Association between Anaesthesia Modality and Clinical Outcomes following Endovascular Stroke Treatment in the Extended Time Window

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ABSTRACT

Background: There is paucity of data on anaesthesia-related outcomes for endovascular treatment (EVT) in the extended window(>6 hours from ischaemic stroke onset). We compared functional and safety outcomes between local anaesthesia(LA) without sedation, conscious sedation(CS) and general anaesthesia(GA).

Methods: Patients that underwent EVT in the early(<6 hours) and extended time windows using LA, CS, or GA, between October 2015 and March 2020, were included from a United Kingdom national stroke registry. Multivariable analyses were performed, adjusted for age, sex, baseline stroke severity, pre-stroke disability, EVT technique, centre, procedural time and IV thrombolysis.

Results: We included 4337 patients: 3193 in the early window (1135 LA, 446 CS, 1612 GA) and 1144 in the extended window(357 LA, 134 CS, 653 GA). Compared to GA, patients treated under LA alone had increased odds of an improved modified Rankin Scale(mRS) at discharge (early: adjusted common(ac)OR=1.50,95%CI 1.29-1.74,p=0.001; extended: acOR=1.29,95%CI 1.01-1.66,p=0.043). Similar mRS at discharge were found in the LA and CS cohorts in the early and extended windows(p=0.21). Compared to CS, use of GA was associated with worse mRS at discharge in the early window (acOR=0.73,95%CI 0.45-0.96,p=0.017) but not in the extended window(p=0.55). There were no significant differences in the rates of symptomatic intracranial haemorrhage or in-hospital mortality across the anaesthesia modalities in the extended window.

Conclusion: LA without sedation during EVT was associated with improved functional outcomes, compared to GA, but not CS, within and beyond 6 hours from stroke onset. Prospective studies assessing anaesthesia related outcomes in the extended time window are warranted.

What is already known on this topic: The optimal anaesthetic technique during endovascular thrombectomy (EVT) remains undetermined, with paucity of data on the clinical outcome in the extended time window.

What this study adds: Using a national stroke registry of the United Kingdom, this large cohort study (n=4337) provides novel real world data to suggest that, compared to local anaesthesia without sedation, the deleterious impact of general anaesthesia on functional outcome may persist in the extended time window cohort, even where there is a higher proportion of 'slow progressors' with more robust collateral circulation.

How this study might affect research, practice or policy: A patient tailored approach to optimal anaesthetic management during EVT should be considered irrespective of the time window whilst awaiting confirmatory data from randomised controlled studies assessing anaesthesia related outcomes in the extended time window.

INTRODUCTION

The optimal anaesthetic technique between local anaesthesia (LA) without sedation, conscious sedation (CS), or general anaesthesia (GA) remains undetermined, with conflicting outcomes reported in previous studies involving acute ischaemic stroke (AIS) patients who underwent endovascular treatment (EVT) predominantly within 6 hours of stroke onset (1-8). Commonly used sedative and hypnotic agents administered during CS and GA are known to disrupt cerebral haemodynamics and cerebral perfusion (9).

However, the potential deleterious clinical impact of CS or GA during EVT on the collateral circulation remains uncertain, particularly in the extended time window (>6 hours from stroke onset) (10, 11). We hypothesised that due to a larger proportion of 'slow progressors' in the extended time window (12), the tenacious collateral supply in these subjects would offset the potential deleterious impact of CS or GA. Hence, we aimed to compare the functional and safety outcomes between LA, CS, and GA in patients undergoing EVT within and beyond 6 hours from stroke onset.

METHODS

Data Source and Study Design

We performed a cohort study on prospectively collected data of patients enrolled in a United Kingdom national stroke registry (Sentinel Stroke National Audit Programme (SSNAP)), according to STROBE guidelines. SSNAP includes all hospital admissions of patients presenting with acute stroke in England, Wales and Northern Ireland (covering 92% of the population in the United Kingdom, UK) (13). Overall case ascertainment of SSNAP is estimated to be over 90% of all acute stroke admissions. Patient data, which include demographic and clinical characteristics, treatments, and outcomes, are submitted

prospectively by clinical teams using a secure web-based case report form with real-time data validation checks to ensure data quality, from the time of admission up to 6 months after stroke.

Pseudonymised individual level data of adult patients (≥18 years) presenting with AIS who received EVT between 1st October 2015 and 31st March 2020 in England and Wales were included. Patients were dichotomised according to the time from onset of stroke, or last known well, to arterial puncture: (i) early window (<6 hours) and (ii) extended window (>6 hours). Within each time window, patients were further divided into three groups: LA, CS, and GA. Patients with missing discharge modified Rankin Scale (mRS) and anaesthetic modality data were excluded. The choice of anaesthetic technique and agents was at the discretion of the individual practitioners and anaesthetists. LA was defined as the use of subcutaneous local anaesthetic injection at the site of the arteriotomy (without sedation), GA required endotracheal intubation and CS required systemic medication for sedation, without requiring advanced airway protection.

Data on anaesthesia conversion from LA or CS to GA, parenchymal imaging findings and clot location were not available. No specific limits were applied to the clinical inclusion criteria, including age, pre-stroke disability and baseline stroke severity National Institutes of Health Stroke Scale (NIHSS).

Outcome measures

Functional outcome was assessed with the mRS, ranging from 0 (no symptoms) to 5 (severe disability/bedridden) and 6 (death), by ordinal shift, and good (mRS≤2 or equivalent to the pre-stroke mRS) or excellent (mRS≤1 or equivalent to the pre-stroke mRS) functional outcome, at ultimate hospital discharge and at 6 months. Other outcomes were early neurological improvement (NIHSS decrease ≥4 between admission and 24 hours or NIHSS 0–1 at 24 hours), early neurological deterioration (24-hour NIHSS increase ≥4 from baseline), and futile recanalisation (mRS 4-6 at hospital discharge or worsening of the pre-stroke disability (mRS 4-5) despite successful reperfusion (modified thrombolysis in cerebral

infarction (mTICI) score of 2b-3). Procedural outcomes were successful reperfusion and complete reperfusion (mTICI score of 3) at the end of EVT. Safety outcomes were in-hospital mortality, any type of intracranial haemorrhage (ICH) and symptomatic ICH (sICH) (ICH with NIHSS increase ≥4 within 24 hours or death). Workflow time metrics were described.

Statistical analysis

Study characteristics were summarised by the anaesthetic modality using descriptive statistics. Continuous variables were expressed as means and standard deviation (SD) and categorical variables were expressed as frequencies or percentages. Comparisons of baseline variables were made using the Chi-square, ANOVA or Student's t-test, wherever applicable. Analyses of binary and ordinal outcomes were expressed as an odds ratio (OR) with a 95% confidence interval (CI).

Multivariable analysis of the outcome measures used ordinal logistic regression for the full-scale mRS and binary regression analysis for the remaining dichotomized clinical outcomes. Adjustment was made for variables of clinical relevance: age (5-year age bands from 60 to 90 years), sex, baseline stroke severity (NIHSS), pre-stroke functional status (mRS), EVT technique, centre, procedural time (mins) and prior intravenous tissue plasminogen activator (IV-tPA). Two-tailed p-value of <0.05 was considered statistically significant. All analyses were conducted using StataSE 16.1.

Ethics

SSNAP has permission to collect patient data without explicit consent, granted by the Confidentiality Advisory Group of the National Health Service Health Research Authority under Section 251. Pseudonymized data use was approved by the Healthcare Quality Improvement Partnership (HQIP) Data Access Request Group. Additional ethical approval was not sought or required for this study. Data access requests should be directed to SSNAP as the data provider and HQIP as the data controller.

RESULTS

We included 4337 patients who underwent EVT at 25 neuroscience centres: 3193 in the early window (1135 LA, 446 CS, 1612 GA) and 1144 in the extended window (357 LA, 134 CS, 653 GA) (Supplemental Figure 1). In the extended window, patients treated under LA had higher pre-stroke morbidity (mRS) compared to the GA group (0(0-1) vs 0(0-0), p=0.004). There was a higher use of stentretrievers only amongst the GA cohort (16.6%) whereas the combined technique of stentretrievers and thromboaspiration (64.1%) with proximal balloon guide catheters (35.0%) were more frequently used in the CS group (Table 1). No significant differences were observed in the remaining baseline characteristics or co-morbidities in the extended and early windows (Supplemental Table 1).

In the extended window, the neuroimaging to groin puncture time was similar across the groups in the extended window (LA: 155.1±*179*.8 mins vs GA: 160.2±*179.3* vs CS: 162.5±*199.3*, p=0.37, Table 1). However, the total procedural time was significantly shorter in the LA group (LA: 51.2±*36*.0 mins vs GA: 62.1±*41.5* vs CS*:* 66.6±*42.7*, p=0.001, Table 1). In the early window, shorter neuroimaging-to-arterial puncture (152.9±*159*.8 mins) and total procedural times (53.0±*33*.3 mins) were recorded in the LA group compared to CS and GA (Supplemental Table 1). Detailed baseline characteristics are presented in Table 1 (extended window) and Supplemental Table 1 (early window).

Outcomes

LA was associated with an increased odds of improving the mRS at discharge compared to GA in the early and extended windows (Table 2, Supplemental Figure 2; early: adjusted common (ac)OR=1.50, 95%CI 1.29-1.74, p=0.001; extended: acOR=1.29, 95%CI 1.01-1.66, p=0.043). However, there was similar mRS at discharge between the LA vs CS cohorts in the early and extended windows (Table 3). In the GA vs CS analysis, use of GA was associated with worse mRS at discharge in the early window (acOR=0.73, 95%CI 0.45-0.96, p=0.017) but not in the extended window (p=0.55) (Table 4).

There were lower rates of in-hospital mortality in the LA cohort compared to GA in the early window (Table 2: LA (10.7%) vs GA (13.4%) aOR=0.73, 95%CI 0.56-0.97, p=0.033) but not in the extended window (p=0.20). No significant differences in the safety outcomes of sICH and in-hospital mortality were identified between the other comparisons of anaesthetic modalities in both time windows (Tables 2-4). The remaining outcomes are detailed in Tables 2, 3 and 4.

DISCUSSION

The findings from this large national stroke registry provide novel real-world data related to the anaesthetic modality of choice during EVT for AIS in the early and extended time windows. The use of LA-only was associated with significantly improved functional outcome (mRS) at hospital discharge compared to GA across both early and extended time windows. However, there was no significant difference in functional outcomes between LA versus CS across both time windows. Although GA was associated with poorer functional outcome compared to CS in the early window, no significant difference in outcome was observed in the extended window.

A post-hoc analysis of 92 patients in the DEFUSE-3 trial (EVT 6-16 hours from stroke onset) concluded that GA (compared to CS) was associated with poorer functional independence (mRS≤2) at 90 days (10). However, in the post-hoc analysis of the DAWN trial (EVT 6-24 hours from stroke onset), GA (compared to CS) was not independently associated with a change in the functional outcome (11). Whilst the findings between the GA and CS cohorts in our study were in line with the findings of the DAWN trial, direct comparisons are challenging due to the lack of detailed information on the factors that determined the selection of anaesthetic approach and the techniques of procedural sedation employed.

During AIS, there is loss of the auto-regulatory capacity of the pial collaterals in the affected region, which increases its susceptibility to fluctuations in the systemic BP. There is growing evidence that even small decreases in the systemic BP are associated with poor functional outcome due to collateral circulation failure and rapidly progressing large infarct volumes (14-16). This would be of particular relevance in 'fast progressors' with poor collaterals who may be more susceptible to changes in the cerebral haemodynamics from intravenous or inhaled anaesthetic agents when undergoing CS or GA. However, our results suggest that the deleterious impact of GA may persist in the extended time window cohort, even where there is a higher proportion of 'slow progressors' with a more robust collateral circulation (12). Although not directly evaluated in our study due to the lack of available data on the intra-procedural BP, one study reported patients treated under CS had a lower average procedural BP and more BP drops compared to patients treated under LA without sedation (17). This mechanism may, in part, explain the improved functional outcomes observed in the LA cohort in our study. Nevertheless, the neurotoxic or neuroprotective effects of sedative/anaesthetic agents and the optimal intra- and peri-procedural BP targets during the acute ischaemia-reperfusion injury remain incompletely understood (18).

The strengths of this study include the large sample size and high quality data within the SSNAP database from standardised case definitions, internal validation and audit trails. There are several limitations. First, due to the observational design, selection bias may have influenced the results. Patient-related factors, including the likelihood of compliance during EVT or the clinical stability would influence the anaesthetic modality decision. Second, there was missing data for certain outcome measures, including the mRS at 6 months. However, near-complete data (99.3%) was available for the primary outcome measure of mRS at discharge which has a high correlation with disability at 3 months (19). Third, data on conversion of LA or CS to GA, the techniques of procedural sedation employed and variables such as ASPECTS, collateral status or clot location were not available in the registry. These variables are key criteria in patient selection

for EVT, and are all strongly associated with clinical outcome. For instance, patients presenting with vertebro-basilar occlusions are more likely to require GA and are likely to have poorer functional outcome. Hence, it would have been informative to understand the selection criteria used to good effect in this cohort. Last, outcome measures were self-assessed rather than evaluated by a core laboratory.

Conclusion:

LA without sedation during EVT was associated with improved functional outcomes, compared to GA, but not CS, within and beyond 6 hours from stroke onset. Prospective studies assessing anaesthesia related outcomes in the extended time window are warranted.

Competing interests & Disclosures:

MAJ receives lecture and consultancy fees from Medtronic. PB has consulting agreements with Phenox, Balt, Neurovasc Technologies, Cerenovus, Perfuze, Brainomix, and Vesalio.

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TABLES

Table 1: Table of characteristics according to the anaesthetic modality: local anaesthesia (LA), conscious sedation (CS), and general anaesthesia (GA) during endovascular treatment in the extended time window (beyond 6 hours from stroke onset).

Feature	LA n (%) / median (IQR) or mean±SD	CS n (%) / median (IQR) or mean±SD	GA n (%) / median (IQR) or mean±SD	P value
Socio-demographics				
Sample size	357	134	653	
Sex (male)	189 (52.9)	65 (48.5)	357 (54.6)	0.42
<60 years	92 (25.7)	49 (36.5)	219 (33.5)	
60-69	73 (20.4)	20 (14.9)	123 (18.8)	
70-79	101 (28.2)	36 (26.8)	178 (27.2)	0.13
80-89	79 (22.1)	26 (19.4)	121 (18.5)	
>90 years	12 (3.3)	3 (2.2)	12 (1.8)	
Baseline characteristics				
NIHSS on admission	15 (8-19)	14.5 (9-19)	16 (9-21)	0.06
Pre-stroke disability (mRS)	0 (0-1)	0 (0-1)	0 (0-0)	**0.004**
IV Thrombolysis	103 (28.8)	32 (23.8)	214 (32.7)	0.09
ThromboAspiration	80 (27.2)	30 (23.8)	179 (31.7)	0.15
StentRetriever	35 (9.8)	16 (11.9)	107 (16.6)	**0.01**
ThromboAspiration & StentRetriever	202 (63.0)	82 (64.1)	305 (51.6)	**0.001**
Proximal Balloon Flow Arrest	101 (28.2)	47 (35.0)	155 (23.7)	**0.01**
Co-morbidities				
Hypertension	160 (44.8)	63 (47.0)	313 (47.9)	0.64
Diabetes	43 (12.0)	21 (15.6)	86 (13.1)	0.56
Atrial fibrillation	73 (20.4)	26 (19.4)	126 (19.2)	0.90
Prior Stroke/TIA	37 (10.3)	23 (17.1)	95 (14.5)	0.08
Congestive heart failure	20 (5.6)	6 (4.4)	33 (5.0)	0.86
Time metrics (mins)				
Onset to Groin Puncture	778.3±508.1	775.3±489.6	737.3±457.9	0.16
Neuroimaging to Arterial Puncture	155.1±179.8	162.5±199.3	160.2±179.3	0.37
Arterial Puncture to End of Procedure	51.2±36.0	66.6±42.7	62.1±41.5	**0.001**

n = number of events, N = number of patients, SD = standard deviation, mRS = modified Rankin scale, TIA = transient ischemic attack, NIHSS = National Institutes of Health Stroke Scale TICI = thrombolysis in cerebral infarction, IV = intravenous.

Table 2: Table of outcomes dichotomised by the anaesthetic modality of local anaesthesia (LA) versus general anaesthesia (GA) in the early (< 6 hours) and extended (> 6 hours) time windows.

Outcome measures	Early Window n/N (%)		Adjusted OR (95% CI)**	P value	Extended Window n/N (%)		Adjusted aOR (95% CI)**	P value
	LA (N=1135)	GA (N=1612)			LA (N=357)	GA (N=653)		
Discharge								
Median mRS (IQR)	3 (1-4)	4 (2-5)	1.50 (1.29 – 1.74)	**0.001***	4 (2-5)	4 (3-5)	1.29 (1.01 – 1.66)	**0.043***†
mRS ≤1	285/1135 (25.1)	309/1612 (19.1)	1.49 (1.19 – 1.85)	**0.001***	64/357 (17.9)	99/653 (15.1)	1.22 (0.81 – 1.84)	0.32
mRS ≤2	467/1135 (41.1)	494/1612 (30.6)	1.58 (1.31 – 1.90)	**0.001***	107/357 (29.9)	164/653 (25.1)	1.10 (0.78 – 1.55)	0.55
6 months								
Median mRS (IQR)	2 (1-3)	2 (1-3)	1.43 (1.08 – 1.89)	**0.010***	2 (1-3)	3 (1-4)	1.56 (0.99 – 2.45)	0.053†
mRS ≤2	214/317 (67.5)	281/495 (56.7)	1.43 (1.01 – 2.01)	**0.039***	76/120 (63.3)	101/200 (50.5)	1.67 (0.97 – 2.89)	0.06
TICI 2b-3	909/1135 (80.0)	1351/1612 (83.8)	0.64 (0.50 – 0.81)	**0.001***	284/357 (79.5)	534/653 (81.7)	0.63 (0.42 – 0.93)	**0.022***
TICI 3	537/1135 (47.3)	819/1612 (50.8)	0.77 (0.65 – 0.92)	**0.005***	175/357 (49.0)	319/653 (48.8)	0.83 (0.61 – 1.12)	0.22
Futile Recanalisation	359/909 (39.4)	699/1351 (51.7)	0.60 (0.49 – 0.73)	**0.001***	200/357 (56.0)	422/653 (64.6)	0.68 (0.48 – 0.95)	**0.025***
ENI	699/1058 (66.0)	966/1569 (61.5)	1.25 (1.03 – 1.50)	**0.020***	182/338 (53.8)	320/629 (50.8)	1.16 (0.85 – 1.57)	0.33
END	74/1058 (6.9)	163/1569 (10.3)	0.63 (0.45 – 0.88)	**0.008***	40/338 (11.8)	109/629 (17.3)	0.56 (0.35 – 0.89)	**0.016***
Any ICH	89/610 (14.6)	188/1281 (14.6)	1.04 (0.77 – 1.41)	0.76	34/244 (13.9)	80/565 (14.1)	1.33 (0.81 – 2.18)	0.24
sICH	15/579 (2.6)	45/1187 (3.7)	0.59 (0.30 – 1.17)	0.13	6/219 (2.7)	22/487 (4.5)	0.51 (0.16 – 1.61)	0.25
In-Hospital Mortality	122/1135 (10.7)	217/1612 (13.4)	0.73 (0.56 – 0.97)	**0.033***	39/357 (10.9)	90/653 (13.7)	0.73 (0.45 – 1.18)	0.20

n = number of events / total number of patients (%), N = number of patients, aOR = adjusted odds ratio, CI = confidence interval, mRS = modified Rankin scale, sICH = symptomatic intracranial haemorrhage, TICI = thrombolysis in cerebral infarction, Futile Recanalization = mRS4-6 despite TICI2b-3 recanalization, ENI = Early neurological improvement (NIHSS improvement by ≥4), END= Early neurological deterioration (NIHSS worsening by ≥4). * = statistically significant **adjusted multivariate analysis for age, sex, baseline NIHSS, pre-stroke disability, centre, EVT technique, procedure time and use of intravenous thrombolysis. Statistical analysis reference is made to 'general anaesthesia'. Analyses performed using binary logistic regression except where denoted with † where ordinal regression was used;

Table 3: Table of outcomes dichotomised by the anaesthetic modality of local anaesthesia (LA) versus conscious sedation (CS) in the early (< 6 hours) and extended (> 6 hours) time windows.

Outcome measures	Early Window n/N (%)		Adjusted OR (95% CI)**	P value	Extended Window n/N (%)		Adjusted aOR (95% CI)**	P value
	LA (N=1135)	CS (N=446)			LA (N=357)	CS (N=134)		
Discharge								
Median mRS (IQR)	3 (1-4)	4 (2-5)	1.13 (0.91 – 1.30)	0.21	4 (2-5)	4 (3-5)	1.22 (0.86 – 1.47)	0.21†
mRS ≤1	285/1135 (25.1)	100/446 (22.4)	1.00 (0.73 – 1.36)	0.98	64/357 (17.9)	22/134 (16.4)	0.95 (0.51 – 1.77)	0.88
mRS ≤2	467/1135 (41.1)	161/446 (36.1)	1.19 (0.91 – 1.54)	0.19	107/357 (29.9)	35/134 (26.1)	1.03 (0.61 – 1.74)	0.89
6 months								
Median mRS (IQR)	2 (1-3)	2 (1-3)	1.29 (0.93 – 1.50)	0.12	2 (1-3)	2.5 (2-3)	1.26 (0.55 – 1.62)	0.38†
mRS ≤2	214/317 (67.5)	72/110 (65.4)	1.24 (0.72 – 2.13)	0.42	76/120 (63.3)	22/42 (52.3)	1.14 (0.47 – 2.79)	0.76
TICI 2b-3	909/1135 (80.0)	341/446 (76.4)	1.13 (0.82 – 1.56)	0.43	284/357 (79.5)	101/134 (75.3)	0.98 (0.56 – 1.72)	0.95
TICI 3	537/1135 (47.3)	212/446 (47.5)	0.84 (0.65 – 1.08)	0.18	175/357 (49.0)	65/134 (48.5)	0.82 (0.53 – 1.29)	0.40
Futile Recanalisation	359/909 (39.4)	143/341 (41.9)	0.95 (0.71 – 1.26)	0.73	200/357 (56.0)	83/134 (61.9)	0.79 (0.47 – 1.35)	0.40
ENI	699/1058 (66.0)	281/427 (65.8)	0.96 (0.73 – 1.26)	0.80	182/338 (53.8)	60/123 (48.7)	1.05 (0.65 – 1.70)	0.83
END	74/1058 (6.9)	42/427 (9.8)	0.70 (0.44 – 1.10)	0.12	40/338 (11.8)	20/123 (16.2)	0.65 (0.31 – 1.34)	0.25
Any ICH	89/610 (14.6)	51/281 (18.1)	0.76 (0.50 – 1.15)	0.20	34/244 (13.9)	17/95 (17.8)	0.98 (0.46 – 2.08)	0.97
sICH	15/579 (2.6)	9/257 (3.5)	0.76 (0.28 – 2.03)	0.59	6/219 (2.7)	5/82 (6.1)	0.17 (0.03 – 1.04)	0.057
In-Hospital Mortality	122/1135 (10.7)	53/446 (11.8)	0.97 (0.65 – 1.44)	0.88	39/357 (10.9)	16/134 (11.9)	0.79 (0.38 – 1.62)	0.53

n = number of events / total number of patients (%), N = number of patients, aOR = adjusted odds ratio, CI = confidence interval, mRS = modified Rankin scale, sICH = symptomatic intracranial haemorrhage, TICI = thrombolysis in cerebral infarction, Futile Recanalization = mRS4-6 despite TICI2b-3 recanalization, ENI = Early neurological improvement (NIHSS improvement by ≥4), END= Early neurological deterioration (NIHSS worsening by ≥4). * = statistically significant **adjusted multivariate analysis for age, sex, baseline NIHSS, pre-stroke disability, centre, EVT technique, procedure time and use of intravenous thrombolysis. Statistical analysis reference is made to 'conscious sedation'. Analyses performed using binary logistic regression except where denoted with † where ordinal regression was used;

Table 4: Table of outcomes dichotomised by the anaesthetic modality of general anaesthesia (GA) versus conscious sedation (CS) in the early (< 6 hours) and extended (> 6 hours) time windows.

Outcome measures	Early Window n/N (%)		Adjusted OR (95% CI)**	P value	Extended Window n/N (%)		Adjusted aOR (95% CI)**	P value
	GA (N=1612)	CS (N=446)			GA (N=653)	CS (N=134)		
Discharge								
Median mRS (IQR)	4 (2-5)	4 (2-5)	0.73 (0.45 – 0.96)	**0.017***	4 (3-5)	4 (3-5)	1.11 (0.78 – 1.56)	0.55†
mRS ≤1	309/1612 (19.1)	100/446 (22.4)	0.68 (0.50 – 0.91)	**0.011***	99/653 (15.1)	22/134 (16.4)	0.72 (0.42 – 1.25)	0.25
mRS ≤2	494/1612 (30.6)	161/446 (36.1)	0.73 (0.56 – 0.95)	**0.021***	164/653 (25.1)	35/134 (26.1)	0.91 (0.57 – 1.46)	0.71
6 months								
Median mRS (IQR)	2 (1-3)	2 (1-3)	1.00 (0.67 – 1.49)	0.97	3 (1-4)	2.5 (2-3)	0.96 (0.51 – 1.78)	0.89†
mRS ≤2	281/495 (56.7)	72/110 (65.4)	0.84 (0.50 – 1.39)	0.50	101/200 (50.5)	22/42 (52.3)	0.74 (0.33 – 1.63)	0.46
TICI 2b-3	1351/1612 (83.8)	341/446 (76.4)	1.77 (1.30 – 2.41)	0.001	534/653 (81.7)	101/134 (75.3)	1.52 (0.90 – 2.57)	0.11
TICI 3	819/1612 (50.8)	212/446 (47.5)	1.09 (0.86 – 1.38)	0.45	319/653 (48.8)	65/134 (48.5)	0.94 (0.62 – 1.42)	0.79
Futile Recanalisation	699/1351 (51.7)	143/341 (41.9)	1.54 (1.17 – 2.02)	**0.002***	422/653 (64.6)	83/134 (61.9)	1.34 (0.84 – 2.16)	0.21
ENI	966/1569 (61.5)	281/427 (65.8)	0.80 (0.62 – 1.03)	0.09	320/629 (50.8)	60/123 (48.7)	0.93 (0.61 – 1.42)	0.75
END	163/1569 (10.3)	42/427 (9.8)	1.06 (0.70 – 1.61)	0.75	109/629 (17.3)	20/123 (16.2)	1.28 (0.71 – 2.30)	0.40
Any ICH	188/1281 (14.6)	51/281 (18.1)	0.73 (0.51 – 1.05)	0.09	80/565 (14.1)	17/95 (17.8)	0.66 (0.35 – 1.25)	0.21
sICH	45/1187 (3.7)	9/257 (3.5)	1.29 (0.58 – 2.86)	0.52	22/487 (4.5)	5/82 (6.1)	0.68 (0.23 – 2.03)	0.49
In-Hospital Mortality	217/1612 (13.4)	53/446 (11.8)	1.22 (0.85 – 1.76)	0.26	90/653 (13.7)	16/134 (11.9)	1.16 (0.62 – 2.15)	0.63

n = number of events / total number of patients (%), N = number of patients, aOR = adjusted odds ratio, CI = confidence interval, mRS = modified Rankin scale, sICH = symptomatic intracranial haemorrhage, TICI = thrombolysis in cerebral infarction, Futile Recanalization = mRS4-6 despite TICI2b-3 recanalization, ENI = Early neurological improvement (NIHSS improvement by ≥4), END= Early neurological deterioration (NIHSS worsening by ≥4). * = statistically significant **adjusted multivariate analysis for age, sex, baseline NIHSS, pre-stroke disability, centre, EVT technique, procedure time and use of intravenous thrombolysis. Statistical analysis reference is made to 'conscious sedation'. Analyses performed using binary logistic regression except where denoted with † where ordinal regression was used.

Supplementary Material

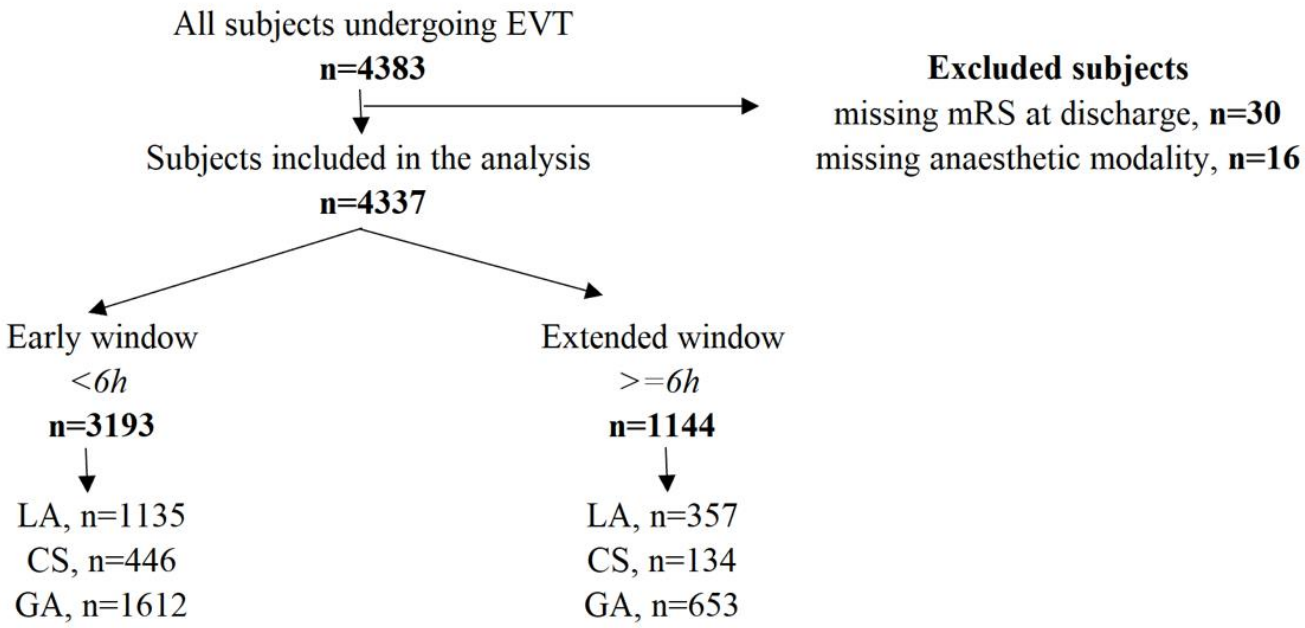
Suppl. Table 1: Table of characteristics according to the anaesthetic modality: local anaesthesia (LA), conscious sedation (CS), and general anaesthesia (GA) during endovascular treatment in the early time window (within 6 hours from stroke onset).

Feature	LA n (%) / median (IQR) or mean±SD	CS n (%) / median (IQR) or mean±SD	GA n (%) / median (IQR) or mean±SD	P value
Socio-demographics				
Sample size	1135	446	1612	
Sex (male)	608 (53.5)	232 (52.0)	908 (56.3)	0.16
<60 years	232 (20.4)	112 (25.1)	444 (27.5)	
60-69	240 (21.1)	87 (19.5)	324 (20.9)	
70-79	359 (31.6)	128 (28.6)	479 (29.7)	0.06
80-89	264 (23.2)	100 (22.4)	331 (20.5)	
>90 years	40 (3.5)	19 (4.2)	34 (2.1)	
Baseline characteristics				
NIHSS on admission	17 (12-21)	18 (13-22)	18 (14-22)	0.97
Pre-stroke disability (mRS)	0 (0-1)	0 (0-1)	0 (0-1)	0.05
IV Thrombolysis	770 (67.8)	320 (71.7)	1119 (69.4)	0.30
ThromboAspiration	343 (30.2)	139 (31.1)	521 (32.3)	0.07
StentRetriever	167 (14.7)	86 (19.2)	270 (16.7)	0.50
ThromboAspiration & StentRetriever	465 (40.9)	170 (38.1)	676 (41.9)	0.34
Proximal Balloon Flow Arrest	224 (19.7)	95 (21.3)	346 (21.4)	0.52
Co-morbidities				
Hypertension	566 (49.8)	212 (47.5)	752 (46.6)	0.24
Diabetes	153 (13.4)	77 (17.2)	222 (13.7)	0.12
Atrial fibrillation	290 (25.5)	97 (21.7)	330 (20.4)	0.007
Prior Stroke/TIA	189 (16.6)	71 (15.9)	250 (15.5)	0.72
Congestive heart failure	61 (5.3)	26 (5.8)	74 (4.6)	0.46
Time metrics (mins)				
Onset to Groin Puncture	221.4±71.4	231.4±66.0	239.5±64.2	**0.001**
Neuroimaging to Arterial Puncture	152.9±159.8	170.2±197.9	168.2±192.7	**0.001**
Arterial Puncture to End of Procedure	53.0±33.3	59.4±35.6	58.7±39.6	**0.001**

n = number of events, N = number of patients, SD = standard deviation, mRS = modified Rankin scale, TIA = transient ischemic attack, NIHSS = National Institutes of Health Stroke Scale TICI = thrombolysis in cerebral infarction, IV = intravenous

Supplemental Figures

Suppl. Figure 1: Flow chart patients that underwent endovascular thrombectomy treatment within and beyond 6 hours from stroke onset, stratified according to the anaesthetic modality used (local anaesthesia (LA), conscious sedation (CS) or general anaesthesia (GA)).



EVT = endovascular thrombectomy, n = number of events, mRS = modified Rankin scale.

Suppl. Figure 2: Distribution of the modified Rankin Scale at discharge comparing local anaesthesia (LA), conscious sedation (CS), and general anaesthesia (GA) during endovascular thrombectomy beyond 6 hours from stroke onset. **A**: LA vs GA, **B**: LA vs CS and **C**: GA vs CS.