RESEARCH ARTICLE

General Anesthesia Compared With Non-GA in Endovascular Thrombectomy for Ischemic Stroke

A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Abstract

Background and Objectives

Endovascular thrombectomy (EVT) for large vessel occlusion ischemic stroke is either performed under general anesthesia (GA) or with non-GA techniques such as conscious sedation or local anesthesia alone. Previous small meta-analyses have demonstrated superior recanalization rates and improved functional recovery with GA when compared with non-GA techniques. The publication of further randomized controlled trials (RCTs) could provide updated guidance when choosing between GA and non-GA techniques.

Methods

A systematic search for trials in which stroke EVT patients were randomized to GA or non-GA was performed in Medline, Embase, and the Cochrane Central Register of Controlled Trials. A systematic review and meta-analysis using a random-effects model was performed.

Results

Seven RCTs were included in the systematic review and meta-analysis. These trials included a total of 980 participants (GA, N = 487; non-GA, N = 493). GA improves recanalization by 9.0% (GA 84.6% vs non-GA 75.6%; odds ratio [OR] 1.75, 95% CI 1.26–2.42, $p = 0.0009$), and the proportion of patients with functional recovery improves by 8.4% (GA 44.6% vs non-GA 36.2%; OR 1.43, 95% CI 1.04–1.98, $p = 0.03$). There was no difference in hemorrhagic complications or 3-month mortality.

Discussion

In patients with ischemic stroke treated with EVT, GA is associated with higher recanalization rates and improved functional recovery at 3 months compared with non-GA techniques. Conversion to GA and subsequent intention-to-treat analysis will underestimate the true therapeutic benefit. GA is established as effective in improving recanalization rates in EVT (7 Class 1 studies) with a high Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) certainty rating. GA is established as effective in improving functional recovery at 3 months in EVT (5 Class 1 studies) with a moderate GRADE certainty rating. Stroke services need to develop pathways to incorporate GA as the first choice for most EVT procedures in acute ischemic stroke with a level A recommendation for recanalization and level B recommendation for functional recovery.

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Glossary

BP = blood pressure; **CS** = conscious sedation; **EVT** = endovascular thrombectomy; **GA** = general anesthesia; **GRADE** = Grading of Recommendations, Assessment, Development, and Evaluations; **LA** = local anesthesia; **mRS** = modified Rankin score; **NTT** = number needed to treat; **OR** = odds ratio; **RCT** = randomized controlled trial; **TICI** = Thrombolysis in Cerebral Infarct.

Endovascular thrombectomy (EVT) for large vessel occlusion ischemic stroke is either performed under general anesthesia (GA) or with non-GA techniques such as conscious sedation (CS) or local anesthesia (LA) alone. Previous observational studies, nonrandomized data from trials, and meta-analysis of nonrandomized comparisons within clinical trials[1-4] suggested harm from GA. These studies may have been confounded by selection bias and differences in blood pressure (BP) management during the procedure, which were rarely reported.[1-4] Previous meta-analyses of randomized controlled trials (RCTs) have reported that GA was at least equivalent[5-8] or superior to non-GA techniques with higher recanalization rates and better functional outcome at 3 months.[8] These meta-analyses pooled data from up to 4 small single-center studies. Current international guidelines, recent reviews, and editorials[9-11] based on these data suggest that these techniques are equivalent, and therefore, the choice of technique is at the discretion of the treating team.

Internationally, there is wide practice variation in the use of LA, CS, or GA for EVT.[1-4,12] If anesthesia or sedation technique is demonstrated to influence outcome, many centers could introduce these changes in practice immediately. The multicenter General Anesthesia vs Sedation for Stroke trial,[13] the largest RCT to date with 351 EVT patients randomized to treatment with GA or non-GA, was published after earlier meta-analyses. The aim of this updated meta-analysis was to compare procedural, functional, and safety outcomes in EVT patients treated with GA or non-GA techniques.

Methods

This systematic review and meta-analysis has been reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[14] The protocol was prospectively registered with International Prospective Register of Systematic Reviews (PROSPERO identifier CRD42022315945).[15] Studies were considered if they fulfilled all the following 3 criteria: RCTs; participants undergoing EVT for large vessel occlusion ischemic stroke; and comparators were GA compared with non-GA techniques such as CS or LA. Trials were excluded if they were not RCTs, did not compare GA with CS/LA, or appeared in a database after the study cutoff period.

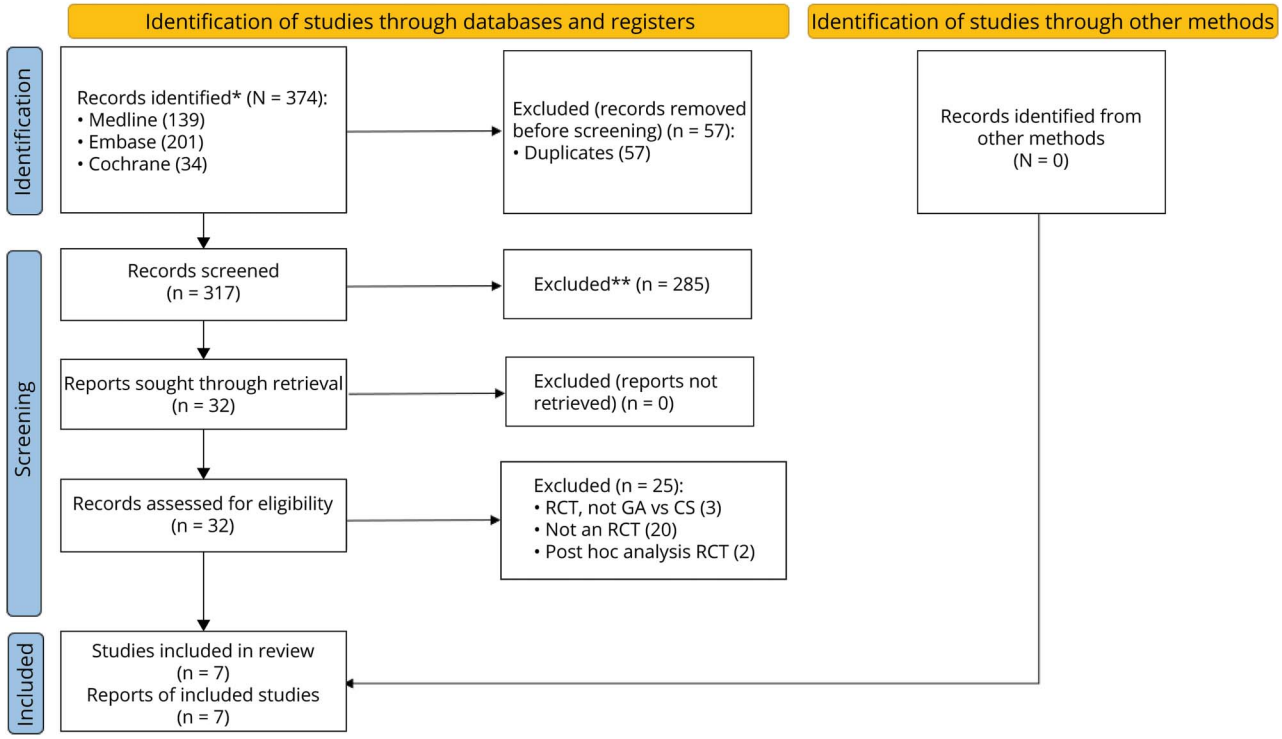
Systematic searches were made on MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials from inception of database until May 1, 2022. There were no restrictions of source language. References from candidate articles were screened for further eligible trials. The search strategy was amalgamated using the 3 criteria listed under eligibility criteria and combined using the Boolean AND operator. The keywords for the population, intervention, and trial design for the detailed search strategy are outlined in eAppendix 1 (links.lww.com/WNL/C648).

One investigator (J.H.) performed comprehensive database searches using the prespecified search criteria. Three investigators (J.H., R.C., and E.B.) performed an initial screening and identified potential trials for a full-text review. Conflicts were resolved by consensus. Full-text articles were read, and relevant publication references were screened for further eligible trials. Summary data were extracted from the published manuscript or supplemental appendix of the included trials. Data items extracted included the authors, journal and year of publication, number of participating sites, country, total number of participants recruited, numbers of participants in each randomized group, and demographic, procedural, and outcome data. Corresponding authors of included trials were contacted for missing outcome data or outcome data in an unclear format.

The primary efficacy measure was good functional recovery as defined by a modified Rankin score (mRS) of 0, 1, or 2 at 3 months. Procedural efficacy was measured by recanalization success as measured by Thrombolysis in Cerebral Infarct (TICI) score of 2b or 3 at procedure completion.[16] Safety endpoints were symptomatic intracerebral hemorrhage and 3-month mortality. These outcomes were all described by an odds ratio (OR) and 95% CI.

Any study that reported an endpoint in an appropriate format (or data could be provided by the corresponding author) was included in a pooled analysis. No further data conversion was required. Individual trial results were tabulated and synthesized and visually displayed in a forest plot. Analysis was performed using Review Manager 5 (RevMan 5.3. Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration, 2014), and studies were combined using a random-effects model. Variability within studies was assessed using the I^2 statistic and χ^2 test. Significant heterogeneity was defined as I^2 >40% and a p value of <0.05 for the χ^2 test. Sensitivity analyses using the leave-one-out method were performed for the recanalization success and functional recovery endpoints. A preplanned subanalysis for functional outcome was performed comparing maintenance anesthesia agents.

Figure 1 Flow Diagram for Systematic Review



CS = conscious sedation; GA = general anesthesia; RCT = randomized controlled trial.

Risk of bias assessment was performed over 5 domains using the Cochrane risk of bias tool version 2 (RoB v2.0)[17]: risk of bias arising from randomization, risk of bias due to deviations from intended interventions; missing outcome data; risk of bias in outcome measurement; and risk of bias in selection of reported result. Each trial was assessed, and these assessments were combined for all included trials. A funnel plot was visually inspected for evidence of reporting bias. Statistical tests of asymmetry were not performed because there were less than 10 included trials.[18] Quality of evidence was assessed using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach.[19]

Standard Protocol Approvals, Registrations, and Patient Consents

This systematic review and meta-analysis was registered prospectively on PROSPERO on March 14, 2022 (PROSPERO 2022 CRD42022315945).[15] This review used summary data from published manuscripts. No patient-level data were used, so informed consent or institutional review board approval was not required.

Data Availability

Data not provided in the article because of space limitations may be shared at the request of any qualified investigator for purposes of replicating procedures and results.

Results

A total of 317 publications were screened and 7 RCTs were included in the systematic review and meta-analysis.[13,20-25] See Figure 1 for study selection flow chart.

The characteristics of the eligible trials are tabulated in Table 1 with procedural, primary, secondary, and safety outcomes. There were a total of 988 EVT patients included of whom 497 were randomized to GA and 491 to non-GA. Successful recanalization (TICI 2b-3) occurred in 84.6% of GA patients and 75.6% of non-GA patients (OR 1.75, 95% CI 1.26–2.42, p = 0.0009). This treatment effect was consistent across the 7 RCTs with low statistical heterogeneity (I^2 = 0%). Functional independence (mRS 0–2) at 3 months occurred in 44.6% of GA patients and 36.2% of non-GA patients (OR 1.43, 95% CI 1.04–1.98, p = 0.03). Five of the 7 trials reported 3-month mRS, and the treatment effect was consistent, with low statistical heterogeneity (I^2 = 8%). The RCTs conducted by Ren et al. and Hu et al. were excluded for this analysis. They did not fulfil inclusion criteria because data were in the incorrect format for pooled analysis, and repeated attempts to contact the authors of these studies for clarification were unsuccessful. There were no differences between GA and non-GA on the safety endpoints of hemorrhagic complications (OR 0.86, 95% CI 0.56–1.31, and p = 0.49) and 3-month mortality (OR 0.83, 95% CI 0.55–1.24, p = 0.35).

Table 1 Demographic and Trial Data for Eligible RCTs With Procedural, Primary, Secondary, and Safety Outcomes

Author, publication year (study)	Study design, period, population	Country and centers	Total patients, (n)	Group, (n)	Age (y)	Sex, male, n (%)	Initial NIHSS
Schönenberger, 2016 (SIESTA)	RCT April 2014–February 2016 EVT, anterior circulation	Germany, single center	150	GA (73) Non-GA (77)	71.8 (12.9)[a] 71.2 (14.7)[a]	48 (65.8) 42 (54.5)	17 (13–20) 17 (14–20)
Löwhagen, 2016 (AnStroke)	RCT 2013–2016 EVT, anterior circulation	Sweden, single center	90	GA (45) Non-GA (45)	73 (65–80)[b] 72 (66–82)[b]	26 (58) 23 (51)	20 (15.5–23) 17 (14–20.5)
Simonsen, 2018 (GOLIATH)	RCT March 2015–February 2017 EVT, anterior circulation	Denmark, single center	128	GA (65) Non-GA (63)	71.0 (10.0)[a] 71.8 (12.8)[a]	36 (55.4) 30 (47.6)	18 (13–21) 17 (15–21)
Sun, 2019 (CANVAS Pilot)	RCT April 2016–June 2017 EVT, anterior circulation	China, single center	40	GA (20) Non-GA (20)	67 (57–77)[b] 60 (45–73)[b]	13 (65) 13 (65)	14 (11–18) 13 (9–17)
Ren, 2020	RCT 2017–2018 EVT, anterior circulation	China, single center	90	GA (48) Non-GA (42)	69.21 (5.78)[a] 69.19 (6.46)[a]	26 (54.2) 24 (57.1)	14 (11–16) 14 (11–16)
Hu, 2021	RCT 2017–2019 EVT, posterior circulation	China, single center	139	GA (72) Non-GA (67)	72.1 (6.8)[a] 71.9 (7.5)[a]	38 (52.78) 32 (50.75)	NR
Maurice, 2022 (GASS)	RCT 2016–2020 EVT, anterior circulation	France, 4 centers	351	GA (174) Non-GA (177)	70.8 (13.0)[a] 72.6 (12.3)[a]	94 (53) 100 (56)	16 (6) 16 (5)

Author, publication year (study)	Initial ASPECTS	IV tPA n (%)	Onset to door time (min)	Door to groin time (min)	Groin puncture to reperfusion (min)	TICI 2b-3 recanalization, n (%)	Procedural BP, mean (SD)
Schönenberger, 2016 (SIESTA)	8 (7–9) 8 (6.25–9)	46 (63.0) 50 (64.9)	NR	75.6 (29.3)[a] 65.6 (19.9)[a]	111.6 (62.5) 129.9 (62.5)	65 (89.0) 62 (80.5)	SBP 144.9 () 147.2 ()
Löwhagen, 2016 (AnStroke)	10 (8–10) 10 (9–10)	33 (73.3) 36 (80)	97 (62–160)[b] 72 (58–119)[b]	34 (18–47)[b] 25 (15–36)[b]	55 (38–110)[b] 74 (37–104)[b]	41 (91.1) 40 (88.9)	MAP 91 (8) 95 (8)
Simonsen, 2018 (GOLIATH)	NR	50 (76.9) 46 (73.0)	159 (122–230)[b] 145 (113–231)[b]	24 (20–27)[b] 15 (12–20)[b]	34 (21–51)[b] 29 (16–51)[b]	50 (76.9) 38 (60.3)	MAP[b] 90 (82–99) 102 (88–111)
Sun, 2019 (CANVAS Pilot)	NR	9 (45) 11 (55)	307 (271–347)[b] 286 (245–333)[b]	29 (25–34)[b] 15 (11–17)[b]	98 (75–123)[b] 87 (66–101)[b]	19 (95) 13 (65)	SBP 123 (21) 148 (33)
Ren, 2020	9 (8–10) 9 (8–10.25)	37 (77.08) 34 (80.95)	247.38 (33.19) 262.86 (62.29)	11.0 (1.64) 11.45 (2.05)	46.98 (15.83) 39.12 (11.86)	42 (87.5) 36 (85.71)	SBP[c] 159.0 (7.5) 161.5 (7.5)

Continued

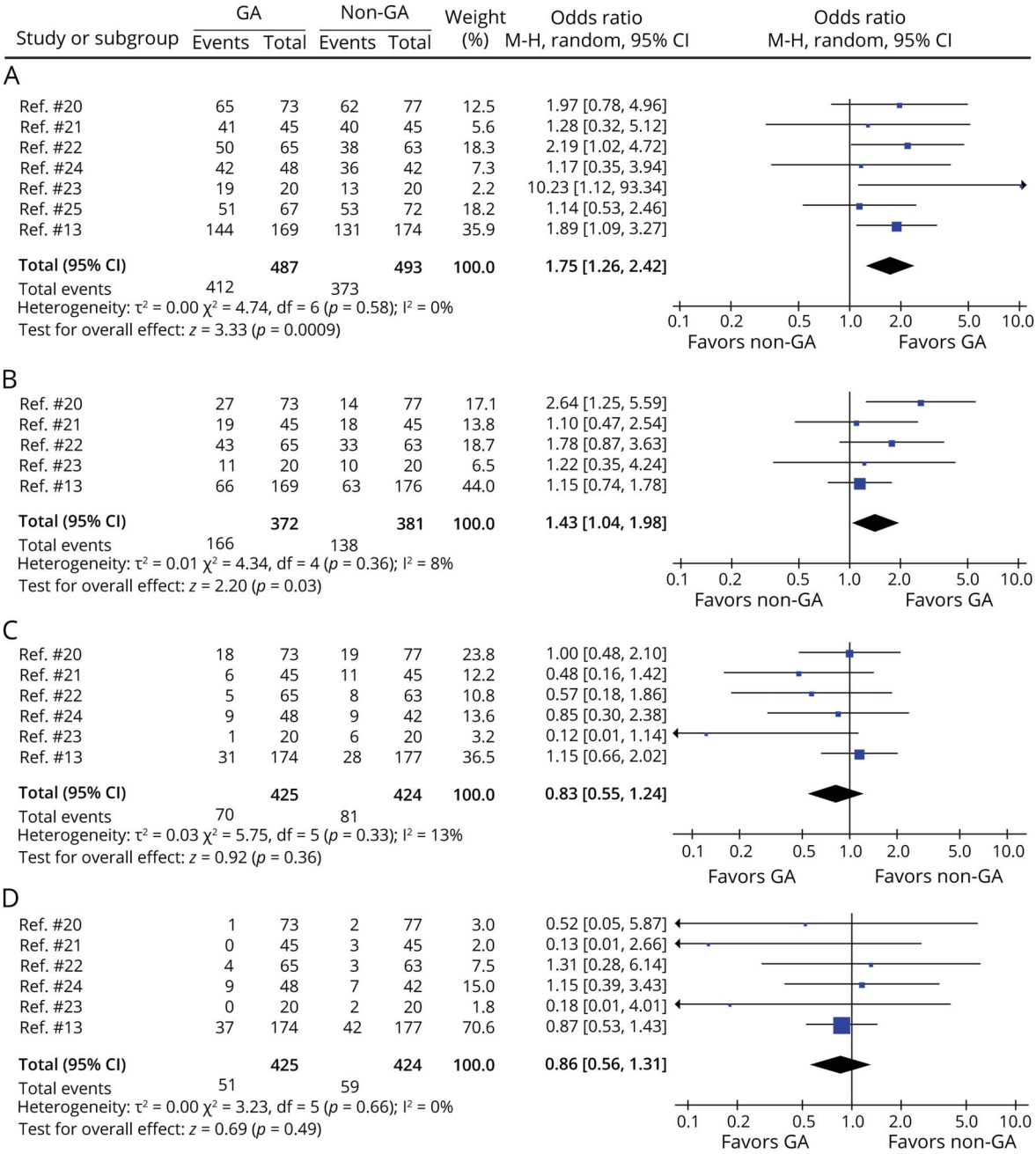
Table 1 Demographic and Trial Data for Eligible RCTs With Procedural, Primary, Secondary, and Safety Outcomes *(continued)*

Author, publication year (study)	Initial ASPECTS	IV tPA n (%)	Onset to door time (min)	Door to groin time (min)	Groin puncture to reperfusion (min)	TICI 2b-3 recanalization, n (%)	Procedural BP, mean (SD)
Hu, 2021	NR	NR	142.3 (39.3) 129.6 (47.3)	NR	130.4 (43.6)[d] 143.3 (45.7)[d]	53 (73.61) 51 (76.12)	156.0 (14.1) 153.1 (11.8)
Maurice, 2022 (GASS)	NR	111 (66) 114 (65)	200 ()[e] 188 ()[e]	69 (44)[a] 60 (39)[a]	51 ()[f] 59 ()[f]	144 (85) 131 (75)	NR[g]

Author, publication year (study)	Change in NIHSS at 24 h, n (IQR)	Favorable outcome (mRS 0–2) at 90 d, n (%)	Any hemorrhagic complication, n (%)	Mortality at 90 d, n (%)	Conversion to GA, n (%)
Schönenberger, 2016 (SIESTA)	5 (−2 to 10) 4 (−2 to 10)	27 (37.0) 14 (18.2)	1 (1.4)[h] 2 (2.6)[h]	18 (24.6) 19 (24.7)	11 (14.3)
Löwhagen, 2016 (AnStroke)	9 (4 to 17) 8 (2.5 to 13)	19 (42.2) 18 (40.0)	0 (0.0)[i] 3 (6.7)[i]	6 (13.3) 11 (24.4)	7 (15.6)
Simonsen, 2018 (GOLIATH)	10 (5 to 14) 7 (0 to 13)	43 (66.1) 33 (52.4)	4 (6.2)[j] 3 (4.8)[j]	5 (7.7) 8 (12.7)	4 (6.3)
Sun, 2019 (CANVAS Pilot)	NR	11 (55) 10 (50)	0 (0.0)[k] 2 (10.0)[k]	1 (5.0) 6 (30.0)	4 (20)
Ren, 2020	NR	NR	9 (18.75) 7 (16.7)	9 (18.75) 9 (20.93)	4 (9.52)
Hu, 2021	NR	NR	NR	NR	2 (3.0)
Maurice, 2022 (GASS)	NR	66 (40) 63 (36)	37 (22)[i] 42 (24)[i]	31 (19) 28 (16)	7 (4.0)

Abbreviations: ASPECTS = Alberta Stroke Program Early CT Score; CS = conscious sedation; EVT = endovascular thrombectomy; GA = general anesthesia; ICH = intracerebral hemorrhage; IQR = interquartile range; IV tPA = IV tissue plasminogen activator; mRS = modified Rankin score; NIHSS = NIH Stroke Scale; NR = not reported; RCT = randomized controlled trial; SCH = subarachnoid hemorrhage; TICI = Thrombolysis in Cerebral Infarction.
[a] Mean (SD).
[b] Median (IQR).
[c] Estimated from Figure 3 in the article by Ren et al.[24] using graph data extraction software.
[d] Recorded as procedure time.
[e] Values imputed from stroke onset to groin puncture and arrival stroke center to groin puncture. Data presented without SD.
[f] Values imputed from stroke onset to recanalization and stroke onset to groin puncture. Data presented without SD.
[g] Cumulative duration of hypotension GA 39 (25) vs CS 36 (31) minutes.
[h] Vessel perforation with ICH, SAH, or both.
[i] Symptomatic ICH.
[j] Intracranial hemorrhage.
[k] Vessel perforation.

Figure 2 Forest Plots of Pooled Effect Estimate for (A) Recanalization Success, (B) Good Functional Recovery, (C) 3-Month Mortality, and (D) Hemorrhagic Complications



Pooled estimates were performed only if trials reported the endpoint and in the correct format. GA = general anesthesia.

A forest plot with the effect estimate for recanalization success (TICI 2b-3[16]) is presented in Figure 2A. The forest plot with the effect estimate for good functional recovery (mRS 0–2) at 3 months is presented in Figure 2B. Forest plots for hemorrhagic complications and 3-month mortality are shown in Figure 2, C and D, respectively.

Prespecified sensitivity analyses were performed leaving out 1 study at a time sequentially for the pooled effect estimate for recanalization and functional recovery endpoints. Recanalization was not sensitive to any trial removal, with ORs ranging from 1.66 to 1.92 (p values from 0.0004 to 0.01) in favor of GA. Good functional recovery was sensitive to the removal of studies conducted by Schonenberger et al. and Simonsen et al. with p values changing to 0.17 and 0.11, respectively. Full results of the sensitivity analyses are summarized in eTables 1 and 2 (links.lww.com/WNL/C648).

Risk of bias assessed by the Cochrane ROB 2.0 tool[17] was low in 5 of the included studies (eTable 3 and

eFigure 1, links.lww.com/WNL/C648) with some concerns in 1 domain in the remaining 2 studies. The funnel plot was symmetric providing no evidence of publication bias (eFigure 2). The overall quality of evidence assessed using the GRADE system was high based on the low risk of bias, consistency of treatment effect, directness of comparison, precision of estimate, and no evidence of publication bias.[19] eTable 4 details the assessment of the quality of evidence for individual trials.

A planned subanalysis comparing trials with a low risk of bias with those with a high risk of bias was not performed because no trial was categorized as high risk. A comparison of 5 low-risk trials with 2 trials with some concerns in 1 domain showed no subgroup effects (eFigure 3, links.lww.com/WNL/C648). A planned subanalysis of trials comparing propofol with sevoflurane as the maintenance anesthesia agent was performed for the recanalization and functional recovery endpoints. Six of the 7 trials used propofol intravenous anesthesia. The forest plot for this subanalysis can be found in eFigure 4.

GA is established as effective in improving recanalization rates in EVT (7 Class 1 studies[13,20-25]) with a high GRADE certainty rating. GA is established as effective in improving functional recovery at 3 months in EVT (5 Class 1 studies[13,20-23]) with a moderate GRADE certainty rating.

Discussion

EVT has revolutionized stroke care in patients with large vessel occlusion with recanalization rates of approximately 71%, and consequent almost doubling of the number who were independent at 3 months.[26] EVT patients with GA were 9.0% more likely to have successful recanalization compared with patients treated with non-GA techniques with a number needed to treat (NNT) of 11.1. This treatment effect was consistent across the 7 RCTs with low statistical heterogeneity (I^2 = 0%). A plausible explanation is that immobility during GA confers superior imaging and procedural conditions making recanalization more likely.

The improved recanalization rates translated into improved functional recovery. EVT patients with GA were 8.4% more likely to be functionally independent at 3 months compared with patients treated with non-GA techniques (GA 44.6% vs non-GA 36.2%), with an NNT of 11.9. Five of the 7 trials reported 3-month mRS, and the treatment effect was consistent, again with low statistical heterogeneity (I^2 = 8%). There were no differences between GA and non-GA on the safety endpoints of hemorrhagic complications and 3-month mortality. These results conflict with previous nonrandomized comparisons where functional recovery was worse with GA.[1-4] Possible explanations for these earlier results include selection bias, treatment delay, and BP confounding.[4,10,11]

A meta-analysis of nonrandomized trial data adjusted for differences in baseline NIH Stroke Scale and time to recanalization, yet functional outcomes remained worse for GA.[26] Observational studies rarely report intraprocedural physiology (including BP), so the potential for residual confounding remains. In comparison, improved reporting of technique, drug choice, dose, and intraprocedural physiology in these RCTs demonstrate largely equivalent BP management (Table 1) in 5 RCTs[13,20,21,24,25] and BP more than 10 mm Hg lower during GA in 2 trials.[22,23] BP is a modifiable risk factor in stroke. This meta-analysis demonstrates that appropriately managed procedural BP reveals a potential therapeutic benefit of GA in EVT.

All RCTs were assessed as being at low risk of bias. A certainty assessment was performed using the GRADE approach.[19] With this updated meta-analysis, there is high confidence that the true treatment effects are similar to our estimates. One trial recruited participants with vertebrobasilar stroke,[25] whereas 6 trials recruited those with anterior circulation stroke only,[13,20-24] with no evidence of subgroup differences in recanalization when comparing anterior and posterior circulation stroke. A comparison for functional outcome could not be performed because Hu et al.[25] did not report functional recovery in a format allowing pooled analysis.

The superiority of EVT with GA for greater recanalization rates and improved functional outcome provides important clinical guidance for anesthesiologists regarding maintenance drug choice and physiologic targets. The 2 common anesthesia maintenance agents (sevoflurane and propofol) have profoundly different effects on cerebral physiology. Propofol is a potent cerebral vasoconstrictor and has minimal effect on cerebral autoregulation.[27,28] Sevoflurane is a cerebral vasodilator at higher doses and impairs normal cerebral autoregulatory responses.[27,29] These physiologic differences could affect cerebral physiology in stroke and subsequent outcome. In addition, propofol and sevoflurane can both reduce cerebral metabolic rate by 60%[29,30] and demonstrate neuroprotection in animal models of neurologic injury.[30-32] Six of the included studies in this analysis used propofol as the primary anesthetic maintenance agent and maintained the statistically significant improvement in clinical outcome (OR 1.54, 95% CI 1.03–2.28, p = 0.03). There was only 1 study that used sevoflurane[21] for maintenance of anesthesia, but there was no evidence of subgroup differences (p = 0.48). RCTs investigating the effect of anesthesia drugs and associated physiology during stroke are required. An RCT comparing different BP targets under GA is underway,[33] and RCT(s) comparing anesthesia maintenance agents[34] and intraprocedural P_aCO_2[35] have been registered.

This study has limitations. Six of the trials were single-center studies. There were variations in both the GA and non-GA arms of the trials regarding drug choice and dose. The improvement in recanalization rates is a robust finding, but the improvement in functional recovery was sensitive to the removal of 2 studies in the sensitivity analysis. There was no evidence of reporting bias at review level with no asymmetry on the funnel plot; however, there was potential for reporting

bias at outcome level because 1 study did not report mRS and another reported in a format unsuitable for pooled analysis. Further data will be available when the CANVAS study (NCT02677415), SEdation Versus General Anesthesia for Endovascular Therapy in Acute Ischemic Stroke (NCT03263117), and Anesthesia Management in Endovascular Therapy for Ischemic Stroke (NCT03229148) trials report results.

In RCTs, GA is associated with higher rates of successful recanalization and functional independence in large vessel occlusion patients treated with EVT when compared with non-GA techniques. This is in contrast to previous observational studies that may have been prone to residual confounding. Conversion to GA and subsequent intention-to-treat analysis will underestimate the true therapeutic benefit. This updated meta-analysis provides high-quality evidence that GA should be the first choice in patients treated with EVT in those centers able to provide expert anesthesiology services. Updated guidelines should incorporate a level 1A recommendation for improved recanalization with GA and level 1B recommendation for functional recovery. Future research should concentrate on drug choice and physiologic targets during GA.

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Appendix Authors

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Douglas Campbell, BM	Auckland City Hospital, New Zealand	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; study concept or design; and analysis or interpretation of data
Elise Butler, MB ChB	Auckland City Hospital, New Zealand	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; study concept or design; and analysis or interpretation of data
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P. Alan Barber, MBChB, PhD, FRACP	University of Auckland, New Zealand	Drafting/revision of the article for content, including medical writing for content; major role in the acquisition of data; study concept or design; and analysis or interpretation of data

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