General Anesthesia Versus Conscious Sedation for Intracranial Mechanical Thrombectomy: A Systematic Review and Meta-analysis of Randomized Clinical Trials

Yu Zhang, MD; Lu Jia, MD; Fang Fang, MD; Lu Ma, MD; Bowen Cai, MD; Andrew Faramand, MD

***Background*—**Endovascular therapy is the standard of care for severe acute ischemic stroke caused by large-vessel occlusion in the anterior circulation, but there is uncertainty regarding the optimal anesthetic approach during this therapy. Meta-analyses of observational studies suggest that general anesthesia increases morbidity and mortality compared with conscious sedation. We performed a systematic review and meta-analysis of randomized clinical trials to examine the effect of anesthetic strategy during endovascular treatment for acute ischemic stroke.

***Methods and Results*—**Systematic review and meta-analysis according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines has been registered with the PROSPERO (International Prospective Register of Ongoing Systematic Reviews) (CRD42018103684). Medline, EMBASE, and CENTRAL databases were searched through August 1, 2018. Meta-analyses were conducted using a random-effects model to pool odds ratio with corresponding 95% CI. The primary outcome was 90-day functional independence (modified Rankin Scale 0–2). In the results, 3 trials with a total of 368 patients were selected. Among patients with ischemic stroke undergoing endovascular therapy, general anesthesia was significantly associated with higher odds of functional independence (odds ratio 1.87, 95% CI 1.15–3.03, I^2=17%) and successful recanalization (odds ratio 1.94, 95% CI 1.13–3.3) compared with conscious sedation. However, general anesthesia was associated with a higher risk of 20% mean arterial pressure decrease (odds ratio 10.76, 95% CI 5.25–22.07). There were no significant differences in death, symptomatic intracranial hemorrhage, anesthesiologic complication, intensive care unit length of stay, pneumonia, and interventional complication.

***Conclusions*—**Moderate-quality evidence suggests that general anesthesia results in significantly higher rates of functional independence than conscious sedation in patients with ischemic stroke undergoing endovascular therapy. Large randomized clinical trials are required to confirm the benefit. **(*J Am Heart Assoc*. 2019;8:e011754. DOI: 10.1161/JAHA.118.011754.)**

Key Words: anesthesia • endovascular treatment • meta-analysis • stroke

Endovascular treatment is a standard-of-care therapy for severe acute ischemic stroke caused by large-vessel occlusion, recommended by international guidelines.[1–4] The continuing debate has focused on best practice for endovascular therapy, including which anesthetic type results in the best outcomes. General anesthesia (GA) with intubation may be associated with less pain and movement and lower aspiration risk.[5] Conscious sedation (CS) with the patient spontaneously breathing may be associated with less time and hemodynamic instability and lower ventilation-associated-complications risk.

Previous systematic review and meta-analyses[6–12] mainly included observational studies,[13–16] which reported worse outcomes from GA compared with CS during endovascular therapy. However, observational studies,[13–16] as well as post hoc analysis of randomized clinical trials (RCTs),[17–19] experience selection bias because patients with more serious stroke are much more likely to be treated under GA. By contrast, individual RCTs were underpowered to detect significant differences in primary outcome, limited by small numbers of events.[20–22] Considering the discrepancy and the limitation of previous studies, we conducted a systematic review and meta-analysis of RCTs to compare the impact of

From the Affiliated Hospital of Chengdu University, Chengdu, Sichuan, China (Y.Z.); Shanxi Provincial People's Hospital, Taiyuan, Shanxi, China (L.J.); West China Hospital, Sichuan University, Chengdu, Sichuan, China (F.F., L.M., B.C.); University of Pittsburgh Medical Center, Pittsburgh, PA (A.F.).

Accompanying Tables S1, S2 and Figure S1 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.011754

Dr Zhang and Dr Jia contributed equally to this work.

Correspondence to: Bowen Cai, MD, West China Hospital, Sichuan University, No. 37, Guo Xue Xiang, Chengdu, Sichuan 610041, China.
E-mail: cbw101@outlook.com

Received February 20, 2019; accepted April 3, 2019.

Clinical Perspective

What Is New?

- This is the first systematic review and meta-analysis of randomized controlled trials comparing anesthetic strategies during endovascular treatment for acute ischemic stroke.
- This study demonstrates that general anesthesia is associated with better functional outcomes than conscious sedation during endovascular treatment for acute ischemic stroke.

What Are the Clinical Implications?

- Our report shows that general anesthesia results in significantly higher rates of functional independence than conscious sedation in patients with ischemic stroke undergoing endovascular therapy.

GA with CS for patients with ischemic stroke undergoing endovascular therapy.

Methods

The data that support the findings of this study are available from the corresponding author upon reasonable request. Ethical approval was not required.

Protocol and Guidance

This systematic review and meta-analysis was prepared concerning the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA),[23] and the Cochrane Handbook for Systematic Reviews of Interventions. The protocol has been registered with the PROSPERO (International Prospective Register of Ongoing Systematic Reviews); registration number CRD42018103684.

Eligibility Criteria

Inclusion criteria were as follows:

1. Population: adult participants (≥18 years) with acute ischemic stroke managed with endovascular treatment.
2. Intervention: GA.
3. Comparison intervention: CS or local anesthesia.
4. Outcome: The primary outcome was functional independence (modified Rankin Scale scores of ≤2) at 90 days. Secondary outcomes were 90-day mortality and successful recanalization (modified Thrombolysis in Cerebral Infarction 2b-3) at 24 hours. Other secondary outcomes (safety outcomes) were symptomatic intracranial hemorrhage, anesthesiologic complication, interventional complication, 20% mean arterial pressure decrease, intensive care unit length of stay, pneumonia, and costs.
5. Study design: RCT.

Exclusion criteria: We excluded post hoc analyses and duplicate reports.

Missing data: We contacted the authors of all unpublished studies as well as any published studies in which data were missing to confirm eligibility and obtain additional details.

Information Sources and Search Strategy

With the assistance of a professional librarian, we searched Medline, EMBASE, and the Cochrane Library at the CENTRAL Register of Controlled Trials from inception to August 1, 2018. We also consulted clinical trial registries (ClinicalTrials.gov, European Union Clinical Trials Register, World Health Organization International Clinical Trials Registry Platform, Stroke Trials Registry, and ISRCTN (International Standard Randomize Controlled Trial Number) Registry). We also searched the references of RCTs, review articles, and systematic reviews on the same topic for eligible articles. We did not use any language restrictions.

For the search strategy, we used the following search terms in various combinations: *endovascular, intra-arterial, intervention, embolectomy, thrombolysis, thrombectomy, ischemia, stroke, cerebrovascular accident, infarct, general anesthesia, conscious sedation, local anesthesia, controlled trials,* and *randomized controlled trial.* (Details of the search strategy are shown in Table S1).

Study Selection

Initially, 2 independent investigators (L.J. and Y.Z.) screened the titles and abstract level, and independently screened the full text of eligible studies. Disagreements were resolved via consensus and by a third author (F.F.). We contacted study authors to obtain missing information and unpublished data when needed to assess the inclusion criteria or when suitable data were not available.

Data Collection Process

Two independent investigators (L.J. and Y.Z.) extracted data from the included RCTs into standardized collection forms. Disagreements were resolved via consensus and by a third author (F.F.).

Assessment of Risk of Bias and Quality of Evidence

Two independent investigators (L.J. and Y.Z.) performed risk assessment using the Cochrane Collaboration risk of bias

tool[24]: sequence generation of the allocation; allocation concealment; blinding of participants, personnel, and outcome assessors; incomplete outcome data; selective outcome reporting; and other sources of bias. Each domain was assessed as either low, unclear, or high risk of bias.

We used the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach to rate the quality of evidence.[25] We used detailed GRADE guidance to assess the overall risk of bias, inconsistency, imprecision, indirectness, and publication bias and summarized results in an evidence profile.

Data Synthesis

All analyses were performed in Review Manager for Windows (RevMan, version 5.3, Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration). Data were abstracted from each study using results reported in an intention-to-treat approach.[26] We calculated odds ratios (OR) and 95% CIs using the Mantel–Haenszel model. For rare events (<5%), we used the Peto method. Statistical heterogeneity among trials was assessed by the Cochran Q test and I^2 test, with I^2 <25% and <50 representing low and high heterogeneity, respectively. The meta-analysis was done using a random-effects model regardless of the level of heterogeneity because the included trials differed meaningfully in clinical and methodological features. A 2-tailed *P* value of <0.05 was considered a criterion for statistical significance.

If a pooled analysis included 10 or more studies, we planned to use a funnel plot to explore the possibility of publication bias.

Sensitivity Analyses

To ensure that estimates remained stable, we conducted sensitivity analyses to examine the impact of using

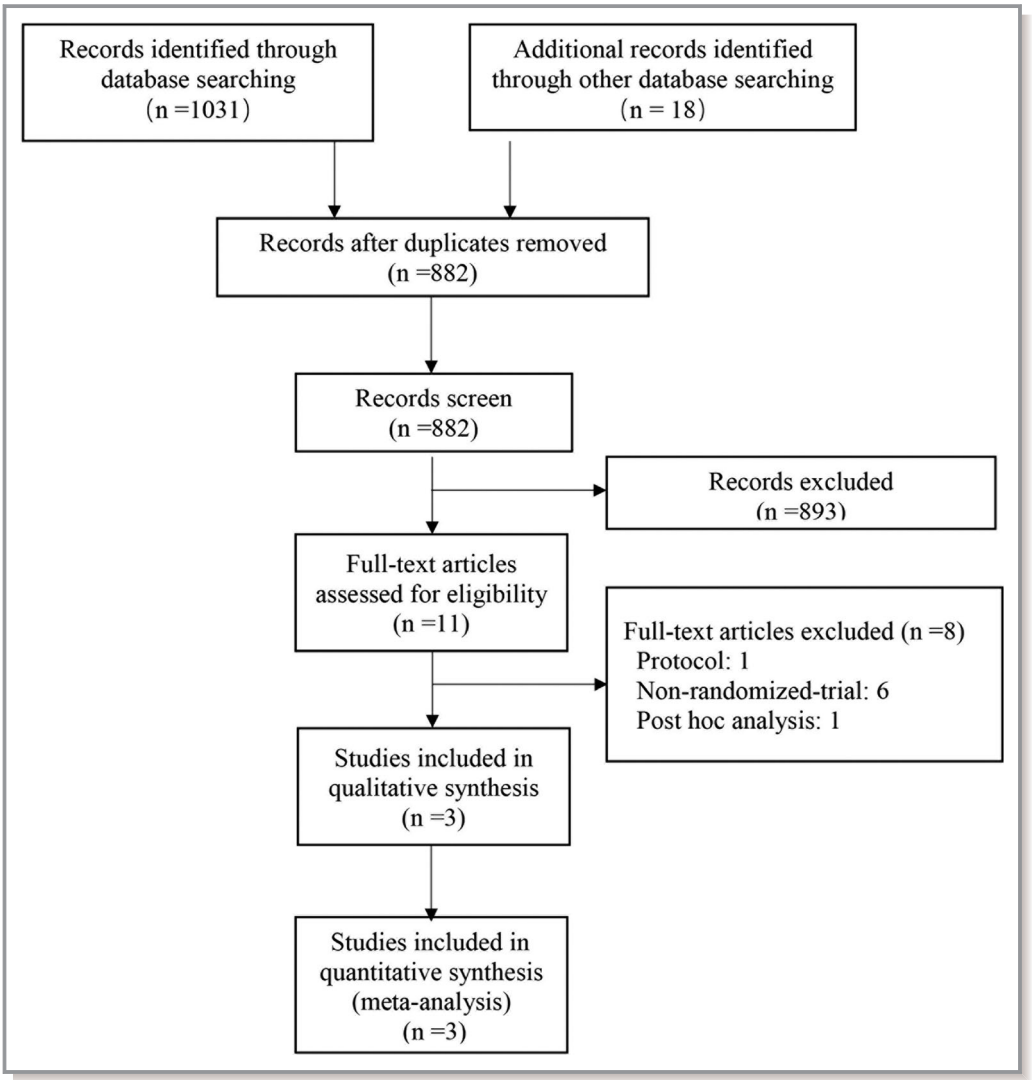

Figure 1. Search strategy and final included and excluded studies.

alternative analysis methods: (1) a random-effects model using the inverse variance method, (2) a fixed-effects model using the inverse variance method, (3) a fixed-effects model using the Mantel–Haenszel method, (4) calculating the risk difference with a random-effects model using Mantel–Haenszel model, and (5) calculating the risk ratios with a random-effects model using the Mantel–Haenszel model.

Results

Study Selection

The search strategy yielded 1049 manuscript abstracts (Figure 1). Eleven pertinent studies were identified and included in full-text review. After review, 8 studies[13–16,27–30] were excluded because they did not meet the inclusion criteria (Table S2). Three trials[20–22] comprising 368 participants were included in the final analysis.

Study Characteristics

Tables 1 and 2 show the characteristics of the included trials and patients. All trials were conducted in Europe. Population sizes were similar, and ranged from 106 to 150. The main inclusion criteria were adults with ischemic stroke, higher National Institutes of Health Stroke Scale (NIHSS) score (>10), and occlusion in the anterior circulation. Mean age ranged from 71 to 73 years, and NIHSS

Table 1. Descriptive Summary of Randomized Trials Characteristics

Trial	SIESTA[20]	AnStroke[21]	GOLIATH[22]
Recruitment period	2014–2016	2013–2016	2015–2017
Country	Germany	Sweden	Denmark
Centers	1	1	2
Number of patients	150	106	128
Inclusion criteria			
Age (y)	≥18	≥18	≥18
NIHSS	>10	≥10 (right-sided occlusion) or ≥14 (left)	>10
Occlusion	Anterior circulation	Anterior circulation	Anterior circulation
Time frame	NR	8 h	6 h
Other	NR	NR	mRS ≤2
Exclusion criteria	Not clearly depict site of vessel occlusion; Not an internal carotid artery or a middle cerebral artery; Intracerebral hemorrhage; Coma; Severe agitation at admission; Loss of airway-protective reflexes of at least absence of gag reflex, insufficient saliva handling, observed aspiration, vomiting, or a combination thereof at admission; Difficult airway; Intolerance of certain medications for sedation or analgesia	Anesthesiologic concerns (airway, agitation, etc); Occlusion of posterior circulation; Intracerebral hemorrhage; Neurological recovery or recanalization before or during angiography; mRS score ≥4; Other comorbidity contraindicating embolectomy	Intubated; Coma; Not living independently; mRS >2
Thrombectomy technique	Stent retriever or direct thrombus aspiration	Stent retriever or Amplatz GooseNeck snare	Stent retriever, direct thrombus aspiration, or intra-arterial thrombolysis
Follow-up, days	90	90	90
Primary end point	Change in NIHSS score 24 h after intervention	Difference in mRS scores at 3 mo	Infarct growth 48 to 72 h after intervention
Secondary outcomes	mRS scores after 90 days, in-hospital and 3-mo mortality, peri-interventional safety, and feasibility.	Composite of death, nonfatal stroke, TIA, or peripheral embolism	mRS scores after 90 days, time and blood pressure levels, and safety end points

mRS indicates modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; NR, not reported; TIA, transient ischemic attack.

Table 2. Baseline Patient Characteristics and Treatment Parameters by Treatment Group Among Included Randomized Trials

	SIESTA 2016[20]		AnStroke 2017[21]		GOLIATH 2018[22]	
	GA (n=73)	CS (n=77)	GA (n=45)	CS (n=45)	GA (n=65)	CS (n=63)
Age, mean (SD) or median (IQR), y	71.8 (12.9)	71.2 (14.7)	73 (65–80)	72 (66–82)	71.0 (10.0)	71.8 (12.8)
Risk factors, N (%)						
Women	25 (34.2)	35 (45.5)	19 (42)	22 (49)	29 (44.6)	33 (52.4)
Hypertension	53 (72.6)	54 (70.1)	27 (60)	22 (49)	39 (60.0)	32 (50.8)
Atrial fibrillation	36 (49.3)	36 (46.8)	18 (40)	18 (40)	24 (36.9)	27 (42.9)
Ischemic heart disease	NR	NR	9 (20)	5 (11)	NR	NR
Antiplatelet therapy	20 (28.1)	24 (32.9)	NR	NR	NR	NR
Hyperlipidemia	20 (27.4)	24 (31.2)	5 (11)	7 (16)	NR	NR
Diabetes mellitus	17 (23.3)	17 (22.1)	9 (20)	7 (16)	9 (13.8)	9 (14.3)
Smoking	9 (12.3)	13 (17.1)	4 (9)	8 (18)	20 (30.8)	20 (31.7)
NIHSS score, mean (SD) or median (IQR)	16.8 (3.9)	17.2 (3.7)	20 (15.5–23)	17 (14–20.5)	18 (13–21)	17 (15–21)
Site of occlusion, N (%)						
Internal carotid artery	1 (1.4)	9 (11.7)	15 (33)	10 (22)	14 (21.5)	13 (20.6)
Middle cerebral artery	46 (63.0)	47 (61.0)	26 (58)	34 (76)	33 (50.8)	39 (61.9)
Tandem	26 (35.6)	21 (27.3)	4 (9)	1 (2)	18 (27.7)	11 (17.5)
Left hemisphere	45 (61.6)	42 (54.5)	26 (58)	17 (38)	39 (60.0)	32 (50.8)
Converted to GA	…	11 (14.2)	…	7 (15.6)	…	4 (6.3)
Time from stroke onset, mean (SD) or median (IQR), minute						
From stroke onset to door	145.0 (83.8)	118.1 (61.5)	NR	NR	159 (122–230)	145 (113–231)
From door to puncture	75.6 (29.3)	65.6 (19.9)	34 (18–47)	25 (15–36)	24 (20–27)	15 (12–20)
Duration of EST	111.6 (62.5)	129.9 (62.5)	55 (38–110)	74 (37–104)	34 (21–51)	29 (16–51)
From onset to reperfusion	NR	NR	254 (206–373)	250 (213–316)	212 (180–288)	216 (162–285)
IV t-PA, N (%)	46 (63.0)	50 (64.9)	33 (73.3)	36 (80)	50 (76.9)	46 (73.0)
Types of endovascular treatment, N (%)						
Stent retriever	60 (82.2)	66 (85.7)	NR	NR	14 (21.5)	12 (19.0)
Direct aspiration	6 (8.2)	4 (5.2)	NR	NR	25 (38.5)	24 (38.1)
Both	16 (21.9)	12 (15.6)	NR	NR	11 (16.9)	10 (15.9)

CS indicates conscious sedation; EST, endovascular stroke treatment; GA, general anesthesia; IQR, interquartile range; IV t-PA, intravenous tissue plasminogen activator; NIHSS, National Institutes of Health Stroke Scale; NR, not reported.

score from 16 to 20. The follow-up period was 90 days across trials.

Risk of Bias and Quality of Evidence

The overall risk of bias was moderate among studies (Figure S1). The nature of the trial interventions precluded blinding of patients and their physicians; random sequence generation and blinding of outcome assessment were considered as low-risk items across trials. GRADE summary findings for all outcomes are shown in Table 3. We did not use funnel plots to assess the existence of possible publication bias because there were only 3 RCTs included in our study.

Efficacy of GA Versus CS

Figure 2 shows the associations between GA versus CS and efficacy. Three trials reported outcomes of functional independence. Overall, 154 out of 368 patients (41.8%) achieved functional independence at 90 days. Patients receiving GA for endovascular therapy had a higher chance of achieving functional independence (OR 1.87, 95% CI 1.15–3.03, I^2=17%). We did not present a funnel plot because there were only 3 trials.

Rates of successful revascularization at 24 hours for GA were 85.2% versus 75.7% for CS (OR 1.94, 95% CI 1.13–3.3, I^2=0%). Among the 3 trials, death occurred in 15.8% of

Table 3. Summary of Findings and Strength of Evidence

Outcome	No. of Patients (Studies)	Relative Effect (95% CI)	I^2	Illustrative Comparative Risks (95% CI, Per 1000)			Strength of Evidence (GRADE)
				CS	GA	Absolute Effect	
Functional independence (mRS scores 0–2)	368 (3)	OR 1.87 (1.15–3.03)	17%	346	497	151 (32–270)	Moderate*
Successful recanalization (mTIMI 2b-3)	368 (3)	OR 1.94 (1.13–3.35)	0%	757	858	101 (22–156)	Moderate*
Mortality	368 (3)	OR 0.74 (0.43–1.27	0%	205	160	−45 (−105 to 42)	Moderate*
Interventional complications	368 (3)	OR 1.76 (0.86–3.61)	0%	76	126	50 (−10 to 152)	Moderate*
Symptomatic intracerebral hemorrhage	368 (3)	OR 0.61 (0.14–2.71)	0%	32	20	−12 (−28 to 51)	Moderate*
Anesthesiologic complications	368 (3)	OR 1.02 (0.28–3.72)	24%	38	39	1 (−27 to 90)	Moderate*
Pneumonia	240 (2)	OR 1.76 (0.38–7.98)	66%	82	135	53 (−49 to 334)	Low*,†
ICU length of stay	150 (1)	MD 17.10 (−13.44 to 47.64)	NR	NR	NR	NR	Moderate*
20% MAP decrease	218 (2)	OR 10.76 (5.25–22.07)	0%	444	896	451 (363–502)	Moderate*

CS indicates conscious sedation; GA, general anesthesia; ICU, intensive care unit; MAP, mean arterial pressure; MD, mean difference; mRS, modified Rankin Scale; NR, not reported; OR, odds ratio; TIMI, thrombolysis in myocardial infarction.
*Imprecision because of the wide CI.
†Inconsistency.

patients among the GA group and 20.5% of patients among the CS group. There was no statistically significant difference between the 2 groups in mortality (relative risk 0.74, 95% CI 0.43–1.27, I^2=0%).

Safety of GA Versus CS

Results of adverse events among both examined groups for all trials are detailed in Figure 3. Pooled estimates suggested that GA was associated with 20% mean arterial pressure decrease (OR 10.76, 95% CI 5.25–22.07). Other meta-analyses showed no significant difference between anesthetic types in rates of symptomatic intracranial hemorrhage (OR 0.51, 95% CI 0.14–1.91), anesthesiologic complication (OR 1.03, 95% CI 0.35–3.03), interventional complication (OR 1.76, 95% CI 0.86–3.61), intensive care unit length of stay (mean difference 17.10, 95% CI −13.44 to 47.64), and pneumonia (OR 1.75, 95% CI 0.38–7.98). To date, no trial has reported quality of life.

Sensitivity Analyses

Similar results were observed for similar primary outcome in all conducted sensitivity analyses: (1) a random-effects model using the inverse variance method (OR 1.87, 95% CI 1.15–3.03), (2) a fixed-effects model using the inverse variance method (OR 1.88, 95% CI 1.21–2.92), (3) a fixed-effects model using the Mantel–Haenszel method (OR 1.88, 95% CI 1.21–2.91), (4) calculating the risk difference with a random-effects model using the Mantel–Haenszel model (risk difference 0.15, 95% CI 0.05–0.24), and (5) calculating the risk ratios with a random-effects model using the Mantel–Haenszel model (risk ratio 1.38, 95% CI 1.01–1.88).

Discussion

In the present systematic meta-analysis of data from 3 RCTs with 368 patients, GA compared with CS results in greater improvement in functional independence at 90 days after acute ischemic stroke. Furthermore, compared with CS, GA was associated with higher rates of successful recanalization at 24 hours but was associated with no significant differences in mortality or symptomatic intracranial hemorrhage.

Compared With Other Studies

To the best of our knowledge, this study is the first meta-analysis of only RCT evaluating CS versus GA for endovascular therapy for ischemic stroke. Previous meta-analyses on this topic, mainly based on observational studies, suggested that GA compared with CS for endovascular therapy decreases neurological recovery and increases mortality and morbidity.[6–12] A post hoc analysis of MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) showed that endovascular therapy with GA did not repeat the treatment benefit in MR CLEAN.[19] The association of GA with worse outcomes after endovascular therapy in observational studies may be explained by blood pressure decreases and a longer delay of time to groin puncture in the GA group, both of which have been associated with worse endovascular treatment outcomes.[31]

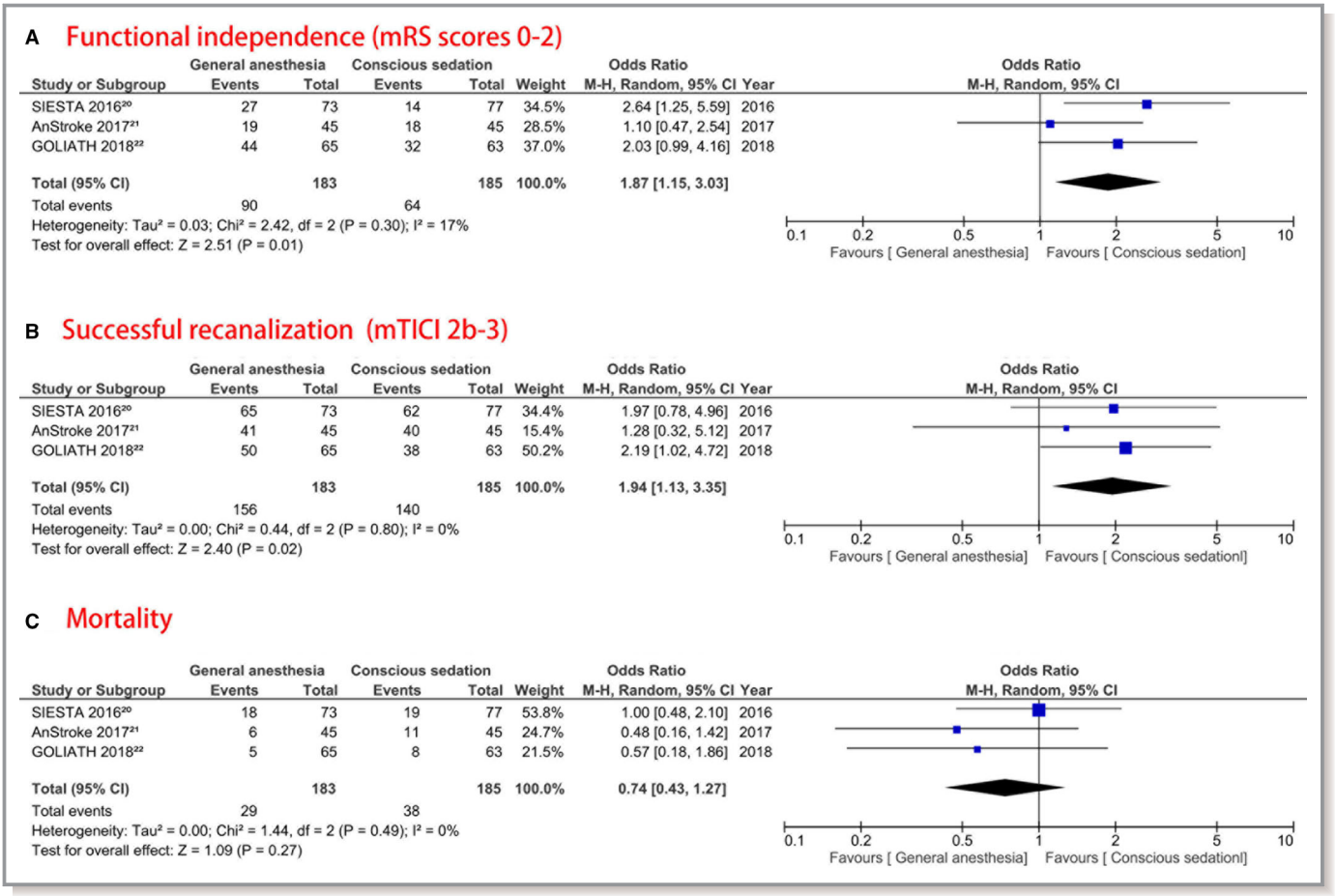

Figure 2. Forest plot of efficacy of all trials evaluating general anesthesia vs conscious sedation. **A**, Functional independence (modified Rankin Scale scores of ≤2) at 90 days. **B**, Successful recanalization (mTICI 2b-3) at 24 hours. **C**, Mortality at 90 days: M-H. M-H indicates Mantel–Haenszel; mRS, modified Rankin Scale; mTICI, modified Thrombolysis in Cerebral Infarction.

Contrary to numerous nonrandomized studies and previous meta-analyses, this study seems to support the idea that endovascular treatment might be performed with greater technical success when patients are under GA. The difference between this study and previous studies might be explained by selection bias of observational studies since GA was often chosen for the patients with more severe illness. In those studies, average baseline NIHSS scores were higher for patients receiving GA than those receiving CS.[8]

There are 3 RCTs to assess whether GA is superior to CS among patients receiving endovascular therapy for stroke. However, 3 trials had different primary outcomes (change in NIHSS at 24 hours, modified Rankin Scale at 3 months, and infarct growth 48–72 hours, respectively) and showed no significant differences in their primary outcomes. The first trial, SIESTA (Sedation versus Intubation for Endovascular Stroke Treatment), found GA versus CS did not result in greater improvement in neurological status in patients with ischemia undergoing endovascular thrombectomy (difference, −3.2 points [95% CI, −5.6 to −0.8]). The second one, AnStroke (Anesthesia During Stroke), showed no difference was found between GA and CS in neurological outcome 3 months after stroke (P=1.00). The last one, GOLIATH (General or Local Anesthesia in Intra Arterial Therapy), concluded GA did not result in worse tissue or clinical outcomes compared with CS. All primary outcomes failed partly because the small sample size may have limited study power to detect clinically relevant differences in outcomes. Interestingly, this meta-analysis of those trials showed mostly positive effects of GA.

Contrary to previous studies,[10,20] we did not find a higher frequency of pneumonia in the GA group. Only 2 trials[20,21] with a total of 240 patients reported pneumonia. The limited information may be underpowered enough to evaluate safety. Observational studies may be more appropriate than trials to evaluate safety because these can involve more people than RCTs.

Future Research

Future studies are needed to systematically study the relationship of disease-, patient-, and treatment-related variables with outcomes following GA for endovascular therapy

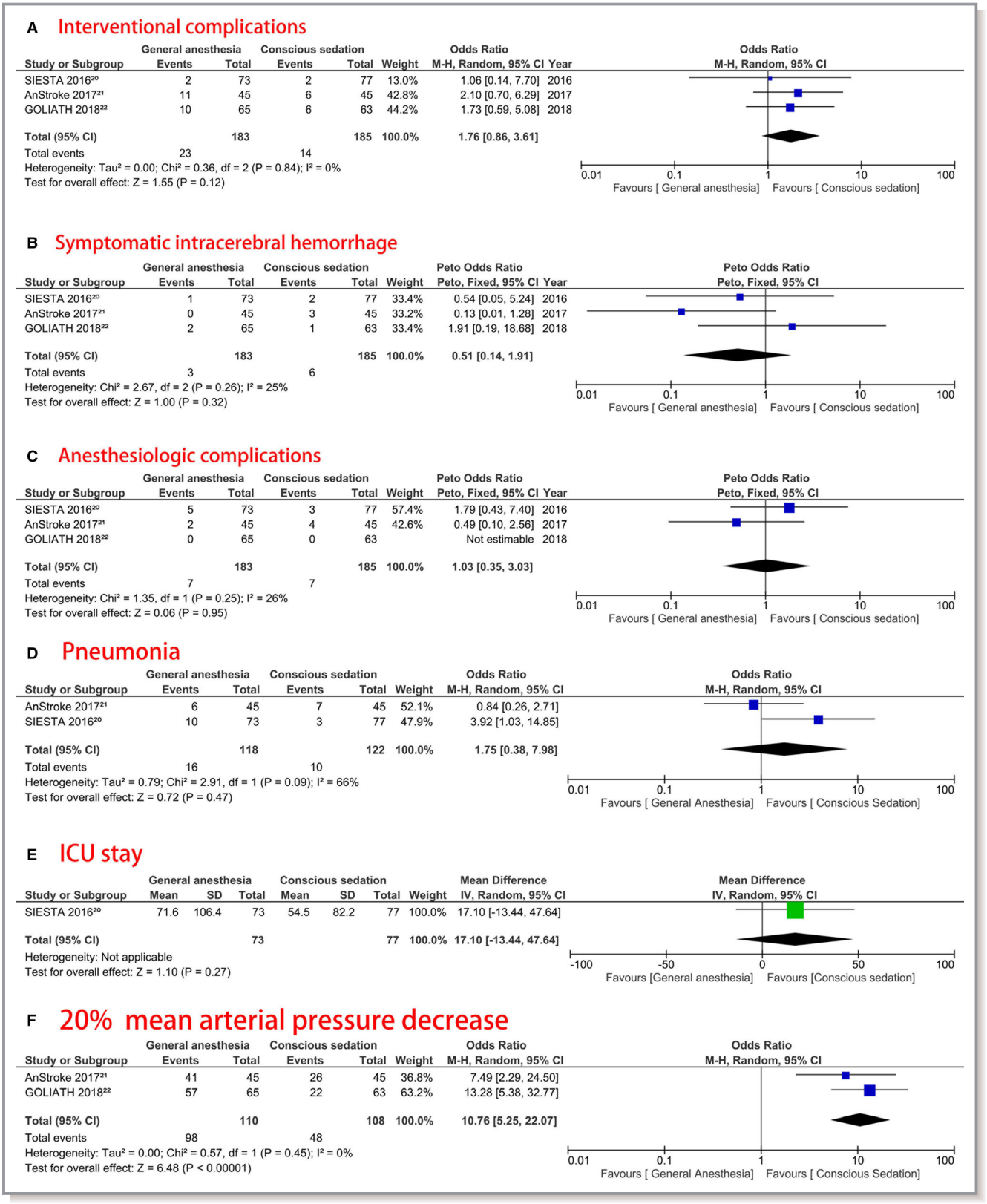

Figure 3. Forest plot of safety of all trials evaluating general anesthesia vs conscious sedation. **A**, Interventional complication. **B**, Symptomatic intracranial hemorrhage. **C**, Anesthesiologic complication. **D**, Pneumonia. **E**, ICU length of stay. **F**, 20% mean arterial pressure decrease. ICU indicates intensive care unit; IV inverse variance; M-H, Mantel–Haenszel.

for the treatment of ischemic stroke, and to identify the ideal patient to undergo GA. Limits on age, GCS (Glasgow Coma Scale), NIHSS score, ASPECTS (Alberta Stroke Program Early CT Score), and, perhaps most importantly, time to treatment, need to be explored. Moreover, longer follow-ups could help provide much more understanding of effectiveness and safety. Finally, cost-effectiveness analyses should be pursued to ascertain the value of GA for endovascular therapy.

Strengths and Limitations

To the best of our knowledge, this study is the first meta-analysis that only involved RCT evaluating the anesthetic strategy of endovascular therapy, which avoided selection bias of retrospective studies and reduced imprecisions of small RCTs. Strengths of this meta-analysis included performing a comprehensive search and duplicate assessment of citation screening, data abstraction, and risk of bias. The meta-analysis implemented a rigorous assessment of the quality of evidence. We have evaluated relative and absolute risks, which are important for making decisions between GA and CS.

We are, however, aware of several limitations. First, our statistical analysis might be imprecise because the studies include relatively few patients and thus have wide CIs around the estimate of the effect, although pooled analysis of these studies yielded statistical significance of primary outcome with low statistical heterogeneity.

Second, the small number of involved RCTs afforded insufficient ability to detect the presence of publication bias.[32,33] However, publication bias is unlikely because all the RCTs had negative results in the primary outcome.

Third, all involved trials were conducted in developed countries, and the management of GA relies more on advanced physical facilities and technical means than CS. Thus, these findings may not apply to less developed countries. Further research in these countries would add to the generalizability.

Fourth, there was a high rate of conversion to GA in the CS group in the included trials (6.3%, 14.2%, 15.6%, respectively), perhaps induced by different strategies in the CS group (ie, monitored anesthetic care or traditional regional anesthesia) and inexperience of the institution or operator with performing intracranial mechanical thrombectomy using CS. The conversion from CS to GA might lead to additional delays in the CS group. Every 5-minute delay in the start of endovascular reperfusion has been estimated to worsen the clinical outcome for 1 in 100 patients.[34] Thus, the high rate of conversion could have reduced the effect of endovascular treatment in the CS group.

Fifth, although there were many similarities to the methodology of the included RCTs, there was also some variability, including eligibility criteria, and the type of devices used for endovascular therapy, which may have a significant influence on outcomes. However, we were unable to assess the effect of important variables because of only 3 trials being included in this review.

Sixth, all included trials were not double-blind study group assignments. Thrombectomy technique, such as the use of a stent retriever, and direct thrombus aspiration, was at the discretion of the neuro-interventionists, which could have introduced bias if patients were treated differently based on knowledge of their assignment.

Conclusions

In contrast with previous meta-analyses of observational studies, this systematic review and meta-analysis found that GA provides beneficial functional independence during endovascular treatment for acute ischemic stroke, compared with CS. Further large RCTs are required to confirm the benefit.

Acknowledgments

The lead author (Zhang) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; no important aspects of the study have been omitted.

Author Contributions

Zhang, Jia, and Fang conceived the study and designed the protocol. Zhang performed the literature search. Zhang and Jia selected the studies. Zhang and Jia extracted the relevant information. Zhang and Jia synthesized the data. Zhang and Faramand wrote the first draft of the paper. Zhang, Jia, Faramand, Ma, Cai, and Fang critically revised successive drafts of the paper and approved the final version. Fang and Cai are the guarantors of the review.

Sources of Funding

This work is supported by the projects of National Natural Science Foundation of China (contract/grant number: 81100925, 81472361), and by . National Key R&D Program of China (No. 2018YFA010860004).

Disclosures

None.

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SUPPLEMENTAL MATERIAL

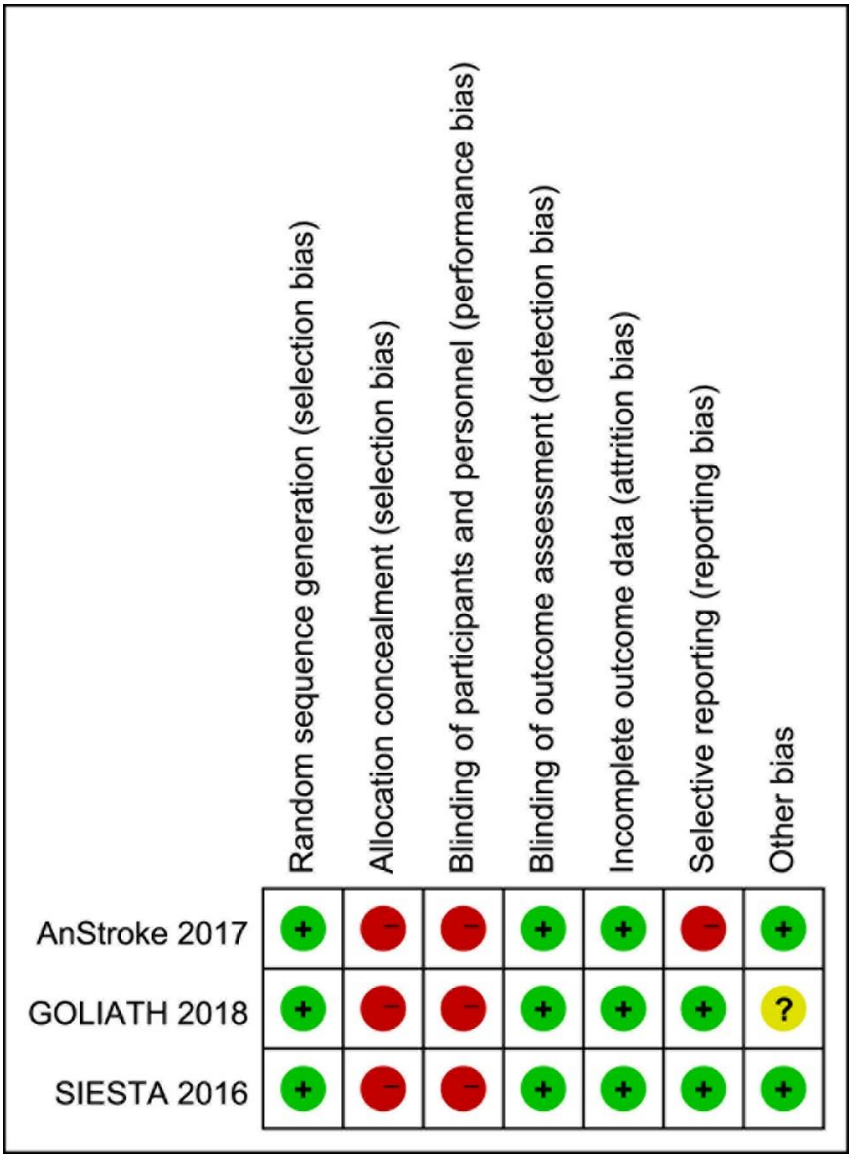
Table S1. Exemplified search strategy for MEDLINE (OvidSP).

#	**Searches**
1	exp cerebrovascular disorders or exp basal ganglia cerebrovascular disease or exp brain ischemia or exp carotid artery diseases or exp carotid artery thrombosis or exp intracranial arterial diseases or exp cerebral arterial diseases/or exp stroke
2	(isch?emi$ adj6 (stroke$ or apoplex$ or cerebral vasc$ or cerebrovasc$ or cva)).tw.
3	((brain or cerebr$ or cerebell$ or vertebrobasil$ or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or middle cerebr$ or mca$ or anterior circulation) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$)).tw
4	Or/ 1-3
5	exp mechanical thrombolysis or exp embolectomy or exp thrombectomy
6	(mechanical adj3 (thrombectom* or thromboembolectom* or thromboembolectom* or thrombolys* or remov* or disrupt* or clot* or embolectom* or recanalis* or recanaliz* or retriev*)).tw.
7	neurothrombectom*.tw. or merci.tw. or penumbra system.tw. or solitaire.tw. or trevo.tw.
8	Or/ 5-7
9	randomized controlled trial. pt. or controlled clinical trial. pt. or randomized. Ab. or placebo.ab. or clinical trials as topic.sh. or randomly. ab. or trial. ti.
10	1 and 4 and 8
11	exp animals/ not humans.sh.
12	10 not 11

Table S2. List of excluded trials and reasons for exclusion.

Study	Reason for exclusion
Abou-Chebl 2010[1]	Not an RCT
Junmaa 2010[2]	Not an RCT
Langner 2013[3]	Not an RCT
Abou-Chebl 2015[4]	Post hoc analysis
Mundiyanapurath 2015[5, 6]	Not an RCT
Just 2016[6]	Not an RCT
Simonsen 2016[7]	Protocol
Athiraman 2018[8]	Not an RCT

Figure S1. Risk of Bias Among Studies.



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