

Original research

Effect of anesthetic strategies on distal stroke thrombectomy in the anterior and posterior cerebral artery

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ABSTRACT

Background Numerous questions regarding procedural details of distal stroke thrombectomy remain unanswered. This study assesses the effect of anesthetic strategies on procedural, clinical and safety outcomes following thrombectomy for distal medium vessel occlusions (DMVOs).

Methods Patients with isolated DMVO stroke from the TOPMOST registry were analyzed with regard to anesthetic strategies (ie, conscious sedation (CS), local (LA) or general anesthesia (GA)). Occlusions were in the P2/P3 or A2–A4 segments of the posterior and anterior cerebral arteries (PCA and ACA), respectively. The primary endpoint was the rate of complete reperfusion (modified Thrombolysis in Cerebral Infarction score 3) and the secondary endpoint was the rate of modified Rankin Scale score 0–1. Safety endpoints were the occurrence of symptomatic intracranial hemorrhage and mortality.

Results Overall, 233 patients were included. The median age was 75 years (range 64–82), 50.6% (n=118) were female, and the baseline National Institutes of Health Stroke Scale score was 8 (IQR 4–12). DMVOs were in the PCA in 59.7% (n=139) and in the ACA in 40.3% (n=94). Thrombectomy was performed under LA±CS (51.1%, n=119) and GA (48.9%, n=114). Complete reperfusion was reached in 73.9% (n=88) and 71.9% (n=82) in the LA±CS and GA groups, respectively (P=0.729). In subgroup analysis, thrombectomy for ACA DMVO favored GA over LA±CS (aOR 3.07, 95% CI 1.24 to 7.57, P=0.015). Rates of secondary and safety

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Distal medium vessel occlusions (DMVOs) have been declared a possible target for thrombectomy but there is currently no evidence on the effects of anesthetic strategies on outcomes and safety.

WHAT THIS STUDY ADDS

⇒ Local anesthesia with and without conscious sedation compared with general anesthesia resulted in similar rates of reperfusion, clinical outcomes, and safety after thrombectomy for DMVO stroke of the anterior cerebral artery and posterior cerebral artery. General anesthesia may facilitate achieving complete reperfusion in DMVO stroke of the anterior cerebral artery.

outcomes were similar in the LA±CS and GA groups.

Conclusion LA±CS compared with GA resulted in similar reperfusion rates after thrombectomy for DMVO stroke of the ACA and PCA. GA may facilitate achieving complete reperfusion in DMVO stroke of the ACA. Safety and functional long-term outcomes were comparable in both groups.

INTRODUCTION

Distal medium vessel occlusions (DMVOs) have been declared a potential next frontier of endovascular

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Conventional anesthetic procedures (ie, local anesthesia with and without conscious sedation or general anesthesia) appear reasonable for DMVO thrombectomy. General treatment recommendations cannot be derived from this study. Further multicenter experience is needed to provide information for ongoing randomized trials.

stroke treatment^{1,2} and, recently, clinical evidence suggested a potential treatment effect of thrombectomy in distal arterial occlusions encouraging ongoing randomized clinical trials (RCTs).^{3–5} Meanwhile, numerous questions regarding procedural details of thrombectomy for DMVOs remain unanswered, including the optimal anesthetic strategy.² Whether local anesthesia (LA), conscious sedation (CS), or general anesthesia (GA) provide a procedural or clinical advantage has been intensively debated for patients with large vessel occlusion (LVO) stroke of the anterior circulation as past studies observed no clear superiority of one strategy.^{6–9} In the subgroup of DMVO stroke, GA may offer a potential advantage as reduced patient movement provides optimal conditions for technically challenging catheter navigations in distal fragile arteries, possibly resulting in better recanalization results and fewer periprocedural complications.

We performed a subanalysis of the TOPMOST registry^{10,11} with regard to anesthetic strategies and hypothesized that GA leads to better procedural results in patients undergoing thrombectomy for DMVO stroke.

METHODS**Study design and protocol**

The TOPMOST (Treatment fOr Primary Medium vessel Occlusion STroke) registry is an international, retrospective, multicenter, observational registry of patients treated for distal cerebral artery occlusions in Europe, the USA and Asia between January 1, 2010 and October 30, 2021.

The study protocol was approved by ethics committee of Hamburg, Germany (Chamber of Physicians, Hamburg; 689–15), in accordance with the Declaration of Helsinki.¹² Patient informed consent was waived by our review board because of the retrospective study design using fully anonymized data. Each of the participating centers obtained ethical approval according to their local protocol for sharing retrospective and fully anonymized data. Parts of the TOPMOST registry have been previously included in studies.^{10,11,13,14} This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies.

Study inclusion criteria and group definitions

In this study we investigated primary isolated DMVOs of the posterior and anterior cerebral arteries (PCA and ACA) (see online supplement eFigures 1 and 2).¹⁵ The main inclusion criteria for this analysis were: acute ischemic stroke due to a primary and isolated occlusion within medium-sized vessel segments of the PCA (ie, P2 or P3) or ACA (ie, A2 to A4) and endovascular treatment (ie, aspiration catheters, stent retrievers, intra-arterial thrombolysis) with or without intravenous thrombolysis (IVT) administration depending on current guideline recommendations.

Procedural characteristics were compared by the initial anesthetic strategy defined as general anesthesia (GA), conscious sedation (CS) or local anesthesia (LA). LA and CS were grouped

together as LA±CS and compared with GA in the main analysis (see online supplemental eFigure 3).

Procedural, clinical and safety outcomes

The primary outcome was the rate of complete reperfusion classified as a modified Thrombolysis in Cerebral Infarction (mTICI) scale score of 3 on the final angiography run. Successful thrombectomy was considered a final reperfusion result of mTICI 2b–3 and a first-pass effect was defined as a mTICI score of 3 after the first reperfusion attempt. Further procedural details such as the number of reperfusion maneuvers, interventional duration (groin puncture to final reperfusion status) and the rate of intervention-related serious adverse events (eg, iatrogenic dissection perforations, distal embolization) were analyzed.

The secondary outcome was the rate of functional outcome assessed with the modified Rankin Scale (mRS) score at day 90 (defining excellent functional outcome as an mRS score 0–1). Early clinical improvement defined as the median change in National Institute of Health Stroke Scale (NIHSS) scores from baseline to discharge was evaluated.

Safety outcomes were the rate of mortality assessed during hospitalization and at 90 days follow-up as well as rates of hemorrhage classified in accordance with the Second European-Australasian Acute Stroke (ECASS II) Study.¹⁶ Primary, secondary and safety outcomes were analyzed and compared by patients receiving GA or LA with or without CS.

Statistical analysis

Standard descriptive statistics were used for all data. Univariable distribution of metric variables was described with median and IQR, and categorical variables as absolute and relative frequencies. The primary outcome (proportions of mTICI 3 at the end of the procedure) was compared between the GA group and the LA±CS group adjusted for age, sex, baseline NIHSS, anterior versus posterior circulation, distal site (P2 and A2 versus P3 and A3/4), and administration of IVT using a multivariable logistic regression model analyzing prespecified subgroups (age, sex, hypertension, circulation site, distal location, IVT, and number of reperfusion attempts). The secondary outcome (proportions of mRS 0–1 at 90 days) was evaluated with univariable and stepwise multivariable logistic regression analysis adjusted for anesthesia strategy, age, sex, circulation site, distal location, prestroke mRS, baseline NIHSS, IVT, and mTICI 2b/3. Safety outcomes were compared by groups of GA and LA±CS. No adjustment for multiple testing was performed and the analyses were regarded as explorative. Local unadjusted two-sided $P < 0.05$ was considered to be statistically significant. Odds ratios (OR) and adjusted ORs (aOR) are presented with 95% confidence intervals. Statistical analyses were carried out with SPSS version 26 (IBM Corporation) and Stata 17.0 (StataMP, StataCorp, Texas, USA).

RESULTS**Baseline characteristics**

A total of 233 patients met the inclusion criteria and were treated endovascularly for primary isolated DMVO in the ACA or PCA. The median age was 75 years (IQR 64–82) and 50.6% (n=118) were women. Patients were admitted with a median NIHSS score of 8 (IQR 4–12), which was significantly higher in the GA group (median 9 (IQR 5–14)) than in the CS±LA group (median 7 (IQR 4–12), $P=0.022$) (table 1). The most common cardiovascular risk factor was arterial hypertension in 76.4% (n=178). DMVOs were located in the ACA in 40.3% (n=94) and in the PCA in 59.7% (n=139). In 25.8% (n=60)

Table 1 Baseline characteristics compared by anesthetic strategy

Baseline and procedural characteristics	All patients (n=233)	LA±CS (n=119)	GA (n=114)	P value
Age, median (IQR)	75 (64–82)	75 (64–83)	76 (64–82)	0.765
Women, % (n)	50.6 (118)	52.1 (62)	53.5 (61)	0.392
Cardiovascular risk factors, % (n)				
Atrial fibrillation	39.5 (92)	36.1 (43)	43 (49)	0.285
Arterial hypertension	76.4 (178)	73.1 (87)	79.8 (91)	0.228
Diabetes mellitus	20.6 (48)	18.5 (22)	22.8 (26)	0.415
Dyslipidemia	42.5 (99)	42 (50)	43 (49)	0.836
Prestroke mRS, median (IQR)	0 (0–2)	0 (0–2)	0 (0–2)	0.552
Missing data	23	20	3	
Admission NIHSS, median (IQR)	8 (4–12)	7 (4–12)	9 (5–14)	0.022*
Baseline imaging, % (n)				
CT	69.1 (161)	81.5 (97)	56.1 (64)	
Occlusion site, % (n)				
ACA	40.3 (94)	33.6 (40)	47.4 (54)	0.032*
PCA	59.7 (139)	66.4 (79)	52.6 (60)	
Distal†	25.8 (60)	27.7 (33)	23.7 (27)	0.480
TOAST classification, % (n)				0.620
Large artery atherosclerosis	17 (35)	17.2 (16)	16.8 (19)	
Cardioembolic	50.5 (104)	53.8 (50)	47.8 (54)	
Small artery occlusion	–	–	–	
Other determined etiology	5.3 (11)	2.2 (2)	8 (9)	
Undetermined etiology	27.2 (55)	26.9 (25)	27.4 (31)	
Missing data	27	26	1	
Time from symptom onset to groin puncture, median (IQR), min	196 (145–300)	197 (135–310)	190 (147–294)	0.944
Missing data	50	24	26	
Intravenous thrombolysis, % (n)	39.1 (91)	37.8 (45)	40.4 (46)	0.692
Local anesthesia only, % (n)	11.6 (27)	22.7 (27)	NA	NA

*Indicating significance.
†Distal=segments of A3, A4 or P3.
ACA, anterior cerebral artery; IVT, intravenous thrombolysis; mTICI, modified Thrombolysis In Cerebral Infarction; NIHSS, National Institute of Health Stroke Scale; PCA, posterior cerebral artery; TOAST, Trial of Org 10 172 in Acute Stroke Treatment.

the occlusions occurred in distal segments (ie, A3, A4, P3). The median time from symptom onset to groin puncture was 196 min (IQR 145–300).

Procedural outcome

Bridging IVT was administered in 39.1% (n=91) of all patients prior to the procedure. Thrombectomies were performed in 48.9% (n=114) of the cases with GA and in 51.1% (n=119) with LA±CS including 11.6% (n=27) with LA only. A successful first-pass effect was observed following thrombectomy under GA and in LA±CS in 42.5% (n=48) and 47.1% (n=56), respectively (P=0.483). Further thrombectomy maneuvers increased the rate of complete reperfusion (mTICI 3) in the GA and LA±CS cohorts to 71.9% (n=82) and 73.9% (n=88), respectively (P=0.729) (figure 1). There were no significant differences in the total number of reperfusion attempts between the two groups (GA: 1 (IQR 1–2) vs LA±CS: 1 (IQR 1–2); P=0.397). The median interventional procedure time from groin puncture to reperfusion was similar in both cohorts (GA: 38.5 min (IQR 25–55) vs LA±CS: 38 min (23–62); P=0.952). Table 2 provides a detailed overview of all procedural outcome results.

In multivariable logistic regression analysis (figure 2), in anterior circulation DMVO the primary outcome (complete reperfusion of mTICI 3) occurred in 42 (77.8%) of 54 patients in the GA group and 21 (52.5%) of 40 patients in the LA±CS group (aOR 3.07, 95% CI 1.24 to 7.57, P=0.015). This effect was significantly different from that observed in patients with posterior circulation DMVO (aOR 0.43, 0.18 to 1.02, interaction P=0.001) (figure 2). In the GA group there was one iatrogenic dissection and two cases of embolization to new territory.

Clinical and functional outcome

The early clinical outcome evaluated by the change in NIHSS from baseline to discharge was higher in the GA group (–3.37 (95% CI –4.94 to –3.66)) than in the LA±CS group (–3 (95% CI –4.16 to –1.9; P=0.028) without adjustment. Unadjusted excellent functional outcome rates at 90 days were significantly higher in the LA±CS group (median mRS 1 (IQR 0–3)) than in the GA group (median mRS 2 (IQR 1–4); P=0.004). In multivariable logistic regression analysis, higher baseline NIHSS scores (aOR 0.86 (95% CI 0.79 to 0.93); P<0.001), pre-stroke mRS (aOR 0.34 (95% CI 0.18 to 0.64); P<0.001), circulation

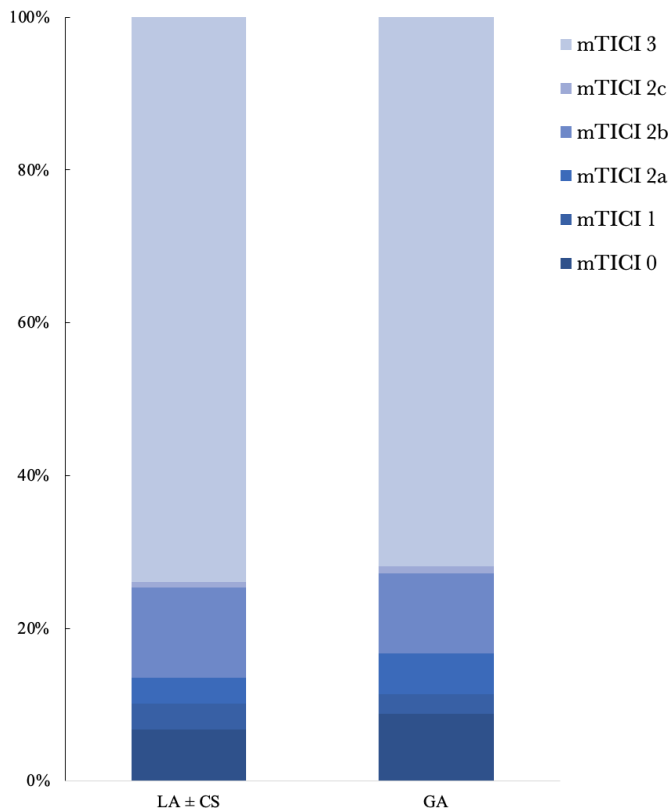


Figure 1 Final angiographic outcome compared by anesthetic strategy. GA, general anesthesia; LA±CS, local anesthesia with or without conscious sedation; mTICI, modified Thrombolysis In Cerebral Infarction Scale.

site (aOR 0.38 (95% CI 0.16 to 0.89); $P < 0.026$), and mTICI 2b–3 (aOR 8.88 (95% CI 2.53 to 31.24); $P < 0.001$) were independently associated with the secondary outcome of mRS 0–1 (see online supplemental eTable 1).

Safety outcome

The overall frequency of sICH was 2.1% ($n = 5$) and did not differ significantly between the LA±CS (2.5%, $n = 3$) and GA (1.8%, $n = 2$) groups ($P = 1.0$). Mortality rates at day 90 were numerically higher in the GA group (17.2%, $n = 15$) than in the LA±CS group (15.7%, $n = 13$; $P = 0.913$).

DISCUSSION

This retrospective multicenter study comparing patients undergoing thrombectomy for DMVO stroke under GA or LA with or without sedation revealed several findings: (1) the distribution of the final reperfusion results was similar in both groups following distal thrombectomy; (2) a significant interaction was observed with regard to the circulation site favoring thrombectomy under GA for DMVO of the ACA; (3) periprocedural complications and safety (ie, sICH and mortality) did not differ significantly between the two anesthetic strategies; (4) excellent functional outcome was independently associated with prestroke mRS, anterior circulation site, baseline NIHSS scores and successful reperfusion.

Whether to perform thrombectomy under GA or CS has been intensively investigated in LVO stroke; however, the evidence remains neutral, ambiguous and inconclusive.¹⁷ Several findings can be derived from the currently available literature. First, retrospective studies and registry data seem to favor CS

for thrombectomy, but important information on the anesthetic strategy decision-making (poor clinical condition vs hospital protocol) and procedural variables (anesthetic protocol, type of anesthetic agent, time metrics, blood pressure management) are usually not reported.¹⁸ In addition, these studies generally found higher baseline NIHSS and lower ASPECTS scores in the GA group, so interpretation of these data remains difficult even after adjustment for crucial confounders.^{6 19–21} Second, randomized evidence must be carefully looked at because RCTs included by the HERMES subanalysis were not designed for this comparison, and the bias of requiring GA for medical reasons rather than protocol-based is also possible in these trials.²² Third, in four dedicated RCTs looking at the effect of anesthesia,^{23–26} GA was associated with a positive treatment effect for improved reperfusion (mTICI 2b/3) in two studies and for independent functional outcome rates (mRS 0–2) in one study. The weight of these studies was high enough that the overall effect size for both endpoints was positive in recent RCT-based meta-analyses.^{7 9} However, these findings must be interpreted with caution since all RCTs were single-center trials and probably not sufficiently powered to detect all treatment effects. Furthermore, the studies showed no substantial differences between groups regarding in-hospital time metrics, which may be associated with the presence of specialized neuroanesthesia teams that performed strict protocol-driven management of GA. Hence, these findings likely do not reflect real-world conditions and may not be generalizable to other populations and not be reproducible in daily clinical practice.²⁷ As a result, current evidence levels of leading associations were rated ‘very low’ and guideline recommendations endorse an individualized patient approach.^{28 29} In this context, our analysis inevitably faces all the challenges of previous studies that investigated the impact of anesthetic strategies on treatment effects after LVO thrombectomy.

Similar to LVO studies, we observed significantly higher baseline NIHSS scores in the GA group compared with the LA±CS group. As already mentioned, this finding may represent a substantial bias showing that patients with a more severe clinical admissions status are rather treated under GA for suspected movement or worsening during the procedure. Additionally, there were significantly more ACA DMVO cases in the GA group than in the LA±CS group. This observation may constitute a higher baseline severity since the NIHSS is naturally higher in ACA than PCA stroke as NIHSS scoring does not encompass all symptoms of the posterior circulation.³⁰

In DMVO stroke, reduced patient movement may have a higher impact on procedural outcomes as it facilitates catheter navigation and therefore serves to prevent complications in distal vessels that are more fragile and susceptible to iatrogenic manipulation. Interestingly, patient movement does not appear to be a major concern for treating interventionalists at the moment, as a recent survey reflected current anesthetic approaches for DMVO strokes worldwide and reported that most interventionalists preferred LA or CA over GA.³¹ Our results do not support this hypothesis, and the distribution of final reperfusion scores was similar in both the GA and LA±CS groups.

In the adjusted subanalysis we observed that, in ACA DMVO stroke, the primary outcome (complete reperfusion) occurred more often in the GA group. This effect was significantly different from that observed in patients with PCA DMVO stroke and suggests that GA facilitates procedural success depending on circulation site, including possible influential factors such as catheter navigation, complex clot removal and an increased level of psychomotor agitation following ACA stroke.^{32 33} However, this finding did not translate into increased periprocedural

Table 2 Procedural and clinical outcome compared by anesthetic strategy

Outcome variables	LA±CS (n=119)	GA (n=114)	P value
Angiographic outcome, % (n)			
FPE	47.1 (56)	42.5 (48)	0.483
Final rate of mTICI3	73.9 (88)	71.9 (82)	0.729
Final rate of mTICI2b/3	86.6 (103)	83.3 (95)	0.491
Total number of attempts, median (IQR)†	1 (1–2)	1 (1–2)	0.397
Groin puncture to reperfusion time, median (IQR), min	38 (23–62)	38.5 (25–55)	0.952
Missing data	8	15	
Neurological outcome			
Early clinical outcome (95% CI)‡	–3 (–4.16 to –1.9)	–3.37 (–4.94 to –3.66)	0.028*
Missing data	22	20	
90-day mRS, median (IQR)	1 (0–3)	2 (1–4)	0.004*
Total rate of mRS 0–1, % (n)	63.9 (53)	40.2 (35)	0.002*
90-day mortality, % (n)	15.7 (13)	17.2 (15)	0.913
Missing data	36	27	
Safety			
sICH, % (n)	2.5 (3)	1.8 (2)	1.0
Periprocedural complications			
Downstream embolization	–	–	NA
Embolization to new territory	–	1.7 (2)	NA
Iatrogenic vessel injury§	1.7 (2)	0.9 (1)	NA

*Indicating significance.

†Regardless of eventual rescue strategies.

‡NIHSS change from baseline to discharge.

§Iatrogenic vessel injury defined as vessel perforation or dissection including large and medium sized vessel segments.

FPE, first-pass effect (mTICI 3 after the first pass); mRS, modified Rankin Scale at 90 days; mTICI, modified Thrombolysis In Cerebral Infarction Scale; sICH, symptomatic intracerebral hemorrhage.

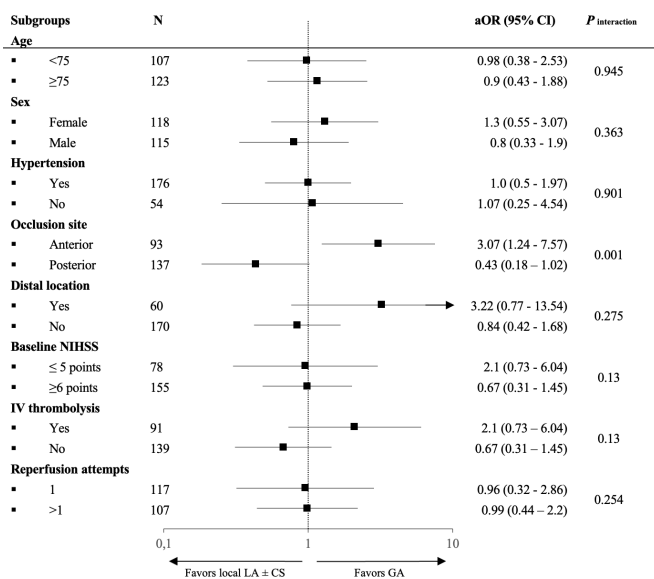


Figure 2 Forest plot of complete reperfusion (mTICI 3) in prespecified subgroups based on multivariable logistic regression analysis. ORs of <1 favor LA±CS over GA. ORs are adjusted for age, sex, baseline NIHSS, circulation site, distal location (P2+A2 vs P3+A3/4) and intravenous thrombolysis. GA, general anesthesia; LA±CS, local anesthesia with or without conscious sedation; NIHSS, National Institutes of Health Stroke Scale.

complications and rates of sICH in the LA±CS group, highlighting the safety of the procedure itself in the whole study cohort.

In DMVO stroke, rapid treatment initiation and reperfusion is crucial since the salvageable tissue is a priori smaller and with it the possible treatment effect of thrombectomy. Thus, GA may have disadvantages in DMVO stroke due to the delay from admission to groin puncture and potentially impaired collaterals by lower blood pressure leading to a poor outcome.² Our results did not corroborate these concerns and, conversely, LA±CS was not associated with better rates of the secondary outcome (excellent functional outcome at 90 days) after adjusting for possible confounders. The results were in line with previous thrombectomy landmark studies showing that increased baseline NIHSS scores, poorer prestroke mRS, advanced age and successful reperfusion were independently associated with improved functional outcomes.³⁴ Interestingly, the anterior circulation site (ie, ACA) was associated with less favorable odds for the secondary outcome in the adjusted model. This finding underlines the challenges faced by ongoing RCTs applying global functional outcome scales focused on motor deficits (eg, mRS) that are not adjusted for circulation sites, and therefore do not adequately reflect neurological recovery of all occlusion locations, particularly in DMVO strokes with a presumably lower treatment effect.^{2,35}

Limitations

Our study has all the limitations that are associated with a non-randomized retrospective multicenter study design,

including missing data regarding details of the anesthetic procedure, imaging, time metrics, and follow-up data. Furthermore, a reporting and selection bias must be anticipated in studies with rarely treated patients by multiple centers. The mTICI scale was initially not designed for the ACA or PCA and reperfusion results were not assessed by an independent core laboratory.³⁶ Data on DMVO treatment in the middle cerebral artery are not yet available in the TOPMOST registry and may have an impact on outcomes. Therefore, the results of the present study must be interpreted with caution and no treatment recommendations can be drawn.

CONCLUSIONS

Among patients with primary isolated DMVO stroke of the ACA and PCA undergoing thrombectomy, neither LA±CS nor GA resulted in higher reperfusion rates. GA may facilitate thrombectomy for distal ACA stroke resulting in higher rates of complete reperfusion. Periprocedural safety and functional outcome were not affected by the anesthetic strategy. An excellent functional outcome at day 90 was independently associated with the prestroke mRS score, circulation site, baseline NIHSS, and successful reperfusion at the end of the procedure.

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Contributors LM, UH, and JF made substantial contributions to the conception and design of the work. Data acquisition was performed by LM, GB, PS, MW, ME, PS, EIP, JK, CM, MRHP, HZ, WN, NA, CK, DB, MT, VM, SF, MM, CW, SL, ME, AJ, DM, MM, ES, SL, LUK, LY, BT, AG, BG, JG, MS, PN, ER, MS, FA, KZ, MMG, MA, AK, PP, AK, FD, MP, TA and RC. LM performed the data analysis. Interpretation of the data was carried out by LM, JF, PCS, UH, GB and PP. LM drafted the manuscript, and all of the other authors revised it critically for important intellectual content. All authors approved the final version to be published. They agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the manuscript are appropriately investigated and resolved. Guarantor: LM.

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