Blood Pressure During Endovascular Treatment Under Conscious Sedation or Local Anesthesia

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Published in:
Neurology

DOI:
10.1212/WNL.0000000000011006
10.1212/WNL.0000000000011006

Published: 12/01/2021

Document Version
Peer reviewed version

Citation for pulished version (APA):
MR-CLEAN Registry Investigators, Samuels, N., van de Graaf, R. A., van den Berg, C. A. L., Nieboer, D., Eralp, I., Treurniet, K. M., Emmer, B. J., Immink, R. V., Majoie, C. B. L. M., van Zwam, W. H., Bokkers, R. P. H., Uyttenboogaart, M., van Hasselt, B. A. A. M., Mühling, J., Burke, J. F., Roozenbeek, B., van der Lugt, A., Dippel, D. W. J., ... van Es, A. C. G. M. (2021). Blood Pressure During Endovascular Treatment Under Conscious Sedation or Local Anesthesia. *Neurology*, *96*(2), e171-e181. https://doi.org/10.1212/WNL.0000000000011006, https://doi.org/10.1212/WNL.0000000000011006

Published Ahead of Print on October 7, 2020 as 10.1212/WNL.0000000000011006

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The most widely read and highly cited peer-reviewed neurology journal
The Official Journal of the American Academy of Neurology

AMERICAN ACADEMY OF NEUROLOGY®

Neurology Publish Ahead of Print
DOI: 10.1212/WNL.0000000000011006

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The Article Processing Charge was funded by the Erasmus University Medical Center.

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Search terms: [2] All Cerebrovascular disease/Stroke; [6] Infarction; [23] Clinical trials Observational study (Cohort, Case control)

Submission type: article

Title character count: 89

Number of references: 31

Number of tables: 3

Number of figures: 4

Word count abstract: 230

Word count paper: 3706

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Study funding:

The authors received no funding for this study. The MR CLEAN Registry is partially funded by unrestricted grants from Toegepast Wetenschappelijk Instituut voor Neuromodulatie, Twente University (TWIN), Erasmus MC University Medical Center, Maastricht University Medical Center, and Amsterdam UMC. The study was additionally funded by the European Union's Horizon 2020 research and innovation program under grant agreement No 777072 (IN-SIlico trials for treatment of acute Ischemic STroke; INSIST), which played no role in study design,

patient enrolment, data collection, analysis, or writing of the manuscript.

Institutional disclosures: Erasmus MC received compensation from Stryker, Medtronic and Bracco Imaging Ltd for activities of A.v.d.L. and D.W.J.D as a consultant. Amsterdam UMC received funds from Stryker® for consultations by CM. MUMC received funds from Stryker® and Codman® for consultations by WZ.

Disclosure: A.v.d.L and D.W.J.D are the recipients of unrestricted grants from Dutch Heart Foundation, Dutch Brain Foundation, The Netherlands Organisation for Health Research and Development, Health Holland Top Sector Life Science, AngioCare BV, Covidien/EV3®, MEDAC Gmbh/LAMEPRO, Top Medical/Concentric, Thrombolytic Science LLC, Stryker, Medtronic and Penumbra Inc. for the conduct of trials of acute treatment for stroke. CM received funds from TWIN Foundation and European Commission, (related to this project, paid to institution); and from CVON/Dutch Heart Foundation, Stryker, Health Evaluation Netherlands (unrelated; all paid to institution) and is shareholder of Nico.lab, a company that focuses on the use of artificial intelligence for medical imaging analysis. Dr. N. Samuels reports no disclosures. Dr. R.A. van de Graaf reports no disclosures. Dr. C.A.L. van den Berg reports no disclosures. Dr. D. Nieboer reports no disclosures. Dr. I. Eralp reports no disclosures. Dr. K.M. Treurniet reports no disclosures. Dr. B.J. Emmer reports no disclosures. Dr. Rogier V. Immink reports no disclosures. DR. R.P.H. Bokkers reports no disclosures. Dr. M. Uyttenboogaart reports no disclosures. Dr. B.A.A.M. van Hasselt reports no disclosures. Dr. J. Mühling reports no disclosures. Dr. J.F. Burke reports no disclosures. Dr. B. Roozenbeek reports no disclosures. Dr. H.F. Lingsma reports no disclosures. Dr. A.C.G.M. van Es reports no disclosures.

Statistical analysis: conducted by Noor Samuels (MD), Rob A. van de Graaf (MD), and Daan Nieboer (MSc), Erasmus MC, University Medical Center.

Acknowledgements: None.

Coinvestigator Appendix : http://links.lww.com/WNL/B252

Abstract

Objective: To evaluate the role of blood pressure as mediator of the effect of conscious sedation (CS) compared to local anesthesia (LA) on functional outcome after EVT.

Methods: Patients treated in MR CLEAN Registry centers with CS or LA as preferred anesthetic approach during EVT for ischemic stroke were analyzed. First, we evaluated the effect of CS on area under the threshold (AUT), relative difference between baseline and lowest procedural mean arterial pressure (ΔLMAP) and procedural blood pressure trend, compared to LA. Second, we assessed the association between blood pressure and functional outcome (modified Rankin Scale, mRS) with multivariable regression. Lastly, we evaluated whether blood pressure explained the effect of CS on mRS.

Results: In 440 patients with available blood pressure data, patients treated under CS (n=262) had larger AUTs (median 228 versus 23 mmHg*min), larger ΔLMAP (median 16% versus 6%) and a more negative blood pressure trend (-0.22 versus -0.08 mmHg/min) compared to LA (n=178). Larger ΔLMAP and AUTs were associated with worse mRS (adjusted common OR (acOR) per 10%-drop 0.87, 95%CI0.78-0.97, and acOR per 300mmHg*min 0.89, 95%CI0.82-0.97). Patients treated under CS had worse mRS compared to LA (acOR 0.59, 95%CI0.40-0.87) and this association remained when adjusting for ΔLMAP and AUT (acOR 0.62, 95%CI0.42-0.92).

Conclusions: Large blood pressure drops are associated with worse functional outcome. However, blood pressure drops do not explain the worse outcomes in the CS group.

Introduction

Post-hoc analyses of the MR CLEAN trial and HERMES collaboration showed that general anesthesia (GA) is associated with worse clinical outcomes than non-GA. In these studies, non-GA was the composite of conscious sedation (CS) and local anesthesia at the groin puncture site only (LA).[1, 2] Furthermore, among patients managed without GA, CS seemed to be associated with worse functional outcome compared to LA.[3, 4]

Previous studies in patients receiving GA during EVT reported worse outcomes in patients who experienced blood pressure drops during the procedure.[5-9] The administration of anesthetic and analgesic agents may cause gradual or sudden declines in blood pressure. This potentially impairs penumbra perfusion before recanalization.[10-12] Considering that hypotension leads to worse outcomes in GA, hypotension might also contribute to worse outcomes in patients treated under CS or LA. Until now, there is limited data on blood pressure parameters during EVT among patient treated under CS or LA.[13, 14]

In the present study, we explored the effect of CS on procedural blood pressure and functional outcome, using patients under LA as control. In addition, we evaluated whether blood pressure drops explain differences in functional outcome between anesthetic regimes.

Methods

Study population

We used data from the MR CLEAN Registry, which is a prospective, multicenter, observational study including all patients who underwent EVT for ischemic stroke due to a large vessel occlusion in the Netherlands from March 2014 until November 2017. Detailed information on the description of variables and the methods of MR CLEAN Registry have been reported

previously.[15] First, centers were excluded if they were non-MR CLEAN trial centers, did not perform EVT under CS or LA as the preferred anesthetic approach, or did not record periprocedural blood pressure as part of protocol care. Second, patients were excluded when they were less than 18 years old, had an occlusion in the posterior circulation or were treated after 6.5 hours of stroke onset. Third, we excluded patients who had no available blood pressure data or were treated under GA as the initial anesthetic strategy during EVT in one of the centers with CS or LA as the preferred anesthetic approach.

To address the risk of bias through selective hemodynamic monitoring and blood pressure data storage in patients at higher risk for hemodynamic instability, we additionally evaluated baseline characteristics of patients treated under CS and LA with and without blood pressure data. Procedural blood pressure values and administered medication were collected retrospectively from patients' records. Study results are reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[16]

Standard protocol approvals, registrations, and patients consents

The MR CLEAN Registry was approved by the medical ethics committee of the Erasmus University MC, Rotterdam, the Netherlands (MEC-2014-235). The institutional review board of each participating center approved the research protocol. At UMC Utrecht, additional approval to participate in the study was obtained from the local research board and ethics committee. The necessity of written informed consent was waived.

Anesthetic management

To limit the risk of confounding by indication, only patients treated in centers that perform EVT under either CS or LA as the preferred anesthetic approach were selected. CS was defined as the administration of any sedative with or without analgesics (e.g. propofol, remifentanil) from 10

minutes before groin puncture until the time of recanalization, not requiring intubation. LA was defined as the use of a local anesthetic (e.g. lidocaine) at the puncture site, without the use of any systemic analgesics or sedatives. Patients converted to GA during the procedure, defined as endotracheal intubation, were analyzed according to the initial anesthetic strategy to limit confounding by indication. The choice of anesthetic agents was at the discretion of the attending anesthesiologist or trained nurse. Anesthetic reports of all patients were reviewed for type, dosages and time of administered anesthetic and vasoactive agents.

Hemodynamic management

Standard hemodynamic monitoring included oxygen saturation, heart rate, non-invasive blood pressure and temperature. Invasive blood pressure monitoring was performed on individual basis as determined by the anesthesiologist. The frequency of blood pressure measurements depends on the local monitoring protocol. Systolic blood pressure, diastolic blood pressure and mean arterial pressure (MAP) values, recorded between 10 minutes before groin puncture and time of recanalization, were retrieved from the patients' procedural anesthesia reports. Since there is no consensus on which blood pressure derived measures are most relevant and what should be avoided (e.g. drops, variability) we focused on three predefined orthogonal definitions that capture different elements of blood pressure drops and variability[17]: [I] area under the threshold (AUT, with MAP on admission as the threshold determined per patient) in mmHg*minute, reflecting both the depth and duration of the relative hypotensive episode; [II] the relative difference between the MAP on admission and the lowest MAP during the EVT procedure, expressed as percentage drop in MAP (ΔLMAP), to account for shorter, larger blood pressure drops; [III] the blood pressure trend during the procedure, defined as the slope for each patient derived from a multilevel linear regression model with "time-since-start procedure" as a

predictor, with a random slope to estimate patient specific trends in blood pressure measurements, for the continuous outcome systolic blood pressure including a random effect for patient to account for within patient variability (Figure 1).[7, 8, 18-20] Hemodynamic intervention was defined as the administration of any inotropes or vasopressors (e.g. ephedrine, phenylephrine) to increase blood pressure or the use of sympathicolytics (e.g. labetalol, clonidine) to lower blood pressure. Blood pressure was regulated according to institutional practices, in general, systolic blood pressure was maintained between 140 and 185 mmHg with a diastolic blood pressure below 105 mmHg based on anesthetic critical care recommendations.[21]

Outcome measures

The primary outcome measure was score on the modified Rankin Scale (mRS). This is a 7-point scale ranging from 0 "no symptoms" to 6 "death", assessed at 90 days after EVT.[22] Secondary outcomes included functional independence (mRS $\leq$ 2), mortality within 90 days post EVT, National Institutes of Health Stroke Scale (NIHSS) score indicating neurologic deficit at 24-48 hours after EVT.[23] Procedure-related outcomes included occurrence of hemodynamic intervention, reperfusion grade, duration of the EVT procedure, and occurrence of procedure-related complications (i.e. vessel perforation, vessel dissection, new thrombus, distal thrombus, hemorrhage, and vasospasm). The reperfusion grade was assessed by the extended thrombolysis in cerebral infarction (eTICI) score on digital subtraction angiography (DSA) which ranges from 0 "no reperfusion or anterograde flow beyond site of occlusion" to 3 "complete reperfusion".[24] Serious adverse events included symptomatic intracranial hemorrhage (sICH, neurologic deterioration of $\geq$ 4 points on the NIHSS, and a compatible hemorrhage on imaging assessed by an independent core laboratory according to the Heidelberg criteria)[25], extracranial hemorrhage, neurologic deterioration (increase of $\geq$ 4 points on the NIHSS), new ischemic stroke (imaging of

new brain tissue infarction with any degree of corresponding neurologic deficit), and pneumonia. Procedure-related complications and eTICI scores were assessed by an independent core laboratory. Investigators who assessed primary and secondary outcomes were not aware of the type of anesthetic management during EVT.

Statistical methods

Baseline characteristics of patients who underwent EVT under CS were compared with patients who received LA during the EVT procedure with a χ^2 test for categorical variables, independent samples *t*-test for normally distributed continuous variables, and Kruskal-Wallis test for non-normally distributed continuous variables. Missing data were imputed using multiple imputations by chained equations based on relevant covariates.[26]

We tested three associations according to a four-step approach: [I] We evaluated the effect of anesthetic modality on the predefined blood pressure parameters (i.e. AUT, ΔLMAP and trend) and hemodynamic interventions during EVT with multivariable linear regression. We adjusted for age, sex, hypertension, diabetes mellitus, atrial fibrillation, history of myocardial infarction, previous stroke, systolic blood pressure on admission, baseline NIHSS, pre-stroke mRS score and treatment center; [II] We assessed the association between the predefined blood pressure parameters and functional outcome. This association was evaluated for all blood pressure parameters separately with ordinal logistic regression adjusted for age, sex, previous stroke, diabetes mellitus, atrial fibrillation, hypertension, history of myocardial infarction, pre-stroke mRS, baseline NIHSS, treatment with intravenous thrombolysis, ASPECTS at baseline, collateral score, time from stroke onset to recanalization, and treatment center; [III] We evaluated the effect of anesthetic modality on functional outcome using an ordinal logistic regression analysis. We adjusted for the following prognostic factors to account for potential

imbalances between both anesthetic modalities: age, sex, previous stroke, diabetes mellitus, atrial fibrillation, hypertension, history of myocardial infarction, pre-stroke mRS score, baseline NIHSS, treatment with intravenous thrombolysis, ASPECTS at baseline, collateral score, time from stroke onset to recanalization, and treatment center; [IV] To evaluate whether procedural blood pressure explained the association between anesthetic modality and functional outcome, we additionally adjusted for the predefined blood pressure parameters that were associated with functional outcome based on multivariable analyses. We repeated step III for secondary outcomes (i.e. functional independence, mortality, early NIHSS, successful reperfusion, duration of procedure, serious adverse events, and procedure-related complications) using the appropriate regression analysis. Step IV was repeated for the secondary outcomes: functional independence, mortality, early NIHSS, and successful reperfusion.

To assess the association between predefined continuous blood pressure parameters and outcome we compared a model containing restricted cubic splines for blood pressure with a model including a linear blood pressure term, based on the log likelihood ratio. Odds ratios for the association between blood pressure and outcome were reported per 300mmHg*minutes for AUT or per 10% drop for DLMAP.[7]

The association between anesthetic approach and functional outcome could possibly be confounded by conversion from LA to CS later on during the EVT procedure as patients who did worse during the procedure received CS later on, and therefore were likely to have worse functional outcome. For that reason, we performed a sensitivity analysis to compare patients receiving CS from the start (<15 min from start EVT) to patients that received LA from the beginning (this group is a composite of LA only and CS administration later on during the procedure, >15 min from EVT start). No correction for multiple testing was performed.

Statistical analyses were performed with R 3.5.0 software (R foundation for Statistical Computing, Vienna, Austria).

Data Availability

Data cannot be made available, as no patient approval has been obtained for sharing coded data. However, R syntax and output files of the analyses will be made available on request.

Results

From the 17 participating centers in the MR CLEAN Registry only 4 centers collected blood pressure data systematically according to protocol and reported LA or CS as the preferred anesthetic approach at start of the EVT (Figure 2).

Study population

Of the 969 eligible patients treated in one of the 4 centers with consistent periprocedural anesthetic management, we included 440 patients with available blood pressure data, who underwent EVT for acute ischemic stroke due to large vessel occlusion, of whom 262/440 (60%) received CS and 178/440 (40%) received LA as procedural anesthetic strategy. Patients treated under CS were less often functionally dependent at presentation (pre-stroke mRS >2; 10/256, 3.8% versus 18/176, 10%) but had a history of previous stroke (44/261, 17% versus 12/178, 6.7%) more often. Mean diastolic blood pressure on admission was lower for patients receiving LA (81, standard deviation [SD] 15 versus 84, SD 16 mmHg; Table 1). We did not find substantial differences in baseline characteristics between patients treated under LA with available blood pressure data (n=178) and without blood pressure data (n=326). Also, no differences between patients treated under CS with available blood pressure data (n=262) compared to patients treated under CS without blood pressure data (n=38) were found.

Procedural management

Average procedural systolic, diastolic and mean arterial blood pressures were lower for patients who were treated under CS (Figure 3, Table 2). AUT and ΔLMAP were larger in the CS group, (median AUT 228 mmHg*min, [interquartile range (IQR) 16-790] versus 23 mmHg*min, [0-200]) and (median ΔLMAP 16%, [5-31] versus 6%, [0-16]). Procedural systolic blood pressure trend was more negative in patients treated under CS compared to LA (-0.22 mmHg, SD 0.39 versus -0.08 mmHg, SD 0.27). Blood pressure elevating medications were administered more often in the CS group than the LA group, 59/262 (23%) versus 6/178 (3.4%). Blood pressure lowering medication was administered in 15/262 (5.7%) of patients in the CS group and in 7/178 (3.9%) of the patients in the LA group. Analgesics were used in 223/262 (85%) patients in the CS group, of which remifentanil was administered most often 116/262 (44%). Sedatives were administered in 142/262 (54%) patients, of which propofol was used most frequently 127/262 (48%) (Table 2). Conversion to GA requiring intubation occurred in 3 patients in the CS group and in 3 patients in the LA group.

I. Association between anesthetic management and procedural blood pressure

CS was associated with larger AUTs (adjusted beta [aβ] 368, [95% CI 242 to 494]) and larger ΔLMAP (aβ 8.1, [95% CI 4.9 to 11.4]) compared to LA based on multivariable linear regression. Furthermore, CS was associated with a more decreasing procedural systolic blood pressure trend (aβ -0.14, [95% CI -0.21 to -0.07]).

II. Association between procedural blood pressure and outcome

Both ΔLMAP (acOR 0.89 per 10% drop from baseline, [95% CI 0.80-0.99]) and AUT (acOR 0.89 per 300mmHg*min, [95% CI 0.82-0.96]) were associated with a shift towards worse functional outcome in multivariable analysis. Procedural blood pressure trend was not associated with functional outcome (acOR 0.85 per mmHg per minute, [95% CI 0.51-1.43]).

III. Association between anesthetic management and outcome

Patients undergoing EVT for acute ischemic stroke under CS were more likely to have poor mRS scores at 90 days compared to LA (acOR 0.59, [95% CI 0.40-0.87]; Table 3, column B, Figure 4). The sensitivity analysis, comparing patients receiving CS from the beginning of the procedure (n = 51) to patients receiving LA from the beginning of the procedure (n = 389), (acOR 0.49, [95% CI 0.26-0.91]), obtained similar results to the primary analysis comparing CS administration at any time point during the procedure to LA. Functional independence at 90 days was less often seen in patients who underwent CS compared to LA (aOR 0.49, [95% CI 0.30-0.83]). There were no differences in all-cause mortality (aOR 1.78, [95% CI 0.96-3.02]), NIHSS at 24-48 hours post-EVT (aβ 1.13 [95% CI -0.38 to 2.64]) and successful reperfusion grades (aOR 1.01, [95% CI 0.66-1.65]) between groups. Procedure duration was almost 20 minutes longer in the CS group compared to the LA group (median 70 [44-90] versus 51 [33-74] minutes). The occurrence of procedure-related complications did not differ between patients treated under CS and LA (9/262, 3% versus 5/178, 4%; aOR 1.45, [95% CI 0.89-2.31]).

IV. Effect of blood pressure on the association between anesthetic management and outcome

Additional adjustment for ΔLMAP and AUT, did not explain the association between anesthetic modality and functional outcome (acOR 0.62, [95% CI 0.42-0.92]; Table 3, column C). Also, ΔLMAP and AUT did not explain the association between anesthetic modality and any of the secondary outcomes.

Discussion

In this study, we evaluated the effect of CS on procedural hypotension, blood pressure trend and hemodynamic interventions compared to LA. Second, we assessed if there was an association between the three predefined blood pressure measures and outcomes. Third, we evaluated the effect of CS on functional outcome compared to LA, and finally we explored if the effect of anesthetic management on outcomes, could be explained by procedural hypotension or blood pressure trend. We found that CS was associated with more blood pressure drops and that these blood pressure drops were related to worse outcomes. However, the blood pressure drops did not explain the effect of CS on functional outcome compared to LA.

Similar to previous studies, we found that patients treated under CS had lower average procedural blood pressure and more blood pressure drops compared to patients treated under LA. Consequently, more hemodynamic interventions were required to increase blood pressure in patients treated under CS.[7, 13, 27]

A drop in MAP from baseline and larger AUT were independently associated with worse functional outcome. Similar, previous studies reported worse functional outcomes in patients with a drop in MAP from baseline of ≥ 10% who received CS or GA during the procedure.[14, 19, 28] A recent study found that larger AUTs were associated with worse functional outcome in patients receiving GA as well as in patients receiving monitored anesthesia care (MAC), which is a composite of CS and LA.[7] In our study, blood pressure drops were relatively mild, especially in the LA group, compared to what has been observed in patients treated under GA (median AUT in our LA group of 23 mmHg*min [0-200] versus 984 mmHg*min [227-1968] in patients treated under GA and median ΔLMAP in our LA group of 6% [0-16] versus 39% [23-49] in patients

treated under GA).[7, 8, 28] The small hemodynamic variability observed in patients treated under LA, underlines the importance of including LA as a treatment arm besides CS and GA in future RCTs focusing on optimal anesthetic and hemodynamic management during EVT.

In this study, patients treated under CS had worse functional outcome compared to patients treated under LA. Hypotension and procedural blood pressure trend did not explain the negative association of CS with functional outcome in our study. Since, there were no large differences in baseline characteristics between patients treated under CS and LA, including neurologic deficit according to the NIHSS at baseline, adjustments for potential covariates did not reduce the effect of CS on outcome compared to LA. Therefore, the effect of CS on functional outcome might be caused by confounders not accounted for in the analyses. The decision to perform EVT under CS is likely to be made by the treating interventionalist and anesthesiologist based on clinical parameters not reflected by the NIHSS score, for example patient agitation and motion. Furthermore, the NIHSS performed in an acute and time-restrained clinical situation might less well comprise mild to moderate neglect, disorientation and aphasia, which could be the determinants of the anesthetic approach. Previous trials reported equivalent functional outcome among patients treated under GA or CS, which is likely due to the strict hemodynamic regimes as part of the anesthetic protocols.[29-31] A pooled analysis of these RCTs suggested that worse outcome after EVT might be associated with blood pressure variability instead of the anesthetic strategy itself. However, conclusions of this study were restricted to the association between blood pressure variability and neurologic outcomes, stratified by anesthetic modality.[28]

In several EVT capable centers with CS or LA as the preferred anesthetic approach during EVT, the involvement of anesthesiologist is limited to patients who are hemodynamic unstable or require GA. Since these results suggest that blood pressure drops and hemodynamic

interventions are seen during both CS and LA, hemodynamic monitoring and rapid treatment of hemodynamic instability during EVT should not be restricted to patients treated under GA only.

Limitations

Our study has several limitations. First, due to the retrospective observational design of this study, results could have been confounded by variables not adjusted for in the analyses. Patients that are more affected at presentation are more likely to get CS and hemodynamic monitoring, meaning residual confounding is present in this cohort. To limit the risk of confounding by indication, we performed a sensitivity analysis for patients who received sedatives or analgesics from the beginning of the procedure. In the sensitivity analysis among patients who received CS from the beginning of the EVT procedure compared to patients receiving LA from the beginning, a similar effect of CS on outcome was found. This suggests that conversion from LA to CS was not directly related to patient's status at baseline and confounding by indication might be less likely. Furthermore, despite we selected centers reporting either CS or LA as the preferred approach we observed that a significant number of patients received the non-preferred initial anesthetic approach. Since we selected centers with CS or LA as preferred anesthetic approach and standard hemodynamic monitoring, the generalizability of our findings to patients treated under different anesthetic or hemodynamic regimes is limited.

Second, there is no consensus on how to quantify procedural hypotension and blood pressure variability. A different quantification of procedural hemodynamics could alter the effect of anesthetics on outcome. Lastly, as heterogeneity in anesthetic approach definitions exist, comparability is difficult since sedation is a continuum ranging from minimal to deep sedation,

with a concomitant variety in physiological effects (e.g. arterial hypotension, bradycardia, respiratory depression).

Conclusions

Hemodynamic interventions to maintain hemodynamic stability are common during EVT under CS and LA. In a cohort of patients treated with EVT under strict blood pressure management, decreases in blood pressure are small and do not explain the differences in functional outcome between patients treated under CS and LA. As blood pressure drops by means of ΔLMAP and AUT are independently associated with worse functional outcome, we advocate to monitor and avoid blood pressure drops (i.e. ensure hemodynamic stability) during EVT. Further randomized controlled trials are needed to determine if hemodynamic interventions improve patient outcomes.

Appendix 1: Authors

Name	Location	Contribution
Noor Samuels, MD	Erasmus MC, University Medical Center, Rotterdam	Study concept and design, data acquisition, statistical analyses, drafting the manuscript
Rob A. van de Graaf, MD	Erasmus MC, University Medical Center, Rotterdam	Study concept and design, data acquisition, statistical analyses, critical revision of the manuscript for intellectual content
Carlijn A.L. van den Berg, BSc	Erasmus MC, University Medical Center, Rotterdam	Major role in data acquisition, statistical analyses, critical revision of the manuscript for intellectual content
Daan Nieboer, MSc	Erasmus MC, University Medical Center, Rotterdam	Statistical analyses, critical revision of the manuscript for intellectual content
Ismail Eralp, MD, PhD	Erasmus MC, University Medical Center, Rotterdam	Critical revision of the manuscript for intellectual content
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Bob Roozenbeek, MD, PhD	Erasmus MC University Medical Center, Rotterdam	Critical revision of the manuscript for intellectual content
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Hester F. Lingsma, PhD	Erasmus MC University Medical Center, Rotterdam	Study concept and design, statistical analyses, interpretation of the data, critical revision of the manuscript for intellectual content
Adriaan C.G.M. van Es, MD, PhD	Erasmus MC University Medical Center, Rotterdam	Study concept and design, interpretation of the data, critical revision of the manuscript for intellectual content

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Figure legends

Figure 1. Schematic illustration procedural blood pressure parameters.

Summary: 1. mean arterial pressure (MAP) value on admission; 2. Lowest MAP; 3. Area under the threshold (AUT); 4. Relative difference between baseline MAP and lowest MAP (ΔLMAP); 5. Average trend (slope). *Abbreviations*: ED, emergency department; EVT, endovascular treatment.

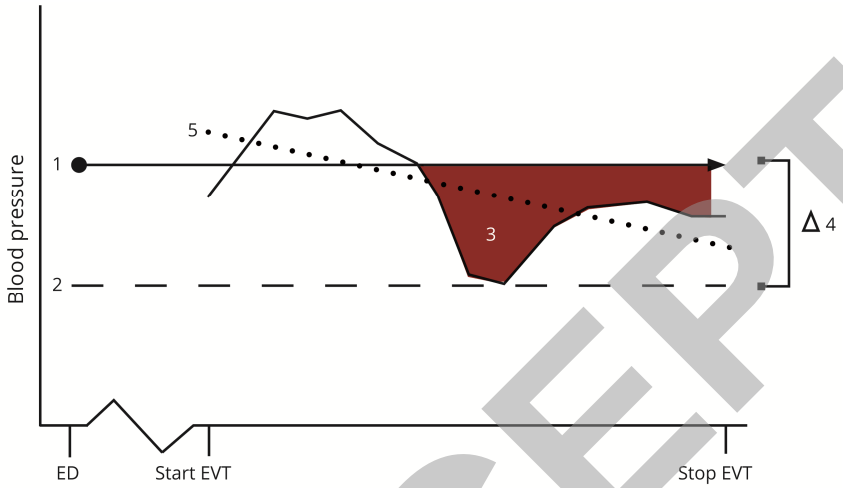

Figure 2. Flowchart of patient selection.

Abbreviations: GA, general anesthesia; LA, local anesthesia; min, minutes; CS, conscious sedation.

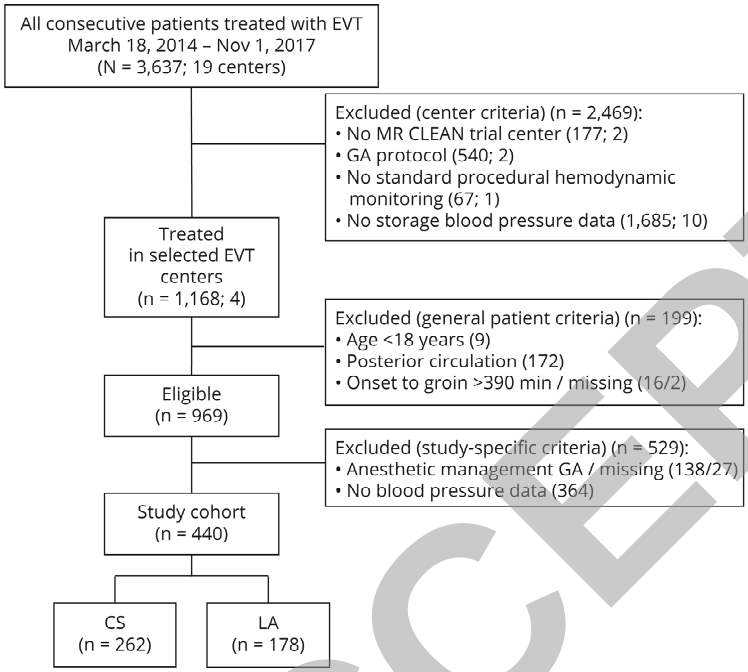

Figure 3. Procedural blood pressure for patients treated under conscious sedation or local anesthesia.

Summary: **A.** Non-smoothed mean systolic blood pressure curves for both anesthetic modalities with 95% tolerance interval (band). **B.** Smoothed mean systolic blood pressure curves during EVT procedure for both anesthetic modalities (continuous line) with 95% tolerance interval (dotted line). *Abbreviations*: min, minutes; mmHg, millimeter of mercury.

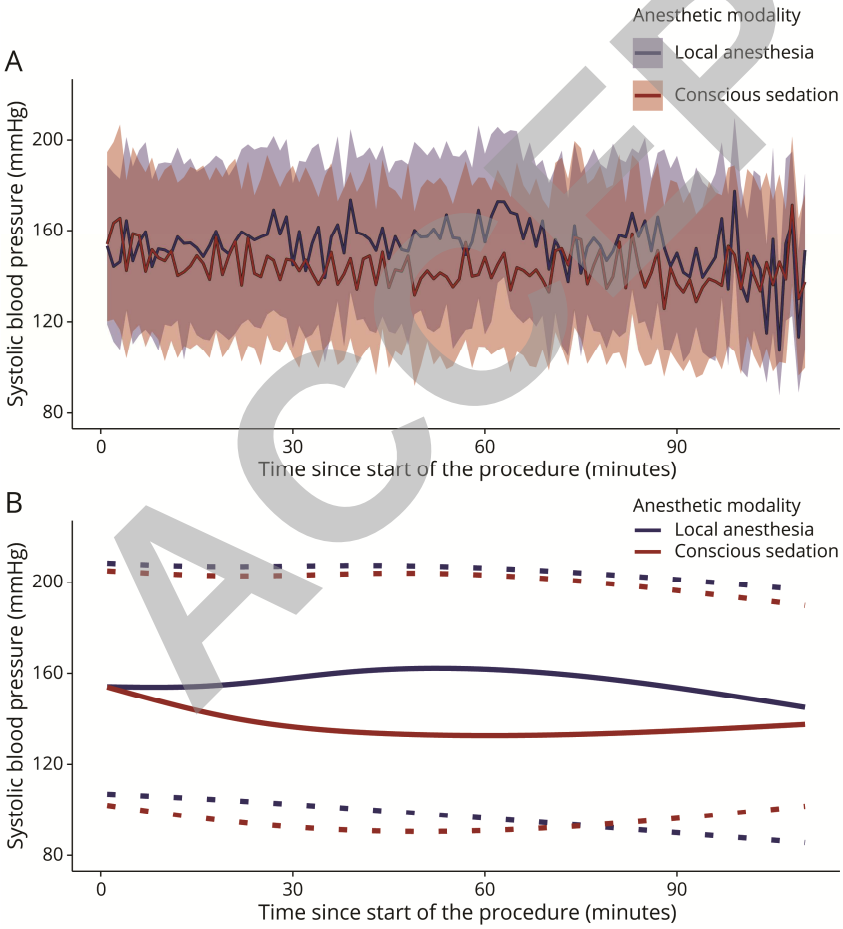

Figure 4. Primary outcome on the modified Rankin Scale by preferred anesthetic method.

Abbreviations: mRS, modified Rankin Scale.

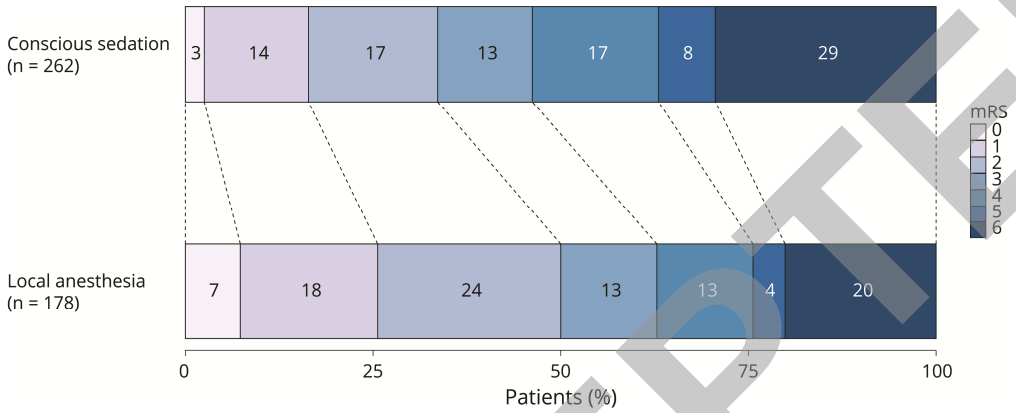

Table 1. Baseline characteristics			
	CS (n=262)	LA (n=178)	Missing
Patient characteristics			
Age, y, mean (SD)	68 (15)	69 (15)	
Male sex, n (%)	128 (49)	103 (58)	
NIHSS, median [IQR]	16 [11-19]	15 [11-19]	
Left hemisphere, n (%)	118 (45)	97 (55)	
Systolic BP, mean (SD)	149 (25)	148 (24)	
Diastolic BP, mean (SD)	84 (16)	81 (15)	
IVT, n (%)	203 (77)	135 (76)	
Center, n (%)			
1, preferred approach CS[a]	134 (70)	58 (30)	
2, preferred approach LA	2 (13)	13 (87)	
3, preferred approach LA	16 (57)	12 (43)	
4, preferred approach CS	110 (55)	95 (45)	
Medical history, n (%)			
Previous stroke	44 (17)	12 (6.7)	1/0
Atrial fibrillation	58 (22)	40 (22)	4/0
Hypertension	124 (49)	94 (53)	8/5
Diabetes mellitus	42 (16)	28 (16)	3/1
Myocardial infarction	29 (11)	24 (14)	6/1
Pre-stroke mRS			6/2
0	182 (72)	133 (76)	
1	35 (14)	18 (10)	
2	29 (11)	7 (4.0)	
>2	10 (3.9)	18 (10)	
Imaging			
Occluded segment, n (%)			7/9
M1	157 (62)	108 (64)	
M2	27 (11)	26 (16)	
ICA	16 (6.3)	5 (3.0)	

ICA-T	55 (22)	30 (18)	
ASPECTS, median [IQR]	9 [8-10]	9 [8-10]	6/9
Collaterals			9/14
Absent	14 (5.5)	9 (5.5)	
filling <50% of occluded area	97 (38)	63 (38)	
>50% but less <100%	99 (39)	65 (40)	
100% of occluded area	43 (17)	27 (16)	
Workflow, min, median [IQR]			
Time from admission ER to groin puncture	41 [28-69]	44 [30-73]	12/7
Time from stroke onset to groin puncture	195 [155-260]	191 [155-244]	

Abbreviations: ASPECTS, Alberta Stroke Program Early Computed Tomography Score; BP, blood pressure; CS, conscious sedation; ED, emergency room; eTICI, extended thrombolysis in cerebral infarction; ICA, internal carotid artery; ICA-T, internal carotid artery terminus; IVT, intravenous thrombolysis; LA, local anesthesia; M(*segment*), middle cerebral artery; min, minutes; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale. Continuous data are presented as mean (standard deviation, SD) for normal distributed data or as median [interquartile range, IQR] for skewed data. [a]Preferred approach changed in 2017 to LA.

Table 2. Procedural anesthetic and hemodynamic data

	CS (n=262)	LA (n=178)
Medication, n.(%)[a]		
Muscle relaxant		
Rocuronium	3 (1.1)	2 (1.1)
Sympatholytics	15 (5.7)	7 (3.9)
Inotropes/vasopressors	59 (23)	6 (3.4)
Clonidine	1 (0.4)	4 (2.2)
Atropine	17 (6.5)	1 (0.6)
Ketanserine	0	1 (0.6)
Ephedrine	16 (6.1)	3 (1.7)
Labetalol	8 (3.1)	2 (1.1)
Epinephrine	2 (0.8)	0
Isoprenaline	2 (0.8)	0
Norepinephrine	20 (7.6)	3 (1.7)
Phenylephrine	24 (9.2)	2 (1.1)

Nimodipine	6 (2.3)	0
Urapidil	0	1 (0.6)
Analgesics	223 (84)	-
Alfentanil	49 (19)	-
Fentanyl	11 (4.2)	-
Morfine	1 (0.4)	-
Remifentanil	116 (44)	-
Sufentanil	46 (18)	-
Sedatives	142 (53)	
Esketamine	12 (4.6)	-
Midazolam	8 (3.1)	-
Propofol	127 (48)	-
Blood pressure values, mmHg		
SBP, median [IQR]	141 [123-164]	155 [135-173]
DBP, median [IQR]	76 [67-84]	80 [70-92]
MAP, median [IQR]	100 [89-115]	107 [94-121]
ΔLMAP, median [IQR][b]	16 [5.2-31]	6.0 [0-16]
AUT, median [IQR][c]	228 [16-790]	23 [0-200]
Trend SBP, mean (SD)[d]	-0.22 (0.39)	-0.08 (0.27)

Abbreviations: AUT, area under threshold; CS, conscious sedation; DBP, diastolic blood pressure; IQR, interquartile range; ΔLMAP, relative difference baseline MAP and lowest procedural MAP; MAP, mean arterial pressure; SBP, systolic blood pressure; SD, standard deviation. [a]

Percentages may add up to more than 100 owing to combined administration of medication. [b] Percentage drop form baseline MAP; [c] mmHg*minute; [d] Beta coefficient.

Table 3. Effect of CS versus LA on outcomes, unadjusted (model A), adjusted for potential confounding variables (model B), and with additional adjustment for blood pressure (model C).

			A	*B*	*C*
	CS (n=262)	LA (n=178)	Unadjusted effect CS vs LA (c)OR (95% CI)	Adjusted effect CS vs LA a(c)OR (95% CI)	Adjusted effect, including ΔLMAP[a] and AUT[b], CS vs LA a(c)OR (95% CI)
Primary outcome, median [IQR]					
mRS at 90 d	4 [2-6]	3 [1-4]	0.56 (0.40 to 0.79)	0.59 (0.40 to 0.87)	0.62 (0.42 to 0.92)
Secondary outcomes, clinical					
mRS ≤2 at 90 d, n (%)	80 (34)	82 (50)	0.53 (0.36 to 0.78)	0.49 (0.30 to 0.83)	0.53 (0.30 to 0.85)
Mortality at 90 d, n (%)	70 (29)	33 (20)	1.51 (0.95 to 2.37)	1.78 (0.96 to 3.02)	1.70 (0.95 to 3.18)
NIHSS 24–48 h, median [IQR]	10 [4-16]	8 [3-15]	1.68 (0.05 to 3.31)[c]	1.13 (-0.38 to 2.64)[c]	0.88 (-0.67 to 2.43)[c]
Secondary outcome, radiological, n (%)					
Successful reperfusion after intervention (eTICI ≥ 2B)	175 (69)	122 (70)	0.96 (0.64 to 1.46)	1.01 (0.66 to 1.65)	1.11 (0.70 to 1.81)
Secondary outcomes, workflow, median [IQR]					
Duration of procedure	70 [44-90]	51 [33-74]	15.9 (9.49 to 22.2)[c]	14.3 (8.17 to 20.50)[c,d]	
Secondary outcomes, safety measures, n (%)					
Procedure-related complications	9 (4)	5 (3)	1.57 (1.01 to 2.45)	1.45 (0.89 to 2.31)	
Symptomatic ICH	13 (5.0)	4 (2.3)	2.27 (0.79 to 8.17)	2.74 (0.87 to 10.4)	
ECH	5 (1.9)	7 (3.9)	0.48 (0.14 to 1.51)	0.52 (0.13 to 1.98)	
Neurologic deterioration	18 (6.9)	8 (4.5)	1.57 (0.69 to 3.90)	1.49 (0.57 to 4.14)	
New ischemic stroke	7 (2.7)	2 (1.1)	2.42 (0.58 to 16.3)	4.80 (0.84 to 20.1)	
Pneumonia	28 (11)	16 (9.0)	1.21 (0.64 to 2.36)	1.04 (0.50 to 2.23)	

Abbreviations: acOR, adjusted common odds ratio; CI, confidence interval; CS, conscious sedation; ECH, extracranial hemorrhage; eTICI, extended thrombolysis in cerebral infarction; ICH, intracranial hemorrhage; IQR, interquartile range; LA, local anesthesia; ΔLMAP, relative difference baseline mean arterial pressure (MAP) and lowest procedural MAP; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; SD, standard deviation.

A. univariable regression analyses. B. multivariable regression analyses (adjusted for age, sex, baseline NIHSS, pre-stroke mRS, history of stroke, hypertension, diabetes mellitus, atrial fibrillation, myocardial infarction, intravenous thrombolysis, ASPECT score at baseline, time between stroke onset and recanalization, center); C. multivariable regression analyses (adjusted for the same variables as in step 2 with an additional adjustment for ΔLMAP and AUT to evaluate if hypotension explains the effect of CS on outcome, i.e. reduces the effect estimate). [a] per 10% drop; [b] per 300mmHg*minutes; [c] reported effect measure is β coefficient; [d] adjustment for time between stroke onset and groin puncture instead of time between stroke onset and recanalization.

Blood pressure during endovascular treatment under conscious sedation or local anesthesia

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Neurology published online October 7, 2020
DOI 10.1212/WNL.0000000000011006