Original Contribution

Anesthesia-Related Outcomes for Endovascular Stroke Revascularization

A Systematic Review and Meta-Analysis

Waleed Brinjikji, MD; Jeffrey Pasternak, MD; Mohammad H. Murad, MD;
Harry J. Cloft, MD, PhD; Tasha L. Welch, MD; David F. Kallmes, MD; Alejandro A. Rabinstein, MD

Background and Purpose—There is currently controversy on the ideal anesthesia strategy during mechanical thrombectomy for acute ischemic stroke. We performed a systematic review and meta-analysis of studies comparing clinical and angiographic outcomes of patients undergoing general anesthesia (GA group) and those receiving either local anesthesia or conscious sedation (non-GA group).

Methods—A literature search on anesthesia and endovascular treatment of acute ischemic stroke was performed. Using random-effects meta-analysis, we evaluated the following outcomes: recanalization rate, good functional outcome at 90 days (modified Rankin Score≤2), symptomatic intracranial hemorrhage, death, vascular complications, respiratory complications, procedure time, and time to groin puncture.

Results—Twenty-two studies (3 randomized controlled trials and 19 observational studies), including 4716 patients (1819 GA and 2897 non-GA) were included. In the nonadjusted analysis, patients in the GA group had higher odds of death (odds ratio [OR], 2.02; 95% confidence interval [CI], 1.66–2.45) and respiratory complications (OR, 1.70; 95% CI, 1.22–2.37) and lower odds of good functional outcome (OR, 0.58; 95% CI, 0.48–0.64) compared with the non-GA group. There was no difference in procedure time between the 2 primary comparison groups. When adjusting for baseline National Institutes of Health Stroke Scale, GA was still associated with lower odds of good functional outcome (OR, 0.59; 95% CI, 0.29–0.94). When considering studies performed in the stent-retriever/aspiration era, there was no significant difference in good neurological outcome rates (OR, 0.84; 95% CI, 0.67–1.06).

Conclusions—Acute ischemic stroke patients undergoing intra-arterial therapy may have worse outcomes when treated with GA as compared with conscious sedation/local anesthesia. However, major limitations of current evidence (ie, retrospective studies and selection bias) indicate a need for adequately powered, multicenter randomized controlled trials to answer this question. **(*Stroke*. 2017;48:00-00. DOI: 10.1161/STROKEAHA.117.017786.)**

Key Words: anesthesia, local ■ confidence intervals ■ humans ■ retrospective studies ■ stroke

Mechanical thrombectomy for treatment of acute ischemic stroke secondary to large vessel occlusion is now standard of care.[1–6] Despite the sizeable treatment effect demonstrated by recently published trials, a substantial proportion of patients do not experience good neurological outcomes, despite successful timely recanalization. Several studies suggest that the choice of anesthetic management during the endovascular recanalization procedure may have a substantial effect on patient outcomes.[7–25] During the past several years, retrospective observational studies have suggested that endotracheal intubation or general anesthesia (GA) is associated with poorer outcomes when compared with conscious sedation (CS)/local anesthesia.[9,10,12,15,26] However, in contrast, recently published randomized controlled trials shows no difference in successful recanalization or neurological outcome.[8] Because of the continuing debate on anesthesia management during intra-arterial treatment of acute ischemic stroke, we performed a meta-analysis of studies comparing outcomes of stroke patients receiving GA and CS/local anesthesia during the procedure.

Methods

Literature Search

To identify comparative studies on GA versus CS during endovascular treatment of acute ischemic stroke, 3 databases were searched from their inception to December 2016: Ovid MEDLINE, Ovid EMBASE, and the Web of Science. The initial search terms were conscious sedation, general anesthesia, and intracranial embolism, and thrombosis or stroke. This was combined with treatment techniques: endovascular, fibrinolytic agents, thromboembolism, catheter, transcatheter, thrombolysis, fibrinolysis, recanalization, embolectomy, or thrombectomy. We also searched references from multiple articles to find any additional studies on anesthesia and outcomes of endovascular treatment of acute ischemic stroke not found in the initial literature search and contacted experts in

Received April 27, 2017; final revision received August 8, 2017; accepted August 11, 2017.

From the Department of Radiology (W.B., H.J.C., D.F.K.), Department of Neurosurgery (W.B., D.F.K.), Department of Anesthesia (J.P., T.L.W.), Division of Preventive Medicine (M.H.M.), Knowledge and Evaluation Research Unit (M.H.M.), and Department of Neurology (A.A.R.), Mayo Clinic, Rochester, MN.

Correspondence to Waleed Brinjikji, MD, Department of Radiology, Mayo Clinic, 200 1st St, SW Rochester, MN 55905. E-mail brinjikji.waleed@mayo.edu

Stroke is available at http://stroke.ahajournals.org DOI: 10.1161/STROKEAHA.117.017786

the field for any additional studies that provided data on anesthesia type and outcomes of stroke intervention. Randomized controlled trials and observational studies were included.

Identified studies from the literature search were then further evaluated for inclusion in the meta-analysis. Inclusion criteria were (1) studies comparing outcomes of 2 groups: GA and CS/local anesthesia and (2) studies reporting separate angiographic or clinical outcomes for GA and CS groups. Exclusion criteria were the following: (1) case reports, (2) studies not separating outcomes by anesthesia type, and (3) noncomparative studies (ie, studies with only 1 group—GA or CS).

Risk of Bias Assessment

Risk of bias assessment of the studies was performed using a modified Newcastle Ottawa scale. This is a tool used for assessing the quality of nonrandomized studies included in systematic reviews and meta-analyses. Each study is judged on 8 items categorized into 3 groups: (1) selection of the study groups, (2) comparability of the study groups, and (3) ascertainment of the outcome of interest.[27] For our topic of interest, the factors that would make a study have low risk of bias include (1) well-defined selection criteria, (2) similar baseline National Institutes of Health Stroke Scale (NIHSS), occlusion location, and treatment paradigms between groups, (3) independent assessment of neurological and angiographic outcomes, and (4) contemporaneous use of GA and CS (ie, studies spanning many years that had high proportions of patients receiving GA in the first time period and high proportions of CS in the latter time period would be considered to have a high risk of bias).

Outcome Variables

For the purposes of this study, patients were divided into 2 groups: (1) GA (GA) and (2) non-GA. In general, patients were considered to have undergone GA if they were intubated at the start of the procedure and were anesthetized using either intravenous or inhaled agents or if they were intubated for any reason before the thrombectomy. Patients were considered part of the non-GA group if they were not intubated at the start of the procedure and were treated under monitored anesthesia care or local anesthesia. Good functional outcome, defined as a modified Rankin Scale (mRS) score of ≤2 at 90 days after endovascular treatment, was the primary end point of this study.[28] Other studied outcomes included 90-day mortality, successful recanalization/angiographic outcome (Thrombolysis in Myocardial Infarction [TIMI] ≥2 or Thrombolysis in Cerebral Infarction [TICI] 2b/3), symptomatic intracranial hemorrhage (ICH), other vascular complications, including dissections and vessel perforations, respiratory complications, including respiratory failure and pneumonia, procedure time, and time to groin puncture.

Statistical Analysis

From each study, we extracted a 2×2 table for binary outcomes and the mean group sample size and a measure of variability for continuous outcomes. Random-effects meta-analysis is used for pooling across studies.[29] The I^2 statistic was used to express the proportion of heterogeneity that is not attributable to chance.[30] Meta-analysis results were expressed as odds ratio (OR) for binary outcomes and weighted mean difference for continuous outcomes with respective 95% confidence intervals (CIs). When assessing continuous outcomes, some studies reported mean values with corresponding standard deviations (SDs), whereas others reported median values with interquartile ranges. If a median and interquartile range were reported, these were converted to a mean and SD based on the assumption of a lognormal distribution of the original measure. We explored the impact of publication bias by constructing funnel plots and testing their symmetry if a sufficient number of studies (>20) was available.

Because, with the exception of 3 studies, the study subjects were not randomized by anesthesia type, we were concerned about lack of similarity between the 2 study groups (ie, patients with worse prognosis receiving 1 of the 2 interventions). Therefore, we conducted meta-regression in which the dependent outcome was the effect size (log of the OR of the primary outcome, the odds of good neurological outcome), and the explanatory variables (independent variables) were initial stroke severity categorized by the baseline average National Institutes of Health Stroke Scale (NIHSS) score and the type of anesthesia (GA versus CS). Studies were weighted in meta-regression using their precision. The results of the meta-regression were presented as an OR adjusted for NIHSS score. Outcomes studied in the meta-regression included good neurological outcome, death, and symptomatic ICH. Because of the small number of studies that had baseline NIHSS, the models of the other meta-regressions were not stable and are not reported. We also performed a sensitivity analysis examining the comparative outcomes including only those studies which used modern mechanical thrombectomy technologies (ie, stent-retrievers and direct thromboaspiration). Studies which relied heavily on intra-arterial tPA (tissue-type plasminogen activator), Merci device or did not specify the type of mechanical thrombectomy technology used were excluded from this sensitivity analysis. We also performed a sensitivity analysis by studying outcomes of the randomized controlled trials (RCTs) only. Meta-analysis and meta-regression were conducted using STATA, version 14 (StataCorp LP, College Station, TX).

Results

Literature Search

A total of 358 articles were found on the initial literature search. Of these, 302 were excluded after reading the abstracts alone because they were not found to be relevant to our study. Of the remaining 56 articles, 13 were excluded because they were conference abstracts, 1 was excluded because of overlapping patient populations, 10 were excluded because they were review articles or editorials, and 15 were excluded for not including information relevant to our study making for a total of 17 studies. One additional study was found when hand searching the contents of review articles, and 4 additional studies were identified by contacting experts in the field. In total, 22 articles with 4716 patients (1819 GA and 2897 non-GA) were included in this study.[7–25,31,32] Three studies randomized patients to GA or CS. All 3 randomized controlled trials were single-center studies performed in the modern stent-retriever era and heavily emphasized control of blood pressure in both GA and CS groups. Ten studies had low risk of bias, 6 studies had moderate risk of bias, and 6 studies had high risk of bias. The largest study cohort had 1079 patients (428 GA and 651 non-GA).

Eighteen of the 22 articles reported mean age in the treatment groups (2 RCTs and 16 non-RCTs). None of these studies demonstrated a statistically significant difference in mean age between groups. Among patients in the GA group, median age was 65.5 years (range, 57–78). Among patients in the non-GA group, median age was 67 years (range, 62–73). Of the 17 studies which reported sex distribution between groups, 1 had a significantly higher proportion of women in the GA group, whereas the others had no difference. None of these studies were the RCTs. The proportion of women was 48.5% in the GA group and 49.0% in the non-GA group. Of the 20 studies that reported occlusion location, all 3 of the RCTs included anterior circulation strokes only. Of the remaining 17 studies, 8 had a higher proportion of posterior circulation strokes than anterior circulation strokes. Hypertension was found in 68.4% of patients in the GA group and 63.6% in the non-GA group. In the GA group, 28.3% of patients were smokers compared with 26.2% for non-GA patients. In the GA group 24.9% had CAD compared with 21.9% of patients in the non-GA group. Summary of included studies is provided in Table 1. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram is provided in Figure 1.

Table 1. Studies Included in Meta-Analysis

Author, Journal, y	No. of GA/ Non-GA Patients	No. of GA/ Non-GA Anterior Circulation Patients	Mean Age of GA/ Non-GA Patients*	No. of HTN GA/ Non-GA Patients*	No. of Smoking GA/ Non-GA Patients*	No. of CAD GA/ Non-GA Patients*	%Female GA/ %Non-GA*	No. Converted from CS to GA	Type of Endovascular Treatment	Study Design	Study Risk of Bias
Abou-Chebl et al[18]; *Stroke*, 2014	196/85	170/82	66/69	148/74	59/28	56/29	48.5/48.2	NA	Solitaire stent-retriever	Post hoc analysis of NASA registry, case–control	M
John et al[17]; *Cerebrovasc Dis*, 2014	91/99	91/99	65/69	NA	NA	NA	59.3/53.5	1/99 (1.0%)	Not specified	Retrospective, single center, case–control	M
Davis et al[21]; *Anesthesiology*, 2012	48/48	29/39	63/62	23/22	17/10	13/5	42.0/19.0	NA	IA tPA and mechanical thrombectomy	Retrospective, single center, case–control	M
Hassan et al[20]; *Neurocrit Care*, 2012	53/83	NA	68/66	36/49	8/10	9/12	49.1/44.6	NA	Endovascular technique not specified	Retrospective, single center, case–control	H
Jumaa et al[24]; *Stroke*, 2010	53/73	53/73	66/67	NA	NA	NA	58.0/53.0	2/73 (2.7%)	IA tPA, Merci, other mechanical	Retrospective, single center, case–control	M
Langner et al[19]; *Rofo*, 2013	19/105	7/87	NA	NA	NA	NA	NA	3/108 (2.8%)	Phenox, penumbra, IA tPA	Retrospective, single center, case–control	H
Li et al[16]; *J Neurosurg Anesthesiol*, 2013	35/74	28/71	62/68	24/55	NA	10/28	40.0/57.0	NA	Merci, penumbra, IA tPA	Retrospective, single center, case–control	H
Nichols et al[23]; *J Neurointerv Surg*, 2010	26/49	26/49	64/64	NA	NA	NA	46.0/39.0	NA	IA tPA, low energy ultrasound	Post hoc analysis of IMS II trial	H
van den Berg[13]; *Stroke*, 2015	70/278	70/278	57/62	37/130	NA	16/43	50.0/56.4	10/278 (3.6%)	Not specified	Post hoc analysis of pretrial cohort of MR CLEAN	L
Schönenberger et al[8]; *JAMA*, 2016	73/77	73/77	72/71	53/54	9/13	NA	34.2/45.5	11/77 (14.3%)	Stent-retriever or aspiration	Randomized controlled trial	L
Janssen et al[10]; *Cardiovasc Interv Radiol*, 2016	53/31	53/31	68/73	38/26	13/8	NA	53.0/58.0	0/31 (0%)	Stent-retriever	Retrospective, single center, case–control	M
Jagani et al[11]; *J Neurointerv Surg*, 2016	38/61	25/60	63/68	29/46	20/26	8/19	45.0/49.0	1/62 (1.6%)	Penumbra, solitaire, Merci	Retrospective, single center, case–control	H
Berkhemer[12]; *Neurology*, 2016	79/137	79/137	63/66	NA	NA	NA	40.5/42.3	6/137 (4.4%)	Stent-retriever	Post hoc analysis of MR CLEAN	L
Just[9]; *Can J Neurolog, Sci*, 2016	42/67	NA	60/63	24/37	25/27	NA	40.0/37.0	1/68 (1.5%)	Not specified	Retrospective, single center, case–control	H
Mundiyanapurath et al[14]; *J Stroke Cerebrovasc Dis*, 2015	29/15	23/13	73/67	NA	NA	NA	55.0/60.0	2/17 (11.8%)	Not specified	Prospective, single center, case–control	L
Abou-Chebl et al[15]; *Stroke*, 2015	147/269	142/263	69/69	108/196	NA	NA	49.0/49.4	NA	EKOS, Merci, penumbra	Post hoc analysis IMS III trial	L
Sugg et al[22]; *AJNR Am J Neuroradiol*, 2010	9/57	8/57	78/66	NA	NA	NA	NA	NA	IA tPA, Merci	Retrospective, single center, case–control	H
Abou-Chebl et al[25]; *Stroke*, 2010	426/554	426/554	NA	NA	NA	NA	NA	NA	IA tPA, Merci, penumbra, stent	Retrospective, multicenter, case–control	L

(*Coantinued*)

Table 1. Continued

Author, Journal, y	No. of GA/ Non-GA Patients	No. of GA/ Non-GA Anterior Circulation Patients	Mean Age of GA/ Non-GA Patients*	No. of HTN GA/ Non-GA Patients*	No. of Smoking GA/ Non-GA Patients*	No. of CAD GA/ Non-GA Patients*	%Female GA/ %Non-GA*	No. Converted from CS to GA	Type of Endovascular Treatment	Study Design	Study Risk of Bias
Bracard et al[31]; *Lancet Neurology*, 2017	67/74	67/74	NA	NA	NA	NA	NA	NA	Stent-retriever	Post hoc analysis of THRACE trial	L
HERMES, ISC, 2017	153/456	153/456	65/67	NA	NA	NA	45.1/48.5	NA	Stent-retriever	Post hoc analysis of 2015 trials	L
Löwhagen Hendén et al[32]; *Stroke*, 2017*	45/45	45/45	73/72	27/22	4/8	9/5	58.0/51.0	7/45 (15.6%)	Stent-retriever and aspiration	Randomized controlled trial	L
GOLIATH, ESOC, 2017*	65/63	65/63	NA	NA	NA	NA	NA	NA	Stent-retriever and aspiration	Randomized controlled trial	L

CAD indicates coronary artery disease; CS, conscious sedation; ESOC, European Stroke Organisation Conference; GA, general anesthesia; GOLIATH, General or Local Anesthesia in Intra Arterial Therapy; H, high; HERMES, Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials; HTN, hypertension; IMS III, Interventional Management of Stroke; ISC, International Stroke Conference; L, low; M, moderate; MR CLEAN, Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; NA, not available; NASA, North American SOLITAIRE Stent-Retriever Acute Stroke Registry; THRACE, Trial and Cost Effectiveness Evaluation of Intra-Arterial Thrombectomy in Acute Ischemic Stroke; and tPA, tissue-type plasminogen activator.

Outcomes

GA was associated with a statistically significant lower odds of favorable functional outcome (ie, mRS≤2) when compared with CS (OR, 0.58; 95% confidence interval [CI], 0.48–0.64; Figure 2). GA patients had statistically significant higher odds of 90-day mortality (OR, 2.02; 95% CI, 1.66–2.45), vascular complications (OR, 1.43; 95% CI, 1.01–2.03), and respiratory complications (OR, 1.70; 95% CI, 1.22–2.37). There was no statistically significant difference in recanalization rates (OR, 1.04; 95% CI, 0.83–1.31) between groups. These findings are summarized in Table 2.

Time to groin puncture was statistically significant longer in the GA group compared with the non-GA group (weighted mean difference, 14.18 minutes; 95% CI, 9.47–18.89). Procedure time was statistically significant shorter in the GA group compared with the non-GA group (weighted mean difference, −4.63; 95% CI, −8.76 to −0.51). Among patients who initially were treated with non-GA, 2.8% (44/1557) were converted to GA.

Study Heterogeneity

I^2 values were <50% for the following outcomes: death at 90 days (I^2=45%), respiratory complications (I^2=11%), symptomatic ICH (I^2=0%), recanalization success (I^2=47%), and vascular complications (I^2=0%). I^2 values were >50% (indicating moderate or substantial heterogeneity) for the following outcomes: mRS ≤2 at 90 days (I^2=71%), time to groin puncture (I^2=64%), and procedure time (I^2=73%).

Meta-Regression and Publication Bias

Adjusting for NIHSS score using meta-regression for the main outcome (odds of having good functional outcomes) yielded an OR of 0.59 (95% CI, 0.29–0.94) for GA. There

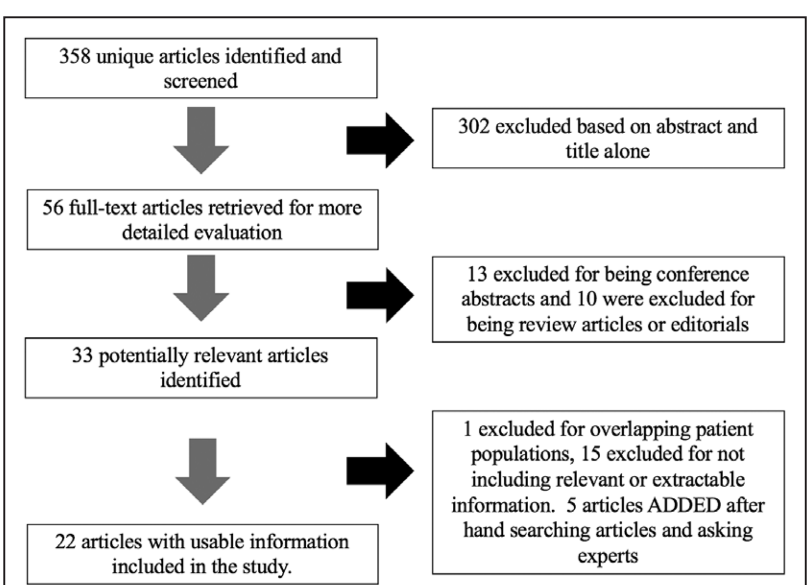

Figure 1. Literature search flowchart.

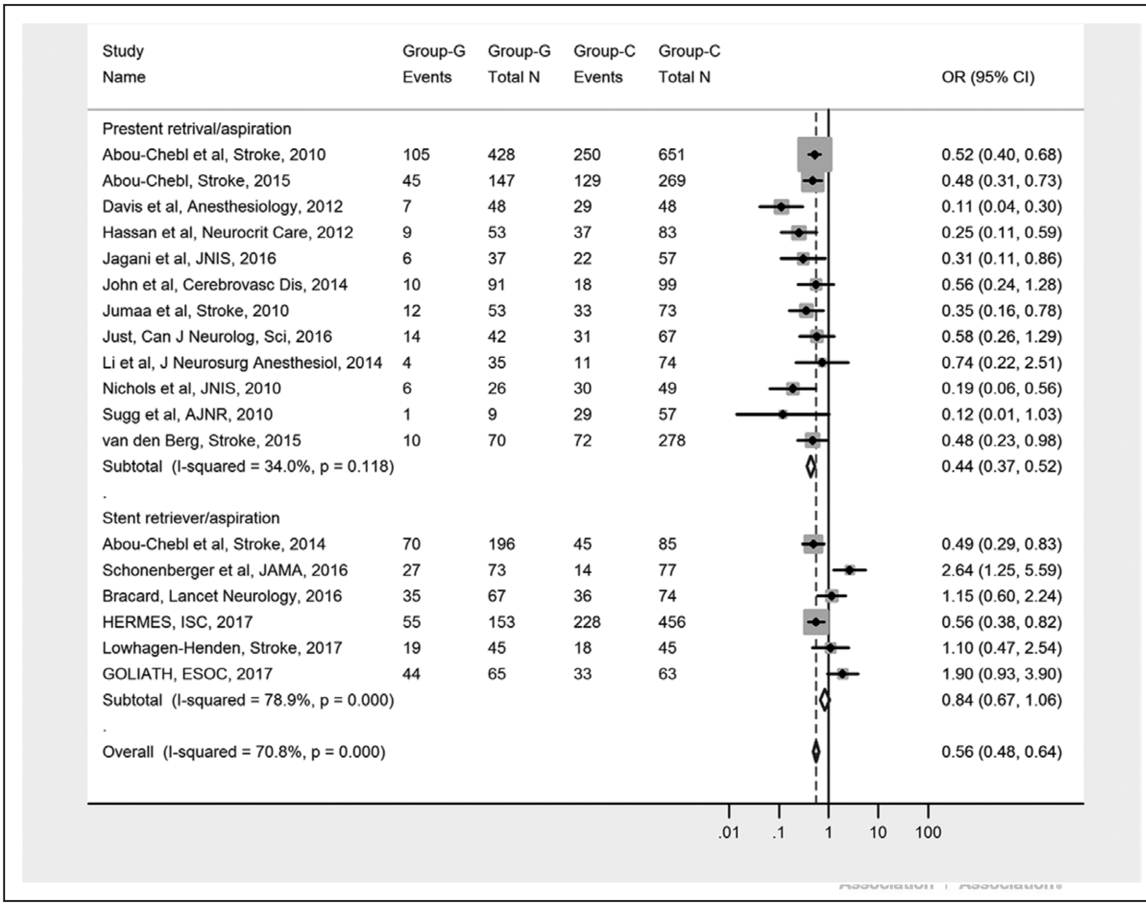

Figure 2. Forest plot of meta-analysis results for good functional outcome (mRS≤2).

was a statistically significant odds of mortality for GA as well (OR, 1.80; 95% CI, 1.23–2.68). There was a nonstatistically significant difference in rates of symptomatic ICH between groups (OR, 1.43; 95% CI, 0.85–2.39). Funnel plot did not suggest publication bias (Figure 3). Statistical evaluation of publication bias showed a *P* value of 0.73.

Sensitivity Analysis

We performed a sensitivity analysis to determine whether anesthesia-related outcomes were different in the prestentriever/aspiration thrombectomy era compared with the modern, stentriever/aspiration thrombectomy era. In the prestentriever era, 12 studies were included, and GA was associated with statistically significant lower rates of good functional outcome compared with non-GA (OR, 0.44; 95% CI, 0.37–0.52).

Table 2. Meta-Analysis Results: Categorical Outcomes

	OR; GA vs Non-GA	95% CI
Death at 3 mo	2.02	1.66–2.45
Modified Rankin Scale score ≤2 at 90 d	0.58	0.48–0.64
Successful recanalization	1.04	0.83–1.31
sICH	1.31	1.01–1.70
Other vascular complications	1.43	1.01–2.03
Respiratory complications	1.70	1.22–2.37

CI indicates confidence interval; GA, general anesthesia; OR, odds ratio; and sICH, symptomatic intracranial hemorrhage.

*Modified Rankin Scale score ≤2 at 90 days.

Only 7 studies have been published to date, including only patients who received stentriever/aspiration thrombectomy. In the modern, stent-retriever/aspiration era, there was a nonstatistically significant lower odds of good neurological outcome for patients receiving GA (OR, 0.84; 95% CI, 0.67–1.06). Prestent-retriever era 90-day mortality was significantly higher in the GA group (OR, 2.69; 95% CI, 2.11–3.45). In the poststent-retriever era, 90-day mortality rates were similar (OR, 1.27; 95% CI, 0.93–1.75).

On performing sensitivity analysis of outcomes including only the RCTs, we found that GA was associated with a statistically significant higher odds of good neurological outcome at 90 days (OR, 1.83; 95% CI, 1.18–2.84).

Discussion

Our meta-analysis shows that patients who received GA had lower rates of good functional outcome and higher rates of mortality and respiratory complications when compared with non-GA patients. In contrast, no difference in recanalization rates or vascular complications were found. Procedure times were faster in the GA group. After adjustment for baseline NIHSS score, GA remained associated with lower odds of good functional outcome. In our sensitivity analysis of studies

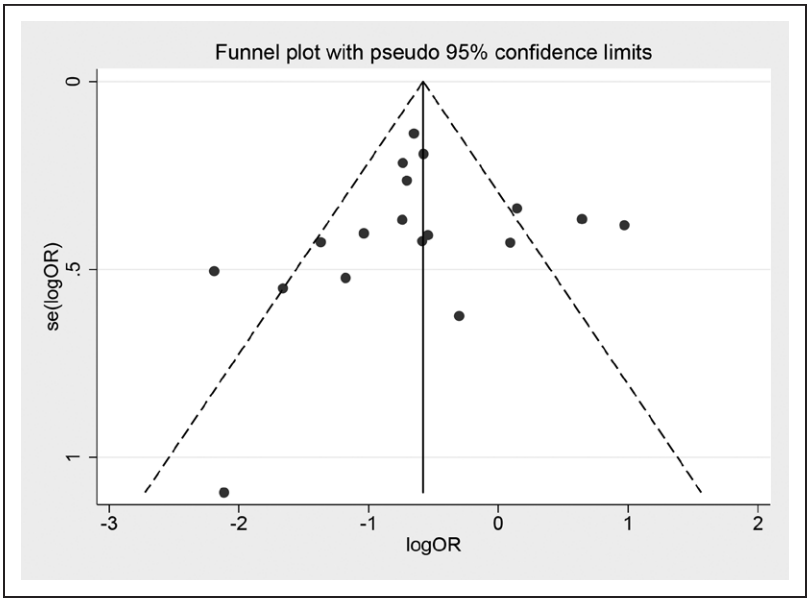

Figure 3. Funnel plot for publication bias.

using modern reperfusion technologies, the use of GA was associated with a nonstatistically significant lower rate of good neurological outcomes. When including the 3 RCTs on this topic, GA was associated with higher rates of good neurological outcome.

Many studies have speculated as to why GA may be associated with poorer neurological outcomes after endovascular treatment for acute ischemic stroke. Delay of treatment is one of the main factors commonly discussed. For example, in the GA versus non-GA subgroup analysis of the MR CLEAN trial, Berkhemer et al[12] reported that door-to-groin puncture times were ≈30 minutes longer in the GA group than in the non-GA group. In our meta-analysis, door-to-groin puncture times were ≈16 minutes longer for the GA group than the non-GA group. Composite data from 5 recently published randomized controlled trials suggest that each hour of delay in door-to-puncture times is associated with a 19% reduction in the likelihood of regaining functional independence.[33] Therefore, it is mechanistically reasonable to hypothesize that the greater time required to induce GA may confer a disadvantage.

Attention has also been paid to the hemodynamic effects of GA and CS during endovascular stroke therapy. Several studies indicate that a pharmacologically induced decrease in blood pressure exceeding 20 to 30 mm Hg in the acute phase of stroke is associated with less favorable outcomes.[34,35] Similarly, in the setting of endovascular stroke therapy, some studies have shown that poor outcome is associated with lower intraoperative blood pressures.[21,36,37] In most studies comparing intraoperative blood pressure between GA and CS during thrombectomy, blood pressure is less with GA.[11,36,37] Therefore, it is mechanistically reasonable to hypothesize that, to the extent that GA increases the likelihood of intraprocedure hypotension, it may confer a disadvantage. Consistent with this hypothesis, in a retrospective study in which intraprocedure blood pressure did not differ between GA (n=91) and CS patients (n=99), 3-month functional status did not significantly differ between groups (adjusted OR [good outcome with CS], 1.57; 95% CI, 0.61–4.02; *P*=0.35).[17]

The principal argument favoring GA is reduced procedure time and improved recanalization rates.[38] For example, in the SIESTA trial, patients undergoing GA had a 10% higher recanalization rate than non-GA patients and had significantly shorter procedure times.[8] Patient movement has also been cited as a potential pitfall of non-GA.[39] Patient movement during the procedure can lead to wire perforation resulting in ICH or dissection. However, our meta-analysis found no difference in vascular complication rates between the GA and non-GA groups. Avoiding emergent endotracheal intubation can also be an advantage of GA compared with CS because this can result in aspiration, airway trauma, and even death.[40–42] Yet, the rate of conversion from non-GA to GA in our study was low (≈3%).

Three randomized trials comparing GA to non-GA have been reported to date. In all studies, baseline NIHSS, occlusion location, demographic characteristics, and various cardiovascular risk factors were similar between groups. Two of these trials demonstrated no difference in the primary outcome (mRS 0–2 at 90 days and NIHSS at 24 hours) between groups, and 2 trials found that GA patients had significantly higher rates of good neurological outcome at 90 days when compared with non-GA patients.[8] However, some limitations of these trials should be considered. First, patients treated in these trials underwent their procedural anesthesia management under the guidance of a highly specialized anesthesia/neurocritical care team with less than a 10-minute delay in puncture time and an exceedingly low rate of procedural hypotension. This limits the generalizability of these studies because many centers (1) do not have anesthesiologists readily available for stroke interventions and (2) do not provide subspecialty anesthetic care for acute ischemic stroke. Furthermore, non-neurological specialists may not be attuned to the delicate needs of blood pressure management and the fast-paced atmosphere of a stroke intervention. Second, there was a high rate of conversion to GA in the non-GA group in both SIESTA (Sedation Versus Intubation for Endovascular Stroke Treatment) and ANSTROKE (Anesthesia During Stroke) (14.2% and 15.6%, respectively). This is substantially higher than the overall rate of 2.8% seen in our meta-analysis. Such a high rate of conversion could result in additional delays in care and potential complications from emergent endotracheal intubation, thus, causing worse outcomes in the CS group on intention to treat analysis. Lastly, because these were all single-center studies, there is a risk of bias given the potential that local practitioners may have been used to perform these procedures primarily under GA before the start of the RCT. Ultimately, larger, multi-institutional RCTs will be needed to further determine the ideal anesthetic management strategy for acute ischemic stroke and improve generalizability.

Limitations

This study has several limitations. Only one of the available studies was randomized by anesthesia type, and that study had a result that contradicted the findings of our meta-analysis. In general, average baseline NIHSS scores were higher for patients receiving GA than those receiving CS. Worse initial stroke severity could contribute to the higher rates of post-treatment morbidity and mortality seen in the GA group. Although we did find a difference when adjusting for baseline NIHSS scores, baseline NIHSS is not a perfect measure in predicting how a patient will fare with various anesthetic techniques. Thus, we were unable to adjust for other important baseline characteristics. The higher baseline NIHSS scores also suggest the possibility of selection bias (ie, more severe strokes may have been more likely to receive GA or be intubated before the procedure because of an inability to preserve airway patency).

Most studies did not stratify outcomes in the GA and non-GA groups based on stroke location (anterior/posterior circulation) or initial ASPECT score (Alberta Stroke Program Early CT Score). In fact, there was a higher rate of anterior circulation occlusions in the non-GA group than in the GA group. It is important to note that the studies from the modern era all including anterior circulation patients only, and there was a significant difference in good neurological outcome rates on this analysis. Most of the studies in this meta-analysis were published in the prestentriever/suction thrombectomy era which limits the applicability of these findings to the modern era of stroke intervention.

Conclusions

This systematic review and meta-analysis of 22 studies and >4500 patients found that acute stroke patients receiving GA had significantly higher rates of morbidity and mortality compared with non-GA patients. However, these findings are based primarily on studies that did not randomize patients by anesthesia type. Additional randomized controlled trials are needed to determine whether there are any differences in outcomes in patients receiving GA versus non-GA.

Disclosures

None.

References

1. Mocco J, Zaidat OO, von Kummer R, Yoo AJ, Gupta R, Lopes D, et al; THERAPY Trial Investigators*. Aspiration thrombectomy after intravenous alteplase versus intravenous alteplase alone. *Stroke*. 2016;47:2331–2338. doi: 10.1161/STROKEAHA.116.013372.
2. Saver JL, Goyal M, Bonafe A, Diener HC, Levy EI, Pereira VM, et al; SWIFT PRIME Investigators. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med*. 2015;372:2285–2295. doi: 10.1056/NEJMoa1415061.
3. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, et al; REVASCAT Trial Investigators. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med*. 2015;372:2296–2306. doi: 10.1056/NEJMoa1503780.
4. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, et al; ESCAPE Trial Investigators. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med*. 2015;372:1019–1030. doi: 10.1056/NEJMoa1414905.
5. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al; EXTEND-IA Investigators. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. 2015;372:1009–1018. doi: 10.1056/NEJMoa1414792.
6. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al; MR CLEAN Investigators. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. 2015;372:11–20. doi: 10.1056/NEJMoa1411587.
7. Sivasankar C, Stiefel M, Miano TA, Kositratna G, Yandrawatthana S, Hurst R, et al. Anesthetic variation and potential impact of anesthetics used during endovascular management of acute ischemic stroke. *J Neurointerv Surg*. 2016;8:1101–1106. doi: 10.1136/neurintsurg-2015-011998.
8. Schönenberger S, Uhlmann L, Hacke W, Schieber S, Mundiyanapurath S, Purrucker JC, et al. Effect of conscious sedation vs general anesthesia on early neurological improvement among patients with ischemic stroke undergoing endovascular thrombectomy: a randomized clinical trial. *JAMA*. 2016;316:1986–1996. doi: 10.1001/jama.2016.16623.
9. Just C, Rizek P, Tryphonopoulos P, Pelz D, Arango M. Outcomes of general anesthesia and conscious sedation in endovascular treatment for stroke. *Can J Neurol Sci*. 2016;43:655–658. doi: 10.1017/cjn.2016.256.
10. Janssen H, Buchholz G, Killer M, Ertl L, Brückmann H, Lutz J. General anesthesia versus conscious sedation in acute stroke treatment: the importance of head immobilization. *Cardiovasc Intervent Radiol*. 2016;39:1239–1244. doi: 10.1007/s00270-016-1411-5.
11. Jagani M, Brinjikji W, Rabinstein AA, Pasternak JJ, Kallmes DF. Hemodynamics during anesthesia for intra-arterial therapy of acute ischemic stroke. *J Neurointerv Surg*. 2016;8:883–888. doi: 10.1136/neurintsurg-2015-011867.
12. Berkhemer OA, van den Berg LA, Fransen PS, Beumer D, Yoo AJ, Lingsma HF, et al; MR CLEAN Investigators. The effect of anesthetic management during intra-arterial therapy for acute stroke in MR CLEAN. *Neurology*. 2016;87:656–664. doi: 10.1212/WNL.0000000000002976.
13. van den Berg LA, Koelman DL, Berkhemer OA, Rozeman AD, Fransen PS, Beumer D, et al; MR CLEAN Pretrial Study Group; Participating Centers. Type of anesthesia and differences in clinical outcome after intra-arterial treatment for ischemic stroke. *Stroke*. 2015;46:1257–1262. doi: 10.1161/STROKEAHA.115.008699.
14. Mundiyanapurath S, Schönenberger S, Rosales ML, Carrilho Romeiro AM, Möhlenbruch M, Bendszus M, et al. Circulatory and respiratory parameters during acute endovascular stroke therapy in conscious sedation or general anesthesia. *J Stroke Cerebrovasc Dis*. 2015;24:1244–1249. doi: 10.1016/j.jstrokecerebrovasdis.2015.01.025.
15. Abou-Chebl A, Yeatts SD, Yan B, Cockroft K, Goyal M, Jovin T, et al. Impact of general anesthesia on safety and outcomes in the endovascular arm of interventional management of stroke (IMS) III trial. *Stroke*. 2015;46:2142–2148. doi: 10.1161/STROKEAHA.115.008761.
16. Li F, Deshaies EM, Singla A, Villwock MR, Melnyk V, Gorji R, et al. Impact of anesthesia on mortality during endovascular clot removal for acute ischemic stroke. *J Neurosurg Anesthesiol*. 2014;26:286–290. doi: 10.1097/ANA.0000000000000031.
17. John S, Thebo U, Gomes J, Saqqur M, Farag E, Xu J, et al. Intra-arterial therapy for acute ischemic stroke under general anesthesia versus monitored anesthesia care. *Cerebrovasc Dis*. 2014;38:262–267. doi: 10.1159/000368216.
18. Abou-Chebl A, Zaidat OO, Castonguay AC, Gupta R, Sun CH, Martin CO, et al. North American SOLITAIRE stent-retriever acute stroke registry: choice of anesthesia and outcomes. *Stroke*. 2014;45:1396–1401. doi: 10.1161/STROKEAHA.113.003698.
19. Langner S, Khaw AV, Fretwurst T, Angermaier A, Hosten N, Kirsch M. Endovascular treatment of acute ischemic stroke under conscious sedation compared to general anesthesia - safety, feasibility and clinical and radiological outcome. *Rofo*. 2013;185:320–327. doi: 10.1055/s-0032-1330361.
20. Hassan AE, Chaudhry SA, Zacharatos H, Khatri R, Akbar U, Suri MF, et al. Increased rate of aspiration pneumonia and poor discharge outcome

among acute ischemic stroke patients following intubation for endovascular treatment. *Neurocrit Care*. 2012;16:246–250. doi: 10.1007/s12028-011-9638-0.
21. Davis MJ, Menon BK, Baghirzada LB, Campos-Herrera CR, Goyal M, Hill MD, et al; Calgary Stroke Program. Anesthetic management and outcome in patients during endovascular therapy for acute stroke. *Anesthesiology*. 2012;116:396–405. doi: 10.1097/ALN.0b013e318242a5d2.
22. Sugg RM, Jackson AS, Holloway W, Martin CO, Akhtar N, Rymer M. Is mechanical embolectomy performed in nonanesthetized patients effective? *AJNR Am J Neuroradiol*. 2010;31:1533–1535. doi: 10.3174/ajnr.A2091.
23. Nichols C, Carrozzella J, Yeatts S, Tomsick T, Broderick J, Khatri P. Is periprocedural sedation during acute stroke therapy associated with poorer functional outcomes? *J Neurointerv Surg*. 2010;2:67–70. doi: 10.1136/jnis.2009.001768.
24. Jumaa MA, Zhang F, Ruiz-Ares G, Gelzinis T, Malik AM, Aleu A, et al. Comparison of safety and clinical and radiographic outcomes in endovascular acute stroke therapy for proximal middle cerebral artery occlusion with intubation and general anesthesia versus the nonintubated state. *Stroke*. 2010;41:1180–1184. doi: 10.1161/STROKEAHA.109.574194.
25. Abou-Chebl A, Lin R, Hussain MS, Jovin TG, Levy EI, Liebeskind DS, et al. Conscious sedation versus general anesthesia during endovascular therapy for acute anterior circulation stroke: preliminary results from a retrospective, multicenter study. *Stroke*. 2010;41:1175–1179. doi: 10.1161/STROKEAHA.109.574129.
26. Brinjikji W, Murad MH, Rabinstein AA, Cloft HJ, Lanzino G, Kallmes DF. Conscious sedation versus general anesthesia during endovascular acute ischemic stroke treatment: a systematic review and meta-analysis. *AJNR Am J Neuroradiol*. 2015;36:525–529. doi: 10.3174/ajnr.A4159.
27. Deeks JJ, Dinnes J, D'Amico R, Sowden AJ, Sakarovitch C, Song F, et al; International Stroke Trial Collaborative Group; European Carotid Surgery Trial Collaborative Group. Evaluating non-randomised intervention studies. *Health Technol Assess*. 2003;7:iii–x, 1–173.
28. Wilson JT, Hareendran A, Hendry A, Potter J, Bone I, Muir KW. Reliability of the modified Rankin Scale across multiple raters: benefits of a structured interview. *Stroke*. 2005;36:777–781. doi: 10.1161/01.STR.0000157596.13234.95.
29. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7:177–188.
30. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327:557–560. doi: 10.1136/bmj.327.7414.557.
31. Bracard S, Ducrocq X, Mas JL, Soudant M, Oppenheim C, Moulin T, et al; THRACE Investigators. Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial. *Lancet Neurol*. 2016;15:1138–1147. doi: 10.1016/S1474-4422(16)30177-6.
32. Löwhagen Hendén P, Rentzos A, Karlsson JE, Rosengren L, Leiram B, Sundeman H, et al. General anesthesia versus conscious sedation for endovascular treatment of acute ischemic stroke: the ANSTROKE Trial (anesthesia during stroke). *Stroke*. 2017;48:1601–1607. doi: 10.1161/STROKEAHA.117.016554.
33. Saver JL, Goyal M, van der Lugt A, Menon BK, Majoie CB, Dippel DW, et al; HERMES Collaborators. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. *JAMA*. 2016;316:1279–1288. doi: 10.1001/jama.2016.13647.
34. Oliveira-Filho J, Silva SC, Trabuco CC, Pedreira BB, Sousa EU, Bacellar A. Detrimental effect of blood pressure reduction in the first 24 hours of acute stroke onset. *Neurology*. 2003;61:1047–1051.
35. Sandset EC, Bath PM, Boysen G, Jatuzis D, Kõrv J, Lüders S, et al; SCAST Study Group. The angiotensin-receptor blocker candesartan for treatment of acute stroke (SCAST): a randomised, placebo-controlled, double-blind trial. *Lancet*. 2011;377:741–750. doi: 10.1016/S0140-6736(11)60104-9.
36. Löwhagen Hendén P, Rentzos A, Karlsson JE, Rosengren L, Sundeman H, Reinsfelt B, et al. Hypotension during endovascular treatment of ischemic stroke is a risk factor for poor neurological outcome. *Stroke*. 2015;46:2678–2680. doi: 10.1161/STROKEAHA.115.009808.
37. Whalin MK, Halenda KM, Haussen DC, Rebello LC, Frankel MR, Gershon RY, et al. Even small decreases in blood pressure during conscious sedation affect clinical outcome after stroke thrombectomy: an analysis of hemodynamic thresholds. *AJNR Am J Neuroradiol*. 2017;38:294–298. doi: 10.3174/ajnr.A4992.
38. Brekenfeld C, Mattle HP, Schroth G. General is better than local anesthesia during endovascular procedures. *Stroke*. 2010;41:2716–2717. doi: 10.1161/STROKEAHA.110.594622.
39. Rossitti S, Pfister M. 3D road-mapping in the endovascular treatment of cerebral aneurysms and arteriovenous malformations. *Interv Neuroradiol*. 2009;15:283–290. doi: 10.1177/159101990901500305.
40. McDonagh DL, Olson DM, Kalia JS, Gupta R, Abou-Chebl A, Zaidat OO. Anesthesia and sedation practices among neurointerventionalists during acute ischemic stroke endovascular therapy. *Front Neurol*. 2010;1:118. doi: 10.3389/fneur.2010.00118.
41. Jabre P, Avenel A, Combes X, Kulstad E, Mazariegos I, Bertrand L, et al. Morbidity related to emergency endotracheal intubation–a substudy of the ketamine sedation trial. *Resuscitation*. 2011;82:517–522. doi: 10.1016/j.resuscitation.2011.01.015.
42. Li J, Murphy-Lavoie H, Bugas C, Martinez J, Preston C. Complications of emergency intubation with and without paralysis. *Am J Emerg Med*. 1999;17:141–143.

Stroke
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association | American Stroke Association

Anesthesia-Related Outcomes for Endovascular Stroke Revascularization: A Systematic Review and Meta-Analysis

Waleed Brinjikji, Jeffrey Pasternak, Mohammad H. Murad, Harry J. Cloft, Tasha L. Welch, David F. Kallmes and Alejandro A. Rabinstein

Stroke. published online September 13, 2017;
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628