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Futile recanalization after endovascular treatment in acute ischemic stroke with large ischemic core

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Abstract

Background Endovascular therapy (EVT) is the treatment of choice for acute ischemic stroke (AIS) with large vessel occlusion. However, in many patients, successful EVT recanalization does not correspond to a clinical improvement, called futile recanalization (FR). We aimed to identify stroke risk factors and patient characteristics associated with FR in AIS with large core infarct (LCI).

Methods A total of 137 patients with AIS with LCI treated by EVT at a single stroke center were retrospectively included from January 2016 to June 2023. LCI was defined by Diffusion-Weighted Imaging-Alberta Stroke Program Early Computed Tomography Score (DWI-ASPECT) <6. Patient age, sex, modified Rankin Scale (mRS), National Institutes of Health Stroke Scale (NIHSS), time to treatment, risk factors, and radiologic findings were collected, and potential associations with FR were analyzed. FR was defined as successful reperfusion with modified Thrombolysis in Cerebral Infarction (mTICI) $\geq$ 2b but without functional independence at 90 days (mRS ≥ 3). A multivariate logistic regression analysis was conducted on the clinical characteristics of patients, based on the presence or absence of FR, and the factors influencing FR.

Results Of 137 patients, 120 showed successful recanalization (mTICI $\geq$ 2b). All patients were divided into FR ($n=80$) and no FR ($n=40$) groups. Older age (odds ratio [OR] 1.052, 95% confidence interval [CI] 1.002–1.105; $p=0.041$), the higher the initial NIHSS score (OR 1.181, 95% CI 1.037–1.344; $p=0.012$), and prior intravenous plasminogen activator (OR 0.310, 95% CI 0.118–0.813, $p=0.017$) were independent influencing factors of FR.

Conclusions The older age, the higher the initial NIHSS, and not receiving intravenous plasminogen activator were independently associated with FR in AIS with LCI. These factors could identify poor responders to EVT recanalization.

Keywords Endovascular treatment, Futile recanalization, Acute ischemic stroke, Large ischemic core

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Introduction

Recent advancements in endovascular interventions have changed the management of patients with large core infarcts (LCI), specifically those with an Alberta Stroke Program Early Computed Tomography Score (ASPECT) of 5 or lower, for whom the benefits of endovascular therapy (EVT) remain uncertain. This cohort was traditionally omitted from early trials due to safety apprehensions. Notably, trials such as SELECT2 (Randomized Controlled Trial to Optimize Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke) and ANGEL-ASPECT (Study of Endovascular Therapy in Acute Anterior Circulation Large Vessel Occlusive Patients With a Large Infarct Core) corroborated findings from RESCUE-Japan LIMIT (Recovery by Endovascular Salvage for Cerebral Ultra-Acute Embolism-Japan Large Ischemic Core Trial), affirming that patients with large ischemic stroke attain superior functional outcomes after EVT compared to best medical treatment [1–3]. These randomized controlled trials provide compelling evidence supporting the extension of EVT to specific subgroups of patients with substantial baseline stroke up to 24 h after the last known well.

There is much that early recanalization can improve the prognosis of AIS with LCI [1, 3]. However, recent randomized clinical trials have shown that many patients undergoing successful recanalization have poor clinical outcomes, termed futile recanalization (FR) [4]. The difference between recanalization success and patient outcomes requires an investigation into the factors that determine the overall efficacy of EVT.

While numerous prior studies have identified predictors of FR following endovascular treatment [5–8], few have specifically examined this issue in patients with LCI. Consequently, this study aimed to identify potential predictors of FR in AIS patients with LCI who underwent endovascular thrombectomy. By identifying precise predictors of FR in this high-risk cohort, our study aims to inform clinical decision-making and optimize therapeutic strategies, ultimately enhancing the efficacy of EVT in AIS patients with LCI.

Methods

Patients

Medical records of AIS patients treated with EVT between January 2016 to June 2022 were identified from the Chonnam National University Hospital (CNUH) stroke registry. We analyzed the data of patients with ischemic anterior circulation stroke with large ischemic core who underwent artery puncture within 24 h from symptom onset and achieved successful angiographic recanalization (defined as modified Thrombolysis in Cerebral Infarction [mTICI] grade 2b or 3). Enrolled patients were >18 years old, examined within 24 h of the last known time the patient was observed to be well, had occlusions of the internal carotid artery (either extracranial or intracranial), M1, or proximal M2 segment of the middle cerebral artery on magnetic resonance angiography (MRA), and had large ischemic cores with Diffusion-Weighted Imaging-Alberta Stroke Program Early Computed Tomography Scores (DWI ASPECTS)<6. At our center, the stroke evaluation protocol includes diffusion MRI and MR angiography as part of the initial examination for ischemic stroke, unless contraindicated. All patients included in this study underwent these imaging procedures. n intravenous thrombolytic (Actilyse) was administered to patients who were diagnosed within 4.5 h of stroke onset. Trevo stent retrievers were used first, and aspiration devices and ballooning devices were utilized as determined by the interventionist's judgement. We examined the modified Rankin Scale (mRS) score at 90 days post-treatment. FR was defined as the poor outcome (mRS score, 3–6) at 90 days despite successful revascularization, and favorable recanalization was defined as functional independence (mRS score, 0–2). Patients were divided into the FR group and the non-FR group accordingly. The Institutional Review Board (IRB) of CNUH approved this study, which was conducted according to the ethical standards laid down by the Declaration of Helsinki (IRB no. CNUH-2020-024).

Data collection

Clinical variables were age, gender, initial National Institutes of Health Stroke Scale (NIHSS), and the presence of cerebrovascular risk factors (hypertension, diabetes mellitus, dyslipidemia, smoking history, and atrial fibrillation). Blood pressure, blood sugar, lipid profile, and complete blood count with differential were measured at arrival. Underlying medical conditions, including hypertension and dyslipidemia, were determined based on the patient's previous medical history and medication use. Additionally, diabetes and dyslipidemia were diagnosed if blood test results, such as lipid profiles and hemoglobin A1c, taken at the time of admission, met the relevant criteria. Hypertension was diagnosed if elevated blood pressure was observed during the hospital stay. A smoker was defined as anyone with a history of smoking within the past five years. Patients were classified into subgroups according to Trials of Org 10,172 in Acute Stroke Treatment (TOAST) classification.

Patients who underwent emergency magnetic resonance imaging (MRI) were targeted, and a large ischemic core was defined by DWI ASPECTS<6. The collateral grade before EVT from cerebral arteriography was defined as described in Higashida et al. [9] In our study, collateral flow grading was assessed using MRA and categorized into four grades. Grade 0 indicates no visible collateral flow to the ischemic area. Grade 1 represents slow collateral flow reaching only the periphery, with some perfusion deficit. Grade 2 shows faster collateral flow but covering only part of the ischemic territory. Grade 3 reflects slow but complete perfusion of the ischemic bed by the late venous phase. Grade 4 indicates rapid and complete collateral flow to the entire ischemic territory. Successful vascular recanalization was defined as a modified thrombolysis in cerebral ischemia (mTICI) scale of 2b or 3 after EVT. Computed tomography or MRI scans were usually performed 24 h after EVT, or when an intracranial hemorrhage was suspected based on clinical symptoms. The radiographic definition of hemorrhagic transformation was classified by the European Cooperative Acute Stroke Study (ECASS2) based on MRI after EVT. Symptomatic intracerebral hemorrhage (ICH) was defined as MRI evidence of ICH and rapid neurological deterioration (an increase in NIHSS by ≥4 points). Our stroke center conducts regular monthly meetings for data quality control, and the imaging analyses of the patients included in this data were performed by two or more neurologists in an anonymized and blinded manner. Any ambiguous findings were discussed during the meetings to minimize errors.

Statistical analysis

All statistical analyses were conducted using SPSS 22.0. A two-sided p-value <0.05 indicated statistical significance. Patients were divided into two groups based on mRS at 3 months after stroke. Univariate analysis was performed to identify clinical and imaging variables associated with functional outcomes. The student's t-test was used for continuous variables, and Chi-squared or Fisher's exact tests were used for categorical variables. Multivariate logistic regression analysis was used for risk factors and adjusted for confounders. We conducted a multivariate analysis and selected variables with significant differences between the two groups in the General Characteristics as covariates. The adjusted variables included age, atrial fibrillation, glomerular filtration rate, initial SBP, initial NIHSS, postprocedural hemorrhagic transformation, and collateral grade before EVT.

Results

A total of 662 patients underwent screening between January 2016 and June 2023. Of 137 patients with AIS with large ischemic core treated by EVT, 120 showed successful recanalization (mTICI≥2b).

These patients were divided into those who had FR ($n=80$) versus those with no FR ($n=40$) (Fig. 1). The included patient cohort consisted of 75 men (62.5%), with a mean age of 71.1±13.8 years and a mean initial NIHSS of 13 (11–17). The mean duration between the last known time the patient was observed to be well and arterial puncture was 342.1±261.2 min, while the mean duration between the last known time the patient was observed to be well and recanalization was 372.4±260.2 min. Forty-eight patients (40.0%) received intravenous thrombolysis, and 91 patients (75.8%) had a poor collateral grade before EVT (0–2). The mean DWI ASPECTS was 4 (3–5). Hemorrhagic transformation post-EVT occurred in 73 patients (60.8%), and symptomatic ICH was observed in 8 patients (6.7%). The vascular occlusion sites were as

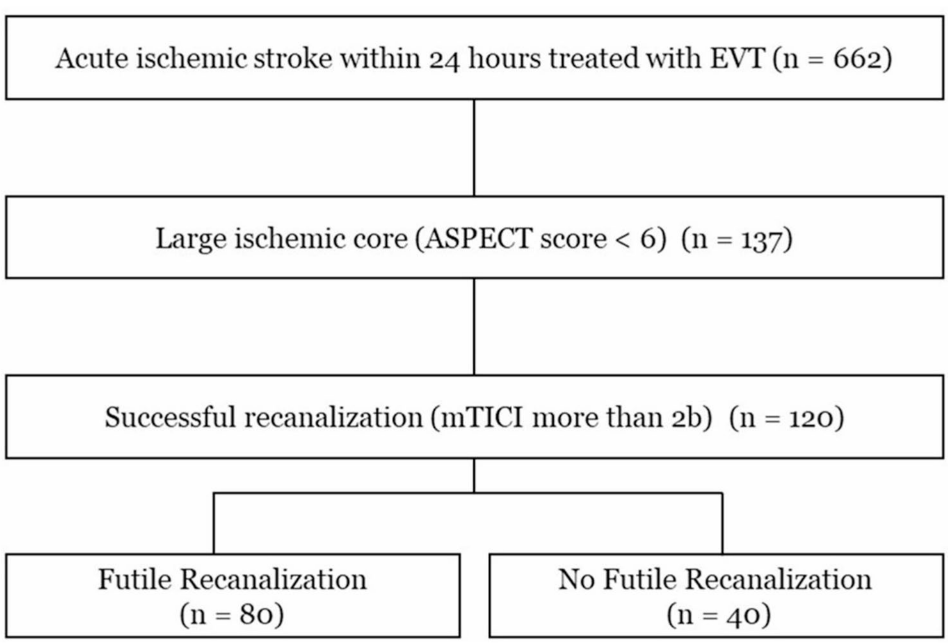

Fig. 1 Flowchart of patient selection

follows: 76 patients (63.3%) had isolated MCA occlusion, while 44 patients (36.7%) had occlusion extending from the ICA. (Table 1).

The FR group comprised 80 patients (75.1%) (Table 2). In univariate analysis, the FR group was significantly older ($p<0.001$), had poorer collateral grades before EVT ($p=0.016$), more frequent atrial fibrillation ($p=0.036$), more instances of post-procedure hemorrhagic transformation ($p=0.001$), higher initial NIHSS scores ($P<0.001$), and higher initial systolic blood pressure ($p=0.035$) compared to the non-FR group. No significant differences between the two groups were observed for inflammatory markers, including the neutrophil-to-lymphocyte ratio, use of intravenous recombinant tissue plasminogen activator (rt-PA), and TOAST classification.

After adjusting for potential confounders in the multivariate logistic regression analysis, factors associated with FR were older age (odds ratio [OR] 1.052, 95% confidence interval [CI] 1.002–1.105; $p=0.041$) and higher initial NIHSS scores (OR, 1.181; 95% CI, 1.037–1.344; $p=0.012$). Additionally, treatment with intravenous rt-PA usage was negatively associated with FR (OR, 0.310, 95% CI, 0.118–0.813, $p=0.017$) (Table 3).

Table 1 Patient baseline Characteristics*

Characteristics	Total ($n=120$)
Age (years, mean and standard deviation)	71.0 ± 13.80
Male (n [%])	75 (62.5) 0
Mean interval between time of stroke onset and puncture (min)	342.1 ± 261.2
Mean interval between time of stroke onset and recanalization (min)	372.4 ± 260.2
Intravenous rt-PA use (n [%])	48 (40.0)0
Initial NIHSS † (IQR)	13 (11–17)
DWI ASPECTS ‡ (IQR)	44 (3–5)
mTICI reperfusion grade §	
2b (n [%])	42 (35.0)0
3 (n [%])	78 (65.0)0
Collateral grade before EVT ¶	
Poor (0–2) (n [%])	91 (75.8)0
Good (3–4) (n [%])	29 (24.2)0
Postprocedural hemorrhagic transformation ‖ (n [%])	73 (60.8)0
HI-1 (n [%])	23 (19.2)0
HI-2 (n [%])	15 (12.5)0
PH-1 (n [%])	12 (10.0)0
PH-2 (n [%])	22 (18.3)0
Symptomatic ICH (n [%])	8 (6.7)0

* Values expressed with "±" are mean ± standard deviation

† Scores on the National Institutes of Health Stroke Scale (NIHSS) range from 0 to 42, with higher scores indicating worse deficits

‡ Alberta Stroke Program Early Computed Tomography Scores (ASPECTS) range from 0 to 10, with lower values indicating a larger infarction

§ A modified TICI reperfusion grade of 2b or higher indicates antegrade reperfusion of more than half the previously occluded target artery ischemic territory

¶ The criteria described in the study of Higashida et al., with lower scores indicating poor collateral circulation (EVT = endovascular therapy)

‖ The radiographic definition of hemorrhagic transformation was classified by European Cooperative Acute Stroke Study (ECASS2) based on MRI after EVT (HI = hemorrhagic infarction; PH = parenchymal hemorrhage; ICH = intracerebral hemorrhage)

Discussion

This study identified predictors of FR in patients with LCI who do not have clinical benefit even after EVT with adequate recanalization. FR after EVT was relatively common in AIS with LCI. Older age, high initial NIHSS score, and no rt-PA before EVT were associated with FR.

The definition of FR is still controversial, but it is generally defined by functional mRS ≥ 3 despite successful vascular recanalization (mTICI 2b–3) [10]. The prevalence of FR may vary depending on the definition, and FR occurs in 32.4–69.6% of patients with AIS due to large vessel obstruction after EVT [5]. Nevertheless, the mechanism, clinical predictors, and management for FR are still lacking. Many trials recently have created some backgrounds for performing EVT even in the presence of a large ischemic core [1–3]. With advancements in endovascular therapy (EVT), successful vascular recanalization can now be achieved in up to 90% of cases. However, despite the administration of appropriate treatment, futile recanalization (FR) remains relatively common. Identifying the factors associated with FR is crucial, as it will provide clinicians with valuable insights for optimizing patient management and facilitating the effective distribution of medical resources [11].

While many studies have already identified predictors of FR in AIS, our study is unique in that it focuses exclusively on patients with LCI. As the criteria for EVT become increasingly liberal and the eligible patient expands, identifying specific characteristics in LCI, where treatment outcomes remain uncertain, could aid in resource allocation, improve decision-making, and better manage patient expectations. In addition, we assessed the ASPECT score using DWI instead of CT. While this may overestimate the true ischemic core, our study's focus on LCI allowed us to detect the ischemic core more sensitively and evaluate its prognostic factors.

Risk factors for FR were assessed in various EVT studies. In the subgroup analysis of DIRECT-MT investigating risk factors for FR, the incidence of FR was higher with increasing age and higher initial systolic blood pressure [6, 12]. In our study, FR was more likely to occur with older age, and the mean age of the FR group was significantly higher than that of the non-FR group (75.1 vs. 63.1, $p<0.001$). Another meta-analysis similarly reported that older age, severity of initial NIHSS score, degree of collateral flow, and initial ASPECT score were associated with FR. In our study, good collateral flow showed significance in univariate analysis; however, it was not associated with FR in multivariate analysis [13].

Table 2 Comparison of factors between favorable and unfavorable group*

Variables	FR (*n* = 80)	Non-FR (*n* = 40)	*P*-value
Age (years)	75.1 ± 10.100	63.1 ± 16.700	< 0.001
Male (n [%])	50 (62.5) 00	25 (62.5) 00	1.000
Risk factors			
Dyslipidemia (n [%])	17 (21.3) 00	10 (25.0) 00	0.643
Atrial fibrillation (n [%])	52 (65.0) 00	18 (45.0) 00	0.036
Hypertension (n [%])	48 (60.0) 00	23 (57.5) 00	0.793
DM (n [%])	24 (30.0) 00	8 (20.0) 00	0.243
Smoking (n [%])	18 (22.5) 00	9 (22.5) 00	1.000
Mean interval between time of stroke onset and puncture (min)	347.5 ± 274.90	331.2 ± 234.20	0.748
Mean interval between time of stroke onset and recanalization (min)	378.8 ± 272.40	359.5 ± 236.50	0.704
Vital signs			
Initial SBP (mmH_2O)	139.1 ± 21.70	1301 ± 21.500	0.035
Initial DBP (mmH_2O)	79.6 ± 12.90	78.8 ± 11.400	0.748
Initial BS (mg/dL)	142.3 ± 46.20	133.4 ± 40.600	0.303
Laboratory			
WBC (10^3/μL)	8.73 ± 4.400	9.28 ± 3.1000	0.475
Lymphocyte (%)	24.25 ± 10.50	27.74 ± 13.300	0.120
Monocyte (%)	7.14 ± 2.400	7.38 ± 2.5000	0.600
Neutrophil (%)	66.49 ± 12.40	62.8 ± 14.900	0.153
NLR	3.93 ± 3.900	3.37 ± 3.1000	0.434
LMR	4.17 ± 5.900	4.06 ± 2.1000	0.913
Total cholesterol (mg/dL)	166.9 ± 41.80	168.4 ± 36.700	0.848
TG (mg/dL)	96.7 ± 50.10	100.3 ± 49.900	0.710
LDL (mg/dL)	101.1 ± 34.20	102.8 ± 29.300	0.786
HDL (mg/dL)	47.9 ± 13.30	46.2 ± 11.600	0.465
MDRD eGFR	78.8 ± 30.70	84.2 ± 36.20	0.391
CKD EPI eGFR	73.2 ± 22.90	81.9 ± 20.00	0.042
Intravenous rt-PA use (n [%])	27 (33.8) 0	21 (52.5) 00	0.048
Initial NIHSS (IQR)	15 (12–17)	11 (8–15)	< 0.001
DWI ASPECTS	4 (3–5)	5 (3–5)	0.920
TOAST			
CE (n [%])	50 (62.5) 0	19 (47.5) 00	0.117
LAA (n [%])	9 (11.3) 0	5 (12.5) 00	0.841
UD (n [%])	20 (25.0) 0	16 (40.0) 00	0.091
mTICI reperfusion grade	0		
2b (n [%])	26 (32.5) 0	16 (40.0) 00	0.417
3 (n [%])	54 (67.5) 0	24 (60.0) 00	0.417
Collateral grade before EVT			
Good (3–4) (n [%])	14 (17.5) 0	15 (37.5) 00	0.016
Postprocedural hemorrhagic transformation (n [%])	57 (71.3) 0	16 (40.0) 00	0.001
HI-1 (n [%])	18 (22.5) 0	5 (12.5) 00	0.190
HI-2 (n [%])	10 (12.5) 0	5 (12.5) 00	1.000
PH-1 (n [%])	10 (12.5) 0	2 (5.0) 00	0.197
PH-2 (n [%])	18 (22.5) 0	4 (10.0) 00	0.095
Symptomatic ICH (n [%])	6 (7.5) 0	2 (5.0) 00	0.605

* Values expressed with "±" are mean ± standard deviation

Abbreviations: DM = diabetes mellitus; SBP = systolic blood pressure; DBP = diastolic blood pressure; BS = blood sugar; WBC = white blood cell; Hgb = hemoglobin; Hct = hematocrit; NLR = neutrophil to lymphocyte ratio; LMR = lymphocyte to monocyte ratio; BUN = blood urine nitrogen; TG = triglyceride; LDL = low density lipoprotein; HDL = high density lipoprotein; rt-PA = recombinant tissue plasminogen activator; NIHSS = National Institutes of Health Stroke Scale; DWI ASPECTS = Diffusion-Weighted Imaging Alberta Stroke Program Early Computed Tomography Scores; TOAST = Trials of Org 10,172 in Acute Stroke Treatment; CE = cardioembolism; LAA = large artery atherosclerosis; OD = other determined; UD = undetermined; mTICI = modified thrombolysis in cerebral infarction; EVT = endovascular therapy; HI = hemorrhagic infarction; PH = parenchymal hemorrhage; ICH = intracerebral hemorrhage

Table 3 Multivariate analysis of the association between factors and functional outcomes after EVT

	Adjusted OR	95% CI	*p*-value
Age	1.052	1.002–1.105	**0.041**
Intravenous rt-PA use	0.310	0.118–0.813	**0.017**
Initial NIHSS	1.181	1.037–1.344	**0.012**
Atrial fibrillation	1.347	0.524–3.462	0.537
Postprocedural HTf	2.356	0.891–6.229	0.084
Good preEVT collaterals	0.386	0.136-1.100	0.075
Initial sBP	1.012	0.991–1.035	0.268
CKD EPI eGFR	1.007	0.980–1.035	0.594

Bold font indicates statistical significance

Abbreviations: OR=odds ratio; CI=confidence interval; SBP=systolic blood pressure; NIHSS=National Institutes of Health Stroke Scale; EVT=endovascular therapy

Adjusted variables: Age, atrial fibrillation, initial SBP, initial NIHSS score, postprocedural hemorrhagic transformation, good preEVT collaterals

Unlike previous studies, our research specifically identified the factors most likely to contribute to FR in patients with AIS and LCI. Since earlier studies on FR did not focus exclusively on patients with LCI, particularly those with low ASPECT scores, discrepancies in the findings between our study and prior research are expected. Our study's emphasis on this distinct patient subgroup provides a more targeted understanding of FR in cases with significant infarct burden.

In our registry, FR occurred in approximately 66% of cases, showing the frequency slightly higher than in other studies. This is likely due to the relatively longer door-to-recanalization time compared to other studies. In a well-designed study, DIRECT-MT, the door-to-recanalization time was around 280 min, whereas it was approximately 380 min in our registry [14]. This high duration is explained by the geographical challenges of our stroke center, which encompasses numerous islands, mountainous terrain, and rural areas. It will serve as a foundation for highlighting the importance of pre-hospital management support in the future.

Previous research has suggested a relationship between FR and high NIHSS scores [7, 8, 15–17]. In patients with severe stroke, while the benefit of EVT was greater compared to medical treatment alone, FR tended to increase as stroke severity escalated. However, despite this increase in FR, the overall advantage of EVT remained more pronounced [8, 18]. This trend was similarly noted in our study. Therefore, it would be unnecessary to exclude patients with large ischemic cores from EVT based on the high NIHSS score. There are controversies about the effect of prior collateral flow status on the FR [5, 17, 19]. In our study, we observed that patients who experienced FR tended to have poor collateral flow. Collateral flow is known to develop poorly in elderly patients or cases of cardioembolic stroke [20–23]. The relatively high prevalence of atrial fibrillation in the FR group, along with older age, might contribute to poor collateral flow within this group. In patients already presenting with a large ischemic core with a small penumbra, the efficacy of collateral flow is diminished, suggesting that the advantage provided by collateral flow might have decreased somewhat. However, although not statistically significant, good collaterals showed a trend of protective effect with an adjusted odds ratio of 0.386. Therefore, a well-designed study with a larger sample size is necessary in the future.

Thrombolysis administered before EVT also exhibited a protective effect against FR (OR 0.310, 95% CI 0.118–0.813, p=0.017). Recent studies have excluded thrombolysis before EVT [24–26], but our data suggest that omitting thrombolysis in patients with large ischemic core does not yield significant benefits and remains advantageous.

Our study had several limitations. First, the study had generalization issues as it was conducted at a single comprehensive stroke center. Second, the retrospective design limited the control of all variables that may influence patient treatment or outcomes. Third, the sample size was relatively small, indicating that a multicenter study targeting a larger population is necessary in the future. Fourth, our study assessed the ASPECT score using DWI, but since most previous studies have typically used CT-based ASPECT scoring, there may be limitations in generalizing our results. Fifth, although we defined functional independence as mRS 0–2 based on the definition of FR, this is stricter than the outcome of mRS 0–3 used in previous large-core trials. Hence, caution is required in interpreting the results, and further studies focusing only on LCI patients may be necessary. Last, since our study lacks information about the final infarct volume, further analysis will be necessary.

In conclusion, FR was prevalent among patients undergoing EVT with a large ischemic core. Older age, high initial NIHSS score, and prior thrombolytic treatment were identified as factors influencing FR. In the future, a well-designed prospective multicenter study is warranted for analyzing the impact of FR.

Abbreviations

AIS	Acute ischemic stroke
EVT	Endovascular treatment; FR = Futile recanalization
LCI	Large core infarction
rt-PA	recombinant tissue plasminogen activator
NIHSS	National Institutes of Health Stroke Scale
DWI ASPECTS	Diffusion-Weighted Imaging Alberta Stroke Program Early Computed Tomography Scores
mRS	modified rankin scale
TOAST	Trials of Org 10172 in Acute Stroke Treatment
mTICI	modified thrombolysis in cerebral infarction
HI	hemorrhagic infarction
PH	parenchymal hemorrhage
ICH	intracerebral hemorrhage

SELECT2	Randomized Controlled Trial to Optimize Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke
ANGEL-ASPECT	Study of Endovascular Therapy in Acute Anterior Circulation Large Vessel Occlusive Patients with a Large Infarct Core
RESCUE-Japan LIMIT	Recovery by Endovascular Salvage for Cerebral Ultra-Acute Embolism-Japan Large Ischemic Core Trial

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Author contributions
Study consent and design: H Kim, MS ParkAcquisition of data: JT Kim, KH Choi, W Yoon, BY Baek, SK Kim, YS Kim, TS KimAnalysis and interpretation of data: H Kim, MS ParkDrafting of the manuscript: H Kim, MS ParkAll authors reviewed the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethical approval/Informed consent
This research was approved by the Institutional Review Board of Chonnam National University Hospital and the requirement for informed consent was waived (IRB No. CNUH-2020-024). This study was performed in accordance with the principles of the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Disclosures
None.

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References

1. Sarraj A, Hassan AE, Abraham MG, Ortega-Gutierrez S, Kasner SE, Hussain MS, et al. Trial of endovascular thrombectomy for large ischemic strokes. N Engl J Med. 2023;388:1259–71.
2. Huo X, Ma G, Tong X, Zhang X, Pan Y, Nguyen TN, et al. Trial of endovascular therapy for acute ischemic stroke with large infarct. N Engl J Med. 2023;388:1272–83.
3. Yoshimura S, Sakai N, Yamagami H, Uchida K, Beppu M, Toyoda K, et al. Endovascular therapy for acute stroke with a large ischemic region. N Engl J Med. 2022;386:1303–13.
4. Nie X, Leng X, Miao Z, Fisher M, Liu L. Clinically ineffective reperfusion after endovascular therapy in acute ischemic stroke. Stroke. 2023;54:873–81.
5. Deng G, Xiao J, Yu H, Chen M, Shang K, Qin C, et al. Predictors of futile recanalization after endovascular treatment in acute ischemic stroke: a meta-analysis. J Neurointerv Surg. 2022;14:881–5.
6. Zhou T, Yi T, Li T, Zhu L, Li Y, Li Z, et al. Predictors of futile recanalization in patients undergoing endovascular treatment in the direct-mt trial. J Neurointerv Surg. 2022;14:752–5.
7. Shi ZS, Liebeskind DS, Xiang B, Ge SG, Feng L, Albers GW, et al. Predictors of functional dependence despite successful revascularization in large-vessel occlusion strokes. Stroke. 2014;45:1977–84.
8. Lee SH, Kim BJ, Han MK, Park TH, Lee KB, Lee BC, et al. Futile reperfusion and predicted therapeutic benefits after successful endovascular treatment according to initial stroke severity. BMC Neurol. 2019;19:11.
9. Higashida RT, Furlan AJ, Roberts H, Tomsick T, Connors B, Barr J, et al. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. Stroke. 2003;34:e109–137.
10. Wang L, Xiong Y. Advances in futile reperfusion following endovascular treatment in acute ischemic stroke due to large vessel occlusion. Eur Neurol. 2023;86:95–106.
11. van der Steen W, van de Graaf RA, Chalos V, Lingsma HF, van Doormaal PJ, Coutinho JM, et al. Safety and efficacy of aspirin, unfractionated heparin, both, or neither during endovascular stroke treatment (mr clean-med): an open-label, multicentre, randomised controlled trial. Lancet. 2022;399:1059–69.
12. Zhang Y, Zhang L, Zhang Y, Li Z, Zhang Y, Xing P, et al. Endovascular recanalization for acute internal carotid artery terminus occlusion: a subgroup analysis from the direct-mt trial. Neurosurgery. 2022;91:596–603.
13. Shahid AH, Abbasi M, Larco JLA, Madhani SI, Liu Y, Brinjikji W et al. Risk factors of futile recanalization following endovascular treatment in patients with large-vessel occlusion: systematic review and meta-analysis. Stroke-Vasc Interv N. 2022;2.
14. Al-Mufti F, Elfil M, Ghaith HS, Ghozy S, Elmashad A, Jadhav AP, et al. Time-to-treatment with endovascular thrombectomy in patients with large core ischemic stroke: the 'late window paradox'. J Neurointerv Surg. 2023;15:733–4.
15. Olivot JM, Heit JJ, Mazighi M, Raposo N, Albucher JF, Rousseau V, et al. What predicts poor outcome after successful thrombectomy in early time window? J Neurointerventional Surg. 2022;14:1051–.
16. Hussein HM, Saleem MA, Qureshi AI. Rates and predictors of futile recanalization in patients undergoing endovascular treatment in a multicenter clinical trial. Neuroradiology. 2018;60:557–63.
17. Ni H, Liu X, Hang Y, Jia Z, Cao Y, Shi H, et al. Predictors of futile recanalization in patients with acute ischemic stroke undergoing mechanical thrombectomy in late time windows. Front Neurol. 2022;13:958236.
18. Badhiwala JH, Nassiri F, Alhazzani W, Selim MH, Farrokhyar F, Spears J, et al. Endovascular thrombectomy for acute ischemic stroke a meta-analysis. Jama-J Am Med Assoc. 2015;314:1832–43.
19. Pan H, Lin CC, Chen LN, Qiao Y, Huang PS, Liu B et al. Multiple-factor analyses of futile recanalization in acute ischemic stroke patients treated with mechanical thrombectomy. Front Neurol. 2021;12.
20. Maguida G, Shuaib A. Collateral circulation in ischemic stroke: an updated review. J Stroke. 2023;25:179–98.
21. Sim JE, Chung JW, Seo WK, Bang OY, Kim GM. Association of systolic blood pressure and cerebral collateral flow in acute ischemic stroke by stroke subtype. Front Neurol. 2022;13:863483.
22. Sinha A, Stanwell P, Beran RG, Calic Z, Killingsworth MC, Bhaskar SMM. Stroke aetiology and collateral status in acute ischemic stroke patients receiving reperfusion therapy-a meta-analysis. Neurol Int. 2021;13:608–21.
23. Arsava EM, Vural A, Akpinar E, Gocmen R, Akcalar S, Oguz KK, et al. The detrimental effect of aging on leptomeningeal collaterals in ischemic stroke. J Stroke Cerebrovasc Dis. 2014;23:421–6.
24. Zi W, Qiu Z, Li F, Sang H, Wu D, Luo W, et al. Effect of endovascular treatment alone vs intravenous alteplase plus endovascular treatment on functional independence in patients with acute ischemic stroke: the devt randomized clinical trial. JAMA. 2021;325:234–43.
25. Suzuki K, Matsumaru Y, Takeuchi M, Morimoto M, Kanazawa R, Takayama Y, et al. Effect of mechanical thrombectomy without vs with intravenous thrombolysis on functional outcome among patients with acute ischemic stroke: the skip randomized clinical trial. JAMA. 2021;325:244–53.
26. Yang P, Zhang Y, Zhang L, Zhang Y, Treurniet KM, Chen W, et al. Endovascular thrombectomy with or without intravenous alteplase in acute stroke. N Engl J Med. 2020;382:1981–93.

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