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Effect of General Anesthesia Versus Conscious Sedation/Local Anesthesia on the Outcome of Patients with Minor Stroke and Isolated M2 Occlusion Undergoing Immediate Thrombectomy: A Retrospective Multicenter Matched Analysis

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BACKGROUND: This study investigates the impact of general anesthesia (GA) versus conscious sedation/local anesthesia (CS/LA) on the outcome of patients with minor stroke and isolated M2 occlusion undergoing immediate mechanical thrombectomy (iMT).

■ METHODS: The databases of 16 comprehensive stroke centers were retrospectively screened for consecutive patients with isolated M2 occlusion and a baseline National Institutes of Health Stroke Scale score ≤5 who received iMT. Propensity score matching was used to estimate the effect of GA versus CS/LA on clinical outcomes and procedure-related adverse events. The primary outcome measure was a 90-day

Key words

- Anesthesia
- M2 occlusion
- Mechanical thrombectomy
- Minor stroke

Abbreviations and Acronyms

ASPECTS: Alberta Stroke Program Early CT Score BMM: Best medical management CS/LA: Conscious sedation/local anesthesia GA: General anesthesia iMT: Immediate mechanical thrombectomy IVT: Intravenous thrombolysis LVO: Large vessel occlusion MCA: Middle cerebral artery mRS: Modified Rankin Scale MT: Mechanical thrombectomy NIHSS: National Institutes of Health Stroke Scale PSM: Propensity score matching RCT: Randomized clinical trial

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RESULTS: Of the 172 patients who were selected, 55 received GA and 117 CS/LA. After propensity score matching, 47 pairs of patients were available for analysis. We found no significant differences in clinical outcome, rates of efficient reperfusion, and procedural-related complications between patients receiving GA or LA/CS (mRS score 0–1, P = 0.815; mRS score 0–2, P = 0.401; all-

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1878-8750/© 2023 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/). cause mortality, P = 0.408; modified Treatment in Cerebral Infarction score 2b–3, P = 0.374; symptomatic subarachnoid hemorrhage, P = 0.082; intraprocedural dissection, P = 0.408; new territory embolism, P = 0.462).

CONCLUSIONS: In patients with minor stroke and isolated M2 occlusion undergoing iMT, the type of anesthesia does not affect clinical outcome or the rate of proceduralrelated complications. Our results agree with recent data showing no benefit of one specific anesthesiologic procedure over the other and confirm their generalizability also to patients with minor baseline symptoms.

INTRODUCTION

esults from randomized trials have defined mechanical thrombectomy (MT) as the standard of care in patients with acute ischemic stroke caused by large vessel occlusion (LVO) in the anterior circulation.¹ Although the influence of numerous clinical and procedural variables on clinical outcomes has been extensively studied, the role of the type of anesthesia is still debated. The use of conscious sedation or local anesthesia (CS/LA), rather than general anesthesia (GA), is less invasive and allows clinical monitoring. It also decreases the risk of hypotension, which can affect blood flow to the ischemic brain. However, there is an increased risk of procedural complications as a result of patient movement and poor airway protection, resulting in longer, and possibly less successful, procedures.² On the other hand, GA is associated with better airway protection, and a more accurate procedure but may delay MT and expose patients to the risk of hypotension.

Data coming from single-center randomized clinical trials (RCTs), meta-analysis of RCTs, post hoc analysis from RCTs, and meta-analysis of retrospective studies are heterogeneous.³⁻⁹ On the other hand, a recent multicenter trial¹⁰ has shown that GA is associated with similar rates of functional independence and major procedure-related complications compared with CS/LA.

Patients with LVO and a baseline National Institutes of Health Stroke Scale (NIHSS) score ≤ 5 represent a challenge concerning the most appropriate acute treatment. The benefit of immediate MT (iMT) is controversial and, in real-world practice, this treatment is considered on a case-by-case basis after careful assessment of individual clinical and radiologic features.¹¹⁻¹⁴ Therefore, in that clinical scenario, the involvement of a more peripheral segment of the middle cerebral artery (MCA) may raise even more skepticism about the appropriateness of an invasive procedure. Consequently, when opting for iMT, also the choice of the more suitable type of anesthesia may be relevant.

We report a large retrospective multicenter analysis of consecutive patients with minor strokes caused by isolated occlusion of the M₂ segment undergoing iMT. The purpose of this study is to evaluate the impact of the type of anesthesia on clinical outcomes and procedure-related complications in this category of patients.

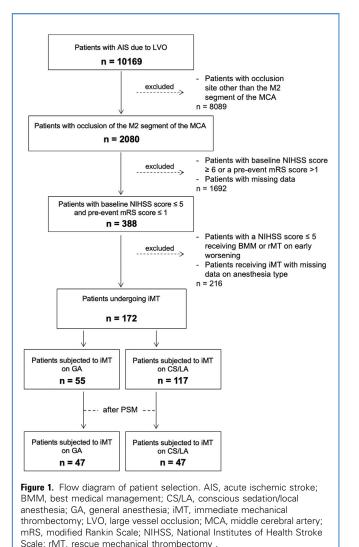
METHODS

Study Participants and Treatment

The prospective databases of 16 comprehensive stroke centers were screened for consecutive patients with acute ischemic stroke caused by LVO admitted between January 2016 and December 2021. This work was conducted in adherence with a study protocol approved by the ethics committee (protocol number 6410/20, ID 3004) of the coordinator hospital. The local ethics committees approved the use of patients' data for this analysis. The need for informed consent was waived because of the retrospective nature of the study.

All patients were diagnosed with an initial noncontrast computed tomography scan followed by multiphase computed tomography angiography to identify the site of occlusion. The Alberta Stroke Program Early CT Score (ASPECTS) was calculated by visual inspection.¹⁵ The state of the collateral leptomeningeal network was graded with the Menon score.¹⁶ Involvement of the M2 segment was defined as an occlusion located either at the genu of the MCA or at the proximal tract of one of the firstorder branches. Caliber dominance was considered present when one division had a larger caliber than the other/s. When this feature could not be assessed because of an occlusion involving the origin of the vessel, branch dominancy was assumed if the missing MCA territory was >50%.^{17,18} Patients with an occlusion site other than the isolated M2 segment, a baseline NIHSS score >6, a pre-event modified Rankin Scale (mRS) score >1 or with missing clinical, endovascular, or radiologic outcome data were excluded. Intravenous thrombolysis (IVT) was administered according to the standard treatment protocol.¹⁹ Patients with a baseline NIHSS score <5 undergoing best medical management (BMM) only (including IVT) or receiving a rescue MT after early clinic worsening during BMM were also excluded. This strategy led to a group of patients with minor stroke and isolated M2 occlusion subjected to iMT. Patients were then divided into 2 cohorts according to the type of anesthesia (GA group vs. CS/LA group). The choice of the anesthesiologic approach was made in adherence with the local protocol or was at the discretion of both the operating neurointerventionalist and anesthesiologist. In this latter case, the decision was made after careful evaluation of the neurologic deficit and its potential impact on the patient's cooperation during the procedure, or on other specific factors (e.g., the respiratory condition or presence of vomiting). However, clinical features favoring a specific anesthesiologic approach were not collected for this study.

MT strategy was planned at the discretion of the interventionalist and performed with a stent-retriever and proximal guide catheter aspiration, direct contact aspiration, or a combination of stent-retriever and distal aspiration. Flow restoration at the end of each procedure was assessed using the modified Treatment in Cerebral Infarction score and based on the percentage reperfusion of the territory supplied by M2, with successful MT corresponding to a score of 2b-3.^{20,21} In each participating center, 2 neuroradiologists with more than 5 years of experience and unaware of clinical outcome reviewed the radiologic and angiographic data of their patients. In cases of doubt or disagreement, DICOM (Digital Imaging and Communications in



Medicine) images were sent to 2 expert neuroradiologists of the coordinating center for re-evaluation and adjudication.

Clinical Variables and Measures of Outcome

Demographics, cardiovascular risk factors, baseline clinical characteristics, imaging data, and therapeutic procedures of the acute phase were collected. Clinical outcome was measured with the 90day mRS score acquired by a trained physician either in person or on the telephone. A 90-day mRS score of 0-1 (excellent neurologic outcome) was chosen as the primary clinical outcome measure given the baseline mild symptoms of patients. Secondary clinical outcome measures were the NIHSS score at 72 hours after MT, an mRS score of 0-2 (functional independence), and death (mRS score = 6) of any cause at 3 months after stroke. The procedural outcome measure was successful reperfusion (modified Treatment in Cerebral Infarction score 2b-3), whereas procedurerelated adverse events included symptomatic subarachnoid hemorrhage, arterial dissection, and new territory embolism defined according to previously established criteria.²²

Statistical Analysis

Baseline clinical and imaging characteristics of patients of both groups were compared using a Pearson χ^2 test or Fisher exact test for categorical variables and the Student t test or Wilcoxon rank sum test for continuous variables, as appropriate. Propensity score matching (PSM) analysis was performed with the nearest neighbor matching method to limit differences in baseline characteristics between patients receiving different types of anesthesia. Covariates used in PSM were all the statistically significant variables at univariate analysis along with other factors relevant for clinical outcome and included age, involvement of a specific M2 branch (superior, middle or inferior branch, the involvement of which may have a different impact on the final clinical outcome²³), presence of coronary artery disease (yes vs. no), administration of IVT (yes vs. no), onset-to-groin time, and involvement of a dominant M2 division (yes vs. no). PSM balance was assessed by checking standardized mean differences between covariates, with a value <0.2 indicating negligible imbalance between the 2 groups, as previously described.²⁴ To determine the effect of anesthesia, coefficients were calculated for each of the clinical and procedural outcome measures with logistic regression and ordinal logistic regression. All P values were 2sided, and a P value <0.05 was considered significant. Missing data were not imputed because these were neither among the outcome variables nor covariates in the propensity score balancing.

All analyses were performed using STATA 15 release 15.1 (StataCorp LLC, College Station, Texas, USA).

RESULTS

A total of 10,169 patients were initially screened and 172 patients with minor stroke and isolated M2 occlusion receiving iMT were selected for this analysis, according to the criteria listed earlier (Figure 1). Concerning the type of anesthesia, in 4 centers, iMT was always performed under GA, whereas 8 centers favored CS/ LA on the base of predefined local protocols. Conversely, in the remaining 2 centers, the type of anesthesia was decided on a case-by-case basis, possibly in relation to individual clinical features that, however, were not collected in this study.

In univariate analysis of the raw study sample, there was a significant difference between patients under GA and those under LA/CS in relation to age (73.4 \pm 3.5 years in the GA group vs. 68.2 \pm 2.6 years in the CS/LA group; P = 0.025), rate of coronary artery disease (27.1% in GA group vs. 9.1% in CS/LA group; P = 0.007), ASPECTS (median, 10, interquartile range, 9–10 in GA group vs. median, 9, interquartile range, 9–10 in CS/LA group; P = 0.002), and MCA branch involvement (P = 0.003) (Table 1).

To evaluate the effect of GA versus CS/LA, all patients were entered in the PSM algorithm, which generated 47 pairs balanced for age, baseline ASPECTS, involvement of a specific M2 branch, presence of coronary artery disease, administration of IVT, onsetto-groin time, and involvement of a dominant M2 division (Table 1). Univariate analysis on the matched cohort showed no difference between patients receiving GA and those receiving CS/LA regarding rates of 90-day excellent neurologic outcome (74.5% in the GA group and 72.3% in the CS/LA group; P = 0.815), the NIHSS score at 72 hours after MT (median, 2, interquartile

Table 1. Univariate Analysis of Demographic, Baseline Clinical, Therapeutic, and Imaging Data in the Entire Cohort of Patients, Stratified by Type of Anesthesia, Before and After Propensity Score Matching

	Before Propensity Score Matching			After Propensity Score Matching		
	CS/LA (n = 117)	GA (n = 55)	P Value*	CS/LA (n = 47)	GA (n = 47)	P Value*
Demographics						
Female, number of patients (%)	53 (45.3)	31 (56.4)	0.176	25 (53.2)	25 (53.2)	1.000
Age, mean (±standard deviation)	68.2 (±2.6)	73.4 (±3.5)	0.025	70.7 (±4.0)	72.4 (±3.6)	0.529
Baseline clinical features						
Atrial fibrillation, number of patients (%)	37 (31.6)	25 (45.5)	0.078	14 (29.8)	21 (44.7)	0.135
Diabetes, number of patients (%)	22 (18.8)	12 (21.8)	0.643	7 (14.9)	7 (14.9)	1.000
Dyslipidemia, number of patients (%)	46 (39.3)	25 (45.5)	0.446	17 (36.2)	20 (42.6)	0.527
Coronary artery disease, number of patients (%)	32 (27.4)	5 (9.1)	0.007	3 (6.4)	3 (6.4)	1.000
Carotid atherosclerosis, number of patients (%)	27 (23.1)	15 (27.3)	0.550	11 (23.4)	15 (31.9)	0.356
COPD, number of patients (%)	13 (11.1)	4 (8.7)	0.650	4 (8.5)	4 (8.5)	1.000
NIHSS baseline, median (IQR)	4 (2—5)	4 (3—5)	0.735	4 (3—5)	4 (3—5)	0.435
Medical therapy and procedural parameters						
Current antiplatelet therapy, number of patients (%)	38 (32.5)	19 (34.5)	0.788	10 (21.3)	13 (27.7)	0.472
Current anticoagulant therapy, number of patients (%)	25 (21.4)	11 (20.0)	0.837	6 (12.8)	11 (23.4)	0.180
Current therapy with statins, number of patients (%)	29 (24.8)	19 (34.5)	0.183	8 (17.0)	13 (27.7)	0.216
Thrombolysis, number of patients (%)	33 (28.2)	18 (32.7)	0.545	14 (29.8)	18 (38.3)	0.384
Onset-to-groin (minutes), median (IQR)	255 (190—346)	345 (220-460)	0.105	272 (220—364)	345 (220-460)	0.849
Groin-to-reperfusion (minutes), median (IQR)	39 (29—45)	41 (30-49)	0.354	38 (28—48)	40 (29—52)	0.349
Baseline imaging data						
Left side, number of patients (%)	72 (61.5)	34 (61.8)	0.972	28 (59.6)	29 (61.7)	0.833
ASPECT, median (IQR)	10 (9—10)	9 (9—10)	0.002	10 (9—10)	9 (9—10)	0.246
Atherosclerotic occlusion, number of patients (%)	11 (9.4)	4 (7.7)	0.718	6 (12.8)	4 (9.1)	0.575
Dominant M2 involvement, number of patients (%)	75 (64.1)	40 (72.7)	0.262	31 (66.0)	34 (72.3)	0.503
Middle cerebral artery branch			0.003			0.194
Superior, number of patients (%)	38 (32.5)	33 (60.0)		21 (44.7)	29 (61.7)	
Middle, number of patients (%)	24 (20.5)	8 (14.5)		6 (12.8)	6 (12.8)	
Inferior, number of patients (%)	55 (47.0)	14 (25.5)		20 (42.6)	12 (25.5)	
Menon score, median (IQR)	5 (4—5)	4 (4—5)	0.925	4 (4-4)	4 (4-4)	0.946

CS/LA, conscious sedation/local anesthesia; GA, general anesthesia; COPD, chronic obstructive pulmonary disease; NIHSS, National Institutes of Health Stroke Scale; IQR, interquartile range; ASPECT, Alberta Stroke Program Early CT Score.

*Statistical significance was considered at P < 0.005, shown in bold type.

range, 1–3) in the GA group and median, 1, interquartile range, o-3 in the CS/LA group; P = 0.837), rates of functional independence (87.2% in the GA group and 80.8% in the CS/LA group; P = 0.401), and of death of any cause (8.5% in the GA group and 4.3% in the CS/LA group; P = 0.408) at 90 days after stroke, respectively. Similar rates of successful recanalization were achieved regardless of the anesthesiologic protocol that was used (89.4% in the GA group and 83.0% in the CS/LA group; P = 0.374). Rates of procedure-related adverse events were higher in

patients receiving CS/LS; however, this difference remained below the threshold of significance (Table 2).

DISCUSSION

Patients with a minor stroke caused by isolated M2 occlusion pose a dual problem during acute management (i.e., the presence of a more distal site of occlusion and minimal symptoms), raising skepticism about the appropriateness of iMT as the preferred

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Table 2. Clinical and Procedural Outcome Data			
	Conscious Sedation/Local Anesthesia (n $=$ 47)	General Anesthesia (n $=$ 47)	Adjusted Estimates*
Clinical outcome measures			
90-day mRS score 0–1, number of patients (%)	34 (72.3)	35 (74.5)	1.12 (0.45–2.79); P = 0.815
NIHSS score at 72 hours, median (interquartile range)	1 (0—3)	2 (1—3)	-0.16 (-1.71 to 1.39); P = 0.837
90-day mRS score 0-2, number of patients (%)	38 (80.8)	41 (87.2)	1.62 (0.53-4.98); P = 0.401
90-day mRS score 6, number of patients (%)	2 (4.3)	4 (8.5)	2.09 (0.36-12.02); P = 0.408
Procedural outcome measures			
mTICI score 2b-3, number of patients (%)	39 (83.0)	42 (89.4)	1.72 (0.51–5.71); <i>P</i> = 0.374
sSAH, number of patients (%)	5 (13.5)	1 (2.2)	0.14 (0.02, 1.28); <i>P</i> =0.082
Intraprocedural dissection, number of patients (%)	4 (8.5)	2 (4.3)	0.48 (0.08–2.74); P = 0.408
New territory embolism, number of patients (%)	3 (8.3)	2 (4.3)	0.50 (0.08-3.16); P = 0.462

All results are expressed as OR (95% CI), except for line 2 (NIHSS score at 72 hours) that reports a coefficient deriving from an ordinal regression.

OR, odds ratio; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; mTICI, modified Treatment in Cerebral Infarction; symptomatic subarachnoid hemorrhage. *Statistical significance was considered at P < 0.05.

recanalization treatment. In this specific group of patients, the benefit of iMT over BMM only has not been clearly shown.^{23,25} In the absence of clear-cut guidelines, in real-world practice, the choice of the most appropriate treatment remains at the discretion of the managing physicians and, in most cases, takes into account the presence or not of potentially disabling symptoms. Therefore, when deciding on iMT, it is crucial to minimize the risk of procedural complications and the choice of the type of anesthesia may be also relevant.

Our results have shown no significant effect of GA or CS/LA on 90-day clinical outcomes. We found a tendency toward higher rates of procedure-related adverse events in only patients receiving CS/LA, likely because of greater difficulties during the endovascular treatment, which, however, remained below the threshold of significance. Unlike previous studies, we did not find higher rates of successful recanalization in patients treated under GA or differences in time metrics of MT between the 2 groups.^{6,26}

Current evidence of the impact of the type of anesthesia on clinical outcomes and procedure-related complications after MT is patchy. Some studies have shown no difference between GA and CS/LA, whereas others have found that GA is associated with a better functional outcome.^{3-6,10} Conversely, evidence from the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Nederlands (MR CLEAN) and a patient-level meta-analysis of the Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke Trials (HERMES) collaboration suggest that CS/LA may be preferable.^{7,8} Reasons in favor of treatment under GA include higher rates of successful reperfusion and airway protection, especially in patients with considerable clinical deterioration.⁶ However, results from the recent Anesthesia Management in Endovascular Therapy for Ischemic Stroke (AMETIS) trial have shown no difference in the rate of postprocedural pneumonias.¹⁰ Limitations of some previous studies include rigid criteria of enrollment concerning anesthetic agents and hemodynamic

management and single-center design, which may reduce the generalizability of their findings.³⁻⁶

The risk of hypotension during the procedure is supposed to be one of the reasons for avoiding GA, especially in patients with poor collateral circulation, because it may lead to greater cerebral hypoperfusion and a larger ischemic infarct.²⁷ Nevertheless, in our study, in which only patients with low baseline NIHSS scores and good collateral circulation were included, we did not observe this difference. Another risk is posed by the elongation of the onset-togroin time. We did not observe a significant difference between patients receiving GA versus CS/LA, but it is conceivable that also a longer onset-to-groin time in association with a procedure under GA would have a limited impact, if any, in patients with minor symptoms because of good collateral circulation.

Overall, our results are not in favor of a specific anesthesiologic approach in patients with M2 occlusion and minor symptoms undergoing iMT. They also agree with a recent report on the effect of the type of anesthesia on both clinical and safety measures in patients with medium-distal occlusions in the anterior and posterior cerebral arteries treated with MT.²⁸ This finding suggests that the choice should be based on the specific characteristics of each patient, to minimize the risk of adverse events, especially in a condition in which the benefit of iMT over BMM still needs to be elucidated.

The main limitation of our study derives from the possible selection bias implicit in its retrospective nature and noncontrolled design. Although clinical records were carefully reviewed, the quality of data collected outside the rigid criteria of a randomized trial could have affected our results. A PSM algorithm was used to minimize differences in baseline characteristics and was calibrated on a set of covariates that we believe are important as predictors of clinical outcome. However, it is possible that other relevant factors were overlooked. Moreover, this statistical approach resulted in a further reduction of our sample size, which may not be large enough to detect significant differences concerning the effect of a

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specific anesthesiologic approach during MT. This aspect is even more relevant in a population of patients with an overall favorable long-term clinical outcome.²³ In most participating centers, the anesthesiologic procedure of choice was based on predefined local protocols rather than tailored to specific clinical features of the individual patient. We believe that this latter aspect of our study may have contributed to minimizing a possible bias deriving from other clinical features of each patient that could have been relevant in the selection of the type of anesthesia and possibly have a role also in long-term clinical outcomes. Of course, the opposite consideration applies to centers without a predefined protocol, in which the clinical path leading to a specific type of anesthesia was not disclosed.

CONCLUSIONS

The type of anesthesia in patients with M₂ occlusion and minor baseline symptoms receiving iMT does not seem to influence the 90-day clinical outcome, as well as the rates of successful recanalization and procedure-related complications. Considering that the benefit of iMT in minor stroke with medium vessel occlusion still needs clarification, the choice of the best anesthesiologic conduct should be tailored to the individual patient necessity to minimize the risk of adverse events.

CRedit AUTHORSHIP CONTRIBUTION STATEMENT

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SUPPLEMENTARY DATA

Supplementary Table 1. Univariate Analysis of Demographic, Baseline Clinical, Therapeutic and Imaging Data in Patients Stratified by Type of Anesthesia, After Propensity Score Matching **Conscious Sedation/Local** Anesthesia (n = 47)General Anesthesia (n = 47) P Value* Demographics Female, number of patients (%) 25 (53.2) 25 (53.2) 1.000 Age, mean (±standard deviation) 0.529 70.7 (±4.0) 72.4 (±3.6) Baseline clinical features Atrial fibrillation, number of patients (%) 14 (29.8) 21 (44.7) 0.135 Diabetes, number of patients (%) 7 (14.9) 7 (14.9) 1.000 0.527 Dyslipidemia, number of patients (%) 17 (36.2) 20 (42.6) Coronary artery disease, number of patients (%) 3 (6.4) 3 (6.4) 1.000 15 (31.9) 0.356 Carotid atherosclerosis, number of patients (%) 11 (23.4) Chronic obstructive pulmonary disease, number of patients (%) 4 (8.5) 4 (8.5) 1.000 4 (3-5) NIHSS score at baseline, median (IQR) 4 (3-5) 0.435 NIHSS score at 72 hours, median (IQR) 0.386 1(0-3)2(1-3)Medical therapy and procedural parameters 0.472 Current therapy with antiplatelet, number of patients (%) 10 (21.3) 13 (27.7) Current therapy with anticoagulant, number of patients (%) 6 (12.8) 11 (23.4) 0.180 0.216 Current therapy with statins, number of patients (%) 8 (17.0) 13 (27.7) Thrombolysis, number of patients (%) 14 (29.8) 18 (38.3) 0.384 Onset-to-groin (minutes), median (IQR) 272 (220-364) 345 (220-460) 0.849 Groin-to-reperfusion (minutes), median (IQR) 38 (28-48) 40 (29-52) 0.349 Baseline imaging data Left side, number of patients (%) 28 (59.6) 29 (61.7) 0.833 Alberta Stroke Program Early CT Score, median (IQR) 10 (9-10) 9 (9-10) 0.246 Atherosclerotic occlusion, number of patients (%) 6 (12.8) 4 (9.1) 0.575 Dominant M2 involvement, number of patients (%) 34 (72.3) 31 (66.0) 0.503 Middle cerebral artery branch 0.194 21 (44.7) 29 (61.7) Superior, number of patients (%) Middle, number of patients (%) 6 (12.8) 6 (12.8) Inferior, number of patients (%) 20 (42.6) 12 (25.5) 4(4-4)4(4-4)0.946 Menon score, median (IQR) NIHSS, National Institutes of Health Stroke Scale; IQR, interquartile range.

*Statistical significance was considered at P < 0.05.