General Anesthesia Compared to Non-GA in Endovascular Thrombectomy for Ischemic Stroke: A Systematic Review and Meta-analysis of Randomized Controlled Trials

Author(s):

Douglas Campbell, BM[1]; Elise Butler, MB ChB[1]; Ruby Blythe Campbell[2]; Jess Ho, MB ChB[3]; P. Alan Barber, MBChB, PhD, FRACP[3]

Corresponding Author:
Douglas Campbell, dcampbell@adhb.govt.nz

Affiliation Information for All Authors: 1. Auckland City Hospital 2. University of Otago 3. University of Auckland

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Abstract

Background and objectives

Endovascular thrombectomy (EVT) for large vessel occlusion ischaemic stroke is either performed under general anesthesia (GA) or with non-GA techniques such as conscious sedation (CS) or local anesthesia (LA) alone. Previous small meta-analyses have demonstrated superior recanalization rates and improved functional recovery with GA compared with non-GA techniques. The publication of further 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 randomised 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 % versus non-GA 75.6%; OR=1.75, 95% CI 1.26 to 2.42, P=0.0009) and the proportion of patients with functional recovery improves by 8.4% (GA 44.6 % versus non-GA 36.2%; OR=1.43, 95% CI 1.04 to 1.98, P=0.03). There was no difference in hemorrhagic complications or 3 month mortality.

Conclusions

In ischemic stroke patients treated with EVT, general anesthesia (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 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 endovascular thrombectomy procedures in acute ischemic stroke with a level A recommendation for recanalization and level B recommendation for functional recovery.

Introduction

Endovascular thrombectomy (EVT) for large vessel occlusion ischaemic 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, non-randomised data from trials and meta-analysis of non-randomised 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 this data suggests 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 centres could introduce these changes in practice immediately. The multicenter General Anesthesia vs Sedation for Stroke (GASS) trial [13], the largest RCT to date with 351 EVT patients randomised 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 (PRISMA) [14]. The protocol was prospectively registered with International Prospective Register of Systematic Reviews (PROSPERO identifier CRD42022315945) [15]. Studies were considered if they fulfilled all three of the following three criteria; randomized controlled trial; participants undergoing EVT for large vessel occlusion ischaemic stroke; comparators were GA compared to non-GA techniques such as CS or LA. Trials were excluded if they were not RCTs, did not compare GA and CS/LA or appeared in a database after the study cut-off period.

Systematic searches were made on Medline, Embase and the Cochrane Central Register of Controlled Trials from inception of database until May 1st 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 three 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 in the Supplement.

One investigator (JH) performed comprehensive database searches using the pre-specified search criteria. Three investigators (JH, RC, EB) performed an initial screen and identified potential trials for 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 was 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 randomised group, 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 of 0, 1 or 2 at 3 months. Procedural efficacy was measured by recanalization success as measured by Thrombolysis in Cerebral Infarct Score (TICI) of 2b or 3 at procedure completion [17]. Safety endpoints were symptomatic intra-cerebral haemorrhage and 3-month mortality . These outcomes were all described by an odds ratio (OR) and 95% confidence interval (CI).

Any study that reported an endpoint in an appropriate format (or the 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 synthesised and visually displayed in a forest plot. Analysis was performed using Review Manager 5 (RevMan 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) and studies were combined using a random effects model. Variability within studies was assessed using the I-squared statistic and chi-squared test. Significant heterogeneity was defined as I-squared > 40% and a p value of <0.05 for the chi-squared test. Sensitivity analyses using the leave-one-out method were performed for the recanalization success and functional recovery endpoints. A pre-planned sub-analysis for functional outcome was performed comparing maintenance anesthesia agents.

Risk of bias assessment was performed over five domains using the Cochrane risk of bias tool version 2 (RoB v2.0) [16]; risk of bias arising from randomization, risk of bias due to deviations from intended interventions; missing outcome data; risk of bias in outcome measurement; risk of bias in selection of reported result. Each trial was assessed and these assessments combined for all included trials. A funnel plot was visually inspected for

evidence of reporting bias. Statistical tests of asymmetry were not performed as there were less than ten 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 14th 2022 (PROSPERO 2022 CRD42022315945 available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022315945).

This review used summary data from published manuscripts. No patient level data was used so informed consent or IRB 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

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

INSERT FIG 1 HERE

The characteristics of the eligible trials are tabulated in Table 1 with procedural, primary, secondary and safety outcomes.

INSERT TABLE 1 HERE

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% non-GA patients (OR=1.75, 95% CI 1.26 to 2.42, P=0.0009). This treatment effect was consistent across the seven randomized controlled trials with low statistical heterogeneity ($I^2 = 0\%$). Functional independence (mRS 0-2) at 3 months occurred in 44.6 % GA patients and 36.2% non-GA patients (OR=1.43, 95% CI 1.04 to 1.98, P=0.03). Five of the seven trials reported three month mRS and the treatment effect was consistent, with low statistical heterogeneity ($I^2 = 8\%$). The RCTs by Ren et al and Hu et al were excluded for this analysis. They did not fulfil inclusion criteria as data was 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 to 1.31, P=0.49) and 3 month mortality (OR=0.83, 95% CI 0.55 to 1.24, P=0.35).

A forest plot with the effect estimate for recanalization success (TICI 2b-3 [17]) 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 Figures 2C and 2D respectively.

INSERT FIG 2 HERE

Pre-specified sensitivity analyses were performed leaving out one 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 odds ratios 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 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 can be found in eTable 1 and eTable 2 in the Supplement.

Risk of bias assessed by the Cochrane ROB 2.0 tool [16] was low in five of the included studies (eTable 3 and eFigure 1 in the Supplement) with some concerns in one domain in the remaining two studies. The funnel plot was symmetric providing no evidence publication bias (eFigure 2 in the Supplement). 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 in the Supplement details the assessment of the quality of evidence for individual trials.

A planned sub-analysis comparing trials with low risk of bias compared to trials with high risk of bias was not performed as no trial was categorized as high risk. A comparison of five low risk trials compares to two trials with some concerns in one domain showed no subgroup effects (eFigure 3 Supplement). A planned sub-analysis of trials comparing propofol with sevoflurane as the maintenance anesthesia agent was performed for the recanalization and functional recovery endpoints. Six of the seven trials used propofol intravenous anesthesia. The forest plot for this sub-analysis can be found in eFigure 4 in the Supplement.

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

Endovascular thrombectomy 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 to patients treated with non-GA techniques with a number needed to treat (NNT) of 11.1. This treatment effect was consistent across the seven randomized controlled trials 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 three months compared to patients treated with non-GA techniques (GA 44.6 % versus non-GA 36.2%), with a NNT of 11.9 Five of the seven trials reported three 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 non-randomized comparisons where functional recovery was worse with GA [1-4]. Possible explanations for these earlier results include selection bias, treatment delay and blood pressure confounding [4,10,11].

A meta-analysis of non-randomized trial data adjusted for differences in baseline National Institute of Health Stroke Scale (NIHSS) and time to recanalization yet functional outcomes remained worse for GA [26]. Observational studies rarely report intra-procedural physiology (including blood pressure) so the potential for residual confounding remains. In comparison, improved reporting of technique, drug choice, dose and intra-procedural physiology in these

RCTs demonstrates largely equivalent BP management (see Table 1) in five RCTs [13,20,21,24,25] and BP more than 10 mm Hg lower during GA in two trials [22,23]. Blood pressure 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 seven RCTs were all 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 six trials recruited 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 as Hu et al [25] did not report functional recovery in a format allowing pooled analysis.

The superiority of EVT with GA in terms of greater recanalization rates and improved functional outcome provides important clinical guidance for anesthesiologists regarding maintenance drug choice and physiological targets. The two 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 physiological differences could impact 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 neurological 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 to 2.28, P=0.03). There was only

one study that used sevoflurane [21] for maintenance of anesthesia, but there was no evidence of subgroup differences (P=0.48). Randomised controlled trials investigating the effect of anesthesia drugs and associated physiology during stroke are required. A 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 in terms of 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 two 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 as one 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 (SEGA; NCT03263117) and Anesthesia Management in Endovascular Therapy for Ischemic Stroke (AMETIS; NCT03229148) trials report results.

Conclusion

In RCTs, general anesthesia 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 centres 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 physiological targets during GA.

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Figures and Tables

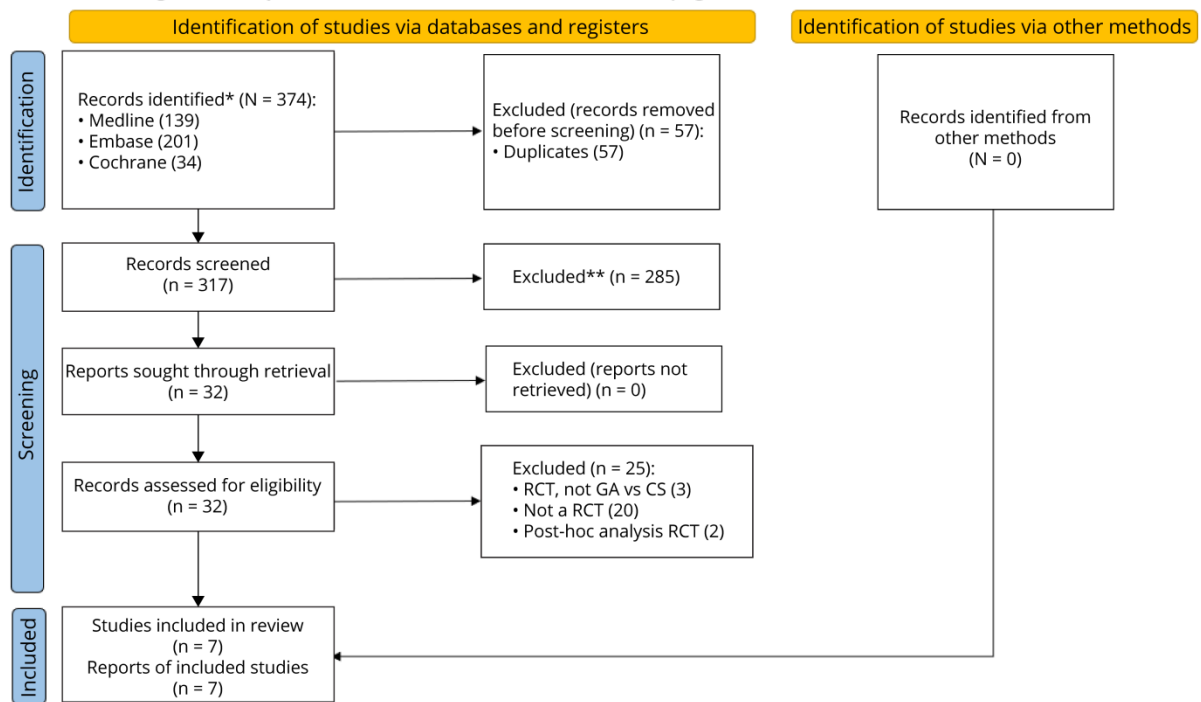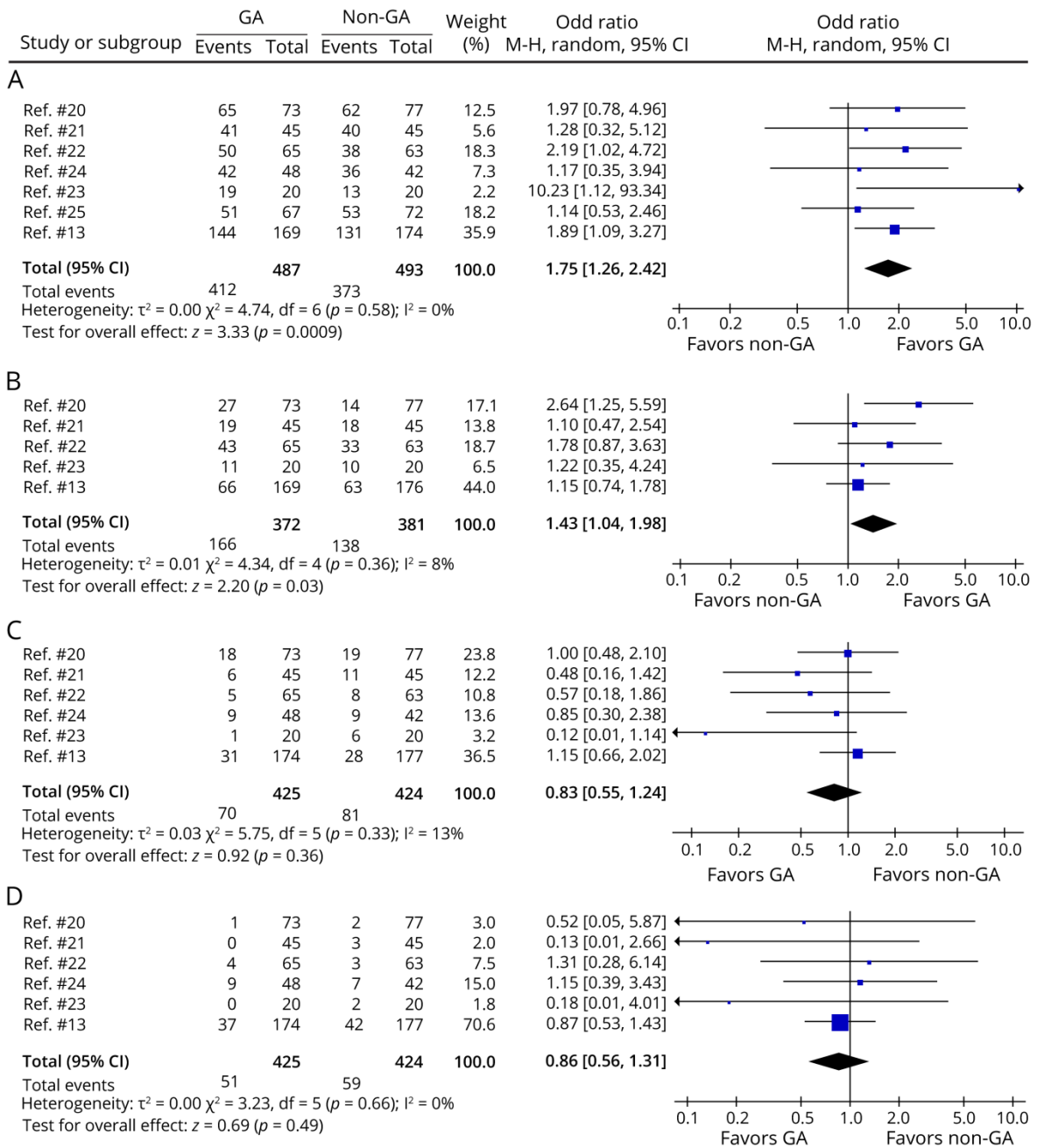**Fig1 Flow diagram for systematic review**

Figure 2. Forest plots of pooled effect estimate for (A) recanalization success (B) good functional recovery (C) 3 month mortality (D) hemorrhagic complications. Pooled estimates were only performed if trials reported the endpoint and in the correct format.

Study or subgroup	GA Events	GA Total	Non-GA Events	Non-GA Total	Weight (%)	Odd ratio M-H, random, 95% CI
A						
Ref. #20	65	73	62	77	12.5	1.97 [0.78, 4.96]
Ref. #21	41	45	40	45	5.6	1.28 [0.32, 5.12]
Ref. #22	50	65	38	63	18.3	2.19 [1.02, 4.72]
Ref. #24	42	48	36	42	7.3	1.17 [0.35, 3.94]
Ref. #23	19	20	13	20	2.2	10.23 [1.12, 93.34]
Ref. #25	51	67	53	72	18.2	1.14 [0.53, 2.46]
Ref. #13	144	169	131	174	35.9	1.89 [1.09, 3.27]
Total (95% CI)		487		493	100.0	1.75 [1.26, 2.42]
Total events	412		373			

Heterogeneity: $\tau^2 = 0.00$ $\chi^2 = 4.74$, df = 6 ($p = 0.58$); $I^2 = 0\%$
Test for overall effect: $z = 3.33$ ($p = 0.0009$)

Favors non-GA — Favors GA

Study or subgroup	GA Events	GA Total	Non-GA Events	Non-GA Total	Weight (%)	Odd ratio M-H, random, 95% CI
B						
Ref. #20	27	73	14	77	17.1	2.64 [1.25, 5.59]
Ref. #21	19	45	18	45	13.8	1.10 [0.47, 2.54]
Ref. #22	43	65	33	63	18.7	1.78 [0.87, 3.63]
Ref. #23	11	20	10	20	6.5	1.22 [0.35, 4.24]
Ref. #13	66	169	63	176	44.0	1.15 [0.74, 1.78]
Total (95% CI)		372		381	100.0	1.43 [1.04, 1.98]
Total events	166		138			

Heterogeneity: $\tau^2 = 0.01$ $\chi^2 = 4.34$, df = 4 ($p = 0.36$); $I^2 = 8\%$
Test for overall effect: $z = 2.20$ ($p = 0.03$)

Favors non-GA — Favors GA

Study or subgroup	GA Events	GA Total	Non-GA Events	Non-GA Total	Weight (%)	Odd ratio M-H, random, 95% CI
C						
Ref. #20	18	73	19	77	23.8	1.00 [0.48, 2.10]
Ref. #21	6	45	11	45	12.2	0.48 [0.16, 1.42]
Ref. #22	5	65	8	63	10.8	0.57 [0.18, 1.86]
Ref. #24	9	48	9	42	13.6	0.85 [0.30, 2.38]
Ref. #23	1	20	6	20	3.2	0.12 [0.01, 1.14]
Ref. #13	31	174	28	177	36.5	1.15 [0.66, 2.02]
Total (95% CI)		425		424	100.0	0.83 [0.55, 1.24]
Total events	70		81			

Heterogeneity: $\tau^2 = 0.03$ $\chi^2 = 5.75$, df = 5 ($p = 0.33$); $I^2 = 13\%$
Test for overall effect: $z = 0.92$ ($p = 0.36$)

Favors GA — Favors non-GA

Study or subgroup	GA Events	GA Total	Non-GA Events	Non-GA Total	Weight (%)	Odd ratio M-H, random, 95% CI
D						
Ref. #20	1	73	2	77	3.0	0.52 [0.05, 5.87]
Ref. #21	0	45	3	45	2.0	0.13 [0.01, 2.66]
Ref. #22	4	65	3	63	7.5	1.31 [0.28, 6.14]
Ref. #24	9	48	7	42	15.0	1.15 [0.39, 3.43]
Ref. #23	0	20	2	20	1.8	0.18 [0.01, 4.01]
Ref. #13	37	174	42	177	70.6	0.87 [0.53, 1.43]
Total (95% CI)		425		424	100.0	0.86 [0.56, 1.31]
Total events	51		59			

Heterogeneity: $\tau^2 = 0.00$ $\chi^2 = 3.23$, df = 5 ($p = 0.66$); $I^2 = 0\%$
Test for overall effect: $z = 0.69$ ($p = 0.49$)

Favors GA — Favors non-GA

Author, publication year (Study)	Study design, period, population	Country and centres	Total patients, (n)	Group, (n)	Age (years)	Sex, male n (%)	Initial NIHSS
Schönenberger 2016 (SIESTA)	RCT April 2014 – February 2016 EVT, anterior circulation	Germany, single centre	150	GA (73) Non-GA (77)	71.8 (12.9)† 71.2 (14.7)†	48 (65.8) 42 (54.5)	17 (13-20) 17 (14-20)
Löwhagen 2016 (AnStroke)	RCT 2013 – 2016 EVT, anterior circulation	Sweden, single centre	90	GA (45) Non-GA (45)	73 (65-80)* 72 (66-82)*	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 centre	128	GA (65) Non-GA (63)	71.0 (10.0)† 71.8 (12.8)†	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 centre	40	GA (20) Non-GA (20)	67 (57-77)* 60 (45-73)*	13 (65) 13 (65)	14 (11-18) 13 (9-17)
Ren 2020	RCT 2017 – 2018 EVT, anterior circulation	China, single centre	90	GA (48) Non-GA (42)	69.21 (5.78)† 69.19 (6.46)†	26 (54.2) 24 (57.1)	14 (11-16) 14 (11-16)
Hu 2021	RCT 2017 – 2019 EVT, posterior circulation	China, single centre	139	GA (72) Non-GA (67)	72.1 (6.8)† 71.9 (7.5)†	38 (52.78) 32 (50.75)	NR
Maurice 2022 (GASS)	RCT, 2016-20 EVT, anterior circulation	France, 4 centres	351	GA (174) Non-GA (177)	70.8 (13.0)† 72.6 (12.3)†	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)† 65.6 (19.9)†	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)* 72 (58-119)*	34 (18-47)* 25 (15-36)*	55 (38-110)* 74 (37-104)*	41 (91.1) 40 (88.9)	MAP 91(8) 95(8)
Simonsen 2018 (GOLIATH)	NR	50 (76.9) 46 (73.0)	159 (122-230)* 145 (113-231)*	24 (20-27)* 15 (12-20)*	34 (21-51)* 29 (16-51)*	50 (76.9) 38 (60.3)	MAP [h] 90 (82-99) 102 (88-111)
Sun 2019 (CANVAS Pilot)	NR	9 (45) 11 (55)	307 (271-347)* 286 (245-333)*	29 (25-34)* 15 (11-17)*	98 (75-123)* 87 (66-101)*	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 [i] 159.0 (7.5) 161.5 (7.5)

Hu 2021	NR	NR	142.3 (39.3) 129.6 (47.3)	NR	130.4 (43.6)[c] 143.3 (45.7)[c]	53 (73.61) 51 (76.12)	156.0 (14.1) 153.1 (11.8)
Maurice 2022 (GASS)	NR	111 (66) 114 (65)	200()[a] 188()[a]	69 (44)† 60 (39)†	51 ()[b] 59 ()[b]	144 (85) 131 (75)	NR [j]

Author, publication year (Study)	Change in NIHSS at 24 hours n (IQR)	Favourable outcome (mRS 0-2) at 90 days n (%)	Any haemorrhagic complication n (%)	Mortality at 90 days 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)[d] 2 (2.6)[d]	18 (24.6) 19 (24.7)	11 (14.3)		
Löwhagen 2016 (AnStroke)	9 (4-17) 8 (2.5-13)	19 (42.2) 18 (40.0)	0 (0.0)[e] 3 (6.7)[e]	6 (13.3) 11 (24.4)	7 (15.6)		
Simonsen 2018 (GOLIATH)	10 (5 to 14) 7 (0 -13)	43 (66.1) 33 (52.4)	4 (6.2)[f] 3 (4.8)[f]	5 (7.7) 8 (12.7)	4 (6.3)		
Sun 2019 (CANVAS Pilot)	NR	11 (55) 10 (50)	0 (0.0)[g] 2 (10.0)[g]	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)[e] 42 (24)[e]	31 (19) 28 (16)	7 (4.0)		
†mean(SD) *median (IQR)							

RCT indicates randomized controlled trial; EVT, endovascular thrombectomy; GA, general anesthesia; CS, conscious sedation; NIHSS, National Institutes of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; IV tPA, intravenous tissue plasminogen activator; NR, not reported; TICI, Thrombolysis in Cerebral Infarction; mRS, modified Rankin Score; SD standard deviation; IQR interquartile range. [a] Values imputed from stroke onset to groin puncture and arrival stroke centre to groin puncture. Data presented without SD [b] Values imputed from stroke onset to recanalization and stroke onset to groin puncture. Data presented without SD [c] Recorded as procedure time [d] Vessel perforation with ICH, SAH, or both [e] Symptomatic ICH [f] Intracranial haemorrhage [g] Vessel perforation [h] Reported as median (IQR) [i] Estimated from Fig 3 using graph data extraction software [j] Cumulative duration of hypotension GA 39 (25) v CS36(31) mins

Table 1. Demographic and trial data for eligible RCTs with procedural, primary,

secondary and safety outcomes.

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General Anesthesia Compared to Non-GA in Endovascular Thrombectomy for Ischemic Stroke: A Systematic Review and Meta-analysis of Randomized Controlled Trials

Douglas Campbell, Elise Butler, Ruby Blythe Campbell, et al.

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