Intracranial artery calcifications profile as a predictor of recanalization failure in endovascular stroke treatment

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ABSTRACT

Background

Acute ischemic stroke with large or medium-vessel occlusion associated with intracranial artery calcification (IAC) is an infrequent phenomenon presumably associated with intracranial atherosclerotic disease. We aimed to characterize IAC and its impact on endovascular treatment outcomes.

Methods

We performed a retrospective cross-sectional study of consecutive patients with stroke treated with thrombectomy from January 2020 to July 2021 in our institution. We described IAC findings (length, density and location pattern) on baseline non-contrast CT. Patients were divided into 3 groups: IAC related to the occlusion location (symptomatic-IAC group), unrelated to the occlusion (asymptomatic-IAC group), and absence of any IAC (non-IAC group). We analyzed the association between the IAC profile and outcomes using logistic regression models. Intracranial angioplasty and stenting were considered rescue treatments.

Results

Of 393 patients included, 26 (6.6%) patients presented a symptomatic-IAC, 77 (19.6%) patients an asymptomatic-IAC and in 290 (73.8%) patients no IAC was observed. The rate of failed recanalization (eTICI 0-2a) before rescue treatment was higher in symptomatic-IAC (65.4%) than in a-IAC (15.6%; *p<0,001*) or non-IAC (13.4%; p<0,001). Rescue procedures were more frequently performed in s-IAC (26.9%) than in a-IAC (1.3%; *p<0,001*) and non-IAC (4.1%; *p<0,001*).

After adjusting for identifiable clinical and radiological confounders, symptomatic-IAC emerged as an independent predictor of failed recanalization (Odds Ratio (OR) 11.89, 95% Confidence Interval (CI) 3.94-35.91; $p<0.001$), adoption of rescue procedures (OR 12.38; 95%CI 2.22-69.09; $p=0.004$) and poor functional outcome (90-day mRS≥3 OR 3.51; 95%CI 1.02-12.00; $p=0.046$).

Conclusions

The presence of intracranial artery calcification related to the occlusion location is associated with worse angiographic and functional outcomes. Therefore, identifying of symptomatic-IAC on baseline imaging may guide optimal endovascular treatment strategy predicting the need for intracranial stenting and angioplasty.

NON-STANDARD ABBREVIATIONS AND ACRONYMS

AIS Acute Ischemic Stroke

ASPECTS Admission Alberta Stroke Program Early CT Score

EVT Endovascular Treatment

IAC Intracranial Artery Calcification

ICAD Intracranial Atherosclerotic Disease

IVT Intravenous Thrombolysis

LVO Large Vessel Occlusion

eTICI modified Thrombolysis in Cerebral Ischemia

NCCT Non-Contrast Computed Tomography

NIHSS National Institutes of Health Stroke Scale

INTRODUCTION

Acute ischemic stroke with large or medium-vessel occlusion associated with intracranial artery calcification (IAC) is an infrequent phenomenon that has been associated with different etiologies such as an intracranial atherosclerotic disease (ICAD) and calcified cardiac emboli. A calcified thrombus has been reported in 2.7-5.9% of patients with an acute ischemic stroke [1,2] and in 1.3-1.8% of patients who underwent endovascular treatment (EVT)[3-5].

Although EVT for acute ischemic stroke has been established as the standard of care among patients with large vessel occlusion [6,7], both ICAD and calcified emboli have been associated with lower recanalization rates. Two recent studies showed that the presence of IAC in the symptomatic vessel was associated with significantly worse angiographic outcomes. Despite these findings, symptomatic IAC was not consistently associated with worse functional outcomes and/or mortality [3,5].

With limited number of studies, the ultimate EVT strategy to achieve best procedural and functional outcomes in patients with an IAC-related acute ischemic stroke remains unclear. We aimed to characterize IAC in acute ischemic stroke patients presenting with a large or medium-vessel occlusion and its impact on EVT procedural results such as recanalization rates, need for intracranial angioplasty and stenting, and clinical outcomes.

METHODS

Anonymized data supporting this study's findings are available for any qualified investigator upon reasonable request to the corresponding author. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statements[8].

Study design and population

We performed a retrospective study based on a prospectively maintained single-center database of patients with an acute ischemic stroke undergoing reperfusion treatments. We selected patients with an intracranial large or medium artery occlusion (intracranial internal carotid, middle cerebral artery, anterior cerebral artery, posterior cerebral artery, intracranial vertebral artery and/or basilar artery) who received EVT from January 2020 to July 2021. Exclusion criteria were admission after 24 hours from stroke symptoms onset, and the presence of isolated extracranial occlusion. The patient selection process is represented in Figure S1. Chart evaluation of eligible patients was conducted by MR-G.

Clinical and radiological parameters:

Recorded demographic and clinical variables included age, sex, baseline mRS, medical comorbidities, stroke severity assessed by National Institutes of Health Stroke Scale (NIHSS), admission Alberta Stroke Program Early CT score (ASPECTS), workflow times (symptom onset, imaging, and groin puncture), and reperfusion therapies administered. In all cases, first-line EVT was performed with commercially available stent retrievers and aspiration catheters. Rescue procedures (intracranial angioplasty +/- intracranial stenting) could be adopted according to neurointerventionalist criteria.

Recanalization was assessed before and after rescue procedures were adopted. The degree of recanalization was determined prospectively by consensus between the interventionalist and the vascular neurologist immediately after the procedure using the expanded Thrombolysis in Cerebral Ischemia (eTICI) score. Patients were considered to achieve successful recanalization if at least 50% of downstream reperfusion was achieved (2TICI $\geq$ 2B).

The location, length and density of the intracranial artery calcifications with intimal pattern were registered on admission non-contrast computed tomography (NCCT) with a slice thickness $\leq$1 mm by MR-G and subsequently validated by MR and MRe. Definite cases of IAC were only included if consensus was reached by the aforementioned evaluators. All intracranial vessels were visually inspected independently of the occlusion location to identify hyperdense lesions or segments. When hyperdensities were identified, a region of interest was drawn over the vessel and/or thrombus to measure the Hounsfield units (HU); IAC was considered for values > 130HU, analogous to cardiology scoring systems[9]. IAC pattern was differentiated into intimal and medial IAC according to a previously validated score, which assesses thickness (1 point for ≥1.5mm, 3 for <1.5mm), circularity (1 point for dot, 2 for <90º, 3 for 90–270º, and 4 for 270–360º), and morphology along the long axis of the artery (1 for irregular/patchy, 4 for continuous, and 0 points for indistinguishable) [10]. The score designates an intimal IAC when ranged from 1 to 6 points, and a medial IAC when ranged from 7-11 points.

Compagne et al. reported that patients with an intimal IAC pattern did not benefit from EVT in contrast to those with a medial IAC pattern [11]. For this reason, we excluded from our analysis patients with a medial IAC calcification pattern as characterized by a thin, continuous, and almost circular calcification (Figure 1). Patients were divided into

3 groups according to the presence of intimal IAC and its association with the acute occlusion: symptomatic-IAC group (s-IAC) where the lesion is associated with the occlusion; asymptomatic-IAC group (a-IAC) where the lesion is not associated with the occlusion and absence of any IAC group (no-IAC).

The primary clinical outcome was the modified Rankin scale (mRS) score at 90 days evaluated through a telephone call by a certified central assessor who was unaware of the IAC findings assignment. Codi Ictus de Catalunya registry (CICAT) is a prospective official mandatory registry of all stroke codes in Catalunya; all included patients are centrally evaluated by trained and certified evaluators (independent from the treating hospitals) who are unaware of potential patient participation in trials or studies. Poor functional outcome was defined as a 90-day mRS score ≥3. All patients were treated according to institutional protocols based on European Stroke Organization guidelines [7] without any investigation or specific treatment performed for the purpose of this study. Data were prospectively recorded in an Institutional database approved by the local ethics committee. Because of the retrospective nature of the study, the need for written informed consent was waived.

Statistical analysis:

Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assure normality of continuous variables. Categorical variables were presented as absolute values and percentages and continuous variables as median (interquartile range (IQR)) or means (± standard deviation (SD)) as indicated. Statistical significance for intergroup differences was assessed by Pearson $\chi 2$ test or Fisher exact test for categorical variables and by Mann-Whitney U test, Student t-test or ANOVA/Kruskal Wallis test as appropriate to continuous variables. Multivariable binary logistic regression analyses were modeled to determine the association between symptomatic-IAC and outcomes, including angiographic results (failed recanalization at first pass and before rescue procedures defined as eTICI 0-2a, final eTICI score), need of rescue procedures, and functional disability. The analyses were adjusted using variables that presented a statistically significant association or clinical relevance with the explored outcome (Tables S1-3 on supplemental material).

A p-value <0.05 was considered statistically significant. All analyses were performed using the IBM SPSS Statistics version 25 software.

RESULTS

From January 2020 to July 2021, a total of 462 patients who presented to our institution with an acute ischemic stroke due to a large or medium-vessel and were treated with EVT were eligible for the study. Of them, we finally included 393 patients who met eligibility criteria. The median age was 77 (IQR 65-85) years old, 48.6% (191 patients) were female, and the median premorbid mRS was 1 (IQR 0-2). Among evaluated patients, 26 patients were found to have a symptomatic-IAC (s-IAC 6.6%), 77 patients were found to have an asymptomatic-IAC (a-IAC: 19,6%), and 290 were found to have no IAC (no-IAC: 73.8%). Table 1 summarizes the baseline characteristics and demographics according to the presence of IAC.

The anatomic distribution of IAC is also shown in table 1; Symptomatic-IAC was more frequently found in the intracranial internal carotid (9/26, 34.6%) and posterior circulation arteries (8/26, 30.7%). Fourteen patients with s-IAC (53.8% of s-IAC) presented additional IAC in other locations unrelated to the occlusion. Median s-IAC attenuation and length were 453±250 HUs and 4.83±2.83 mm, respectively. There were no differences in terms of attenuation and length of the IAC between s-IAC group and a-IAC group. There were no differences in terms of stroke severity, ASPECTS, workflow times, or rate of intravenous thrombolysis (IVT) between the 3 groups (Table 1).

Angiographic and clinical outcomes

The most frequent first-line EVT technique was combination of stent retrieval and distal aspiration (316/393, 80.4%). As compared to patients in non-IAC group, patients in the s-IAC group had longer groin puncture to reperfusion time (64 minutes (IQR 40-89) vs 38 (IQR 24-67), p=0.002). The rate of failed reperfusion without rescue procedures (65.4% vs 15.6% in a-IAC and 13.3% in non-IAC groups, p<0.001) and the use of rescue procedures (26.9% vs 1.3% in a-IAC and 4.1% in non-IAC groups, p<0.001) were higher in the s-IAC patients (Table 2). The presence of s-IAC was not significantly associated with higher number of thrombectomy passes. Detailed information on the angiographic and clinical outcomes is presented in Table 2.

When the IAC intimal pattern was included in the multivariable logistic regression model with potential confounders (such as age, ASPECTS, tandem occlusion, onset to groin time, intravenous thrombolysis, and first-line EVT technique), symptomatic-IAC emerged as an independent predictor of failed recanalization at first pass (eTICI 0-2a 73.1% vs 53.2% in a-IAC and 40.7% in non-IAC, p=0.008; OR 4.37 (95%CI 1.47-13.0)), failed recanalization without rescue procedures (eTICI 0-2a 65.4% vs 15.6% in a-IAC and 13.4% in non-IAC, p<0.001; OR 11.89 (95%CI 3.94-35.91)) and need of rescue procedures (26.9% vs 1.3% in a-IAC and 3.8% in non-IAC, p=0.004; OR 12.38 (95%CI 2.22-69.09)). Pre-procedural intravenous thrombolysis was not associated with recanalization rates (Table 3, Figure 2A).

Among patients with s-IAC who underwent rescue procedures, final successful recanalization (TICI 2b-3) was achieved in 71.4% of cases (Figure 2B). Thus, rescue procedures in s-IAC patients resulted in an improvement of recanalization. However, failed recanalization rates were still higher (28.6% vs 14.3% in a-IAC and 10.3% in non-IAC, p=0.189; OR 3.94 (95% CI 0.51-30.52)).

The presence of s-IAC was not significantly associated with hemorrhagic complications (Table 2). After adjusting for identifiable confounders in the clinically-targeted multivariable analysis, s-IAC was an independent predictor of 90-day disability (mRS 3-6 80.8% in s-IAC vs 76.6% in a-IAC and 62.3% in non-IAC, p=0.046; OR 3.51 (95%CI 1.02-12.00) comparing with a-IAC and non-IAC groups (Table 3, Figure 3).

DISCUSSION

Our study shows that up to 6% of the patients undergoing EVT for an acute stroke harbor a calcification at the occlusion location that is identifiable on admission CT imaging. The presence of a s-IAC predicted worse procedural and functional outcomes. However, recanalization rates improved with rescue procedures such as intracranial angioplasty and stenting. Preprocedural identification of s-IAC could lead to the early consideration of rescue treatments. This becomes important since the conventional tools for mechanical thrombectomy such as aspiration and/or stent retriever alone may not be sufficient in this disease process and the sequelae of recurrent thrombectomy attempts, such as thrombus fragmentation and microvascular impairment could be detrimental leading to worse outcomes.

Intracranial artery calcification within the symptomatic vessel has been proposed as a potential and infrequent marker of a worse angiographic outcomes in multiple studies [1-

[3,5,12,13]. An in-vitro model of calcified occlusions suggested the triple combination of a stent retriever, local aspiration and flow arrest using a balloon guide catheter as the best first-line approach [14]. However, there is a paucity of data to guide the optimal EVT strategy to achieve the best clinical outcomes in these patients.

Our study shows that acute ischemic stroke associated with IAC is not a rare phenomenon. Symptomatic IAC was observed in up to 6.6% of the patients receiving EVT in our institution, which is slightly higher than previous studies reports [3,5]. However, our study includes both anterior and posterior circulation occlusions and IAC located in medium size intracranial vessels, while previous studies included only patients with an anterior circulation stroke.

Although previous studies have hypothesized an embolic etiology of symptomatic IAC [1,2], clinical and radiological characteristics of these patients favor an ICAD etiology. Intimal calcification pattern (Figure 1) related to atherosclerotic luminal stenosis can occur in all major cerebral arteries and is a major cause of territorial hypoperfusion and artery-to-artery embolism[15]. No significant correlation between medial calcification and luminal stenosis has been established yet, although it is thought to affect arterial stiffening with consequent compliance deterioration and vasodilation limitation [16,17]. Furthermore, EVT in AIS with underlying ICAD has been described as more complex and technically challenging, with a higher probability of recanalization failure [18,19]. Thus, the presence of intimal IAC on imaging can be considered as an adjunct biomarker in the diagnosis of ICAD in addition to other imaging biomarkers and modalities such as the presence intracranial plaque and perfusion imaging.

In our series, successful recanalization (eTICI $\geq$ 2b) was achieved with first-line technique in only 26.9% of s-IAC cases, as opposed to 84.4% and 86.6% of a-IAC and non-IAC groups, respectively. Accordingly, s-IAC was associated with the need of endovascular rescue procedures, as intracranial angioplasty and stent deployment, and worse functional outcomes. Despite recanalization rates and the need of rescue procedures between asymptomatic-IAC and non-IAC groups being similar, worse outcomes were observed in asymptomatic-IAC patients. Intracranial artery calcifications (both symptomatic and asymptomatic) could also be associated with poor prognosis because of higher prevalence of vascular risk factors, older age, arterial wall stiffening, or microvascular impairment.

As previously reported [3,5], IVT before EVT did not lead to a higher or lower rate of recanalization. Intracranial stent deployment requires concomitant administration of intravenous antiplatelet therapy, which might increase the risk of intracranial bleeding if IVT has been administered. Our limited cohort does not allow us to achieve conclusions related to concomitant IVT administration. Further studies are warranted to assess the safety of IVT administration where s-IAC seen on initial imaging and where intracranial stenting and peri-procedural antiplatelet therapy are anticipated.

In the case of s-IAC related occlusions where rescue procedures such as stenting and/or angioplasty were performed, the rate of recanalization rose to values closer to the asymptomatic-IAC group and non-IAC group rates. Early adoption of rescue procedures might lead to successful reperfusion through decreasing the number of thrombectomy attempts. This translates to improved clinical outcomes due to several reasons such as shorter procedural time, decreased arterial wall damage or thrombus fragmentation and/or microvascular impairment [20,21].

The feasibility, safety and efficacy of rescue intracranial stenting after failed thrombectomy in patients with anterior circulation LVOs had been suggested in two retrospective studies [22-24] and is being tested in prospective randomized clinical trials (NCT03955835 and NCT03993340). More studies are needed in order to optimize patient selection for these procedures. The presence of symptomatic-IAC on initial imaging could be considered for this purpose.

If a symptomatic-IAC related occlusion is identified on baseline stroke imaging, we suggest that intracranial angioplasty and stent deployment be considered among the first-line treatment options; the strategy might include initial loading of antiplatelet drugs and gentle debulking of the lesion with a stent-retriever to avoid repetition of unsuccessful thrombectomy attempts that could cause endothelial denudation and plaque activation. Further studies are warranted to specifically evaluate the safety and clinical efficacy of primary intracranial stenting in patients with symptomatic-IAC related occlusion.

Limitations

Our study has some limitations. Main limitations include a retrospective analysis, the lack of independent imaging core lab adjudication and the self-reported eTICI evaluation. Additionally, the standard EVT approach in our center is a combined stent retriever and distal aspiration technique, with rare use of balloon guide catheter, followed by as needed rescue procedures at the discretion of the treating neurointerventionalists. Different approaches may have led to different angiographic results; however, our overall rate of recanalization is comparable to other prospective series. Finally, our study has been performed in a single center and the results need to be reproduced in multicenter studies to confirm our findings.

CONCLUSIONS

The presence of intracranial artery calcification related to the occlusion location among patients with an acute ischemic stroke is not infrequent and it is associated with worse angiographic and functional outcomes. Identification of symptomatic-IAC on baseline stroke imaging may help to anticipate the optimal endovascular treatment strategy and suggest the need for rescue procedures, such as intracranial stenting and angioplasty.

Table 1. Baseline characteristics and demographics

Footnote:

*Combination of stent retrieval and distal aspiration

† P value indicate differences between the three groups: Pearson χ2 test for categorical variables and ANOVA/Kruskal Wallis test as appropriate to continuous variables. $P < 0.05$ was considered statistically significant.

mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; CTP: Computed Tomography Perfusion; ASPECTS: Admission Alberta Stroke Program Early CT Score; ADAPT: A Direct Aspiration First Pass Technique; IAC: Intracranial Artery Calcifications.

	Symptomatic IAC (n=26)	Asymptomatic IAC (n=77)	No IAC (n=290)	P value†
Age (years) [median, IQR]	80 (66-87)	82 (72-88)	72 (63-83)	<0.001
Gender (female) [n, %]	12 (46.2%)	29 (37.7%)	150 (51.7%)	0.087
Risk factors [n, %]				
Former or current smoker	9 (34.6%)	23 (29.9%)	81 (27.9%)	0.901
Hypertension	**18 (69.2%)**	**65 (84.4%)**	**190 (65.5%)**	**0.006**
Diabetes mellitus	9 (34.2%)	21 (27.3%)	60 (20.7%)	0.161
Atrial fibrillation	4 (15.4%)	27 (35.1%)	72 (24.8%)	0.083
Ischemic heart disease	5 (19.2%)	17 (22.1%)	41 (14.1%)	0.199
Previous stroke	6 (23.1%)	12 (15.6%)	61 (21.0%)	0.528
Dyslipidemia	11 (42.3%)	43 (55.8%)	120 (41.4%)	0.074
Premorbid mRS [median, IQR]	**1 (1-2)**	**1 (1-3)**	**0 (0-2)**	
0	6 (23.1%)	10 (13.0%)	84 (29.0%)	
1	9 (34.6%)	30 (39.0%)	118 (40.7%)	**0.001**
2	7 (26.9%)	17 (22.1%)	57 (19.7%)	
3-4	1 (3.8%)	20 (26.0%)	31 (8.7%)	
TOAST classification				
Cardioembolic	6 (23.1%)	43 (55.8%)	168 (57.9%)	
Large-vessel atherosclerosis	15 (57.7%)	16 (20.8%)	47 (16.2%)	**<0.001**
Other determined etiology	0 (0%)	4 (5.2%)	22 (7.4%)	
Undetermined etiology	5 (19.2%)	14 (18.2%)	53 (18.2%)	
Baseline NIHSS [median, IQR]	15 (9-22)	16 (10-21)	16 (10-20)	0.923
Tandem occlusion [n, %]	4 (15.4%)	11 (14.3%)	38 (13.1%)	0.924
Occlusion level [n, %]				
Intracranial ICA	9 (34.6%)	9 (11.7%)	46 (15.9%)	
ACM M1	4 (15.4%)	35 (45.5%)	134 (46.2%)	
ACM M2	5 (19.2%)	16 (20.8%)	78 (26.9%)	**<0.001**
ACM M3	0 (0%)	2 (2.6%)	1 (0.3%)	
ACA	0 (0%)	3 (3.9%)	5 (1.7%)	
ACP	0 (0%)	6 (7.8%)	10 (3.4%)	
AV	5 (19.2%)	0 (0%)	4 (1.4%)	
AB	3 (11.5%)	6 (7.8%)	12 (4.1%)	
Wake-up stroke [n, %]	11 (42.3%)	35 (45.5%)	106 (36.6%)	0.359
Onset to groin time [mean ± SD]	501.8 ± 368.6	438.8 ± 321,3	416.0 ± 299.2	0.368
ASPECTS [median, IQR] [n, %]	10 (8 – 10)	10 (8-10)	9 (8-10)	0.558
Intravenous thrombolysis	4 (15.4%)	18 (23.4%)	96 (33.1%)	0.061
Primary endovascular technique [n, %]				
Combined technique*	**19/26 (73.1%)**	**69/77 (89.6%)**	**228/290 (78.6%)**	
ADAPT	**1/26 (3.8%)**	**6/77 (7.8%)**	**39/290 (13.4%)**	**<0.001**
Stent retriever + balloon guide catheter	**1/26 (3.8%)**	**2/77 (2.6%)**	**19/290 (6.6%)**	
Other	**5/26 (19.2%)**	**0/77 (0%)**	**4/290 (1.4%)**	

Number of IAC [mean ± SD]	2±1.06	1.62±0.96	-	<0.001
IAC location [n, %]	26	115	-	<0.001
Intracranial ICA	9 (34.6%)	47 (40.9%)		
ACM M1	4 (15.4%)	4 (3.5%)		
ACM M2	5 (19.2%)	1 (0.9%)		
ACM M3	0 (0%)	2 (1.7%)		
ACA	0 (0%)	3 (2.6%)		
ACP	0 (0%)	0 (0%)		
AV	5 (19.2%)	55 (47.8%)		
AB	3 (11.5%)	3 (2.6%)		
Maximal length (mm) [mean ± SD]	4.83±2.83	5.37±3.15	-	0.590
Maximal density (HU) [mean ± SD]	453±250	541±257	-	0.106
Coexistence of asymptomatic IAC [n, %]	14/26 (53.8%)	-	-	-

Table 2. Angiographic and clinical outcomes.

Footnote:

*P value indicate differences between the symptomatic-IAC patients and asymptomatic-IAC and non-IAC patients, respectively: Pearson χ2 test for categorical variables and Mann-Whitney U test or Student t-test as appropriate to continuous variables. P < 0.05 was considered statistically significant.

NIHSS: National Institutes of Health Stroke Scale; eTICI: expanded Thrombolysis in Cerebral Ischemia; PH: Parenchymal hemorrhage; mRS: modified Rankin Scale; IAC: Intracranial Artery Calcifications.

	Symptomatic IAC	**Asymptomatic IAC**		**No IAC**	
	(n=26)	**(n=77)**	**P value***	**(n=290)**	**P value***
Angiographic					
Frequency of rescue procedures [n, %] Angioplasty Angioplasty+stenting	7/26 (26.9%) 0/7 7/7	1/77 (1.3%) 0/1 1/1	**<0.001**	12/290 (4.1%) 2/12 10/12	**<0.001**
Groin to reperfusion time [median, IQR]	64 (40-89)	53 (31-78)	0.118	38 (24-67)	**0.002**
Number of passes [median, IQR]	2 (1-3)	2 (1-2)	0.990	2 (1-2)	0.782
First pass eTICI 0-2a [n, %]	19/26 (73.1%)	41/77 (53.2%)	0.076	118/290 (40.7%)	**0.001**
eTICI 0-2a without rescue procedures [n, %]	17/26 (65.4%)	12/77 (15.6%)	**<0.001**	39/290 (13.3%)	**<0.001**
Final eTICI 0-2a	12/26 (46.2%)	11 (14.3%)	**<0.001**	30/290 (10.3%)	**<0.001**
Clinical					
NIHSS at 24 hours [median, IQR]	16 (5-23)	13 (6-20)	0.401	10 (4-18)	0.114
Intracerebral hemorrhage (PH 1-2) [n, %]	2/24 (8.3%)	14/77 (18.2%)	0.346	32/288 (11.1%)	0.500
Symptomatic intracerebral hemorrhage [n, %]	1/24 (4.2%)	1/77 (9.1%)	0.676	22/288 (7.6%)	0.454
90-day mortality [n, %]	11/25 (42.3%)	31/77 (40.3%)	0.854	78/289 (27.0%)	0.097
90-day mRS score 3-6 [n, %]	21/26 (80.8%)	59/77 (76.6%)	0.661	180/289 (62.3%)	**0.060**

Table 3. Multiple logistic regression analyses for symptomatic intracranial artery calcification as a poor prognostic factor

Footnote:

Covariates included in the multivariable analysis were: Age, ASPECTS, tandem occlusion, intracranial occlusion location, onset to groin time, thrombolysis and first-line endovascular technique for angiographic outcomes. Age, premorbid mRS, hypertension, Atrial fibrillation, onset to groin time, NIHSS at onset, number of passes and intracranial occlusion location for clinical outcomes (see table S1-3).

eTICI: expanded Thrombolysis in Cerebral Ischemia; mRS: modified Rankin Scale.

Angiographic and clinical outcomes	OR	95% CI	P value
Failed recanalization at first pass (eTICI 0-2a)	4.37	1.47-13.0	0.008
Failed recanalization without rescue procedures (eTICI 0-2a)	11.89	3.94-35.91	<0.001
Failed final recanalization (eTICI 0-2a) **OR adjusted to symptomatic-IAC with rescue procedures*	3.94	0.51-30.52	0.189
Need of rescue procedures (angioplasty and/or stenting)	12.38	2.22-69.09	0.004
90-day mortality	2.39	0.90-6.36	0.081
90-day mRS score 3-6	3.51	1.02-12.00	0.046

Figure 1. Intracranial artery calcification (IAC) with intimal pattern (yellow arrows) located in intracranial internal carotid artery (ICA) and M1 segment t of right MCA [A], intracranial ICA [B], basilar artery [C] and M2 segment of left MCA [D]. We did not consider in our study when an intracranial artery calcification presented medial pattern (dotted yellow arrow), such as right vertebral artery [E] and bilateral ICA [F].

Figure 2. (A) Angiographic outcomes defined by eTICI score before rescue treatment. (B) Final angiographic outcomes after rescue treatment.

IAC; Intracranial Artery Calcifications; eTICI: modified Thrombolysis in Cerebral Ischemia

Figure 3. Functional outcome at 90 days.

IAC; Intracranial Artery Calcificarions; mRS: modified Rankin Scale

CONTRIBUTORSHIP

MR-G, MRe, and MRi contributed to the conception and design of the study. MR-G, MRe, MRu, JK, PL, MDDL, AG-T, MO-G, CP, FR, SB, MM, NR-V, DR-L, JJ, JP, DH, CM, AT and MRi contributed to the acquisition and analysis of data. MR-G drafted the manuscript and prepared the figures with significant contributions from MRe, MRu, AT, and MRi. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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DISCLOSURES

Carlos A Molina reported receiving personal fees from AstraZeneca for consultant services outside the submitted work. Alejandro Tomasello reported receiving personal fees from Anaconda Biomed, Balt, Medtronic, Perflow, and Stryker outside the submitted work. Marc Ribo reported receiving personal fees from Anaconda Biomed, AptaTargets, Cerenovus, Medtronic, Methinks, Philips, Sanofi, Stryker, Balt and Rapid AI outside the submitted work; he has a modest ownership of NoraHealth. No other disclosures were reported. Authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

DATA

Anonymized data supporting this study's findings are available reasonably to the corresponding author from any qualified investigator.

SUPPLEMENTAL MATERIAL

Figure S1

Tables S1–S3

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