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Original Article

# “Real life” impact of anesthesia strategy for mechanical thrombectomy on the delay, recanalization and outcome in acute ischemic stroke patients

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## ABSTRACT

**Background and purpose.** – Choice of anesthesia type on outcome for mechanical thrombectomy (MT) in acute ischemic stroke remains controversial. The goal of our research was to study the impact of anesthesia strategy on the delay, angiographic and neurological outcome of MT performed under general anesthesia (GA) vs. conscious sedation (CS).

**Methods.** – This prospective, single-center observational study included patients with anterior circulation large vessel occlusion (ACLVO) strokes treated with MT within 6 hours of symptom onset. All time metrics were evaluated. Angiographic and clinical outcomes were assessed by recanalization rate (mTICI) and 3-month functional independence (mRs). Complications and mortality rate were recorded as safety outcomes.

**Results.** – In total, 303 consecutive thrombectomies were performed, 86.8% under GA. NIHSS was higher in GA, with median of 19.0 for GA and 16.5 for CS ( $P=0.049$ ). Median time from arrival in hospital (door) to groin puncture was 83 min (IQR=45.0–109.5) for GA compared to 72 min (IQR=35.0–85.3) for CS,  $P=0.170$ . Median time from arrival in the angi suite to groin puncture was 20 min (IQR=15.0–29.0) for GA compared to 15 min (IQR=10.0–20.0) for CS,  $P=0.017$ . There were no significant differences in recanalization time metrics, successful revascularization rate, functional independence and mortality rate at three months.

**Conclusions.** – GA induced a 5 to 10 minutes delay for groin puncture, without impact on recanalization time metrics, or neurological outcome at 3 months. Our results demonstrate that a well-organized workflow is associated with reasonable delay in performing GA for MT, without effect on outcome compared to sedation.

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## Introduction

Prospective, randomized trials in acute stroke have recently demonstrated the clinical benefit of mechanical thrombectomy (MT) for anterior circulation large vessel occlusion (ACLVO) [1–7]. However, best practice standards in several aspects of the

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procedure have not yet been determined. For instance, anesthesia strategy is not standardized and is often largely driven by institutional and physician constraints. Anesthesia for MT can be divided in two administration methods, general anesthesia (GA) or conscious sedation without intubation (CS). It is commonly believed that disadvantages of GA include the increased delay in treatment time and the potential negative impact of anesthetic agents, such as a decrease and fluctuation of arterial pressure (AP) that could impair cerebral perfusion [8]. Potential advantages of GA include improved procedural safety, recanalization effectiveness and control of the airway. Previous observational studies and RCTs (randomized controlled studies), have demonstrated comparative revascularization rates and significantly improved clinical outcomes for CS [9–18]. On the contrary, three newly published single center RCTs on anesthesia in MT, found no advantages of CS over GA (19–21). The goal of this large data set was to study the “real life” effect of anesthesia strategy on feasibility, delay, safety, efficacy and clinical outcomes of MT. Our objective was to compare our own patient series against previously published reports taking into consideration anesthesia strategy (GA or CS).

## Methods

### Study design

This prospective single-center, observational study was performed to identify differences in patients treated under GA and CS. The study enrolled 303 consecutive ACLVO patients treated by MT within 6 hours of symptom onset.

This study was conducted from January 1, 2014 until the July 1, 2016. Our center is the referring hospital for a region spanning 45,000 km<sup>2</sup> with a population of almost 3 million. Eleven stroke units refer patients to our center for MT. Among the 303 patients, 114 (38%) were admitted to another regional stroke center and then referred to us (drip and ship method), and 189 (62%) were directly admitted to our hospital (Mothership).

### Imaging

Our department is equipped with four magnetic resonance (MR) units including two 3Tesla MR units dedicated to neuroradiology and two computed tomography (CT)-scans available 24/7. When possible and if no contra-indications exist, acute strokes are evaluated by MR. The imaging protocol takes 10 minutes and includes diffusion weighted imaging (DWI), time of flight (TOF) MR angiography (MRA), T2\*, fluid attenuation inversion recovery (FLAIR), gadolinium cervical angiography and perfusion. In cases of contra-indication to MR, a CT/CTA/CT perfusion scan is performed. The Alberta Stroke Program Early CT score (ASPECTS) was calculated on DWI (MR ASP) or CT (CT ASP) to assess the extent of ischemic core (22). Among the 303 patients, 243 were evaluated by MR (80.2%) and 60 (19.8%) by CT.

### Clinical assessment

All patients in our study were evaluated by a stroke neurologist and the National Institutes of Health Stroke Scale (NIHSS) score calculated for stroke severity. After imaging confirmed ACLVO stroke, vital parameters such as AP, pulse, and respiration rates were monitored continuously. If no contraindications, an intravenous tissue-type plasminogen activator (IV tPA) at full dose (0.9 mg/kg) was administered within 4.5 h from symptom onset.

### Intervention

After imaging confirmed ACLVO stroke, all cases were discussed between the stroke neurologist and the interventional neuroradiologist. Patients were transferred to the angiography suite only if groin puncture could be done within 6 hours from stroke onset or TLSW (time last seen well).

Our anesthesiology team is available 24/7 and is trained for the procedure. GA is the standard practice for MT patients in our center. In some cases, however, when the patient is considered calm and cooperative, or in cases where intubation is cause for concern, MT is performed under CS. There is no absolute or defined algorithm, and the choice is at the discretion of the neurointerventionalist and anesthesiologist.

In our series, the vast majority of general anesthesia cases consisted of intubation and mechanical ventilation using a rapid sequence induction using intravenous etomidate and suxamethonium followed by sufentanil and volatile agent (sevoflurane) use. Conscious sedation consisted of intravenous midazolam and sufentanil without intubation. AP was controlled to avoid a decrease of more than 20% baseline values, by using intravenous fluid challenge, ephedrine or phenylephrine if necessary. Arterial pressure was monitored and maintained in a narrow range for all the patients (GA and CS) from the moment the patient entered the angiography suite.

MT was performed by stentrievers or via direct aspiration. In all cases, any occurrence of a hemorrhagic event was evaluated systematically at the end of the procedure by a flat panel CT. All patients were extubated immediately after the procedure in the angiography suite and transferred to the recovery room and thereafter in in neuro-intensive care unit. Revascularization rates for all patients were assessed by two independent interventional neuroradiologists, using the modified Thrombolysis in Cerebral Infarction (mTICI) scale. Successful revascularization was defined as grade 2b or 3.

### Follow up

In all cases, a 24-hour MR or CT (in cases of MR contraindications) was performed, and any existence of a hemorrhagic transformation noted. Hemorrhagic infarction, type 1 (HI1) is defined by small petechiae along the margins of the infarction, and type 2 (HI2) is defined by more confluent petechiae within the infarction area, both without mass effect. Parenchymal hematoma, type 1 (PH1) is defined by one or more blood clots occupying 30% or less of the infarcted area with a mild mass effect, and type 2 (PH2) is defined by blood clots in more than 30% of the infarcted area with a clinically significant mass effect. Subarachnoid hemorrhage (SAH) is defined as hemorrhage in the subarachnoid space. Symptomatic intra-cerebral hemorrhage (SICH) is defined as parenchymal hemorrhage leading to a neurological deterioration of at least 4 points NIHSS score worsening. Modified Rankin Scale (mRs) score was assessed at 3 months after discharge. Good clinical outcome was defined as mRs 0 to 2.

### Statistical analysis

Statistical analyses were performed using SPSS software v. 23.0 (SPSS Inc., Chicago, IL, USA). Descriptive data for all groups and variables were expressed as a mean  $\pm$  SD (for continuous measures), Median (IQR), or the percentage of a group for discrete variables. Categorical data were analyzed using the Pearson chi-square test. A normal distribution was tested using the Kolmogorov-Smirnov test. If the data were normally distributed, the *t*-test was used. Non-parametric data were analyzed using the Mann-Whitney *U*-test. Logistic regression model was used to determine predictors of

**Table 1**  
Baseline patient's characteristics.

	CS	GA	Total	P-value
No.	40	263	303	
Age, median, (IQR)	73 (24.8)	70 (20.5)	71 (21)	$P=0.336$
Onset NIHSS median, (IQR)	15.5 (10)	18 (7)	18 (7)	$P=0.030$
Pre mRS 0 n, (%)	36 (90)	223 (85)	259 (86)	$P=0.383$
Pre mRS 1 n, (%)	4 (10)	30 (11)	34 (11)	$P=0.792$
ASPECTS DWI median, (IQR)	7 (1)	7 (3)	7 (0)	$P=0.013$
ASPECTS CT median, (IQR)	9 (2.5)	9 (2)	9 (2)	$P=0.639$
NIHSS Pre-treatment, median, (IQR)	16.5 (9.3)	19 (6.5)	18 (7)	$P=0.049$
IV tPA n, (%)	20 (50)	176 (66.9)	196 (64.7)	$P=0.045$
LVO n, (%)				
Left-side occlusion	14 (35.0)	152 (57.8)	166 (54.8)	$P=0.008$
M1	21 (53)	117 (44)	138 (46)	$P=0.343$
M2	7 (18)	29 (11)	36 (12)	$P=0.238$
ICA T	8 (20)	56 (21)	64 (21)	$P=0.852$
Cervical ICA	1 (2.5)	12 (4.6)	13 (4.3)	$P=0.548$
TANDEM	3 (8)	47 (18)	50 (17)	$P=0.099$
Total	40 (100)	263 (100)	303 (100)	$P=0.114$

**Table 2**  
Time metrics.

	Present study			
	CS	GA	Total	P-value
Times (min): median (IQR)				
Onset to IV tPA	136 (55)	150 (64)	148 (62)	$P=0.186$
Onset to groin	216 (139)	240 (125)	240 (127)	$P=0.286$
Door to groin	72 (50)	83 (65)	80 (60)	$P=0.170$
Room to groin	15 (10)	20 (14)	20 (13)	$P=0.017$
Onset to recanalization	280 (123)	305 (121)	305 (122)	$P=0.755$
Door to recanalization	115 (82)	133 (79)	132 (81)	$P=0.127$
Room to recanalization	70 (54)	73 (47)	72 (48)	$P=0.472$
Groin to recanalization	45 (45)	42 (35)	42 (37)	$P=0.806$

different type of anesthesia. All reported  $P$ -values were two-sided; differences were considered significant when  $P$ -value was  $<0.05$ .

## Results

### Patient baseline characteristics

In the study period, 303 thrombectomies were performed for ACLVO stroke. Among the 303 cases, 263 (86.8%) were performed under GA and 40 (13.2%) under CS. Mean age was 67.5 (SD = 15.3) years. Overall 38% patients were transferred to our center from another regional stroke unit (drip and ship), 95 (36.1%) in GA and 19 (47.5%) in CS. Patient characteristics for the entire population, GA and CS group are detailed in [Table 1](#).

Onset NIHSS Score was higher in the GA group, with a significant difference on univariate ( $P=0.030$ ) but not on multivariate ( $P=0.154$ ) regression analysis.

Pre-treatment NIHSS Score was higher in the GA group, with a significant difference on univariate ( $P=0.049$ ) but not on multivariate ( $P=0.586$ ) regression analysis.

ASPECTS was calculated on DWI in 243/303 patients (80.2%) and on CT in 60/303 (19.8%), with median (IQR) of 7.0 (58.0–79.0) and 9.0 (8.0–10.0) respectively. DWI ASPECTS was found to be significantly lower in GA group in multivariate regression (odds ratio 0.52, 95% CI 0.28–0.99;  $P=0.045$ ).

Concerning the thrombus location, there was a significant difference in stroke location with a higher proportion of left hemispheric stroke in GA patients (57.8% vs. 35.0%) in multivariate regression (odds ratio 5.16, 95% CI 1.18–22.51;  $P=0.029$ ).

### Procedure time metrics

[Table 2](#) displays the time metrics in the global population and in the GA/CS groups.

**Table 3**  
Per/Post-procedure complications, primary and secondary outcomes.

	CS	GA	Total	P-value
No.	40	263	303	
SAH n, (%)	0	3 (1.1)	3 (1)	$P=0.497$
Intracranial vessel perforation n, (%)	1 (2.5)	2 (0.8)	3 (1)	$P=0.300$
Cervical carotid dissection n, (%)	1 (2.5)	3 (1.1)	4 (1.3)	$P=0.482$
ENT n, (%)	4 (10)	6 (2)	10 (3)	$P=0.031$
SICH at 24 h n, (%)				
HI1	0	2 (0.8)	2 (0.7)	$P=0.580$
HI2	0	3 (1.1)	3 (1.0)	$P=0.497$
PH1	0	5 (1.9)	5 (1.7)	$P=0.379$
PH2	0	3 (1.1)	3 (1.0)	$P=0.497$
SAH	1 (2.5)	1 (0.4)	2 (0.7)	$P=0.123$
Total	1 (2.5)	14 (5.3)	15 (5.0)	$P=0.443$
AICH at 24 h n, (%)				
HI1	3 (7.5)	23 (8.7)	26 (8.6)	$P=0.793$
HI2	4 (10.0)	20 (7.6)	24 (7.9)	$P=0.601$
PH1	3 (7.5)	24 (9.1)	27 (8.9)	$P=0.736$
PH2	0	10 (3.8)	10 (3.3)	$P=0.071$
SAH	0	2 (0.8)	2 (0.7)	$P=0.580$
Total	10 (25.0)	79 (30.0)	89 (29.4)	$P=0.514$
mTICI n, (%)				
2b/3	32 (80)	209 (79.5)	241 (79.5)	$P=0.938$
2a/1	5 (12.5)	31 (11.8)	36 (11.9)	$P=0.896$
0	3 (7.5)	23 (8.7)	26 (8.6)	$P=0.793$
Total	40 (100)	263 (100)	303 (100)	
NIHSS day1, median, (IQR)	11 (13.3)	12 (16)	12 (15)	$P=0.102$
3 months mRS 0–2 n, (%)	22 (58)	135 (53)	157 (54)	$P=0.568$
3 months mRS 6 (mortality) n, (%)	4 (11)	42 (16)	46 (16)	$P=0.347$

Median time from arrival in our hospital, door to groin puncture was 83 min (IQR = 45.0–109.5) for GA compared to 72 min (IQR = 35.0–85.3) for CS (odds ratio 1.01, 95% CI 1.00–1.02;  $P=0.032$ ) in the univariate, but not significant in the multivariate analysis ( $P=0.170$ ). Median time from arrival in the angi suite, room to groin puncture was 20 min (IQR = 15.0–29.0) for GA compared to 15 min (IQR = 10.0–20.0) for CS, significant in the multivariate analysis (odds ratio 1.14, 95% CI 1.02–1.26;  $P=0.017$ ).

### Technique

MT was feasible in 90.1% (273/303) of the procedures. Stentriever were used in 87.4% of the cases (265/303), 89.0% (234/263) in GA and 77.5% (31/40) in CS. Direct aspiration alone or in combination with a stentriever was used in 18.5% of cases (56/303), 17.9% (47/263) in GA and 22.5% (9/40) in CS. Median number of stentriever deployments was 2 (IQR = 1.0–3.0) in the global population and in both groups. There was a significant difference in the number of 3rd passage attempts performed, 15% under GA versus 32% in CS in univariate ( $P=0.023$ ), but not in the multivariate regression analysis ( $P=0.555$ ).

### Procedural complications

Procedural complications are detailed in [Table 3](#). Embolization into new vascular territories (ENT) was significantly higher in CS on the univariate (odds ratio 0.25, 95% CI 0.07–0.88;  $P=0.010$ ) but not on the multivariate analysis ( $P=0.999$ ).

### Post-procedural complications

Post-procedural complications are detailed in [Table 3](#). Symptomatic hemorrhages occurred in 15/303 cases overall (5%), of which 12/15 (80%) were previously treated with IV tPA. Asymptomatic hemorrhages occurred in 89/303 (29.4%), of which 59/89 (66.3%) were previously treated with IV tPA. There was no

statistical difference in symptomatic and asymptomatic hemorrhages between groups.

Hemorrhagic infarction, type 1 (HI1) is defined by small petechiae along the margins of the infarction, and type 2 (HI2) is defined by more confluent petechiae within the infarction area, both without mass effect. Parenchymal hematoma, type 1 (PH1) is defined by one or more blood clots occupying 30% or less of the infarcted area with a mild mass effect, and type 2 (PH2) is defined by blood clots in more than 30% of the infarcted area with a clinically significant mass effect:

- subarachnoid hemorrhage (SAH);
- symptomatic intra-cerebral hemorrhage (SICH) is defined as parenchymal hemorrhage leading to a neurological deterioration of at least 4 points NIHSS score worsening.

### Clinical outcome

There were no significant differences in the rate of successful recanalization, 24 h post-treatment NIHSS, 3 months good clinical outcome and mortality rate. Three-month clinical evaluation was performed in 97% (293/303) of patients, 10 patients did not have neurological follow-up and were lost to follow-up. Primary and secondary outcomes are provided in Table 3.

### Discussion

There is an ongoing debate concerning the optimal anesthesia strategy for MT procedures. Several previous reports firmly suggest CS is the optimal solution, considered as safe as GA and providing better clinical outcomes at 3-month follow-up [10–15]. It has also been speculated that GA could even erase the benefit of MT [16]. On the other hand, three newly released RCTs reports aiming to compare the influence of GA and CS on early neurological improvement (SIESTA, ANSTROKE, GOLIATH) have demonstrated no evidence of CS superiority over GA, displaying even a slight benefit for GA [19–21].

The proportion of GA patients (87%) in our study is substantially higher than other recently published RCTs. Differences in patient baseline NIHSS, pre-treatment NIHSS and MR ASPECTS (higher stroke volume), and left side LVO strokes between GA/CS were consistent with our policy that CS is reserved for clinically less severe patients. Although this demonstrates a clear bias in favor of CS patients, there was no difference in 3 months clinical outcome.

In our study, the time from onset to IV tPA (mean 2h28 min) was higher than in all previously reported multicentric RCTs, except THRACE [6], but lower than in the GA group of HERMES pooled data [18]. Retrospective study from the pre-trial cohort of the centers that participated in the MR CLEAN trial [16], and the Brinjikji et al. [14] meta-analysis, showed longer time metrics for GA compared to the non-GA group. Our study demonstrates overall time loss in the range of 5 to 10 minutes for GA (time from door-to-groin and room to groin). However, this time loss was later compensated by a shortened procedure time, and finally time room to recanalization was similar in both groups. In our study, GA did not delay recanalization times, which is coherent with the SIESTA trial results. Delay to start the procedure, with compensating shorter procedural time in GA was equally found in other RCTs [17,18].

In our series with GA considered the standard modality, the rate of successful recanalization (TICI 2b/3: 79.5%), good clinical outcome (3M mRs 0–2: 54%) and mortality rate (16%) complements those of the recent positive RCTs, despite a longer delay from onset to IV and onset to groin. It is in the range of the highest CS results in previous observational studies. In their meta-analysis, Campbell et al. showed significantly worse clinical outcome in patients

treated under GA compared to non-GA [18]. It is worth considering that included studies were performed in the centers with preference for non-GA practice, and without uniform anesthesia protocol for either GA or non-GA [18]. There were signals of benefit in favor of general anesthesia consistent across primary and secondary endpoints of the GOLIATH, ANSTROKE and SIESTA studies, which is coherent with our results. SIESTA even suggested better functional outcomes in the GA group, though as a secondary endpoint. Our findings support the results of the SIESTA trial, yet our study demonstrates a higher rate of successful recanalization (TICI 2b/3 GA: 79.5%, CS: 80%) (TICI 2b/3 AG: 65%, CS: 62%), and a higher rate of good clinical outcomes (3M mRs 0–2 GA: 53%, CS: 58%) compared to SIESTA (3M mRs 0–2 GA: 37%, CS: 18%).

Procedural and post-procedural complications showed no statistical difference between GA and CS and demonstrated similar rates to other RCTs. The percentage of ENT in our study (3%) is lower than in all the RCTs. In the univariate analysis, the global rate of complications was higher in CS, undoubtedly due to a significant difference in ENT. Additionally, there was a significant lower number of third stentriever passages required to obtain a complete recanalization when the procedure was performed under GA. Although there is no definitive explanation for these findings, they could suggest MT performed under GA is more efficient, safer and faster.

All these findings could support the argument that a possible drop in AP during general anesthesia may negatively impact outcome [23,24]. The MR CLEAN subgroup analysis showed similar high infarct volume in the GA and control group [25,26]. The cause for this may be the absence of cerebral autoregulation mechanisms in the collateral circulation which, makes the penumbra region highly vulnerable to decreases in AP [27]. As part of our workflow experience, AP values during the peri-procedural period are kept within a strict range (such as in SIESTA trial), not allowing large fluctuations. It is also possible that other factors such as availability and clinical experience of anesthesiology teams in high volume centres may influence differences between studies.

The main limitations of our series include non-randomization of our patients and our single center experience. There was an imbalance in the number of patients between the two groups (GA/CS: 40 vs. 263) with bias in the inclusion criteria (more severe patients in GA group).

### Conclusions

In the “real life” context, MT for ACLVO strokes can be performed under general anesthesia with angiographic and clinical results comparable to previously reported randomized clinical studies. Although GA was performed in patients with more severe strokes, there was no difference in recanalization rates and functional outcomes at 3 months. GA was associated with a delay for MT start times in the range of 5 to 10 minutes, however there was no delay for final recanalization time metrics. Immobility under GA could have provided more precise interventions, with less ENT and minimized 3rd pass retrievals. Additional multicentric randomized trials are necessary to better assess benefits and drawbacks of both types of anesthesia.

### Disclosure of interest

The authors have not supplied their declaration of competing interest.

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