Antiplatelet therapy increases symptomatic ICH risk after thrombolysis and thrombectomy

Running Title: Prior antiplatelet therapy and mechanical thrombectomy

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Abstract

Background and Purpose: The influence of chronic treatment by antiplatelet drug (APD) at stroke onset on the outcomes of patients with acute ischemic stroke (AIS) treated with combined intravenous thrombolysis (IVT) and endovascular therapy (EVT) is unclear. We investigated whether prior APD use influences the risk of symptomatic intracranial hemorrhage (sICH) and functional outcome in AIS patients ~~optimally~~ treated with combined reperfusion therapy.

Methods: A single-center retrospective analysis of AIS patients with proximal intracranial occlusion who underwent IVT and EVT between January 2015 and May 2017. The main outcomes were the incidence of sICH using the Heidelberg Bleeding Classification and patients' functional status at 90 days, as defined by the modified Rankin scale (mRS). Outcomes were evaluated according to ~~prior use of~~ daily exposure to APD and associations were assessed using multivariate logistic regression analysis.

Results: This study included 204 patients: 71 (34.8%) were taking APD before AIS. Patients with chronic treatment by APD at stroke onset had a higher rate of sICH (26.7% *vs*. 3.7%; $p<0.001$) and worse functional outcome (mRS > 2) at 90 days (69% *vs*. 36.8%; $p<0.001$). Prior APD use was associated with an increased likelihood of sICH (OR 9.8; 95%CI [3.6–31.3], $p<0.05$) and of functional dependence at 90 days (OR 5.72; 95%CI [2.09–1.72], $p<0.001$), independent of confounders on multivariate analysis.

Conclusions: Chronic treatment by APD at stroke onset in AIS patients with proximal intracranial occlusion treated using IVT and EVT increases the risk of sICH and worsens

the functional prognosis. Further investigation to refine acute revascularization strategies in this population might be required.

Introduction

Recanalization of the intracranial brain supplying arteries is one of the main predictors of good long-term functional outcome and low mortality in patients with acute ischemic stroke (AIS) (1). For patients admitted within 4.5 hours of symptom onset of IS related to proximal occlusion of an intracranial artery, the optimal revascularization strategy is the combination of intravenous thrombolysis (IVT) and endovascular therapy (EVT) (2,3). However, reperfusion therapies are associated with an increased risk of symptomatic intracranial hemorrhage (sICH) (2,4,5). While in most cases ICH observed following revascularization therapy does not affect the functional outcome at 3 months, large parenchymal cerebral hemorrhages and sICH can significantly worsen a patient's functional prognosis and increase mortality (6,7).

One potential risk factor for hemorrhagic infarction is pre-stroke daily antithrombotic use (8,9). Approximatively 30 to 40% of stroke patients are already treated chronically with an antiplatelet drug (APD) at admission (10,11). While such treatment has been associated with a significantly increased risk of sICH after IVT (12), no statistically significant association with a worse functional outcome has been established, even after adjusting for confounders. As a consequence, withholding IVT is not recommended in this population (12).

Recent studies have suggested the absence of an increased risk of sICH related to EVT alone (2). A meta-analysis of the major trials that compared the effects of EVT combined with the best available medical treatment (including IVT) for patients within the 4.5-hour time-window after symptom onset of acute IS versus the best medical treatment alone highlighted the safety of EVT in terms of secondary ICH (2). However,

a significant number of patients did not receive IVT and no analysis was performed including APD use as a potential confounder (13,14).

Therefore, this study specifically examined whether prior APD treatment influenced the rate of sICH and functional outcome evaluated at 3 months post-stroke in IS patients with proximal intracranial artery occlusion treated with the optimal reperfusion strategy, defined as a combination of IVT and EVT, within 4.5 h after symptom onset.

Materials and Methods

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study population

This was a retrospective analysis of a prospectively compiled database of consecutive patients admitted to our institution due to an AIS related to a proximal intracranial artery occlusion, and who were eligible for reperfusion strategy combining IVT and EVT. We included consecutive patients older than 18 years admitted between January 2015 and May 2017. Patients received IVT and endovascular treatment using either a stent-retriever or contact aspiration, according to the European Stroke Organization recommendations for AIS (15). No APD was used during acute procedure and until the brain imaging performed 24h after stroke symptoms onset.

Patients were excluded if they fulfilled one or more of the following criteria: (1) missing information on the use of APD before admission; (2) no follow-up brain imaging at 24 h, (3) emergency stenting requiring acute APD administration and (4) no 3-month modified Rankin Scale (mRS) data. The mRS was performed at 3 months by a

stroke neurologist during a planned post-stroke follow-up visit, or by a trained stroke nurse via a phone interview. The study population is part of the ObA2 regional cohort (National commission for data protection CNIL authorization n°911201). Each patient were asked for non-opposition for the use of clinical, biological and imaging data as collected in standard care.

Study variables

Antiplatelet therapy before stroke was the main variable of interest, and was self-reported by patients or their families and verified during hospitalization.

The following data, known for their prognostic value or association with ICH, were also recorded at baseline: (1) demographics (age and gender); (2) vascular risk factors [arterial hypertension, diabetes, dyslipidemia, smoking, coronary heart disease, atrial fibrillation, and history of previous stroke or transient ischemic attack (TIA)]; (3) pre-stroke mRS score; (4) between-hospital transfer; (5) admission blood pressure (systolic and diastolic); (6) admission serum glucose level; (7) stroke severity (NIHSS) at hospital admission; (8) occlusion topography (internal carotid, middle (M1 or M2), anterior (A1) or posterior (P1) cerebral arteries; (9) ASPECTS at admission; (10) number of microbleeds and extent of leukoaraiosis according to the Fazekas score evaluated on pre-treatment MRI; (11) time from symptom onset to the onset of thrombolytic therapy and groin puncture; (12) modified Treatment in Cerebral Ischemia (mTICI) score; and (13) stroke etiology according to the TOAST classification. Atherosclerosis was defined by the presence of intra or extracranial supraaortic vessel stenosis > 50 % identified during conventional angiography for EVT. Cardio-embolic mechanism was diagnosed when major cardio-embolic origin was identified after a minimal cardiological work-up

including, 48h ECG-recording and transthoracic echocardiography. Dissection and other sources were grouped in the other determined mechanism subgroup. Patients with two or more causes identified were excluded from the undetermined etiology subgroup and are presented as a group named multiple potential causes. Undetermined mechanisms defined patients with negative or incomplete evaluation.

Diagnoses of ICH and sICH

Computed tomography (CT) or magnetic resonance imaging (MRI) was performed routinely in all patients 24~36 h after revascularization treatment or in case of neurological deterioration and assessed for ICH according to the Heidelberg Bleeding Classification (HBC) (15). Symptomatic ICH was also defined according to HBC (16) as newly observed ICH associated with any of the following conditions: (1) NIHSS score increase by > 4 points compared with immediately before worsening; (2) NIHSS score increase by > 2 points in one category; and (3) deterioration leading to intubation, hemicraniectomy, external ventricular drain placement, or any other major interventions. An additional necessary condition for sICH was that the symptom deterioration could not be explained by causes other than the observed ICH.

Functional outcomes at 3 months

The primary outcome was the level of disability, assessed by the mRS at 3 months (17,18). A good functional outcome was defined as an mRS score of 0–2.

Statistical analysis

The main outcomes were the patients' functional status at 90 days and the incidence of sICH. We recorded parenchymal hematoma (PH) as a secondary outcome.

The statistical analyses were performed using R statistical software (ver. 3.5.0; R Development Core Team, Vienna, Austria). Means (standard deviations) and medians (25^{th} – 75^{th} percentiles) were used to describe the distribution of continuous variables; percentages described categorical variables.

The two groups (Chronic treatment by APD at stroke onset APD use *vs.* no APD use) were compared statistically using the Pearson χ^2 test or, in the case of small expected frequencies, Fisher's exact test. Continuous variables were compared using Student's *t*-test. Outcomes were compared according prior APD use status. Furthermore, the associations of prior APD use with the different outcomes were assessed using univariate and multivariate logistic regression models adjusting for potential confounders. Logistic regression models were used to adjust for the main confounding factors identified on the basis of a literature review and some variables that differed significantly ($p<0.05$) in the univariate analyses between the APD and no-APD groups. For each model, the maximum number of confounding factors that could be adjust for was defined according to the 1 variable per 10 events criterion (19). Assumption of the models (log-linearity of the associations) was systematically checked. Variables leading to convergence issues in the models were excluded. The results of the regression analyses are expressed as odds ratios (ORs) with corresponding confidence intervals (CIs). A *p*-value <0.05 was considered significant.

Results

Study population

Between January 2015 and May 2017, 236 consecutive patients received IVT in combination with EVT at our center; this study included 204 of these patients (**Figure 1**).

The population characteristics are summarized in the first column of **Tables 1** and **2**. The mean patient age was 69.3 ± 14.0 years; 53.9% were men, the median pre-stroke mRS score was 0 [0–1], and the median NIHSS score was 16 [11.5–20].

Of the 204 patients, 133 (65.2%) did not take APD before hospitalization. Of the 71 patients (34.8%) on long-term APD, 62 (87.3%) received aspirin, 7 (9.9%) clopidogrel, and 2 both aspirin and clopidogrel. None of the patients were treated by ticagrelor or prasugrel. ADP were used by 15% of patients ~~in~~ for primary prevention and by 85% ~~in~~ for secondary prevention for acute stroke, heart or peripheral artery disease.

Occlusion of the anterior circulation as noted in 93.1% (190/204) of the patients.

Successful recanalization (mTICI score ≥ 2b) was achieved in 91% of the study population.

ICH occurred in 134 patients (65.7%) and sICH in 24 patients (11.7%). Among the patients with ICH, 18.4% had a sICH. The 3-month good functional outcome and mortality rates were 48% and 15.2%.

Comparison of the APD and no-APD groups

Table 1 compares the baseline characteristics of patients with and without APD pretreatment. Patients in the APD group were significantly older (p=0.01), had more cardiovascular risk factors [hypertension (p<0.01), diabetes (p<0.01), dyslipidemia

(p<0.001)], and were more likely to have a vascular history than those in the no-APD group. The rate of glycaemia on arrival was also significantly higher in patients from the APD group. Pre-stroke mRS, NIHSS score, blood pressure on arrival, ASPECTS, occlusion topography, Fazekas score, and number of microbleeds did not differ between the two groups.

Table 2 compares the evolution and outcomes of patients with and without AP pretreatment. The successful recanalization (mTICI 2b and 3) rate did not differ between the two groups. However, there was a significant difference in the distribution of mTICI scores between the two groups (p<0.05). In the APD group 60.6% (43/71) of the patients had an mTICI score of 3, versus 52.6% (70/133) in the no-ADP group. However, favorable reperfusion (final mTICI 2b-3) rate was similar between groups (93.2 vs 87.3 %, p = 0.16).

The APD group had significantly higher rates of ICH (76.1% *vs*. 60.15%, p<0.001), ~~PH (40.5% *vs*. 10.5%, p<0.001)~~, and sICH (26.7% vs. 3.75, p<0.001) than the no-ADP patients. The proportion of patients with 3-month functional independence (mRS score ≤ 2) was significantly lower in the APD group than in the no-ADP group (31% *vs*. 63.15%, p<0.001). **Figure 2** shows the distribution of mRS scores in both groups. There was no significant difference in mortality between the two groups (22% *vs*. 13%, p=0.142).

Multivariate analysis

Tables 3a and 3b show the associations of baseline characteristics (age and NIHSS) and radiological variables (ASPECT and TICI) with the occurrence of sICH in the multivariate logistic regression analyses. Chronic treatment by APD at stroke onset was the only variable independently associated with a higher likelihood of sICH in both models (OR, 9.8; 95% CI: 3.6–31.35, $p<0.001$ and OR, 9.4; 95% CI: 3.5–30, $p<0.001$).

Table 4 depicts the associations of baseline clinical and radiological parameters with 3-month functional dependence (mRS > 2) in the multivariate logistic regression analyses. Chronic treatment by APD at stroke onset was independently associated with a higher likelihood of functional dependence at 90 days (OR, 5.72; 95% CI: 2.09–17.2, $p<0.001$). Stroke severity (NIHSS) at admission ($p<0.001$), blood glucose level at admission ($p<0.05$), and time from symptom onset to recanalisation ($p=0.01$) were also independently associated with a poor functional outcome at 3 months.

Furthermore, no patient with sICH had an mRS score ≤ 2 at 3 months, and mortality was significantly higher in these patients [sICH, 14 patients (56%); no-sICH, 19 patients (10.4%), $p<0.001$].

Discussion

Although 30 to 40% of patients admitted due to AIS are on chronic APD treatment at admission, modification of the acute revascularization strategy is not recommended by guidelines in this population (3,15). Our study demonstrates that, independently of demographic, clinical, and biological characteristics, patients with pre-stroke APD

212 treatment (i) have higher rates of asymptomatic and symptomatic ICH and (ii) a worse
213 functional prognosis at 3 months.

214 In accordance to the current literature, 34.8% of the patients included in this study
215 were on long-term APD before their stroke. Although the clinical and imaging
216 characteristics of our patients were similar to those described in the major endovascular
217 trials of AIS related to proximal intracranial artery occlusion (2,20), we observed a higher
218 frequency of ICH in our population [65.7% in total, with 43.9% hemorrhage infarction
219 (HI) and 21.2% PH] than in previous studies (i.e: 36 % in total with 23% HI and 13% PH
220 in THRACE study) (21). This high incidence is likely a consequence of methodology.
221 First, 85% of the post-revascularization imaging analyses performed at our center used
222 T2* MRI sequences, while most other studies used CT to detect and classify ICH (22,23).
223 While CT readily detects ICH, it frequently underestimates the incidence of ICH
224 following reperfusion therapy, i.e., at a rate a 50% to 70% in post-mortem studies, which
225 is highly similar to the results observed using T2* MRI sequences (24,25). Better
226 sensitivity of MRI over CT for the detection of HI, and a shift in classification from HI
227 to PH according to use of MRI versus CT, have clearly been established (26,27) and
228 account for most of the difference between the results reported here and those in previous
229 studies. Second, the updated HBC (16) includes a proportion of patients with ICH outside
230 the infarcted area compared with the more widely used European Cooperative Acute
231 Stroke Study (ECASS) classification (28). In addition, use of the HBC could explain the
232 high rate of sICH observed in our population (12%) compared with the typical rate of 5%
233 reported in studies using the ECASS III, National Institute of Neurological Disorders and
234 Stroke (NINDS), or Safe Implementation of Thrombolysis in Stroke-Monitoring Study
235 (SITS-MOST) definitions of sICH (2,21). In the present study, the increased rate of PH-

2 in the subgroup of patients treated by APD before the acute ischemic event supports the association between sICH and pre-stroke APD treatment. Finally, of the patients with ICH, 17.9% had sICH, which is a similar rate to other studies (19–27%) (28). Although mean delays between symptoms onset and revascularization were not different between patients chronically treated by APD and those without APD we cannot exclude that the risk of ICH might be influenced by this parameter which will have to be investigated in further studies.

The second objective of this study was to assess the influence of pre-stroke APD treatment on functional outcome. Overall, in our population, the rates of good functional outcome at 3 months (mRS score ≤ 2) and mortality were close to those found in previous studies (51.2% and 15.9%, respectively) (2,21). The fact that the higher rates of ICH and sICH were not associated with worse functional outcome also supports the hypothesis that the high rate of ICH was mainly attributable to better detection and categorization of ICH. Interestingly, APD treatment at the time of stroke onset was independently associated with the functional status at 3 months. This association could be related to two main factors. First, sICH, which is associated with pre-stroke APD treatment, is a well-known cause of increased mortality and poor functional prognosis (22). In this study, no patient with sICH had a mRS score ≤ 2 at 3 months, and mortality was significantly higher in these patients. Second, the occurrence of hemorrhagic transformation, even moderate, may delay the start of APD or anticoagulant treatment following stroke, thereby increasing the risks of re-occlusion and early recurrence (especially since a cardioembolic mechanism is frequently found in this population). Indeed, several studies have shown that early initiation of antithrombotic therapy after cerebral infarction partially reduces the risk of recurrent stroke and improves functional outcomes (29,30). All together these

results suggest that patients chronically treated by APD at stroke onset deserve greater attention and personalized revascularization strategies. Recent studies found that EVT alone is non-inferior to EVT combined to IVT in patients with intracranial proximal artery occlusion (31,32); since APD use is associated with a significant increase in the risk of ICH after IVT, the benefit of performing EVT alone in patients on chronic APD treatment at stroke onset and presenting directly at a comprehensive stroke center with a proximal occlusion is questionable. In case of IVT, two strategies might be discussed to reduce the risk of ICH among patients previously treated by APD, either using a low-dose IVT with alteplase IV (0.6 mg/kg), recent studies and meta-analyses (33) suggesting a similar efficacy and a better safety profile among patients chronically treated by APD compared with the standard dose, or using tenecteplase, which carries a potentially lower risk of hemorrhagic transformation (34,35). On the other hand the higher rate of excellent recanalization (TICI-3) among patients previously treated by APD potentially suggest the benefit of platelet inhibition in reperfusion strategies and will need further investigations.

Several limitations of our study need to be acknowledged. First, the modest sample size and retrospective analysis of prospectively collected data were important methodological shortcomings. Unfortunately, data on other potential risk factors described in the literature, like fluctuations in blood pressure in the acute phase (31) or collaterality (32), were unavailable in our electronic records database and thus were not evaluated as potential confounders. However, the strength of the association between pre-treatment with APD and the risk of sICH and poor functional prognosis strongly supports a critical role of APD in these complications. Second, 12% of the eligible patients had to be excluded, mainly because of the absence of mRS data at 3 months, which limits the statistical power of this study. However, patients with missing outcome data had clinical

characteristics comparable with those of our population, and their exclusion thus probably did not influence the results. Third, more than one imaging modality was used to determine the severity of hemorrhagic infarction (85% MRI and 15% CT). However, the patients who had CT were mainly those who had worsened clinically and required emergency follow-up imaging. In these patients, there was significantly more PH (PH-1 and PH-2) and, according to several studies, the concordance rate between MRI and CT is very high for bleeding classified as PH (26,27). Fourth, patients with vertebro-basilar artery occlusion were included while their functional prognosis is usually worse than patients with occlusion of the anterior circulation. However, this subgroup represented only 6.3% of this population and these patients were well-balanced between APD and non-APD groups, suggesting the low influence of these patients on our results. Fifth, the low number of symptomatic ICH limited the number of variables included in the models; therefore we cannot exclude that additional parameters might influence the risk of post-thrombolytic sICH. In addition, some factors not recorded in this database such as cocaine consumption or chronic treatment by statins (38,39) have been reported to increase the risk of post-thrombolytic sICH and should be evaluated in the future. Finally, the biological efficacy of APD was not evaluated in the patients upon arrival at the emergency room, so we could not assess the potential relationship between the level of platelet inhibition and outcome.

Conclusions

Chronic APD treatment at stroke onset in AIS patients treated with IVT and EVT significantly increases the risk of sICH and poor functional outcome at 90 days, which

might justify evaluation of acute stroke reperfusion strategy on an individual patient basis. Further studies should be conducted to validate our results.

Statement of Ethics:

Because of its retrospective observational nature, this study was exempt from ethical committee approval.

Conflict of Interest Statement:

The authors have no conflicts of interest to declare.

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Author Contributions:

MC, GM, IS, TT acquired the data, analyzed the results, drafted the manuscript and critically reviewed the manuscript. RG performed statistical analysis and analyzed the results. FG, SD, SO, PR, SS, JB, acquired the data and critically reviewed the manuscript.

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466 **Tables**

467 **Table 1**: Comparison of patients with and without prior antiplatelet drugs

468 **Baseline characteristics**

	Population	**No APD**	**APD**	***p*-value**
	N=204	n=133	n=74	
Demographic and clinical characteristics				
Age, mean ± SD (y)	69.26 ± 13.9	67.56 ± 14.78	72.44 ± 11.75	0.01
Men, n (%)	110 (53.9)	71 (53.4)	39 (54.9)	0.83
Pre-stroke mRS score, median [Q1-Q3]	0 [0-1]	0 [0-1]	0 [0-1]	0.2
Transfer from another hospital, n (%)	92 (45.1)	58 (43.6)	34 (47.9)	0.56
Hypertension, n (%)	122 (59.8)	69 (51.9)	53 (74.6)	<0.001
Diabetes, n (%)	31 (15.2)	14 (10.5)	17 (23.9)	0.01
Dyslipidemia, n (%)	72 (35.3)	34 (25.5)	38 (53.0)	<0.001
Current smoker, n (%)	48 (23.5)	30 (22.6)	18 (23.3)	0.65
Previous stroke or TIA, n (%)	30 (14.7)	7 (5.2)	23 (33.3)	<0.001
Coronary heart disease, n (%)	26 (12.7)	0 (0)	26 (36.2)	<0.001
Atrial fibrillation, n (%)	38 (18.6)	21 (15.8)	17 (23.9)	0.15
Baseline NIHSS score, median [Q1-Q3]	16 [11.5-20]	16 [12-20]	16 [11-20]	0.896
Systolic blood pressure, mean ± SD	144.67± 26.77	144.14 ± 28.31	145.66 ± 23.78	0.7
Diastolic blood pressure, mean ± SD	78.33 ± 19.41	79.88 ± 20.14	75.42 ± 17.75	0.12
Blood glucose, g/L, mean ± SD	1.24 ± 0.32	1.2 ± 0.27	1.32 ± 0.37	0.01
Imaging characteristics				
Admission CT, n (%)	133 (64.3)	87 (65.4)	46 (62.2)	0.64
ASPECTS CT, median [Q1-Q3]	10 [9-10]	10 [9-10]	10 [9-10]	0.9
ASPECTS CBV, median [Q1-Q3]	9 [7-10]	9 [8-10]	9 [7-10]	0.76
Admission MRI, n (%)	73 (37.8)	46 (34.6)	27 (38.03)	0.63
ASPECTS DWI, median [Q1-Q3]	8 [6-9]	8 [6-9]	8 [6.7-8]	0.58
Occlusion site, n (%)				0.26
M1	101 (49.5)	69 (51.9)	34 (45.1)	
M2	32 (15.7)	21 (15.8)	11 (15.5)	
P1	4 (1.9)	3 (2.2)	1 (1.1)	
P2	1 (0.5)	0 (0)	1 (1.1)	
VA	1 (0.5)	1 (0.7)	0 0)	
BA	7 (3.4)	5 (3.7)	2 (2.8)	
T carotid	25 (12.25)	11 (8.2)	14 (19.7)	
Tandem ICA- MCA	31 (15.2)	22 (16.5)	9 (12.7)	
Tandem BA – PCA	1 (0.5)	1 (0.7)	0 (0)	
Fazekas score > 2, n (%)	28 (15.7)	18 (14.9)	10 (17.4)	0.65
Fazekas PV score, median [Q1-Q3]	1 [0-2]	1 [0-2]	1 [0-2]	0.54
Fazekas WM score, median [Q1-Q3]	1 [0-2]	1 [0-2]	1 [0-2]	0.50
MB, median [Q1-Q3]	0 [0-0]	0 [0-0]	0 [0-0]	0.84

mRS, modified Rankin Scale; TIA, transient ischemic attack; CT, computed tomography; ASPECTS, Alberta Stroke Program Early CT Score; NIHSS, National Institutes of Health Stroke Scale; CBV, cerebral blood volume; MRI, magnetic resonance imaging; DWI, diffusion-weighted imaging; VA, vertebral artery; BA, basilar artery; ICA, internal carotid artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; PV, periventricular; WM, white matter; MB, microbleeds

476 **Table 2**: Comparison of patients with and without prior APD

477 **Therapy and outcomes**

	Population n=204	**No APD** n=133	**APD** n=71	***p*-value**
Therapy				
IVT				
Onset-rt-PA time, mean ± SD	155.44± 46.11	155.7 ± 45.2	152.4 ± 47.8	0.66
EVT				
Onset-punction time, mean ± SD	260.45 ± 91.56	256.3 ± 100.6	267.5± 74.1	0.4
Onset-recanalization time, mean ± SD	307 ± 97.4	301.9 ± 106.7	315.7 ± 79.3	0.34
Number of passage, mean ± SD	2.37 ± 1.7	2.39 ± 1.77	2.32 ± 1.57	0.77
Anesthesia modality				0.75
General, n (%)	28 (13.7)	19 (14.3)	9 (12.7)	
Local/Sedation, n (%)	176 (86.2)	114 (85.7)	62 (87.3)	
mTICI at end of procedure, n (%)				0.03
1	3 (1.5)	3 (2.3)	0 (0)	
2a	15 (7.3)	6 (4.5)	9 (12.7)	
2b	73 (35.7)	54 (40.6)	19 (26.7)	
3	113 (55.4)	70 (52.6)	43 (60.6)	
Good recanalization (mTICI ≥ 2b), n (%)	186 (91.2)	124 (93.2)	62 (87.3)	0.16
Follow-up imaging				
MRI, n (%)	174 (85.2)	118 (88.7)	56 (78.9)	0.06
ICH, n (%)	134 (65.7)	80 (60.15)	54 (76.1)	<0.001
HI-1	46 (22.5)	36 (27.1)	10 (14.1)	
HI-2	45 (22.1)	30 (22.6)	15 (21.1)	
PH-1	20 (9.8)	7 (5.3)	13 (18.3)	
PH-2	21 (10.3)	7 (5.3)	14 (19.7)	
SAH	2 (0.9)	0 (0)	2 (2.8)	
IVH	1 (0.5)	0 (0)	1 (1.4)	
PH, n (%)	41 (21.3)	14 (10.5)	27 (40.5)	<0.001
Outcomes				
SICH, n (%)	24 (11.8)	5 (3.75)	19 (26.7)	<0.001
Craniectomy, n (%)	9 (4.4)	4 (3.0)	5 (7)	0.33
mRS score at 90 days, median [Q1-Q3]	2 [1-4]	2 [1-3]	2 [2-5]	<0.001
mRS score at 90 days ≤ 2, n (%)	106 (51.9)	84 (63.15)	22 (31)	<0.001
Mortality, n (%)	31 (15.2)	17 (13)	14 (19.7)	0.19
Stroke Mechanism: TOAST				0.07
Unknown	63 (30 .9)	42 (31.6)	21 (29.5)	
Atherosclerosis	36 (17.6)	25 (18.8)	11 (15.5)	
Cardio-embolic	93 (45.6)	56 (42.1)	37 (52.1)	
Other	10 (4.9)	10 (7.5)	0 (0)	
Multiple potential causes	2 (1)	0 (0)	2 (2.8)	

IVT, intravenous thrombolysis; EVT, endovascular therapy; rt-PA, recombinant tissue plasminogen activator; mTICI, modified Treatment in Cerebral Ischemia score; MRI, magnetic resonance imaging; ICH, intracranial hemorrhage; SICH, symptomatic intracranial hemorrhage; mRS, modified Rankin Scale; HI, hemorrhage infarction; PH, parenchymal hematoma; SAH, subarachnoid hemorrhage; IVH, intraventricular hematoma

Table 3: Predictors of SICH – Clinical (n = 203) and Radiological (n = 190) models – multivariate analysis

Characteristics	**OR**	**[95% CI]**	***p*-value**
Clinical Model			
Age	1.012	[0.98-1.05]	0.47
Prior APD	9.35	[3.55-29.41]	**<0.001**
Baseline NIHSS score	1.067	[0.99–1.16]	0.10
Radiological Model			
Prior APD	9.35	[3.55-29.41]	**<0.001**
ASPECT	0.80	[0.64-1.01]	0.06
Successful recanalization	0.68	[0.19-2.85]	0.57

APD, antiplatelet drug; NIHSS, National Institutes of Health Stroke Scale

Table 4: Predictors of a poor functional outcome (mRS > 2) – multivariate analysis (137 patients)

Characteristics	**OR**	**[95% CI]**	***p*-value**
Age	1.03	[0.98–1.09]	0.21
Pre-stroke mRS	26.7	[3.71-284.97]	**<0.001**
Prior APD	5.72	[2.09-17.2]	**<0.001**
Baseline NIHSS score	1.2	[1.08-1.34]	**<0.001**
Blood glucose	4.8	[1.04-25.77]	**0.04**
ASPECT	0.73	[0..53-0.99]	**0.04**
Fazekas score > 2	0.83	[0.2-3.45]	0.8
Onset-to-recanalization time	1.01	[1-1.01]	**0.01**
ICH	2.49	[0.79-8.6]	0.12
Successful recanalization	0.42	[0.06-2.63]	0.2427

mRS, modified Rankin Scale; APD, antiplatelet drug; NIHSS, National Institutes of Health Stroke Scale; ICH, Intracerebral hemorrhage

Figures

Figure 1. Patient flow chart

IVT, intravenous thrombolysis; EVT, endovascular therapy; APD, antiplatelet drug

Figure 2. Comparison of the distribution of modified Rankin Scale (mRS) scores at 3 months between the APD and No APD groups