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SAFETY AND EFFICACY OF EMERGENT DUAL ANTIPLATELET THERAPY AFTER CAROTID STENTING IN ACUTE ISCHAEMIC STROKE WITH TANDEM LESIONS

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ABSTRACT

Background: Optimal periprocedural antithrombotic management after emergent carotid artery stenting (eCAS) for acute ischaemic stroke (AIS) due to atherothrombotic tandem lesions (TL) remains controversial.

Methods: Population-based observational study in Catalonia (Spain), including adult AIS patients with atherothrombotic TL treated with endovascular treatment and eCAS (January 2017–March 2023). Emergent dual antiplatelet therapy (DAPT) was compared with other regimens (single or no antiplatelet therapy). The primary outcome was a composite of sICH (symptomatic intracranial haemorrhage) and 30-day mortality. Secondary outcomes included any haemorrhagic transformation (HT), the ordinal shift in 90-day modified Rankin Scale (mRS) score and acute stent thrombosis within 72 hours, adjusted with inverse probability of treatment weighting.

Results: Among 297 patients (mean age 70.6 ± 10.3 years), 86 (29.0%) received emergent DAPT. The composite outcome occurred less frequently in the DAPT group (10.5% vs. 25.6%), aOR 0.41 (95% CI 0.18–0.94, $p=0.035$). The DAPT group showed better 90-day functional outcome in the adjusted shift analysis (commonOR 1.94, 95% CI 1.19–3.15, $p=0.008$), without differences in overall HT (aOR 0.71, 95% CI 0.37–1.34, $p=0.291$) and stent thrombosis rate (10.5% vs 7.1%, $p=0.336$, insufficient events for adjusted analysis). Among patients receiving DAPT within 24 hours, outcomes did not differ according to whether it was initiated emergently or deferred.

Conclusions: Emergent DAPT during eCAS resulted in a lower rate of the composite outcome (sICH and 30-day mortality) and better 90-day functional outcome, without differences in stent thrombosis or overall HT rate. These findings support the safety of emergent DAPT after eCAS, although residual confounding cannot be excluded.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Emergent carotid artery stenting (eCAS) during endovascular therapy may improve outcomes in acute ischaemic stroke due to atherothrombotic tandem lesions, but concerns about haemorrhagic transformation have led to highly variable periprocedural antithrombotic practice.

WHAT THIS STUDY ADDS

Emergent DAPT was associated with a lower rate of the composite outcome of sICH and 30-day mortality, and with a better 90-day functional outcome. Early ischaemic and procedural factors, rather than the timing of antithrombotic escalation, appear to be the main drivers of haemorrhagic outcomes after eCAS. Among patients receiving DAPT 24 hours after eCAS, the timing of its initiation (emergent vs. deferred within 24 hours) did not appear to influence outcomes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

These findings suggest that antithrombotic decisions after eCAS need not be driven by haemorrhagic concerns, and that both emergent and deferred DAPT strategies are reasonable options depending on the clinical context.

INTRODUCTION

Tandem lesions (TL), defined as the coexistence of an acute intracranial large vessel occlusion (LVO) and a significant stenosis or occlusion of the ipsilateral extracranial internal carotid artery (ICA), account for up to 20% of acute ischaemic strokes (AIS) treated with endovascular therapy (EVT)¹. TL have been associated with worse functional outcomes compared to isolated intracranial LVOs, likely due to increased clot burden, reduced collateral flow secondary to cervical occlusion, lower recanalization rates and the need for more complex and prolonged endovascular procedures^{2,3}.

In patients with atherothrombotic TL, growing evidence suggests that emergent carotid artery stenting (eCAS) performed during EVT may be more beneficial for treating the cervical carotid lesion, compared to a conservative strategy. Specifically, prior studies have consistently shown better recanalization rates and improved 90-day and long-term functional outcomes, without a significant increase in the risk of haemorrhagic transformation (HT)⁴⁻⁷. Although results from ongoing randomised clinical trials are pending⁸⁻¹², eCAS continues to expand in these setting, likely reflecting supportive observational data and improvements in procedural techniques¹³.

Nevertheless, considerable variability persists regarding the early antithrombotic regimen used once eCAS is decided^{14,15}. To date, no randomised controlled trials have specifically addressed the optimal antithrombotic regimen after eCAS. Although current guidelines recommend dual antiplatelet therapy (DAPT) after an elective carotid artery stenting to prevent acute stent thrombosis¹⁶, antithrombotic management in the setting of emergent stenting remains non-standardised¹⁷ and often conditioned by each practitioner's risk-benefit assessment and concerns of HT. Despite the uncertainty, there are two main strategies according to the antithrombotic regimen after eCAS: emergent initiation of a high-intensity antithrombotic therapy (DAPT) during EVT; or deferred initiation after performing a follow-up CT.

We hypothesize that emergent DAPT initiated during EVT after eCAS in patients with atherothrombotic TL is safe and may improve functional outcome. The aim of this study was to investigate if emergent DAPT immediately initiated after eCAS is associated with an increased rate of any HT of the infarct, compared to less intensive periprocedural regimens. Secondly, we aimed to assess its potential benefit in terms of functional outcome and explore the risk of

early complications. Additionally, given that DAPT has become the standard of care at 24 hours after eCAS, we explored whether its emergent initiation confers additional benefit in preventing acute stent thrombosis over deferred initiation after imaging confirmation.

METHODS

Study design and population

The SECURIS (Stenting Extracranial Carotid Artery stenosis dURING endovascular treatment in patients with acute Ischaemic Stroke) study was an observational study based on data from the Catalonia Stroke Code Registry (CICAT), a prospective, population-based, mandatory registry that collects data on all consecutive patients treated under the Stroke Code protocol across Catalonia. Study design, data collection, and reporting adhered to the STROBE statement guidelines¹⁸ are published elsewhere⁶.

For this preplanned study, patients who underwent EVT for AIS in any of the ten comprehensive stroke centres (CSC) that perform EVT in Catalonia between January 2017 and March 2023 were identified. Inclusion criteria were as follows: 1) age ≥ 18 years old; 2) previous modified Rankin Scale (mRS) score 0-3; 3) time from symptom onset or last time seen well (LTSW) ≤ 24 hours; 4) AIS with large vessel occlusion (LVO) of anterior circulation including terminal ICA (TICA), segments M1/M2 of the middle cerebral artery (MCA) or segment A1 of the anterior cerebral artery (ACA); 5) concomitant atheromatous stenosis of cervical ICA $\geq 50\%$ according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria¹⁹; 6) treatment with any EVT modality; and 7) eCAS placement during EVT.

Exclusion criteria were: 1) lack of critical follow-up data (mRS score at 90 days and follow-up computed tomography (CT) within the first 36 hours after treatment), 2) lack of information about the emergent antithrombotic regimen used during eCAS placement, 3) anticoagulation during EVT; and 4) a non-atheromatous aetiology of ICA stenosis (e. g., dissection).

The study protocol was approved by the Ethics Committee of Hospital de la Santa Creu i Sant Pau (IIBSP-SEC-2023-136) and the CICAT scientific committee. The need for written informed consent was waived due to the retrospective nature of the study.

Study variables

Demographic data (age, sex); relevant previous medical history (prior mRS score, hypertension, dyslipidaemia, diabetes, ischemic heart disease, antithrombotic treatment, previous stroke, smoking); index event characteristics and metrics (baseline National Institute of Health Stroke Scale [NIHSS] score, Alberta Stroke Program Early CT Score (ASPECTS), occlusion site, vital signs, time from onset to hospital arrival, door-to-needle and door-to-groin puncture times); treatment

data (prior intravenous thrombolysis [IVT], total number of passes (without distinguishing between intracranial and extracranial passes), EVT-associated complications (arterial perforation, artery dissection or distal embolism), general anaesthesia use, final modified Thrombolysis In Cerebral Infarction [mTICI²⁰]) and radiological data on the presence of HT in the follow-up CT performed within 36 hours were collected directly from the CICAT registry as described in the main study⁶. Successful recanalization was defined as a final mTICI score ≥ 2 b. Neurologists of each 10 participating CSC collected additional data from electronic health records: stroke aetiology according to Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria²¹, degree of ICA stenosis according to the NASCET criteria¹⁹ in the angiographical series previous to stent decision, and classification of HT in the follow-up CT scan according to the European Cooperative Acute Stroke Study-II (ECASS-II) criteria²², but including also any remote parenchymal haemorrhage (PH), subarachnoid or intraventricular haemorrhage²³. Also, antithrombotic regimen was assessed at four time points: during EVT, initiated later but within the first 24 hours post-EVT, initiated at 24 hours post-EVT and at discharge. At each time point, antithrombotic treatment was classified as: DAPT, single antiplatelet therapy (SAPT), or no antithrombotic treatment. Specific antithrombotic drugs were assessed. The decision to perform eCAS or angioplasty alone, as well as the use of prior IVT, the antithrombotic regimen, and its timing of initiation, was at the discretion of each treating physician.

Study outcomes

The primary outcome was a composite of sICH (symptomatic intracranial haemorrhage according to ECASS-II criteria) on the 24-36 hours follow-up CT, or early mortality within the first 30 days from eCAS. The secondary outcomes were: 1) the presence of any category of HT on the 24-36 hours follow-up CT, 2) the shift on the mRS score at 90 days of follow-up, and 3) acute thrombosis of the stent within 72 h after the procedure detected by any diagnostic modality.

The mRS score at 90 days of follow-up was assessed centrally through a structured telephone interview conducted by certified central evaluators who were blinded to the clinical information, and was assessed using the full-scale range (from 0 to 6). Stent thrombosis detection and screening was not standardised and depended on local protocols. Post-procedural vascular imaging was performed at the discretion of each treating team, and the specific imaging modality used was not systematically recorded; hence it was considered an exploratory outcome.

Statistical analysis

Categorical variables were reported using counts (n) and percentages (%), and quantitative variables were reported as means and standard deviations (SD) or medians and interquartile range (IQR) if non-normally distributed according to the Shapiro-Wilk test.

Univariable analyses were performed using the χ^2 test for categorical variables and the Student t test or Wilcoxon Rank Sum test, as appropriate, for continuous variables, comparing patients who received emergent DAPT and those who received other regimens. For the multinomial exploratory analyses, ANOVA test for continuous variables (or Kruskal-Wallis test when a non-parametric test was required) were used to compare differences between different antithrombotic regimens and agents during EVT.

To reduce treatment-selection bias, inverse probability of treatment weighting (IPTW) was constructed using a logistic model for the main binary comparison (DAPT vs. no-DAPT) and a multinomial logistic model for the exploratory analysis of three groups. Individual propensity score (PS) was estimated using a logistic regression model including pre-treatment covariates likely to influence treatment allocation or the primary outcome: age, baseline NIHSS, ASPECTS, previous IVT, atrial fibrillation, number of passes, successful recanalization and prior antiplatelet therapy. Stabilization weights were used with trimming to the 99th percentile to avoid extreme weights. Balance after the IPTW was assessed by visual inspection of propensity score overlap using density plots (see Supplemental Figure 1) and using standardised mean differences (SMDs), with SMD <0.10 considered adequate balance (see Supplemental Table 1 and Supplemental Figure 2). Since atrial fibrillation had an SMD of 0.10 after the IPTW (the limit of acceptable balance), a doubly robust strategy was used, including this variable directly in all outcome models in addition to the IPTW. Models were further adjusted by imbalances detected in the bivariate analysis between groups. For binary outcomes, logistic regression with robust standard errors was used. Ordinal logistic regression was used for the mRS shift. Results are expressed as odds ratios with 95% confidence intervals.

Two pre-planned sensitivity analyses were performed. First, an analysis restricted to patients who were receiving DAPT 24 hours after the procedure, comparing emergent vs delayed initiation. This analysis was applied because DAPT represents the standard of care after CAS¹⁶, and deviations from this regimen after 24 hours were presumed to reflect underlying clinical conditions (such as haemorrhagic complications, neurological worsening, or medical complications) that could directly affect outcome measures. Second, an exploratory multinomial analysis with different antithrombotic strategies (SAPT with ASA, SAPT with tirofiban, DAPT with ASA+tirofiban and DAPT with ASA+clopidogrel).

Analyses were conducted using available data only; no imputation of missing data was performed. A two-tailed p-value <0.05 was considered significant. All statistical analyses were performed using Stata version 17.0 (StataCorp, College Station, TX).

RESULTS

Study population

Among 578 patients from the SECURIS study, 344 underwent eCAS. Of those, 297 patients were finally included in the analysis (see detailed Flowchart in Figure 1). Separately, 33 additional patients who underwent eCAS were excluded from the original SECURIS cohort⁶ due to missing follow-up data, and could therefore not be considered for this analysis.

Clinical and radiological characteristics of the patients are summarized in Table 1. Mean age was 70.6 years-old (SD=10.3), and 58 patients (19.5%) were women. During EVT, 86 patients (29%) received DAPT, 120 patients (40.4%) received SAPT and 91 patients (30.6%) did not receive any antithrombotic agent. Patients under DAPT underwent general anaesthesia more frequently and had lower baseline NIHSS scores. Otherwise, they had similar baseline characteristics than patients who received other regimens (see Supplemental Table 1). As general anaesthesia was markedly imbalanced between groups, it was included in the adjusted models in addition to the IPTW. A sensitivity analysis comparing estimates with and without adjustment for general anaesthesia is presented in Supplemental Table 2.

All patients who received emergent DAPT received ASA or lysine acetylsalicylate as first antiplatelet agent. The second agent administered was clopidogrel in 70/86 (81.4%) patients, tirofiban in 15/86 (17.4%) patients and ticagrelor in 1/86 (1.2%) patient (see Supplemental Table 3). Information about different antithrombotic regimens received and its time of initiation is represented in Supplemental Figure 3, showing that the proportion of patients under DAPT increased over time.

Primary outcome

All the outcomes are summarized in Table 2. Altogether, 9 (10.5%) patients presented the composite outcome on the DAPT group and 54 (25.6%) in the no-DAPT group (p=0.004). After adjustment, patients who received emergent DAPT had a significant lower rate of the composite outcome than patients with other regimens (aOR 0.41, 95% CI 0.18-0.94, p=0.035).

Secondary outcomes

There were no statistical differences in the overall HT rate (26.7% in the DAPT group vs 36.5% in the no-DAPT group (aOR 0.71, 95% CI 0.37-1.34, p=0.291)). Patients who received emergent DAPT had lower medians of 90-days mRS score than those who received other regimens (median

2 [IQR 1-4] Vs 3 [IQR 1-5], $p=0.016$) (see 90-day mRS distribution among groups in Figure 2), with a significant shift towards better outcomes after adjustment (cOR 1.94 (95% CI 1.19-3.15) $p=0.008$).

Acute stent thrombosis within 72 hours from EVT was detected in 24 (8.1%) patients, with insufficient events for adjusted analyses. Although it occurred more frequently in the DAPT group, this difference was not statistically significant (10.5% vs 7.1%, $p=0.336$) (see Table 2).

Sensitivity analyses

The first sensitivity analysis included only patients who were under the election regimen (DAPT), 24 hours after the procedure. Among the analysed population, 200 patients were receiving DAPT 24 hours after eCAS (67.3%); 86 (43.5%) received emergent DAPT, and 114 (57%) initiated DAPT later within the first 24 hours. Outcomes were consistent with the main analysis, including the presence of any HT, functional outcome and mortality (see Supplemental Table 4). Stent thrombosis was not included due to the small size of events and high risk of bias.

In the exploratory multinomial analysis comparing different antithrombotic strategies (see Supplemental Table 5), DAPT showed a more favourable mRS shift than SAPT-tirofiban (cOR 3.35, 95% CI 1.51-7.41, $p=0.003$), and SAPT-tirofiban a less favourable shift than SAPT-aspirin (cOR 0.45, 95% CI 0.21-0.99, $p=0.048$), without differences in the primary outcome. Clopidogrel and tirofiban did not differ significantly as the second DAPT agent, although the low number of events precluded adjusted analysis.

DISCUSSION

In this large, population-based cohort of patients with atherothrombotic tandem lesions treated with EVT and eCAS, we found that emergent DAPT initiation was safe (with lower rates of the composite outcome of sICH and early mortality) and associated with better 90-day functional outcome, without differences in the overall HT and acute stent thrombosis rate. Our results are relevant in several ways.

First, emergent DAPT during EVT was associated with a lower rate of both the composite outcome of sICH and early mortality and sICH alone, with sICH rates comparable to previous series (3.6% in the MeCAS registry²⁴ and 2% reported by Farooqui M. et al²⁵). Besides, there were no differences between groups in the overall HT rate, even after adjusting by using PS including determinant variables, such as age, prior IVT or ASPECTS. Altogether, our findings are consistent with previous studies suggesting that, despite the theoretical concern about HT, a more intensive antithrombotic regimen after eCAS is safe^{15,26,27} and other factors (such as higher intraprocedural

heparin doses, a greater number of thrombectomy passes, and lower ASPECTS) may play a more relevant role in HT risk²⁸. This lower risk of HT, which may seem counterintuitive, supports the idea that HT (and specially its more severe forms) after eCAS is more strongly driven by baseline ischaemic injury and procedural complexity than by the timing of antithrombotic escalation. In fact, in the first SECURIS publication, only higher baseline NIHSS scores, number of passes and arterial perforation during the procedure predicted the presence of relevant HT⁶. Importantly, baseline NIHSS was slightly lower in the DAPT group and this imbalance could have contributed to confounding by indication, with patients perceived to be at lower haemorrhagic risk being more likely to receive emergent DAPT. Nevertheless, baseline NIHSS was included in the PS, and SMD after IPTW indicated adequate balance between groups. However, residual confounding cannot be completely excluded.

Second, emergent DAPT was associated with a better 90-days mRS scores distribution, although this association was sensitive to the inclusion of general anaesthesia in the model (see Limitations) and was attenuated to a non-significant trend without it. This likely reflects that, even though emergent DAPT may contribute to better functional prognosis after eCAS, other well-established variables included in our PS (such as baseline NIHSS, ASPECTS, or the number of thrombectomy passes) probably exert a more robust influence¹⁵. It may also suggest the presence of confounding by indication, whereby clinicians tend to prescribe emergent DAPT more readily in patients who appear clinically more favourable.

Third, no significant differences in acute stent thrombosis were observed among emergent antithrombotic regimens, in contrast to prior reports suggesting improved stent patency with more intensive antithrombotic strategies²⁹. The rate of acute stent thrombosis in our cohort was lower than previously reported (8.1% within 72 hours vs approximately 20% within 24 hours)¹⁴, and relevant intraprocedural factors (including suboptimal stent expansion, residual stenosis, early device thrombosis, plaque characteristics, or technical aspects of the procedure¹⁴), were not systematically captured, which may have influenced both detection and treatment decisions. Besides, the detection of acute stent thrombosis was not protocolised and relied on non-standardised, locally determined imaging, likely leading to underestimation of its true incidence. Hence, these results should be interpreted cautiously.

Exploratory agent-comparisons showed worse 90-day functional outcome with SAPT-tirofiban than with SAPT-aspirin or DAPT, without differences in the primary outcome. Given the small subgroup size and the counterintuitive direction relative to tirofiban's antiplatelet potency, this likely reflects confounding by indication rather than a true pharmacological effect, and larger studies are needed to clarify this question.

Finally, our results did not change after excluding from the analyses those patients who were not under the election regimen (DAPT)¹⁶ 24 hours after eCAS. Globally, this translates into the fact that, once patients are transitioned to DAPT within the first 24 hours, its emergent initiation may not be a major determinant of efficacy outcomes, with other factors (as previously discussed) likely playing a more prominent role. From a clinical standpoint, our results suggest that both strategies (emergent DAPT and deferring DAPT initiation until a 24-hour imaging confirmation) may be safe and reasonable. In patients perceived to be at higher haemorrhagic risk, deferring DAPT initiation until a control CT scan is available within 24 hours may not translate into worse clinical outcomes.

The main strength of this study is that it is based on a mandatory, population-based registry, which not only reflects real-life clinical practice but also ensures standardised documentation of key clinical and procedural variables, thereby enhancing its external validity. Second, the use of IPTW as a robust adjustment method helps mitigate the confounding inherent to non-randomised comparisons. Third, the detailed information regarding both the specific antithrombotic agents used and the timing of their initiation allowed us to directly address a common and clinically relevant question in daily practice that has been little explored in previous literature: how and when patients should be transitioned to DAPT after eCAS.

Several limitations should be acknowledged. First, its observational design may have led to inherent bias from unmeasured or imprecisely captured confounders. General anaesthesia illustrates this limitation: although it was incorporated into the doubly-robust adjustment given the baseline imbalance between groups, its clinical indication in each case (e.g., agitation, airway compromise, or anticipated procedural complexity) was not systematically captured. Excluding it from the adjustment attenuated the DAPT association with 90-day functional outcome to a non-significant trend, underscoring the sensitivity of this finding to residual confounding. Second, despite constructing the PS by including the variables that, based on clinical judgment, most strongly influence the choice of antithrombotic regimen, unmeasured confounders that influence both treatment selection and outcomes and differences in local protocols remain and may have led to residual confounding by indication. Third, although the emergent antithrombotic regimen initiated during EVT was systematically captured, the timing and conditions of early antithrombotic initiation within the first 24 hours were heterogeneous across centres and practitioners, varying in the exact time of administration, whether prior neuroimaging was obtained, and the clinical criteria used to guide the decision. This heterogeneity may have introduced high variability in the deferred DAPT group of the sensitivity analysis, where the boundary between “emergent” and “deferred” initiation was defined by the 24-hour antithrombotic record rather than by a standardised clinical protocol. Fourth, prior

antiplatelet therapy was included in the IPTW rather than used to classify the emergent antithrombotic regimen, given that information regarding therapeutic adherence or time of last dose was unavailable, making it impossible to determine the biological degree of platelet inhibition at the time of EVT. Although patients on chronic antiplatelet therapy may have had residual platelet inhibition at the time of eCAS, which could have influenced the outcomes, we believe this approach better reflects the pragmatic clinical reality of acute stroke care, where such information is rarely available at the time of treatment decisions. Fifth, the DAPT group itself was pharmacologically heterogeneous, including clopidogrel, tirofiban, and ticagrelor as second antiplatelet agents, which precludes conclusions about the optimal specific agent and may have introduced additional unmeasured variability in bleeding and thrombotic risk. Determining the true pharmacological benefit from a specific agent would require standardised surveillance protocols, extended follow-up, and larger cohorts. Sixth, acute stent thrombosis was collected retrospectively by local investigators and was not systematically screened for, which may have led to detection bias, so our results must be interpreted with caution. Seventh, the registry did not distinguish intracranial from extracranial passes, which precludes a precise analysis of the relationship between intracranial passes and HT. Similarly, CT perfusion was not systematically performed and CT softwares vary between centers; therefore, ischaemic core volume was not collected. ASPECTS was used as a surrogate, consistent with routine clinical practice at the participating centers, but cannot fully capture infarct burden.

In conclusion, in this population-based study of patients with AIS due to TL treated with EVT and eCAS, emergent initiation of DAPT was associated with lower rates of the composite outcome (sICH and 30-day mortality) and better 90-day functional outcome, without differences according to the timing of DAPT initiation within 24 hours. Further randomised evidence is warranted to establish the better antithrombotic regimen (including timing of initiation and specific agents) after eCAS.

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TABLES

Table 1. Patients clinical and radiological characteristics according to antithrombotic regimen during EVT

	Total (n=297)	DAPT (n=86)	SAPT (n=120)	No AT (n=91)	p*
Demographics					
Age, mean (SD)	70.6 (10.3)	70.8 (10.7)	70.3 (10.4)	70.7 (10.0)	0.823
Sex (female), n (%)	58 (19.5)	23 (26.7)	22 (18.3)	13 (14.3)	0.103
Prior medical history					
Prior mRS, mdn (IQR)	0 (0-1)	0 (0-1)	0 (0-1)	0 (0-1)	0.854
Current smoking, n (%)	110 (37.2)	33 (38.4)	43 (35.8)	34 (37.8)	0.923
Hypertension, n (%)	194 (65.5)	58 (67.4)	81 (67.5)	55 (61.1)	0.570
Diabetes, n (%)	81 (27.4)	27 (31.4)	31 (25.8)	23 (25.6)	0.609
Dyslipidemia, n (%)	151 (51.0)	48 (55.8)	57 (47.5)	46 (51.1)	0.500
Ischaemic heart disease, n (%)	49 (16.6)	17 (19.8)	20 (16.7)	12 (13.3)	0.517
Atrial fibrillation, n (%)	28 (9.4)	7 (8.1)	8 (6.7)	13 (14.3)	0.153
Prior ischaemic stroke, n (%)	33 (11.2)	8 (9.3)	14 (11.7)	11 (12.2)	0.805
Prior AT therapy, n (%)					0.088
- None	174 (58.6)	45 (52.3)	74 (61.7)	55 (60.4)	
- SAPT	94 (31.7)	34 (39.5)	38 (31.7)	22 (24.2)	
- DAPT	8 (2.7)	0 (0.0)	3 (2.5)	5 (5.5)	
Prior statin therapy, n (%)	123 (41.4)	39 (45.4)	51 (42.5)	33 (36.3)	0.499
Stroke severity and acute phase variables					
Baseline NIHSS score, mdn (IQR)	17 (12-20)	16 (10-20)	18 (13-22)	16 (12-19)	0.022
Systolic Blood Pressure (mmHg), mdn (IQR)	152 (135- 169)	149 (132- 163)	156 (136- 169)	153 (138- 168)	0.101
Glycemia (mg/dL), mdn (IQR)	126 (107- 159)	129 (106- 159)	129 (109- 169)	120 (104- 144)	0.164
ASPECTS, mdn (IQR)	9 (8-10)	9 (8-10)	9 (7-10)	9 (8-10)	0.296
IVT, n (%)	107 (36.0)	37 (43.0)	40 (33.3)	30 (33.0)	0.276
Endovascular treatment					
Number of passes, mdn (IQR)	1 (1-2)	1 (1-2)	1 (1-3)	1 (0-1)	0.005
mTICI $\geq$ 2b, n (%)	275 (92.6)	82 (95.4)	113 (94.2)	80 (87.9)	0.117
General anaesthesia, n (%)	72 (24.2)	45 (52.3)	19 (15.8)	8 (8.8)	<0.001
Arterial perforation ^a , n (%)	6 (2.3)	0 (0)	3 (3.4)	3 (3.5)	0.253
Artery dissection ^a , n (%)	19 (7.3)	6 (7.1)	7 (7.8)	6 (7.0)	0.977
Distal embolism ^a , n (%)	19 (7.3)	7 (8.3)	5 (5.6)	7 (8.1)	0.731
Puncture-recanalization (min), mdn (IQR)	63 (40-93)	58.5 (40-80)	67 (44.5- 97)	61 (39- 100)	0.186
TOAST classification					
Atherothrombotic, n (%)	275 (91.6)	81 (94.2)	111 (92.5)	83 (91.2)	0.751
Undetermined (two/more causes), n (%)	22 (7.4)	5 (5.8)	9 (7.5)	8 (8.8)	0.751

Abbreviations: ASPECTS, Alberta Stroke Program Early CT Score; AT, antithrombotic; CI, confidence interval; DAPT, dual antiplatelet therapy; IQR, interquartile range; IVT, intravenous thrombolysis; LTSW, last time seen well; mdn, median; mRS, modified Rankin Scale; mTICI: modified Thrombolysis In Cerebral Infarction; NIHSS, National Institute of Health Stroke Scale; OR, odds ratio; SAPT, single antiplatelet therapy; SBP, systolic blood pressure; SD, standard deviation.

*p values from one-way ANOVA for age; Kruskal-Wallis test with ties correction for remaining continuous variables; chi-squared or Fisher's exact test for categorical variables.

^aArterial perforation, arterial dissection and distal embolism available for 259 patients.

Table 2. Outcomes according to emergent antithrombotic regimen

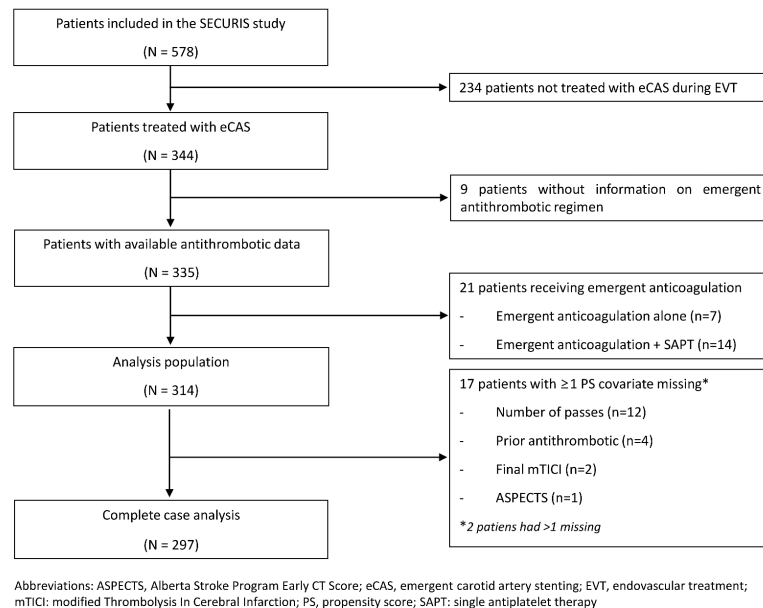
	No-DAPT (n=211)	DAPT (n=86)	p	aOR (95% CI)*	p
Primary outcome					
sICH or 30-day mortality, n (%)	54 (25.6)	9 (10.5)	0.004	0.41 (0.18–0.94)	0.035
- sICH, n (%)	34 (16.1)	4 (4.7)	0.007	0.27 (0.09–0.88)	0.029
- 30-day mortality, n (%)	32 (15.2)	9 (10.5)	0.287	0.71 (0.29–1.70)	0.438
Secondary outcomes					
Any HT, n (%)	77 (36.5)	23 (26.7)	0.107	0.71 (0.37–1.34)	0.291
Any PH, n (%)	37 (17.5)	6 (7.0)	0.019	0.29 (0.10–0.85)	0.023
- PH1, n (%)	14 (6.7)	2 (2.3)	0.130	0.22 (0.05–0.97)	0.046
- PH2, n (%)	22 (10.6)	4 (4.7)	0.104	0.41 (0.11–1.56)	0.191
90-days shift in mRS, mdn (IQR)	3 (1–5)	2 (1–4)	0.016	1.94 (1.19–3.15)†	0.008
Stent thrombosis <72h, n (%)	15 (7.1)	9 (10.5)	0.336	–	–

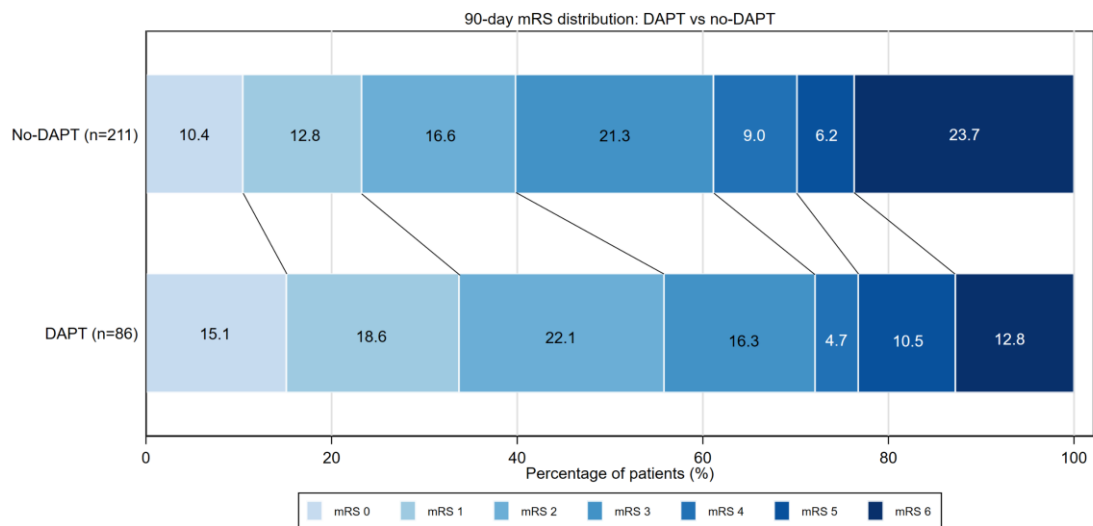
Abbreviations: AT: antithrombotic; aOR: adjusted odds ratio; CI: confidence interval; HT: haemorrhagic transformation; mdn: median; mRS: modified Rankin Scale; PH: parenchymal haemorrhage; sICH, symptomatic intracranial haemorrhage.

*Adjusted using inverse probability of treatment weighting (IPTW) with doubly robust estimation including atrial fibrillation and general anaesthesia in the outcome model.

†Results expressed as common OR (cOR) from ordinal logistic regression; cOR >1 indicates shift towards lower (better) mRS scores.

FIGURES

Figure 1. Participant flowchart**Figure 2. mRS Score Distributions at 3 months of follow-Up according to emergent antithrombotic regimen**



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