, et al. Clinical and safety outcomes of endovascular therapy 6 to 24 hours after large vessel occlusion ischemic stroke with tandem lesions. *J Stroke* 2023; 25: 378–387.
26. Broocks G, Hanning U, Bechstein M, et al. Association of thrombectomy with functional outcome for patients with ischemic stroke who presented in the extended time window with extensive signs of infarction. *JAMA Netw Open* 2022; 5: e2235733.
27. Al-Mufti F, Elfil M, Ghaith HS, et al. Time-to-treatment with endovascular thrombectomy in patients with large core ischemic stroke: the "late window paradox." *J Neurointerv Surg* 2023; 15: 733–734.
28. Yuan G, Sang H, Nguyen TN, et al. Association between time to treatment and outcomes of endovascular therapy vs medical management in patients with large ischemic stroke. *Neurology* 2025; 104: e210133.
29. Almallouhi E, Al Kasab S, Hubbard Z, et al. Outcomes of mechanical thrombectomy for patients with stroke presenting with Low Alberta Stroke Program Early Computed Tomography Score in the early and extended window. *JAMA Netw Open* 2021; 4: e2137708.
30. Gupta R, Horev A, Nguyen T, et al. Higher volume endovascular stroke centers have faster times to treatment, higher reperfusion rates and higher rates of good clinical outcomes. *J Neurointerv Surg* 2013; 5: 294–297.
31. Nguyen HT, Ton MD, Vu DL, et al. Post-market registry of stroke patients treated with medtronic neurothrombectomy devices in Southeast Asia: PROSPR-SEA. *Stroke* 2023; 3: e000318.
32. Al Kasab S, Almallouhi E, Jumaa M, et al. Outcomes of adjunct emergent stenting versus mechanical thrombectomy alone: the RESCUE-ICAS registry. *Stroke* 2025; 56: 390–400.
33. Powers WJ, Rabinstein AA, Ackerson T, 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.
34. Nguyen TN, Nogueira RG, Qureshi MM, et al. Noncontrast CT selected thrombectomy vs medical management for late-window anterior large vessel occlusion. *Neurology* 2024; 102: e209324.
35. Huo X, Nguyen TN, Sun D, et al. Association of mismatch profiles and clinical outcome from endovascular therapy in large infarct: a post-hoc analysis of the ANGEL-ASPECT trial. *Ann Neurol* 2024; 96: 729–738.
36. Sarraj A, Hassan AE, Abraham MG, et al. Endovascular thrombectomy for large ischemic stroke across ischemic injury and penumbra profiles. *JAMA* 2024; 331: 750–763.
37. Global, Regional, and National Burden of Stroke and its risk factors. 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet Neurol* 2024; 23: 973–1003.
38. Health VMo. *Guidelines for stroke diagnosis and treatment (3312 QD-BYT)*. Hanoi, Vietnam: Vietnam Ministry of Health, 2024.
39. Requena M, Olivé-Gadea M, Muchada M, et al. Direct to angiography suite without stopping for computed tomography imaging for patients with acute stroke: a randomized clinical trial. *JAMA Neurol* 2021; 78: 1099–1107.
40. Yogendrakumar V, Vandelanotte S, Mistry EA, et al. Emerging adjuvant thrombolytic therapies for acute ischemic stroke reperfusion. *Stroke* 2024; 55: 2536–2546.
41. Abdalkader M, Siegler JE, Lee JS, et al. Neuroimaging of acute ischemic stroke: multimodal imaging approach for acute endovascular therapy. *J Stroke* 2023; 25: 55–71.
42. Paul U, Koneru M, Siegler JE, et al. A cortically-weighted versus total Alberta Stroke Program Early Computed Tomography Score in thrombectomy outcome models. *J Stroke Cerebrovasc Dis* 2024; 33: 107607.
43. Huo X, Sun D, Chen W, et al. Endovascular treatment for acute large vessel occlusion due to underlying intracranial atherosclerotic disease. *Semin Neurol* 2023; 43: 337–344.