

Anesthetic Management and Outcome in Patients during Endovascular Therapy for Acute Stroke

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ABSTRACT

Background: Studies of endovascular treatment for acute ischemic stroke have identified general anesthesia as a predictor for poor outcome in comparison with local anesthesia/sedation. This retrospective study attempts to identify modifiable factors associated with poor outcome, while adjusting for baseline stroke severity, in patients receiving general anesthesia.

Methods: We reviewed charts of 129 patients treated between January 2003 and September 2009. The primary outcome was the modified Rankin Score of 0–2 for 3 months poststroke. Predictors of neurologic outcome included baseline National Institutes of Health Stroke Scale score, blood glucose concentration, and age. Additional risk factors evaluated were prolonged stroke onset-treatment interval and systolic blood pressure less than 140 mmHg. Choice of local anesthesia or general anesthesia was recorded.

Results: The study group was 96 out of 129 patients for whom modified Rankin Scale scores were available; 48 patients received general anesthesia and 48 local anesthesia. The proportion of patients with “good” outcomes were 15% and 60% in the general anesthesia group and local anesthesia group, respectively ($P < 0.001$). Lowest systolic blood pressure and general anesthesia were correlated ($r = -0.7$, $P < 0.001$). Independent predictors for good neurologic out-

What We Already Know about This Topic

- Recent retrospective case series have reported an association between general anesthesia and poor outcome, but data of intraoperative management and consideration of baseline neurologic status were not available

What This Article Tells Us That Is New

- Systolic blood pressure less than 140 mmHg and general anesthesia were predictors of poor neurologic outcome in patients requiring endovascular therapy for acute stroke

come were local anesthesia, systolic blood pressure greater than 140 mmHg, and low baseline stroke scores.

Conclusions: Adjusted for stroke severity, patients who received general anesthesia for treatment are less likely to have a good outcome than those managed with local anesthesia. This may be due to preintervention risk not included in the stroke severity measures. Hypotension, more frequent in the general anesthesia patients, may also contribute.

ENDOVASCULAR arterial revascularization for acute stroke improves outcome of patients with large vessel occlusion,^{1–8} for whom the results of intravenous thrombolysis are poor. At our center, emergency endovascular therapy has been offered to patients with severe disabling stroke due to occlusions of the carotid, middle cerebral, and basilar arteries presenting for treatment within 6 h of stroke onset.

Anesthetic management during an endovascular intervention includes local anesthesia and a range of sedation up to and including general anesthesia. In addition to patient

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comfort, anesthetic intervention may be required to reduce patient movement and maintain physiologic stability and airway control. In published reports of endovascular treatment for acute stroke,¹⁻⁸ details concerning anesthetic management during interventions are scarce. Little mention has been made of potential anesthetic factors that may influence neurologic outcome.

Four recent retrospective reviews⁹⁻¹² have reported a strong and worrisome association between general anesthesia and poor neurologic outcome and death; opinions are divided as to the clinical implications of these findings.¹³⁻¹⁵ The contribution of anesthetic management in poor outcome remains unclear, because in the reported studies the major determinant of outcome, the baseline stroke severity, was not controlled; the patients that received general anesthesia tended to be "sicker." Nichols *et al.*¹¹ have suggested that selection of patients with more severe stroke contributed to the poor outcome in the patients that received deep sedation or general anesthesia.

In our center we reserve general anesthesia for patients who cannot cooperate and those with acute critical events, such as airway obstruction. Despite the likelihood that these patients are sicker, we speculated that there may be additional factors that contribute to poor outcome that we could modify with the expectation of improving outcome. Specifically, we speculated that perioperative blood pressures may have been influenced by anesthetic management and could plausibly have contributed to the observed differences in neurologic outcome. In an attempt to address this question, we have retrospectively reviewed patients undergoing endovascular treatment for acute stroke at our center, comparing those treated with local anesthesia or light sedation to patients treated with general anesthesia.

Materials and Methods

Institutional Review Board approval (University of Calgary Conjoint Ethics Committee, University of Calgary, Calgary, Alberta, Canada) was obtained for review of the stroke database and patient hospital records; the requirement for individual patient consent was waived. The study was a retrospective cohort study of neurologic outcome in patients receiving endovascular therapy for acute ischemic stroke from January 2003 to September 2009. Neurologic outcome was measured with the modified Rankin Score (mRS), recorded 3 months after the stroke onset. We anticipated that the main independent contributor to stroke outcome would be the baseline stroke severity, measured with the National Institutes of Health Stroke Scale (NIHSS) score, assigned at the time of diagnosis in the emergency department. Patient characteristics that we postulated could influence outcome were age and comorbidities. Treatment factors that we thought might contribute to outcome included time-to-treatment, hypotension or hypertension (systolic blood pressure less than 140 mmHg or greater than 180 mmHg, respectively),^{16,17} and hyperglycemia.¹⁸ The blood pressure

values that we used correspond to the limits of the range of systolic blood pressure that is associated with best outcome.^{16,17} In our analysis, we sought to adjust for the effects of baseline stroke severity to identify modifiable factors that may improve the neurologic outcome, specifically in patients for whom general anesthesia is required. Since the patient database was small (less than 200 individuals), we decided that evaluation of the effects of specific anesthetic agents on outcome was not feasible and we did not collect data with respect to the anesthetic drugs.

During the study period, patients with thromboembolic stroke involving middle cerebral artery occlusion, extracranial internal carotid occlusion, intracranial carotid "T" occlusion, and basilar artery occlusion were offered intra-arterial thrombolysis. The Calgary Stroke Program serves a population of 1.5 million and is centralized at the Foothills Medical Center, where approximately 150 patients requiring thrombolysis are managed at each year. Patients with significant clinical symptoms and proximal occlusions are considered for endovascular thrombolysis.¹⁹

We use a "good" x-ray film-computed tomography scan occlusion paradigm and prefer not to intervene in patients with poor scans (baseline Alberta Stroke Program Early Collimated Tomography Score of less than 4). Detailed criteria for patient selection have been previously described.²⁰

Information for each patient was identified from the database, the paper chart, the electronic record, and the automated anesthesia record (when available). Charts were reviewed by two neurologists and three anesthesiologists. The baseline data recorded at the time of neurologic diagnosis in the emergency department included patients' demographics (age, sex), comorbidities, and neurologic condition (NIHSS score, stroke type and territory, and Glasgow Coma Scale). Data for factors contributing to secondary brain injury included the elapsed times from stroke to intravenous thrombolytic administration and systemic factors (perioperative blood pressure and blood glucose concentration). In the local anesthesia group, blood pressure was measured with an oscillometric noninvasive blood pressure cuff at frequencies that varied from patient-to-patient. In patients receiving general anesthesia blood pressure, blood measure was measured either with the oscillometric method above or with an arterial cannula, and recorded at 5-min intervals.

During the study period the decision to involve the anesthesia service was made on a case-by-case basis by the interventional team (the stroke neurologist and the neuroradiologist). The choice of anesthetic technique was made collectively by the neurologist, radiologist, and anesthesiologist. For some patients we were able to retrieve a specific indication for general anesthesia such as preintervention aspiration or airway obstruction and decreased level of consciousness. For patients managed with local anesthesia, conscious sedation, when required, was provided with intermittent doses of midazolam (2.5 mg) and fentanyl (25 mcg), typically administered by the stroke neurologist every

15 to 30 min. Once deep sedation was judged to be required, patients received light general anesthesia with tracheal intubation, mechanical ventilation and neuromuscular block, provided by an anesthesiologist. Monitoring for all patients included electrocardiography, pulse oximetry, and noninvasive blood pressure measurements. For patients receiving general anesthesia, end-tidal volatile agent concentration and carbon dioxide were also monitored. General goals were to maintain blood pressure, as measured directly with an arterial cannula when possible, to within 10% of preanesthetic values.

All procedures were performed in a dedicated biplane neuroangiography suite (Siemens Axiom Artis, Siemens, Erlangen, Germany) by four experienced neurointerventionalists. Under sterile conditions, selective angiography and intra-arterial therapy were provided using a femoral artery for vascular access. Reconstituted recombinant tissue plasminogen activator was applied to the thrombus and combined, when appropriate, with mechanical thrombus disruption and retrieval with the microcatheter. Recanalization of the symptomatic vessel was assessed angiographically. Anticoagulation was maintained during the procedure with unfractionated heparin, using a 2,000 U intravenous bolus at the beginning of the procedure. Control angiograms were obtained every 3 to 4 min to monitor progression of the aspiration and to reposition the reperfusion catheter to a new thrombus face. The procedure was terminated if satisfactory reperfusion was achieved or if there was no progress after 2 h. Thrombectomy devices and intra-arterial tissue plasminogen activator were used at the discretion of the neurointerventionalist and the stroke neurologist, according to device availability and specific patient anatomy. The baseline and final perfusion were documented by the neurointerventionalist with the Thrombolysis in Myocardial Infarction scores (0–3; 0 = no perfusion, 3 = complete perfusion).²¹

Statistical Considerations

The purpose of the analysis was, after adjusting for baseline stroke severity, to identify factors that were predictive of good outcome in the patient cohort. We performed univariate analysis to identify the patient variables that were distributed unevenly between the patients who received local anesthesia and those who received general anesthesia. In the univariate analysis, no adjustment for multiple comparisons was applied and statistical significance was inferred for $P < 0.05$. We then ran a correlation coefficient matrix among the proposed independent variables to identify the presence of multicollinearity. Next we applied binomial logistic regression analysis to two hypothetical models; in both models good neurologic outcome (mRS 0–2) was the dependent variable, and in both models we adjusted for baseline stroke severity. In the first model we examined the contribution of stroke severity, anesthetic type, and blood glucose. In the second model we examined the contribution of stroke severity, hypotension, and blood glucose.

Data were entered into a Microsoft Excel® spreadsheet (Microsoft Corporation, Redmond, WA) and verified with the original sources for internal consistency. Statistical analysis was performed with STATA® (StataCorp LP, College Station, TX) and graphics were created with Sigmaplot® 11 (Systat Software, Inc., San Jose, CA). Numerical data were evaluated for normality with the Shapiro–Wilk statistic; data that were not normally distributed was described with the median and the interquartile range and compared using the Mann–Whitney rank sum test. Rates and proportions of patients within subgroups were evaluated with the Pearson product moment coefficient. Outcomes were characterized by the relative risk for good outcome (mRS 0–2), which meant the multiple of risk of the good outcome in patients treated with local anesthesia compared with those treated with general anesthesia. Zhang and Yu have suggested²² that relative risk may be preferable to adjusted odds ratio in study populations such as the present one, in which the outcome of interest is common, because the odds ratio may exaggerate a risk association. *Post hoc* estimates of mean blood pressure were calculated using the formula (systolic blood pressure + 2 diastolic blood pressure)/3, and were reported as mean values \pm SD. Maximum and minimum mean blood pressures were compared between the local and general anesthesia groups using two-way ANOVA using the Holm–Sidak method to adjust for multiple comparisons.

To estimate the impact of excluding patients with incomplete data on the results, we assigned each patient (when possible) a Houston Intra-arterial Therapy score² that has been validated to predict the likelihood of good outcome after endovascular intervention for acute ischemic stroke. The scoring system combines age (more than 75 yr, 1 point), NIHSS score (more than 18, 1 point), and baseline glucose concentration (more than 8.3 mm, 1 point) to quantify the preintervention likelihood of poor outcome. Houston Intra-arterial Therapy scores of 0–3 were associated with poor outcomes in 44%, 67%, 97%, and 99% of patients, respectively.²

Results

Patient Characteristics

During the study period, the database contained 129 patients who were listed as having received intracerebral endovascular therapy. Outcome determinations could be retrieved in 97 patients. For one patient, the anesthetic management could not be determined, leaving a total study cohort of 96. The characteristics of the study patients are summarized in table 1. Characteristics that were not evenly distributed between the general and local anesthesia groups were sex, NIHSS score, diabetes mellitus, blood glucose, minimum systolic and diastolic blood pressures, and the discharge destination.

Table 1. Baseline Patient Characteristics and Postintervention Destination

	General Anesthesia (n = 48)	Local Anesthesia (n = 48)	P Value	Missing Data (n = 33) (General Anesthesia = 5)
Demographics				
Age in years (mean, SD)	63 (14)	62 (15)	0.72	60 (16)
Male Sex (% , n)	58% (28)	81% (39)	0.03	58% (20)
Clinical (% , n)				
NIHSS (median, IQR)	19.5 (9)	16 (9.5)	0.03	18 (5)
Hypertension	48% (23)	46% (22)	1.00	48% (16)
Atrial fibrillation	21% (10)	27% (13)	0.63	18% (6)
Ischemic heart disease	27% (13)	10% (5)	0.07	27% (9)
Smoking	35% (17)	21% (10)	0.17	30% (10)
Diabetes mellitus	25% (12)	4% (2)	0.01	3% (1)
Obesity	15% (8)	7% (4)	0.82	6% (2)
Valvular heart disease	2% (1)	10% (5)	0.20	12% (4)
Stroke mechanism			0.14	
Large vessel atherosclerosis	34% (16)	19% (9)		24% (8)
Cardioembolic	32% (15)	42% (20)		26% (9)
Other	13% (6)	6% (3)		12% (4)
Undetermined	21% (10)	33% (16)		36% (12)
Stroke Territory				
Middle cerebral artery	60% (28)	79% (34)	0.08	79% (26)
Left hemisphere	64% (18)	56% (19)	0.68	42% (14)
Basilar artery	40% (19)	21% (9)	0.08	21% (7)
Physiological				
Glucose (mm) (mean, SD)	8.0 (1.9)	7.2 (1.9)	0.04	6.8 (1.9)
Minimum SBP (mmHg)	104 (17)	137 (20)	<0.001	127 (25)
Minimum DBP (mmHg)	76 (11)	56 (10)	<0.001	72 (15)
Maximum SBP (mmHg)	165 (24)	162 (27)	0.50	159 (27)
Maximum DBP (mmHg)	91 (20)	91 (12)	0.92	92 (13)
Minimum MAP (mmHg)	72 (15)	96 (15)	<0.001	76 (17)
Maximum MAP (mmHg)	116 (14)	114 (14)	0.69	101 (18)
Discharge Destination				
PACU/Direct to ward	14	39	<0.001	27
ICU	34	9		6
Unknown		1		

DBP = diastolic blood pressure; ICU = intensive care unit; IQR = interquartile range; MAP = mean arterial pressure; NIHSS = National Institutes of Health Stroke Scale; PACU = postanesthesia care unit; SBP = systolic blood pressure.

Clinical Outcome at 3 Months

For the primary outcome, 22 patients (23%) had no or minimal neurologic deficits (mRS 0–1), 37 patients (39%) were functionally independent (mRS 0–2) (fig. 1), and 25 patients died (26%). When clinical outcomes were evaluated according to anesthetic management, significantly fewer of the patients that received general anesthesia (7/48, 15%) had good outcomes than in the group managed with local anesthesia (29/48, 60%). The relative risk of a good outcome for patients receiving general anesthesia was 0.31 (95% CI, 0.14–0.66), or stated alternatively, the relative risk of good outcome with local anesthesia was 3.2 (1.5–6.8). Mortality was more likely in the patients that received general anesthesia than in those managed with local anesthesia (relative risk: 2.3, or 1.1–3.7; $P = 0.039$).

Analysis of Factors Predicting Outcome

There were 37 patients who had a good outcome, making it feasible to model the contribution of three factors using

binary logistic regression analysis. This technique was chosen to allow us to identify risk factors while adjusting for the baseline stroke severity. First we evaluated the correlation between factors that were biologically relevant to stroke: age, presence of diabetes mellitus, coronary artery disease or atrial fibrillation, periprocedural blood sugar, and minimum recorded values of systolic and diastolic blood pressure (Correlation Matrix, appendix 1). Since the correlation analysis identified the possibility that general anesthesia and blood pressure were colinear variables, we constructed two models including either type of anesthesia (general or local) or blood pressure nadir (less than or greater than 140 mmHg) but not both together, blood sugar to the nearest mM and NIHSS score in 5-point increments. The results (tables 2 and 3) show that, after adjusting for baseline stroke severity, both the selection of local anesthesia and lowest systolic blood pressure equal to or greater than 140 mmHg were predictors of good outcome.

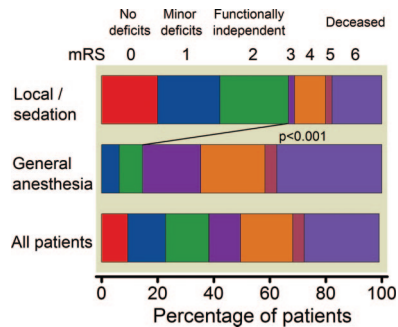


Fig. 1. Neurologic outcome by modified Ranking Scale in all patients ($n = 96$) and in patients who received general anesthesia ($n = 48$) or local anesthesia, mild sedation. No patient who received general anesthesia recovered without a deficit (scale, 0), and the percentage of patients that had a good neurologic outcome (scale, 0–2) was much lower than among patients that received local anesthesia (dotted line). mRS = modified Ranking Scale.

Blood Pressure during the Endovascular Procedure

In patients managed with general anesthesia the average lowest recorded systolic blood pressure (104 ± 17 mmHg) was lower than that observed in the patients managed with local anesthesia (134 ± 32 mmHg; $P < 0.001$) (fig. 2). The lowest systolic blood pressure was 140 mmHg or greater in 60% of patients managed with local anesthesia, compared with 4% of patients with general anesthesia ($P < 0.0001$, Fisher exact test). Diastolic and mean arterial pressures showed a similar pattern (table 1). Systolic blood pressures above 180 mmHg have been associated with poor neurologic outcome;²³ nine patients (20%) in both the general and local anesthesia groups had highest systolic blood pressure measurements greater than 180 mmHg ($P = 1.00$, Fisher exact test). To examine the worst case scenario, in patients managed with local anesthesia, 44% of patients had maximum and minimum systolic blood pressures that were within the range of 140–180 mmHg; in patients managed with general anes-

sia, none had maximum and minimum systolic pressures that lay within this range.

Post hoc estimation of mean blood pressure showed that the highest mean blood pressures were 115 ± 15 mmHg (local anesthesia group) and 115 ± 19 mmHg (general anesthesia group). The lowest mean blood pressures were 97 ± 13 mmHg (local anesthesia group) and 71 ± 10 mmHg (general anesthesia group). The lowest mean pressure in the local anesthesia group differed from the general anesthesia group (two-way ANOVA, $P < 0.001$).

Timing of Therapy and Concurrent Treatments

Pretreatment with intravenous thrombolytic therapy and the promptness of either intravenous or intra-arterial therapy may influence outcome. We examined the distribution of these variables with respect to patients receiving local anesthesia/sedation or general anesthesia. The interval times that could be calculated from information in the medical record included the time from stroke onset to arrival in the emergency department, from stroke onset to intravenous therapy, and from stroke onset to intra-arterial therapy. The results (fig. 3) show that interval times for administration of intravenous and intra-arterial treatment did not differ between the patients ultimately managed with local anesthesia/sedation compared to those managed with general anesthesia (Mann–Whitney rank sum test, $P = 0.173$, 0.871 for intra-arterial and intravenous therapy intervals, respectively).

Patient Selection Bias

Stroke Severity. The patients who received general anesthesia had more severe strokes than those managed with local anesthesia (table 1, fig. 4). The proportion of patients receiving general anesthesia increased as the stroke severity increased from minor (8/30) to severe 23/32 ($P = 0.008$) (fig. 4). With respect to the vascular territory of the strokes, the basilar artery was involved in 19/48 (40%) of patients in

Table 2. Logistic Regression Analysis of 96 Patients Undergoing Endovascular Therapy for Acute Stroke

Model 1				
Logit P (mRS < 3) = $3.75 - (2.06 \times \text{General Anesthesia}) - (0.50 \times \text{NIHSS score per 5 point increment}) - (0.25 \times \text{Blood Glucose, mm})$				
Predictor	$\beta \pm \text{SE}$	Wald's Chi-square	Relative Risk (CI_{95})	P Value
Constant	3.75 ± 1.32	8.00		
General Anesthesia	-2.06 ± 0.54	14.74	0.31 (0.14–0.66)*	0.002
NIHSS score (per 5 point increment)	-0.50 ± 0.21	5.93	0.8 (0.6–0.9)	0.006
Blood glucose (per mm increase)	-0.25 ± 0.16	2.44	0.9 (0.7–1.1)	0.178
Test				
Overall model evaluation				
Likelihood ratio test		35.38	<0.001	
Pearson Chi-square Statistic		102.87	0.186	
Goodness-of-fit test				
Hosmer–Lemeshow test		15.03	0.058	

* Alternately, the relative risk of good outcome with local anesthesia is: 3.2 (CI_{95} 1.5–6.8).

mRS = modified Rankin Score; NIHSS = National Institutes of Health Stroke Scale.

Table 3. Logistic Regression Analysis of 96 Patients Undergoing Endovascular Therapy for Acute Stroke

Model 2				
Logit P (mRS < 3) = 3.13 -(1.84*Lowest BP < 140)-(0.52*NIHSS score per 5 point increment)-(0.33*Blood Glucose, mm)				
Predictor	b ± SE	Wald's Chi-square Test	Relative Risk (CI ₉₅)	P Value
Constant	3.13 ± 1.26	6.12		0.013
Lowest SBP < 140 mmHg	-1.84 ± 0.62	8.88	0.59 (0.40–0.87)	0.008
NIHSS score (per 5 point increment)	-0.52 ± 0.19	7.64	0.8 (0.6–0.96)	0.019
Blood glucose (per mm increase)	-0.33 ± 0.16	4.48	0.8 (0.6–0.95)	0.016
Test				
Overall model evaluation		Chi-square	P	
Likelihood ratio test		28.58	<0.001	
Pearson Chi-square Statistic		88.43	0.557	
Goodness-of-fit test				
Hosmer-Lemeshow test		6.77	0.562	

BP = blood pressure; mRS = modified Rankin Score; NIHSS = National Institutes of Health Score; SBP = systolic blood pressure.

the general anesthesia group and 9/48 (20%) of patients in the local anesthesia group ($P = 0.078$).

Critical Events. The periprocedural critical events, summarized as one event per patient, that were retrieved from notes in the patient charts are summarized in table 4. Although the frequency of events was similar in the two treatment groups ($P = 0.30$), the proportion of patients with critical events and poor outcome was greater in the patients receiving general anesthesia ($P = 0.008$).

Patients with Missing Data. For 33 patients, charts were available, but it was not possible to determine neurologic outcome. The patient characteristics are summarized in table 1. The excluded patients had a higher NIHSS score than the local anesthesia group ($P < 0.05$), similar to that observed in the general anesthesia group. The excluded patients had higher mean blood pressures than the general anesthesia

group ($P < 0.001$), not different from the local anesthesia-treated patients. The frequency of diabetes mellitus and the glucose values in excluded patients were less ($P = 0.001$) than in the general anesthesia group and similar to the local anesthesia group ($P = 1.0$).

We were able to assign Houston Intra-arterial Therapy scores² (see Materials and Methods) to 30/33 patients. If outcomes in the present cohort of patients were similar to previously reported,² the excluded patients would be expected to have generated 10 more patients with good outcome, nine managed with local anesthesia and one managed with general anesthesia. After inclusion of these results, the proportion of patients with good outcome in the local anesthesia group would change to 38/70 (54%) as compared with 8/53 (15%) in the patients who received general anesthesia (chi-square test result = 18.5, $P < 0.001$).

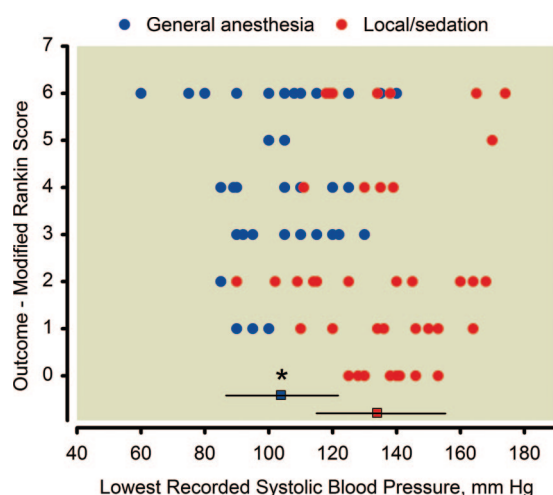


Fig. 2. Scattergram showing the modified Rankin score of individual patients according to their lowest recorded systolic blood pressure. Blue circles denote patients that received general anesthesia. Mean lowest systolic blood pressures (± 1 SD) in the general anesthesia and local anesthesia groups are denoted by the blue and red boxes, respectively. * $P < 0.05$.

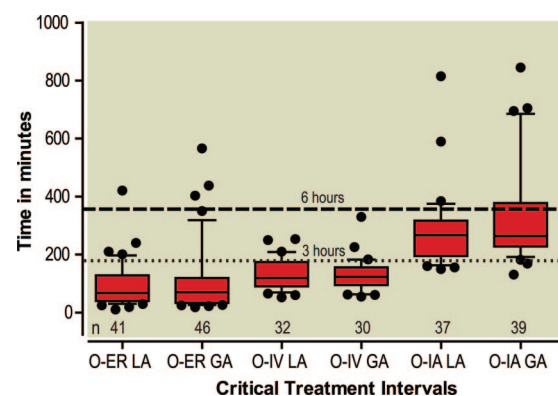


Fig. 3. Interval times for stroke (time 0) to arrival in the emergency department (O-ER), stroke to intravenous thrombolysis (O-IV), and stroke to intraarterial thrombolysis (O-IA). The data are shown as the median and 25–75 quartiles with the error bars representing the CI₉₅. Outliers are shown as individual filled circles. The time thresholds for initiation of intravenous (dotted line) and intra-arterial therapy (dashed line) are provided for reference. GA = general anesthesia; LA = local anesthesia; n = the number of patients within each treatment category at the indicated time interval.

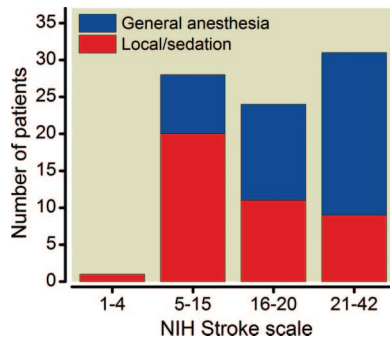


Fig. 4. Numbers of patients receiving local anesthesia/mild sedation (red bar) versus general anesthesia (blue bar) as a function of preintervention stroke severity, measured by the National Institutes of Health Stroke Score. The proportion of patients receiving general anesthesia increased with stroke severity ($P = 0.008$).

Discussion

The results show that baseline stroke severity, lowest systolic blood pressure greater than 140 mmHg, and the use of light sedation or local anesthesia are independent predictors of good neurologic outcome following endovascular treatment of acute stroke. These results must be interpreted with caution. Although we adjusted for stroke severity while evaluating the influence of blood pressure, anesthetic technique, and glucose concentration, the characterization of stroke severity by NIHSS score likely has limitations. It is possible that the NIHSS score fails to capture aspects of stroke severity that are then revealed by the contributions to poor outcome of labile blood pressure or the need for general anesthesia. In addition, NIHSS score may not capture the effects of the preintervention critical events (table 4) that were associated with poor outcome in a higher proportion of patients in the general anesthesia group. According to this hypothesis, the baseline stroke severity, if completely characterized, would be the sole predictor of the outcome of therapy. The results are also consistent with the hypothesis that hypoten-

sion induced by general anesthesia enhances the ischemic insult. In the latter model, maintenance of blood pressure until flow is restored may result in improved outcomes, potentially in all patients, not just those who require general anesthesia.

The present study has several important limitations: small size, data limitations with respect to blood pressure measurements, retrospective design, and nonstandardized anesthetic management. After an initial review of the charts, the small number of patients and nonstandardized anesthetic management lead us to conclude that information concerning the details of anesthetic management would not be meaningful, and we chose not to retrieve that data. In a prospective study with two standardized anesthetic techniques, the sample size of each group required to identify an improvement in good outcomes from 15% (present study) to 30% would be estimated to be 43 ($\alpha = 0.05$, power = 0.80) for a total of 86 patients treated with general anesthesia.

The relationship of blood pressure with clinical outcomes in patients with acute stroke is controversial. Although the most recent American Heart Association guidelines²⁴ state that “Drug-induced hypertension, outside the setting of clinical trials, is not recommended for treatment of most patients with acute ischemic stroke,” this may apply to a pharmacologically lowered blood pressure. Two studies showed that on admission, approximately 70% of stroke patients had a blood pressure greater than 170/110 mmHg,²⁵ which then declined during the first week of hospitalization.^{25,26} The relationship between systolic pressure and outcome has been reported as u-shaped or j-shaped, with systolic blood pressures outside the range of 140–180 mmHg being associated with poor outcome.²³ Blood pressure decreases during the acute phase of ischemic stroke are also associated with poor neurologic outcome.¹⁷ However, it is not known to what extent blood pressure is a “marker” for severe stroke and to what extent it is a pathophysiological “factor” in stroke outcome.

Table 4. Perioperative Critical Events

Complication	General Anesthesia		Local Anesthesia	
	No. of Patients (n = 48)	Poor Outcome	No. of Patients (n = 48)	Poor Outcome
Airway obstruction/difficult intubation/hypoxia prior to intervention	4	4	3	3
Perforation/subarachnoid hemorrhage	1	1		
Decreased level of consciousness prior to intervention	5	5		
Arrhythmia/hypotension	2	2	1	1
Pulmonary aspiration prior to intervention	4	4	1	
Intracerebral hemorrhage	1	1	2	1
Angioedema from tPA			2	
Total Patients with events	17 (35%)	17	11 (23%)	5*

* $P = 0.008$.

tPA = tissue plasminogen activator.

In previous studies the timing of the “baseline” values reported was not consistent; in one study the baseline was an average of all values recorded in the emergency department,¹⁷ and in another the baseline value was the single last value recorded before randomization.²³ These arbitrary selections represent “postevent” measurements that may deviate significantly from the patient’s true “baseline” values. In our study, because we included all patients for who outcome was available, we could not determine a way to consistently assign a “baseline” value. We therefore chose to retrieve what we thought were the most physiologically relevant values that would be available in the majority of patient charts: the highest and lowest systolic pressures. We then analyzed the data using a “good” range of 140–180 mmHg.²⁷ Since these are single measurements and are not time-weighted, our analysis may exaggerate the importance of individual readings. However, we feel that this is justified in a hypothesis-generating study. Refinements such as the use of 24 h monitoring,²⁶ weighted-average mean blood pressure,²⁸ and pulse pressure²⁸ have been used in small studies to try to improve the prognostic value of blood pressure measurements, but to our knowledge, have not gained widespread acceptance.

More relevant to anesthetic management is, “What to do if the blood pressure falls outside the range described above?”, as appears to have happened in many of the patients who received general anesthesia. The most recent systematic reviews that we could find^{27,29} reported that there was “insufficient evidence to decide whether drugs that raise or lower blood pressure should be used in the treatment of acute stroke.”²⁹ In a recent randomized clinical trial designed to examine blood pressure management in acute stroke, the hypotensive limb of the study was “terminated early because of recruitment problems.”³⁰ This study emphasizes the dilemma for the anesthesiologist: We have little or no evidence to guide our management, because few stroke patients experience significant hypotension in the absence of pharmacotherapy. If a patient, anxious and confused with new onset hemiparesis, has a blood pressure of 170 mmHg systolic that drops to 120 systolic with mild sedation, what is the effect on his or her stroke? If his or her blood pressure before the stroke was usually 130 mmHg systolic, would that make a difference with respect to the target blood pressure? Is it appropriate to take the time to apply invasive monitoring, and administer vasopressor therapy expectantly, while potentially delaying recanalization? Finally, most of these anesthetics are provided as emergencies, sometimes with little or no warning, always in “unprepared” patients. How can we best develop a team that can meet the challenges of these patient scenarios?

In particular, future studies should assess blood pressures maintained during the critical period before recanalization and reperfusion, including invasive and noninvasive systolic, diastolic, and measured mean pressures. Since the maintenance of adequate perfusion pressure is probably most important before recanalization has reestablished blood flow, the timing of hypotension may be critically important.

The small sample size means that there are few patients in each treatment category. For example, to decide whether general anesthesia is associated with harm to patients, the category that will help to answer the question is the group of patients that is expected to have a good outcome (low NIHSS) and is assigned to receive a general anesthetic. In our study the size of this group was only 34 patients, and therefore only 30–60% (10–20 patients) in this category can be predicted to have a good outcome. These considerations provide a partial explanation for the inability of the analysis to distinguish between selection to receive general anesthesia and the major confounder, periprocedural hypotension.

In this cohort of patients the main predictor of neurologic outcome, the baseline stroke severity, was worse in patients who received general anesthesia (fig. 2). This finding is not surprising, given that the usual practice in our institution during the study period was to proceed with endovascular therapy under local anesthesia unless there were specific indications for general anesthesia. In this cohort of patients, the provision of general anesthesia did not appear to be associated with a delay of therapy.

In conclusion, our retrospective review has replicated previous reports that patients managed with general anesthesia, and its concomitant relative systolic hypotension, during endovascular therapy for acute ischemic stroke have a much lower likelihood of good neurologic outcome, compared to patients managed with local anesthesia. Since avoidance of general anesthesia is not always possible, prospective studies of patient in this high risk group will be important to guide our management.

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Appendix 1. Pearson Product Moment Correlation Coefficient Matrix

	General Anesthesia	Minimum SBP	Minimum DBP	Age	A.Fib.	CAD	Diabetes	Glucose
General Anesthesia	1.0	−0.66*	−0.70*	0.04	−0.07	0.21	0.30	0.20
Min. SBP		1.0	0.76*	−0.00	−0.06	−0.081	−0.13	−0.143
Min. DBP			1.0	−0.28	−0.09	−0.19	−0.23	−0.26
Age				1.0	0.312	0.134	0.06	0.19
A.Fib.					1.0	0.23	0.04	0.20
CAD						1.0	0.33	0.327
Diabetes							1.0	0.52*
Glucose, mm								1.0

* $P < 0.001$ following Bonferroni correction for multiple comparisons.

A.Fib. = atrial fibrillation; CAD = coronary artery disease; DBP = diastolic blood pressure; SBP = systolic blood pressure.

ANESTHESIOLOGY REFLECTIONS

Lucien Morris: “Put the Kettle On!”



After clinically pioneering his iconic “Copper Kettle” in Wisconsin in the spring of 1948 as one of Professor Ralph Waters’ residents, Dr. Lucien Morris (*left*, 1914–2011) would eventually report on “A New Vaporizer for Anesthetic Agents” in the November 1952 issue of *ANESTHESIOLOGY*. Dr. Morris would teach anesthesiology and the virtues of “the world’s first precision vaporizer” from academic professorships in Iowa City, Seattle, Toronto, and Toledo. A towering intellectual, he insisted that I call him Lucien but also that I understand that his prototype machine’s copper table top (*lower right*) was critical for proper “transfer of heat ... to the liquid to be vaporized.” When I proudly escorted the irascible professor past one of the copper vaporizing cylinders that I had removed (for display purposes) from one of his machines, Lucien wryly observed, “Why, George, you have amputated my Copper Kettle!” (Copyright © the American Society of Anesthesiologists, Inc. This image also appears in the *Anesthesiology Reflections* online collection available at www.anesthesiology.org.)

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