Anesthetic management during endovascular treatment of acute ischemic stroke in the MR CLEAN Registry

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ARTICLE CLASS OF EVIDENCE

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Abstract

Objective

To compare outcomes after endovascular treatment (EVT) for acute ischemic stroke with 3 different types of anesthetic management in clinical practice, as anesthetic management may influence functional outcome.

Methods

Data of patients with an anterior circulation occlusion, included in the Dutch nationwide, prospective Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) Registry between March 2014 and June 2016, were analyzed. Patients were divided into 3 groups defined by anesthetic technique performed during EVT: local anesthesia only (LA), general anesthesia (GA), or conscious sedation (CS). Primary outcome was the modified Rankin Scale score at 90 days. To compare functional outcome between groups, we estimated a common odds ratio (OR) with ordinal logistic regression, adjusted for age, sex, prestroke modified Rankin Scale score, baseline NIH Stroke Scale score, collaterals, and time from onset to arrival at intervention center.

Results

A total of 1,376 patients were included. Performed anesthetic technique was LA in 821 (60%), GA in 381 (28%), and CS in 174 (13%) patients. Compared to LA, both GA and CS were associated with worse functional outcome on the modified Rankin Scale score at 90 days (GA cOR_{adj} 0.75; 95% confidence interval [CI] 0.58–0.97; CS cOR_{adj} 0.45; 95% CI 0.33–0.62). CS was associated with worse functional outcome than GA (cOR_{adj} 0.60; 95% CI 0.42–0.87).

Conclusions

LA is associated with better functional outcome than systemic sedation in patients undergoing EVT for acute ischemic stroke. Whereas LA had a clear advantage over CS, this was less prominent compared to GA.

Classification of evidence

This study provides Class III evidence that for patients with acute ischemic stroke undergoing EVT, LA improves functional outcome compared to GA or CS.

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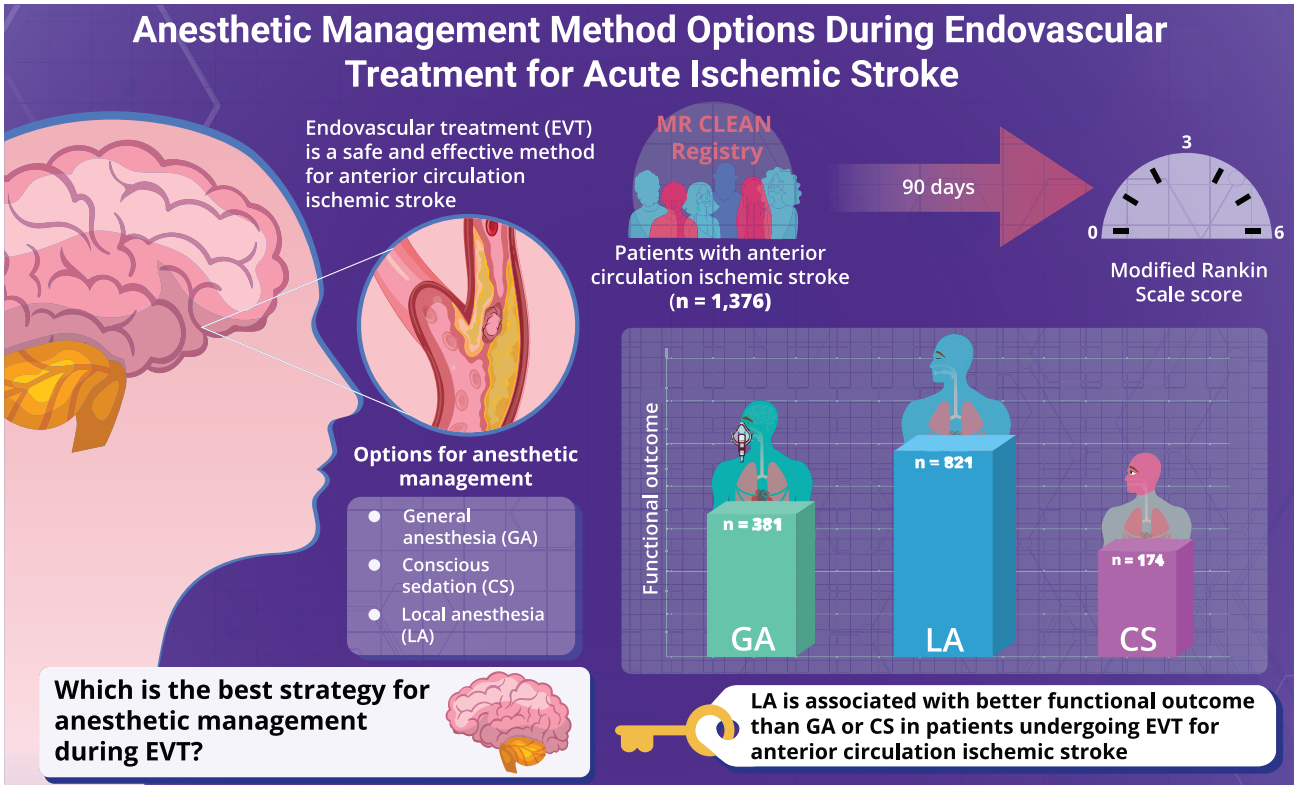
Coinvestigators are listed at links.lww.com/WNL/B16.

Glossary

ASPECTS = Alberta Stroke Program Early CT Score; **CI** = confidence interval; **cORadj** = adjusted common odds ratio; **CS** = conscious sedation; **CTA** = CT angiography; **DSA** = digital subtraction angiography; **eTICI** = extended Thrombolysis in Cerebral Ischemia; **EVT** = endovascular treatment; **GA** = general anesthesia; **ICH** = intracranial hemorrhage; **LA** = local anesthesia; **MR CLEAN** = Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; **mRS** = modified Rankin Scale; **NIHSS** = NIH Stroke Scale; **sICH** = symptomatic intracranial hemorrhage.



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Endovascular treatment (EVT) is safe and effective for anterior circulation ischemic stroke.[1] However, the best strategy for anesthetic management during EVT is unclear. In general, 3 approaches are described: general anesthesia (GA), conscious sedation (CS), and local anesthesia (LA). The 2015 American Heart Association guidelines state that the choice of anesthetic approach should be based on individual patient characteristics, and additional evidence is needed to determine the optimal standard approach.[2]

A recent meta-analysis of 7 randomized clinical trials showed that EVT with GA was associated with worse outcomes than EVT without GA,[3] which is in line with previously published results.[4] Confounding by indication may have contributed to worse outcomes with GA in observational studies. Three single-center randomized clinical trials, in which patients were randomized to receive either GA or CS, found no difference in outcome between these 2 approaches.[5–7] Anesthetic management was strictly protocolled in these trials, with specific attention to maintaining blood pressure at a certain level. In both treatment groups, the same medication was used, the difference being lower dose and absence of intubation in the CS group. Finally, a recent single-center study found that patients undergoing EVT with LA had superior outcomes compared to those with CS. However, LA was not compared to GA in this study.[8]

LA can provide an advantage over GA and CS, as potentially harmful decreases of blood pressure and potential toxic effects of sedating medication are avoided. We aimed to compare outcomes of patients treated with 3 different anesthetic approaches during EVT: LA, GA, or CS.

Methods

Patients enrolled in the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) Registry from its start on March 16, 2014, until June 15, 2016, were included in this study. The MR CLEAN Registry is a nationwide, multicenter,

observational study, in which patients who underwent EVT in the Netherlands were prospectively registered. In the following text, we describe the definitions that were used in the MR CLEAN Registry.[9] All patients undergoing an EVT procedure (defined as entry into the angiography suite and arterial puncture) for acute ischemic stroke in the anterior and posterior circulation have been registered in the MR CLEAN Registry. EVT consisted of arterial catheterization with a microcatheter to the level of the occlusion, followed by mechanical thrombectomy or thrombus aspiration, with or without delivery of a thrombolytic agent. The method of EVT for each patient was left to the discretion of the treating physicians. Inclusion criteria for the present study were start of EVT (arterial puncture) within 390 minutes after symptom onset; age ≥18; and occlusion of intracranial carotid artery (ICA, ICA-T) or middle (M1/M2) or anterior (A1/A2) cerebral artery, demonstrated by baseline CT angiography (CTA). Previously described definitions were used to assess Alberta Stroke Program Early CT Score (ASPECTS) on baseline noncontrast CT and collateral status on single-phase CTA.[10,11] All imaging was assessed by an independent core laboratory.

Anesthetic management

GA was defined as unconsciousness and the need for airway protection (i.e., tracheal intubation, laryngeal mask). CS was defined as administration of systemic medication with the intention to sedate the patient during the procedure, without the need for advanced airway protection. LA was defined as administration of a local anesthetic at the puncture site, without the use of systemic medication in order to sedate the patient.

The preferred approaches for anesthetic management were center-specific, with the exception of one interventionist who preferred CS in a center in which LA was the generally preferred approach. Two centers changed their protocol from GA to LA in the study period. Logistics and the means of execution of GA and CS were left to the treating physicians.

Outcome measures

The primary outcome measure was the modified Rankin Scale (mRS)[12] score at 90 days, which was assessed as part of usual care for all patients with stroke in all centers. The mRS score is a common measure of patient functional outcome after stroke, ranging from 0 (no symptoms) to 6 (death). Local investigators were instructed to assess mRS scores at 90 days (range 14 days either way) by telephone, according to standardized scheme.[13] Anesthetic management was registered by treating interventionists, and study staff was unaware of anesthetic management during follow-up mRS assessment.

Good functional outcome was defined as mRS score 0–2. Other outcome measures were NIH Stroke Scale (NIHSS)[14] score postintervention by a certified assessor, successful reperfusion according to postintervention digital subtraction angiography, duration of interventional procedure, and safety. Reperfusion was assessed according to the extended Thrombolysis in Cerebral Ischemia (eTICI) score,[15] which ranges from grade 0 (no reperfusion) to grade 3 (complete reperfusion). Successful reperfusion was defined as eTICI 2B or higher. In case lateral or anterior view were missing on final digital subtraction angiography (DSA), the maximum eTICI score was 2A. DSA was scored by a core laboratory, which was blinded for clinical outcome.

Safety outcomes were symptomatic intracranial hemorrhage (sICH), ischemic stroke progression, pneumonia, and mortality at 90 days. Intracranial hemorrhage (ICH) was classified symptomatic if the patient had died or had a decline on the NIHSS of at least 4 points, and imaging findings were related to clinical deterioration (Heidelberg criteria).[16] sICH was evaluated by the adverse events committee, consisting of 2 neurologists and 1 radiologist, after assessment of medical reports and classification of ICH on imaging. The definition of ischemic stroke progression was decline of at least 4 points on the NIHSS and an ICH as the cause of the deterioration was excluded with CT. The decision to classify as progression of ischemic stroke was done by the complication committee after reviewing the medical reports. The diagnosis of pneumonia was based on standard clinical practice, and was not standardized across the study.

Statistical analysis

Standard statistics were used to analyze baseline characteristics. Logistic regression was used to estimate the association between the performed anesthetic technique and outcomes. We performed adjustment for age, sex, prestroke mRS score, baseline NIHSS score, collaterals, and onset to arrival to intervention center. To compare functional outcome between anesthesia groups, we analyzed the shift on the mRS with ordinal logistic regression analysis. In addition, we adjusted for center (in which EVT was performed) in a multilevel regression analysis.

We performed the following sensitivity analyses. First, to address possible confounding by indication, we compared outcomes among the 3 anesthetic techniques according to the center-specific preferred approach. In this analysis, patients who received a different procedure than the standard procedure, based on individual patient characteristics or practical feasibility, were analyzed according to the initial preferred procedure. Second, we repeated the main analysis after excluding 1 center that had previously reported results of LA vs CS.[8]

Missing data in MR CLEAN registry

Missing NIHSS scores were retrospectively scored with a standardized score chart based on information from the reported neurologic examination.[9] If successful reperfusion was not achieved during EVT, the time of last contrast bolus injection was used as a proxy for time of reperfusion. Any mRS score of 0–5 assessed within 30 days was considered missing. These values were therefore replaced by mRS scores derived from multiple imputation for the (multivariable) regression

analysis.[17] Multiple imputation was performed with Stata/SE 14.1 (StataCorp, College Station, TX) with the following variables: age, sex, baseline NIHSS score, diabetes mellitus, previous myocardial infarction, previous stroke, prestroke mRS score, atrial fibrillation, IV thrombolysis prior to EVT, systolic blood pressure, baseline ASPECTS, occlusion segment, CTA collateral status, time from symptom onset to start of EVT, time from symptom onset to successful reperfusion, eTICI score at the end of the intervention, and NIHSS score after 24–48 hours. All descriptive analyses include patients with complete data, while all regression models include all patients with imputed data.

Classification of evidence

This interventional study provides Class III evidence that for patients with acute ischemic stroke undergoing EVT, both GA and CS were associated with worse functional outcome on the mRS at 90 days compared to LA (GA adjusted common odds ratio [cOR_{adj}] 0.75; 95% confidence interval [CI] 0.58–0.97; CS cOR_{adj} 0.45; 95% CI 0.33–0.62).

Standard protocol approvals, registrations, and patient consents

The MR CLEAN Registry was approved by the ethics committee of the Erasmus University MC, Rotterdam, the Netherlands (MEC-2014-235). With this approval, it was approved by the research board of each participating center. At UMC Utrecht, approval to participate in the study was obtained from their own research board and ethics committee.

Data availability

Source data will not be made available because of legislative issues on patient privacy, but detailed analytic methods and study materials, including log files of statistical analyses, will be made available to other researchers on request to the first author.

Results

Patient characteristics

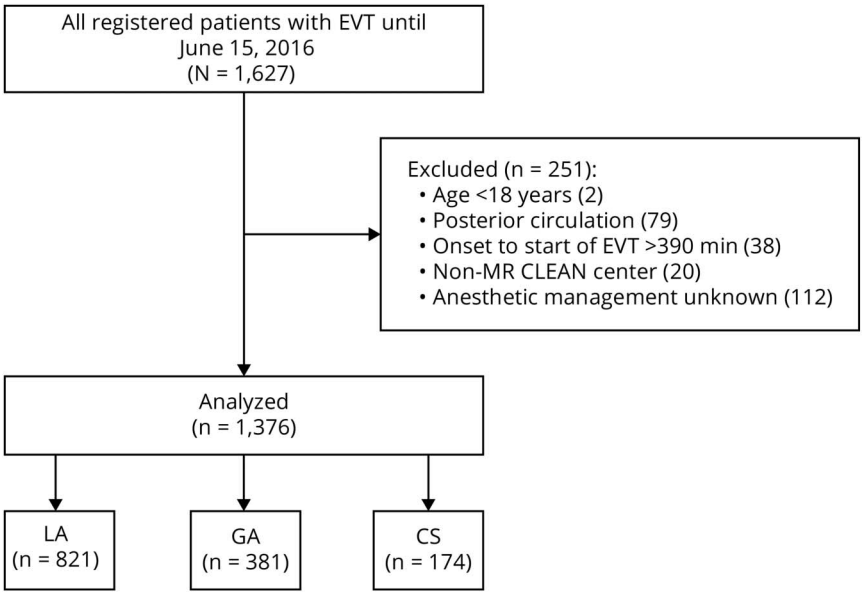
In the MR CLEAN Registry, 1,627 patients were registered until June 15, 2016. We included 1,376 patients in the present study (figure 1). The performed anesthetic technique was LA in 821 (60%), GA in 381 (28%), and CS in 174 (13%) patients (table 1).

Age was higher in the LA group, while median NIHSS score was lower compared to the GA and the CS group. In the CS group, prestroke functional status was better, and history of ischemic stroke was less frequent. Occlusion site and collateral score on baseline CTA were comparable, although good collaterals (grade 3) were slightly more frequent with LA and CS compared to GA. Both the percentage of patients who were transferred from a primary stroke center to an intervention center (59% [CS] vs 53% [LA], and 54% [GA]), and the duration from onset to arrival in the intervention center (median 140 [CS] vs 135 [LA], and 135 [GA] minutes), was slightly higher in the CS group (table 1).

Intervention characteristics

Successful reperfusion (eTICI ≥2B) in patients who underwent an attempt for thrombus retrieval was achieved most frequently with GA, in 227 of 352 (64%), less so with LA, in 416 of 706 (59%), and least frequently with CS, in 81 of 156 (52%) ($p = 0.02$; table 2). Of note, an eTICI 2A score on DSA

Figure 1 Flowchart of MR CLEAN registry patients included for the analysis according to performed anesthetic technique



CS = conscious sedation; EVT = endovascular treatment; GA = general anesthesia; LA = local anesthesia; MR CLEAN = Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands.

Table 1 Baseline characteristics (according to performed anesthetic technique)

	LA (n = 821)	GA (n = 381)	CS (n = 174)	*p* Value	Missing, n
Age, y, median (IQR)	72 (61–80)	69 (55–78)	69 (58–78)	<0.01	0
Male sex, n (%)	445 (54)	208 (55)	89 (51)	0.73	0
NIHSS, median (IQR)	15 (11–20)	17 (12–20)	16 (11–19)	0.02	29
Clinical localization: left hemisphere, n (%)	425 (52)	230 (61)	87 (50)	0.04	0
Systolic pretreatment blood pressure, mm Hg, mean (SD)	149 (24)	148 (24)	154 (26)	0.07	40
IV alteplase treatment, n (%)	644 (78)	294 (77)	131 (75)	0.51	3
Medical history, n (%)					
Atrial fibrillation	195 (24)	73 (19)	40 (23)	0.22	18
Hypertension	433 (53)	175 (46)	88 (51)	0.08	18
Diabetes mellitus	143 (17)	55 (14)	33 (19)	0.30	8
Hypercholesterolemia	268 (33)	108 (28)	38 (22)	0.01	40
Current smoking	186 (23)	79 (21)	48 (28)	<0.01	13
Ischemic stroke	149 (18)	66 (17)	19 (11)	0.06	9
Prestroke modified Rankin Scale score, n (%)				<0.01	26
0	557 (68)	228 (60)	134 (77)		
1	111 (14)	51 (13)	12 (7)		
2	54 (7)	40 (11)	8 (5)		
>2	99 (12)	62 (16)	20 (11)		
Imaging					
Level of occlusion on noninvasive vessel imaging (CTA), n (%)				0.97	73
ICA (intracranial)	47 (6)	24 (6)	8 (5)		
ICA-T	174 (21)	78 (21)	37 (21)		
M1	453 (55)	205 (54)	97 (56)		
M2	98 (12)	48 (13)	18 (10)		
Other: M3 and ACA	9 (1)	6 (2)	1 (1)		
ASPECTS subgroups, n (%)				0.01	63
0–4	50 (6)	25 (6)	14 (8)		
5–7	159 (19)	102 (27)	48 (28)		
8–10	571 (69)	241 (63)	103 (59)		
Collaterals, n (%)				0.11	105
Grade 0	53 (6)	30 (8)	10 (6)		
Grade 1	246 (30)	121 (32)	51 (29)		
Grade 2	288 (35)	151 (40)	58 (33)		
Grade 3	169 (21)	54 (14)	40 (23)		
Transfer from primary stroke center, n (%)	438 (53)	206 (54)	103 (59)	0.37	0
Onset to arrival intervention center, min, median (IQR)	135 (60–190)	135 (65–185)	140 (61–198)	0.78	67

Abbreviations: ACA = anterior cerebral artery; ASPECTS = Alberta Stroke Program Early CT Score; CS = conscious sedation; CTA = CT angiography; LA = local anesthesia; GA = general anesthesia; ICA = intracranial carotid artery; IQR = interquartile range; NIHSS = NIH Stroke Scale.

Table 2 Intervention characteristics

	LA (n = 821), n (%)	GA (n = 381), n (%)	CS (n = 174), n (%)	*p* Value
Performed procedure				0.06
Attempt made for thrombus retrieval	706 (86)	352 (92)	156 (90)	
Target occlusion was not accessible	44 (5)	9 (2)	9 (5)	
No target occlusion was present on DSA	66 (8)	19 (5)	8 (5)	
Other reason for no attempt for thrombus retrieval	5 (1)	1 (0)	1 (1)	
Successful reperfusion (eTICI 2B or higher)[a]	416 (59)	227 (64)	81 (52)	0.02
Excellent reperfusion (eTICI 2C or higher)[a]	337 (41)	170 (45)	56 (32)	0.01
Complete reperfusion (eTICI 3)[a]	276 (34)	114 (30)	44 (25)	0.05
Missing 2-directional view on DSA in patients reaching eTICI 2A, n/n (%)	62/176 (35)	15/65 (23)	9/39 (23)	0.10
Stent retriever as first treatment modality[a]	582 (82)	219 (62)	120 (77)	<0.01
Onset to start of EVT (arterial puncture), min, median (IQR)	200 (155–255)	225 (170–270)	210 (160–277)	<0.01
Onset to reperfusion/last contrast bolus, min, median (IQR)	258 (215–320)	287 (232–335)	272 (223–346)	<0.01
Start of EVT (arterial puncture) to reperfusion/last contrast bolus, min, median (IQR)	55 (33–79)	55 (30–82)	62 (40–85)	0.21
Median duration of interventional procedure, min, median (IQR)	63 (40–88)	62 (40–90)	70 (46–92)	0.21

Abbreviations: CS = conscious sedation; DSA = digital subtraction angiography; eTICI = extended Thrombolysis in Cerebral Ischemia; EVT = endovascular treatment; LA = local anesthesia; GA = general anesthesia; IQR = interquartile range.
[a] In patients in whom an attempt was made for thrombus retrieval (LA, n = 706; GA, n = 352; CS, n = 156 patients).

as a result of missing 2-directional view was most frequently given in the LA group (35%; compared to 23% in GA or CS of eTICI 2A scores). In these patients, successful reperfusion might be underreported. Both onset to start of EVT (LA 200, GA 225, CS 210 minutes median) and onset to reperfusion (LA 258, GA 287, CS 272 minutes median) were shorter with LA compared to GA and CS (table 2).

Concerning anesthetic management, administration of low-dose systemic opioids for analgesic purpose was still reported as LA by 1 intervention center: in 19/821 patients (2%) with LA as reported technique, a bolus of alfentanil (n = 8; 100–500 μg), sufentanil (n = 10; 2.5–10 μg), or remifentanil (n = 1, dose unknown) was administered IV just before pulling back the stent retriever for thrombectomy.

Clinical outcomes

Functional outcome

Compared to LA, both GA and CS were associated with worse functional outcome on the mRS at 90 days (GA cOR_{adj} 0.75; 95% CI 0.58–0.97; CS cOR_{adj} 0.45; 95% CI 0.33–0.62) (table 3). After adjustment for center in which EVT was performed, we found similar results (GA cOR_{adj} 0.73; 95% CI 0.52–1.02; CS cOR_{adj} 0.51; 95% CI 0.33–0.78). CS was associated with worse functional outcome on the mRS compared to GA (cOR_{adj} 0.60; 95% CI 0.42–0.87) (table 4).

mRS score at 90 days was available for 1,264 patients. Functional independence (mRS score 0–2) was reached in 41% with LA, 35% with GA, and 25% with CS ($p < 0.01$). An mRS score 0–1 was more frequent in the LA group (23%) vs the GA group (14%) and the CS group (9%) ($p < 0.01$; table 5 and figure 2).

We performed a sensitivity analysis, in which groups were based on center level preference for anesthetic management. In the case LA or CS was the preferred approach, this was changed to GA in 8% of the patients. In the case GA was the preferred approach, 90% of the patients underwent GA. The associations with mRS score had a similar direction compared to our main analyses (according to actually performed anesthetic technique). When applied as standard of care, GA showed a nonsignificant trend towards worse functional outcome on the mRS (cOR_{adj} 0.86; 95% CI 0.67–1.10). The negative effect of CS remained significant in this setting (cOR_{adj} 0.68; 95% CI 0.51–0.90).

Compared to the main analysis, we found similar results after excluding one center that had reported results of LA vs CS earlier.[8]

Safety outcomes

Occurrence of sICH was similar in all groups. In the CS group, occurrence of pneumonia was more frequent (20% vs 11% [LA] and 10% [GA]; $p < 0.01$). Mortality was lowest with LA (27%) compared to GA (32%) and CS (36%) ($p = 0.04$) (table 5).

Table 3 Association between actually performed anesthetic management and outcomes: general anesthesia (GA) or conscious sedation (CS) compared to local anesthesia (LA)

	LA, OR	GA		CS	
		Unadjusted, OR (95% CI)	Adjusted, OR (95% CI)	Unadjusted, OR (95% CI)	Adjusted, OR (95% CI)
mRS at 90 days[a]	1	0.75 (0.59 to 0.94)	0.75 (0.58 to 0.97)	0.57 (0.42–0.77)	0.45 (0.33–0.62)
mRS 0–1 at 90 days[a]	1	0.54 (0.38 to 0.76)	0.60 (0.41 to 0.89)	0.34 (0.20–0.60)	0.29 (0.16–0.51)
mRS 0–2 at 90 days[a]	1	0.79 (0.60 to 1.03)	0.79 (0.58 to 1.08)	0.46 (0.31–0.69)	0.35 (0.23–0.54)
mRS 0–3 at 90 days[a]	1	0.77 (0.59 to 0.99)	0.70 (0.52 to 0.95)	0.56 (0.40–0.80)	0.41 (0.28–0.61)
sICH	1	0.94 (0.55 to 1.59)	0.92 (0.54 to 1.57)	0.98 (0.49–1.98)	1.00 (0.50–2.03)
Ischemic stroke progression	1	1.24 (0.82 to 1.88)	1.19 (0.78 to 1.83)	1.74 (1.06–2.86)	1.82 (1.10–3.02)
Pneumonia	1	0.89 (0.60 to 1.33)	0.89 (0.59 to 1.34)	1.97 (1.28–3.03)	2.23 (1.44–3.48)
Mortality at 90 days	1	1.27 (0.97 to 1.68)	1.39 (1.00 to 1.93)	1.46 (1.01–2.11)	1.96 (1.28–3.01)
NIHSS postintervention (24–48 hours)	1	β 0.88 (−0.31 to 2.07)	β 0.19 (−0.86 to 1.25)	β 2.33 (0.78–3.88)	β 2.47 (1.13–3.82)

Abbreviations: CI = confidence interval; OR = odds ratio; mRS = modified Rankin Scale; NIHSS = NIH Stroke Scale; sICH = symptomatic intracranial hemorrhage. Analyses were adjusted for age, sex, prestroke mRS, baseline NIHSS score, collaterals, and duration from onset to arrival at the intervention hospital.
[a] N = 1,264; mRS score at 90 days was missing for 112 patients.

Discussion

In the current nationwide observational study, LA was associated with better functional outcome and lower mortality rate than GA or CS, and we found worse outcome with CS compared to GA. Cerebral complications were essentially the same with all 3 techniques. Occurrence of pneumonia was most frequent with CS. In the Netherlands, LA is the preferred anesthetic approach during EVT for acute ischemic stroke in most hospitals. As the preferred approach, the negative effect of CS remained prominent, whereas GA only led to slightly worse functional outcome compared to LA.

In a post hoc analysis of randomized EVT trials, GA was compared with non-GA, which includes CS and LA. As in our study, GA was associated with worse functional outcome.[3]

Previous randomized trials comparing GA to CS[5–7] showed that clinical outcomes were not worse for GA. In our study, CS was associated with worse functional outcome compared to GA, which may have been caused by a higher incidence of pneumonia due to differences in airway support. This indicates that, whenever sedative support is necessary, GA might be a better option than CS.

Table 4 Association between anesthetic management and outcomes: conscious sedation compared to general anesthesia

	Unadjusted, OR (95% CI)	Adjusted, OR (95% CI)
mRS at 90 days[a]	0.76 (0.55 to 1.07)	0.60 (0.42–0.87)
mRS 0–1 at 90 days[a]	0.64 (0.35 to 1.19)	0.48 (0.25–0.91)
mRS 0–2 at 90 days[a]	0.59 (0.39 to 0.91)	0.44 (0.27–0.71)
mRS 0–3 at 90 days[a]	0.74 (0.50 to 1.08)	0.59 (0.38–0.91)
sICH	1.05 (0.48 to 2.27)	1.09 (0.50–2.38)
Ischemic stroke progression	1.40 (0.81 to 2.42)	1.52 (0.87–2.66)
Pneumonia	2.21 (1.34 to 3.63)	2.51 (1.50–4.20)
Mortality at 90 days	1.15 (0.75 to 1.75)	1.41 (0.85–2.35)
NIHSS postintervention (24–48 hours)	1.45 (−0.26 to 3.16)	2.28 (0.74–3.82)

Abbreviations: CI = confidence interval; OR = odds ratio; mRS = modified Rankin Scale; NIHSS = NIH Stroke Scale; sICH = symptomatic intracranial hemorrhage. Analyses were adjusted for age, sex, prestroke mRS, baseline NIHSS score, collaterals, and duration from onset to arrival at the intervention hospital.
[a] N = 1,264; mRS score at 90 days was missing for 112 patients.

Table 5 Outcomes (n = 1,376; anesthetic management was unknown for 112 patients) according to performed anesthetic technique

	LA (n = 821), n (%)	GA (n = 381), n (%)	CS (n = 174), n (%)	*p* Value
mRS at 90 days, median (IQR)[a]	3 (2–6)	4 (2–6)	4 (3–6)	<0.01
mRS 0–1 at 90 days[a]	180 (23)	46 (14)	15 (9)	<0.01
mRS 0–2 at 90 days[a]	319 (41)	117 (35)	39 (25)	<0.01
mRS 0–3 at 90 days[a]	432 (56)	162 (49)	66 (42)	<0.01
sICH	48 (6)	21 (6)	10 (6)	0.97
Ischemic stroke progression	69 (8)	39 (10)	24 (14)	0.08
Pneumonia	93 (11)	39 (10)	35 (20)	<0.01
Mortality at 90 days	210 (27)	107 (32)	57 (36)	0.04
NIHSS postintervention (24–48 hours), median (IQR)	10 (3–17)	13 (4–18)	13 (7–18)	<0.01

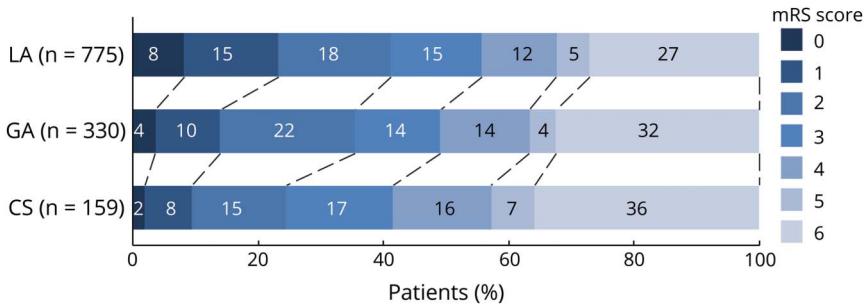
Abbreviations: CS = conscious sedation; GA = general anesthesia; IQR = interquartile range; LA = local anesthesia; mRS = modified Rankin Scale; NIHSS = NIH Stroke Scale; sICH = symptomatic intracranial hemorrhage.
[a] N = 1,264; mRS score at 90 days was missing for 112 patients.

LA could provide an advantage over GA and CS, because it avoids exposure to side effects of sedating medication, mainly prolonged arterial hypotension. In the sensitivity analysis, we found that the conversion rate from LA or CS to GA was low (8%), and comparable to the rate that was reported in previous randomized studies (6%–16%).[5–7]

Aside from the positive influence on functional outcome, we advocate the use of LA as this offers the possibility to clinically assess the patient during the procedure, is a less complex technique, and is likely to reduce health care costs.

This study has limitations. First, the standard approach for anesthetic management varied per center, so differences between centers could have influenced differences in outcomes. Nevertheless, functional outcome was similar after adjustment for center in a multilevel regression analysis. Second, in one center, the protocol for LA also included IV administration of opioids, which potentially had a sedating effect. However, only 2% of patients in the LA group actually received systemic opioids, and doses were low. Therefore, the influence on the results should be minimal. Third, our patients were not randomized for anesthetic management. In order to minimize indication bias, we performed a sensitivity analysis, which was based on the preferred, standard approach for type of anesthetic management. However, selection bias could not be ruled out. Preferably, the effect of anesthetic management would be assessed with a multicenter randomized trial, in centers with different preexisting protocols, minimizing the influence of preference of centers for the arm consistent with their previous protocol. Fourth, we were not able to report on the experience of patients during the endovascular procedure. As thrombectomy can be painful under LA, future studies should investigate a possible psychological effect after EVT. Finally, types of sedating medication that were used with GA and CS and periprocedural blood pressure values were not systematically recorded. As a result, we were not able to report these at this time. Notwithstanding, we describe a large number of patients, who were prospectively enrolled in a nationwide registry. Our study is

Figure 2 Distribution of the modified Rankin Scale (mRS) score at 90 days according to performed anesthetic technique: local anesthesia (LA), general anesthesia (GA), and conscious sedation (CS)



N = 1,264; mRS score at 90 days was missing for 112 patients.

the first to compare all 3 anesthetic techniques, representing current differences in clinical practice.

LA only is associated with better functional outcome than systemic sedation in patients undergoing EVT for acute ischemic stroke. Whereas LA had a clear advantage over CS, this was less prominent compared to GA.

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Disclosure

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Appendix 1 Authors

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Marie Louise E. Bernsen, MD	Rijnstate Hospital, Arnhem	Author	Critical review of the manuscript
Jeannette Hofmeijer, MD, PhD	Rijnstate Hospital, Arnhem	Author	Patient enrollment, critical review of the manuscript
Jasper M. Martens, MD, PhD	Rijnstate Hospital, Arnhem	Author	Critical review of the manuscript
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Appendix 2 Coinvestigators

Coinvestigators are listed at links.lww.com/WNL/B16.

References

1. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet 2016;387:1723–1731.
2. Powers WJ, Derdeyn CP, Biller J, et al. American Heart Association/American Stroke Association focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2015;46:3020–3035.
3. Campbell BCV, Zwam WH, Goyal M, et al. Effect of general anesthesia on functional outcome in patients with anterior circulation ischaemic stroke having endovascular thrombectomy versus standard care: a meta-analysis of individual patient data. Lancet 2018;17:47–53.
4. Brinjikji W, Pasternak J, Murad MH, et al. Anesthesia-related outcomes for endovascular stroke revascularization: a systematic review and meta-analysis. Stroke 2017; 48:2784–2791.
5. Schönenberger S, Uhlmann L, Hacke W, et al. Effect of conscious sedation vs general anesthesia on early neurological improvement among patients with ischemic stroke undergoing endovascular thrombectomy: a randomized clinical trial. JAMA 2016; 316:1986–1996.
6. Löwhagen Hendén P, Rentzos A, Karlsson JE, et al. General anesthesia versus conscious sedation for endovascular treatment of acute ischemic stroke: The AnStroke trial (anesthesia during stroke). Stroke 2017;48:1601–1607.
7. Simonsen CZ, Yoo AJ, Sørensen LH, et al. Effect of general anesthesia and conscious sedation during endovascular therapy on infarct growth and clinical outcomes in acute ischemic stroke. A randomized clinical trial. JAMA Neurol 2018;75:470–477.
8. Graaf van de RA, Samuels N, Mulder MJHL, et al. Conscious sedation or local anesthesia during endovascular treatment for acute ischemic stroke. Neurology 2018;91:e19–e25.
9. Jansen IGH, Mulder MJHL, Goldhoorn RB, et al. Endovascular treatment for acute ischemic stroke in routine clinical practice: prospective, observational cohort study (MR CLEAN Registry). BMJ 2018;360:k949.
10. Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy: ASPECTS Study Group: Alberta Stroke Programme Early CT Score. Lancet 2000;355:1670–1674.
11. Tan IY, Demchuk AM, Hopyan J, et al. CT angiography clot burden score and collateral score: correlation with clinical and radiologic outcomes in acute middle cerebral artery infarct. AJNR Am J Neuroradiol 2009;30:525–531.
12. Swieten van JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. Stroke 1988;19:604–607.
13. Janssen PM, Visser NA, Dorhout Mees SM, Klijn CJM, Algra A, Rinkel GJE. Comparison of telephone and face-to-face assessment of the modified Rankin Scale. Cerebrovasc Dis 2010;29:137–139.
14. Brott T, Adams HP Jr, Olinger CP, et al. Measurements of acute cerebral infarction: a clinical examination scale. Stroke 1989;20:864–870.
15. Noser EA, Shaltoni HM, Hall CE, et al. Aggressive mechanical clot disruption: a safe adjunct to thrombolytic therapy in acute stroke? Stroke 2005;36:292–296.
16. Kummer von R, Broderick JP, Campbell BC, et al. The Heidelberg bleeding classification: classification of bleeding events after ischemic stroke and reperfusion therapy. Stroke 2015;46:2981–2986.
17. Donders AR, van der Heijden GJ, Stijnen T, Moons KG. Review: a gentle introduction to imputation of missing values. J Clin Epidemiol 2006;59:1087–1091.