REVIEW ARTICLE

Is General Anesthesia for Endovascular Thrombectomy Helpful or Harmful?

E. L. Harrison, Michael D. Hill

ABSTRACT: Endovascular thrombectomy (EVT) has significantly improved outcomes for patients with acute ischemic stroke due to large vessel occlusion. However, despite advances, more than half of patients remain functionally dependent 3 months after their initial stroke. Anesthetic strategy may influence both the technical success of the procedure and overall outcomes. Conventionally, general anesthesia (GA) has been widely used for neuroendovascular procedures, particularly for the distal intracranial circulation, because the complete absence of movement has been considered imperative for procedural success and to minimize complications. In contrast, in patients with acute stroke undergoing EVT, the optimal anesthetic strategy is controversial. Nonrandomized studies suggest GA negatively affects outcomes while the more recent anesthesia-specific RCTs report improved or unchanged outcomes in patients managed with versus without GA, although these findings cannot be generalized to other EVT capable centers due to a number of limitations. Potential explanations for these contrasting results will be addressed in this review including the effect of different anesthetic strategies on cerebral and systemic hemodynamics, revascularization times, and periprocedural complications.

RÉSUMÉ : L'anesthésie générale dans la thrombectomie endovasculaire a-t-elle une influence favorable ou défavorable? La thrombectomie endovasculaire (TEV) a permis d'améliorer grandement les résultats cliniques chez les patients ayant subi un accident vasculaire cérébral (AVC) ischémique aigu, attribuable à l'occlusion d'un gros vaisseau. Toutefois, malgré les progrès, plus de la moitié des patients se trouvent encore en état de dépendance fonctionnelle trois mois après leur AVC initial. Il est possible que les modalités d'anesthésie influent tant sur la réussite technique de l'intervention que sur l'ensemble des résultats. Il est pratique courante d'effectuer les interventions neuroendovasculaires sous anesthésie générale (AG), surtout dans les cas de circulation intracrânienne distale, puisque l'absence complète de mouvement est considérée comme essentielle à la réussite de l'intervention, et que l'AG permet de réduire le plus possible les risques de complications. En revanche, chez les patients soumis à une TEV pour un AVC aigu, les modalités optimales d'anesthésie prêtent à controverse. D'après des études sans répartition aléatoire, l'AG aurait un effet défavorable sur les résultats, tandis que, dans certains essais comparatifs à répartition aléatoire récents de modalités d'anesthésie, on a observé une amélioration ou du moins une non-détérioration des résultats chez les patients soumis, ou non, à l'AG; toutefois, il est impossible d'appliquer les résultats obtenus à d'autres centres en mesure d'effectuer des TEV en raison d'un certain nombre de limites. L'article de synthèse portera donc sur des explications plausibles de ces résultats divergents, dont l'effet de différentes modalités d'anesthésie sur l'hémodynamique générale et cérébrale, le temps nécessaire à la revascularisation et les complications périopératoires.

Keywords: Interventional neuroradiology, Anesthesia, Stroke, Endovascular, Clinical, Cerebrovascular disease

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Introduction

Endovascular thrombectomy (EVT) is the standard of care for patients with acute ischemic stroke (AIS) due to large vessel occlusion (LVO).[1] Efficacy is dependent on timely recanalization of the occluded artery. Despite significant improvements in clinical outcomes with EVT, more than half of patients remain functionally dependent (as defined by a modified Rankin scale (mRS) score of greater than two) 3 months after their initial stroke.[2] It may be that additional factors, such as anesthetic strategy, influence both the technical success of the procedure and overall outcomes.

The optimal anesthetic strategy for those undergoing EVT is controversial; at present, GA is routinely used at some centers, used only for specific patient types or situations or eschewed completely. Options include local anesthetic (LA) use at the arterial access site only, conscious or procedural sedation (CS) without intubation, or general anesthesia (GA) with full airway control and optional use of neuromuscular blockade. The distinction between CS and GA is generally drawn at the use of intubation for full airway control.

Proposed advantages and disadvantages associated with each type of anesthesia are shown in Table 1. Conventionally, GA has

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Table 1: Advantages and disadvantages by anesthetic strategy

	Advantages	Disadvantages
GA	Decreased patient movement* Avoids need for urgent intubation in case of deterioration Airway protection Pain control	Hemodynamic changes - Hypertension with laryngoscopy required for intubation - Preintubation hypotension (induction agent induced) Potential for delayed time to recanalization Need for additional workforce (nursing, anesthetics, ICU)
CS	Enables intraprocedural neurologic assessment Lower cost**	Lack of airway protection – increased risk of aspiration
LA	Enables intraprocedural neurologic assessment Lower cost**	Lack of airway protection***

CS=conscious sedation; GA=general anesthesia; ICU=intensive care unit; LA=local anesthetic.
*Theoretically increasing chance of successful recanalization and reducing risk of distal embolization and vessel perforation/dissection.
**Less medication, monitoring, staffing, need for ICU admission compared with GA.
***Lower risk of aspiration compared with CS.

been widely used in neuro-intervention for elective endovascular procedures such as the coiling of intracranial aneurysms. Particularly, distally in the intracranial circulation, the complete absence of movement has been widely considered essential for both technical procedural success and to minimize complications and therefore a major advantage of GA.

Initial nonrandomized studies evaluating anesthetic choice suggested an association with adverse outcomes and GA.[3–18] A post hoc analysis of MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in The Netherlands), in which sites prespecified their anesthetic technique prospectively, demonstrated that the beneficial effect of EVT on clinical outcomes was nullified in those treated with GA.[19] The HERMES (Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke) collaboration meta-analysis reported that patients treated with GA had poorer outcomes compared with those managed without GA; the benefit of EVT on functional outcomes was reduced but still observable.[20] More recently, five single center RCTs have published contrasting results, reporting either improved or no significant difference in clinical outcomes according to anesthetic strategy.[21–25] This stark contrast between larger multicenter cohort studies showing a negative association between GA use and outcomes and smaller single center randomized trials showing improved or no difference in outcomes with GA is the fundamental source of ongoing controversy in the field.

Different anesthetic strategies have variable effects on cerebral and systemic hemodynamics, revascularization times, and periprocedural complications (see Figure 1). Interpretation of results from nonrandomized studies is affected by confounding by indication and selection bias. Patients with more severe stroke and multiple comorbidities, the very factors that predict poorer outcome overall, are more likely to be managed under GA. Anesthetic practices in the HERMES trials varied substantially, in contrast with the highly specified protocols of the most recent anesthesia-specific RCTs.

The objective of this review is to examine the influence of different anesthetic management strategies on clinical outcomes in those with AIS due to LVO of the anterior circulation, with secondary consideration of potential underlying mechanisms.

Clinical Results

Retrospective Studies

Observational, predominantly retrospective studies, which have attempted to evaluate the association between anesthetic strategy and clinical outcomes among patients with AIS managed with EVT, have reported mixed results (see Table 2). CS has been associated with improved functional outcomes[3–14] and reduced mortality[4–7,9,13,14] compared with GA; others have reported no difference in outcomes between CS and GA.[26–31] LA has similarly been associated with better functional outcomes compared with GA,[15–18] often with reduced mortality,[15,16] although these findings are contrasted by those from a subanalysis of Trial and Cost Effectiveness Evaluation of Intra-arterial Thrombectomy in Acute Ischemic Stroke[32] and a prospective study by Wu et al.[33] Only two studies have directly compared outcomes in those managed with CS versus LA. Work from 1034 patients in the Endovascular Treatment in Ischemic Stroke registry in France reported higher rates of good functional outcome with CS versus LA (mRS 0–2 at 3 months CS 52% vs LA 40%, $p = 0.028$).[34] A retrospective review from one of the MR CLEAN centers reported contrasting results (mRS 0–2 at 3 months CS 22% vs LA 47%, OR 0.4 [0.2–0.8]).[35] Both Goldhoorn et al. and Cappellari et al. retrospectively evaluated outcomes in patients with LA, CS, or GA. In both studies, those managed with LA had improved functional outcomes (Goldhoorn mRS 0–2 GA 35%, CS 25%, LA 41%, $p \leq 0.01$; Cappellari mRS 0–2 GA 42.5%, CS 46.6%, LA 52.4%, $p \leq 0.001$) and reduced mortality (Goldhoorn GA 32%, CS 36%, LA 27%, $p = 0.04$; Cappellari GA 21.5% CS 19.7% LA 14.8%, $p \leq 0.001$).[36,37] The range of rates of good outcome among these various studies is large implying likely differences in the populations under study. Interpretation of results from these nonrandomized studies is limited (inherent bias in trial design, combination of LA and CS into single comparator group); however, findings suggest improved outcomes in those managed without GA and point toward better outcomes in patients managed with LA rather than CS. In addition to improved outcomes, patients managed without GA have a shorter length of stay as reported by powers (GA 8.02 days (5.35–12.18 days), CS 5.93 days (3.31–8.85 days), $p = 0.03$),[13] and Bekelis et al. (GA 19.6 days, CS 11.7 days, unadjusted

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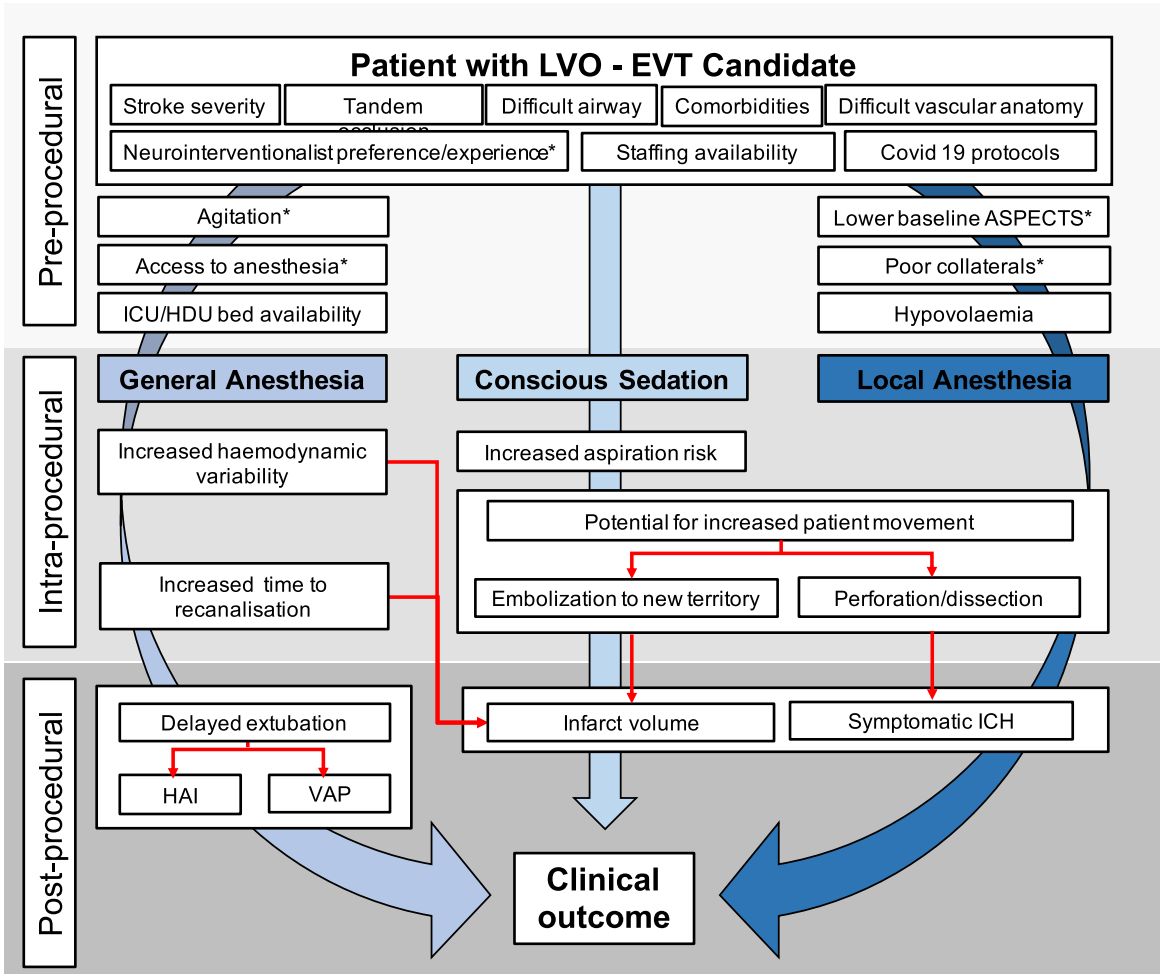

Figure 1: *Anesthesia and EVT – key variables.*

difference 7.9 (CI 5.1–10.7)[38] and a reduced cost of hospitalization (GA $USD 34,903 ($25,530–55,444), CS $26,775 ($18,790–39,935), $p \leq 0.0001$).[7]

Anesthesia-Specific RCTs

Five single center RCTs have examined the influence of anesthetic strategy on outcomes among patients with AIS due to anterior circulation LVO (see Tables 3–5). Overall rates of functional independence (mRS 0–2 at 90 days) were variable, ranging from 27.3% in SIESTA[25] to 59.4% in GOLIATH.[21] Similar variability was seen in the HERMES trials, with the most comparable (by anesthetic strategy) reporting functional independence in 32.6% patients in MR CLEAN (38% GA),[41] 60.0% in Solitaire With the Intention For Thrombectomy as PRIMary Endovascular Treatment (37% GA),[42] and 71.0% in Extending the Time for Thrombolysis in Emergency Neurological Deficits – Intra-Arterial (36% GA).[43] Only two of the anesthesia-specific RCTs, ANSTROKE and the work by Ren et al., specifically evaluated the impact of anesthetic outcome on functional status 3 months poststroke.[23,24]

SIESTA (Sedation versus Intubation for Endovascular Stroke Treatment) randomized 150 patients (73 GA, 77 CS) from the University of Heidelberg in Germany. GA was the standard of care prior to trial commencement; CS was the intervention in the trial. The CS protocol, implemented 6 months prior to study commencement, targeted a Richmond Agitation Sedation Scale of −3 to −2. There was no difference in primary outcome, change in NIHSS at 24 hours, between groups (GA mean −3.2, CS mean −3.6, difference −0.4 (−3.4–2.7) $p = 0.82$), although patients managed with GA were significantly more likely to achieve functional independence at 3 months (GA 37%, CS 18.2%, difference −18.8 (−32.8 to −4.8), $p = 0.01$).[25]

ANSTROKE (Anesthesia During Stroke Trial) randomized 90 patients (45 GA, 45 CS) from Sahlgrenska University Hospital in Sweden who presented within 8 hours of onset. GA was considered the intervention, suggesting CS was the standard of care prior to trial enrollment. Neither the primary endpoint of percentage of patients that achieved an mRS of 0–2 at 3 months (GA 42.2%, CS 40%, $p = 1.00$) nor the median mRS at 3 months (GA 3 (1–4), CS 3 (1–5.5), $p = 0.5001$) differed by anesthetic strategy.[24]

In GOLIATH (General Or Local anesthesia in Intra Arterial Therapy), both GA and CS were routinely used at the Aarhus University Hospital, Denmark prior to trial commencement. Similar to ANSTROKE, no target level of sedation was provided

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Table 2: Nonrandomized studies

Author, year	N (patients)	Method	Outcomes (%)	Complications (%)	Mortality (%)	Summary
CS vs GA						
Improved functional outcomes with CS vs GA						
Sugg et al. (2010)[3]	65 GA 13.8% CS 87.7% CV NS	2007–2009 Single center Retrospective	**mRS 0–2** CS 50.9, GA 11.1; $p = 0.033$ **Recanalization (TICI 2–3)** CS 70, GA 77	**Complications** CS 3.5, GA 22; $p = 0.0288$	**In hospital** CS 29.8, GA 55.6	Increased good functional outcomes + reduced complications with CS c.w GA
Abou-Chebl et al. (2010)[4]	960 GA 44% CS 54% CV NS	2005–2009 Multicenter Retrospective	**Poorer functional outcome with GA (3 months)** OR 2.33 (1.63–3.44); $p = 0.0001$	**SICH** GA 9.3, CS 9.1	**Higher mortality with GA** OR 1.68 (1.23–2.30); $p = 0.0001$	Better functional outcomes (OR 2.33) + reduced mortality with CS c.w GA
Jumaa et al. (2010)[5]	126 GA 42% CS 58% CV NS	Single center 2006–2009 Retrospective	**mRS 0–2 (3–6 months)** GA 23, CS 46; $p = 0.009$ **Recanalization (TICI 2–3)** GA 70, CS 82	**Intraprocedural** GA 15, CS 6 **Pneumonia** GA 30, CS 13.7; $p = 0.024$	**In hospital** GA 31, CS 43; $p = 0.011$	Increased good functional outcomes + lower rates of pneumonia + mortality with CS c.w GA
Hassan et al. (2013)[6]	907 GA 42.7% CS 57.3% CV 3.5%	2006–2010 Multicentre Prospective	**mRS 0–2 (at discharge)** CS 68.2, P-GA 42, U-GA 50 CS vs GA $p \leq 0.001$ P-GA vs U-GA $p = 0.73$		**In hospital** CS 4.4, P-GA 17, U-GA 13 CS vs GA $p \leq 0.001$ P-GA vs U-GA $p = 1.00$	Increased good functional outcomes + lower rates of pneumonia + mortality with CS c.w GA. Outcomes + mortality similar for P-GA + U-GA
McDonald et al. (2015)[7]	1014 GA 50% CS 50% CV NA	2006–2013 Multicentre Retrospective propensity matched	**Discharge home** GA 14, CS 23; $p = 0.0007$ **Discharge to LTC** GA 52, CS 57	**SAH or ICH** GA 11, CS 12 **Pneumonia** GA 17, CS 9.3; $p = 0.0005$	**In hospital** GA 25, CS 12; $p \leq 0.0001$	Increased discharge home + lower rates of pneumonia + mortality with CS c.w GA
Van den Berg et al. (2015)[8]	348 GA 20.1% CS 79.8% CV 3.7%	2002–2013 Multicentre Retrospective	**mRS 0–2 (at discharge)** CS 25.9, GA 14.3; $p = 0.04$ **Recanalization (TICI 2b-3)** CS 42.6, GA 48.6	**SICH** CS 11.9, GA 11.4 **Pneumonia** CS 14.7, GA 12.9	**In hospital** CS16.5, GA 21.4	Increased good functional outcomes with CS c.w GA
Just et al. (2016)[9]	109 GA 38.5% CS 61.5% CV NS	2000–2013 Single center Retrospective	**mRS (at discharge) >2** GA 76.2, CS 62.7; $p = 0.032$ **mRS (3 months) > 2** GA 66.7, CS 53.7		**In hospital** GA 40.5, CS 17.9; $p = 0.009$ **3 months** GA 42.9, CS 20.9; $p = 0.014$	Increased good functional outcomes + reduced mortality with CS c.w GA
Jagani et al. (2016)[10]	99 GA 38.4% CS 61.6% CV 1.6%	2008–2015 Single center Retrospective	**mRS 0–2** CS 39, GA 16; $p = 0.02$	**ICH** CS 28, GA 35	**3 months** CS 18, GA 30	Increased good functional outcomes with CS c.w GA
Slezak et al. (2017)[11]	401 GA 69% CS 31% CV 7.4%	2010–2015 Single center Prospective	**mRS 0–2** CS 47.4, GA 32; $p = 0.02$ **Recanalization (TICI 2–3)** CS 85.9, GA 88.3	**SICH** CS 6.8, GA 8 **Pneumonia** CS 16.5, GA 25.3; $p = 0.048$	**3 months** CS 20.7, GA 28.9	Increased good functional outcomes + reduced rates of pneumonia with CS c.w GA
Eker et al. (2018)[12]	97 GA 33% CS 67% CV 10%	2012–2015 Multicentre Retrospective	**mRS 0–2** GA 50.0, CS 66.2* **Recanalization (TICI 2b-3)** GA 68.8, CS 78.5	**SICH** GA 0, CS 0 **Pneumonia** GA 34.4, CS 12.3; $p = 0.02$		Increased good functional outcomes + reduced rates of pneumonia with CS c.w GA

Table 2. *Continued*

Author, year	N (patients)	Method	Outcomes (%)	Complications (%)	Mortality (%)	Summary
Powers et al. (2019)[13]	92 GA 28% CS 72% CV 6.1%	2016–2017 Multicentre Retrospective	mRS 0–2 GA 23, CS 53; $p = 0.009$ Recanalization (TICI 2b-3) GA 69, CS 79	SICH GA 4, CS 8 Pneumonia GA 3.8, CS 1.5	3 months GA 19, CS 12; $p = 0.04$	Increased good functional outcomes + reduced mortality with CS c.w GA
Feil et al. (2021)[14]	6635 GA 67% CS 24.9% CV 3.3%	2015–2019 Multicentre Retrospective	**mRS 0–2** CS 42.1, GA 34.2, CV 33.5; $p \leq 0.001$ **Recanalization (TICI 2b-3)** CS 83.0, GA 84.2, CV 82.6	**Periprocedural** CS 15.0, GA 21.0, CV 28.3; $p \leq 0.001$ **Vessel complications** CS 2.5, GA 2.9, CV 6.4; $p = 0.007$ **ICH** CS 1.7, GA 2.8, CV 5.9; $p \leq 0.001$	**3 months** CS 23.4, GA 32.4, CV 26.0; $p \leq 0.001$	Increased good functional outcomes + reduced complications + mortality with CS c.w GA. Mortality similar for CV
No difference in functional outcomes for CS vs GA						
Li et al. (2013)[26]	109 GA 32.1% CS 67.9% CV NS	2006–2012 Single center Prospective	**mRS 0–2 (at discharge)** GA 11, CS 15 **Recanalization (TICI 2–3)** GA 63, CS 76	**Pneumonia** GA 21, CS 16	**In hospital** GA 40, CS 22; $p = 0.045$	No difference in functional outcome by anesthetic strategy but reduced mortality with CS c.w GA
John et al. (2014)[27]	190 GA 47.9% CS 52.1% CV NS	2008–2012 Single center Retrospective	**mRS 0–2 (30 days)** CS 22.8, GA 14.9 **Recanalization (TICI 2b-3)** CS 48.5, GA 57.8	**Parenchymal hematoma** CS 10.1, GA 26.3; $p = 0.003$	**In hospital** CS 13.3, GA 25.8; $p = 0.04$	No difference in functional outcome by anesthetic strategy. Reduced parenchymal hematoma + mortality with CS c.w GA
Peng et al. (2018)[28]	149 GA 29.5% CS 70.5% CV 0%**	2015 Multicentre Prospective	**mRS 0–2 (3 months)** CS 53.3, GA 61.4 **Recanalization (TICI 2b-3)** CS 86.4, GA 84.1	**SICH** CS 4.8, GA 2.3	**3 months** CS 12.4, GA 11.4	No difference in functional outcomes, complications or mortality by anesthetic strategy
Shan et al. (2018)[29]	228 GA 50% CS 50% CV NA	2014–2016 Multicentre Prospective Propensity matched	**mRS 0–2** GA 41.2, CS 46.5 **Recanalization (TICI 2b-3)** GA 86.0, CS 81.6	**SICH** GA 21.9, CS 12.3	**In hospital** GA 26.3, CS 21.9 **3 months** GA 31.6, CS 21.9	No difference in functional outcomes, complications or mortality by anesthetic strategy
Rohde et al. (2019)[30]	56 GA 50% CS 50% CV NA	2012–2015 Multicentre Retrospective Propensity matched	**mRS 0–2 (at discharge)** GA 60.4, CS 60.4	**Pneumonia** GA 0, CS 14.3 **SICH** 0 both groups	**In hospital** 0 both groups	No difference in functional outcomes, complications or mortality by anesthetic strategy
Byrappa et al. (2021)[31]	155 GA 29% CS 71% CV NS	2015–2018 Single center Retrospective	**mRS 0–2 (at discharge)** GA 33.3, CS 49.9 **mRS 0–2 (3 months)** GA 22.2, CS 58.8 **Recanalization (TICI 2b-3)** GA 84.4, CS 78.0		**In hospital** GA 11.4, CS 7.4	No difference in functional outcome or mortality by anesthetic strategy
Bekelis et al. (2017)[38]	1174 GA 37.6% CS 62.4% CV NS	2009–2013 Multicentre Retrospective	**Functional outcomes not recorded**		**In hospital** GA 25.6, CS 18.1; $p \leq 0.001$	Reduced mortality with CS c.w GA

LA vs GA

Improved functional outcome with LA vs GA						
Davis et al. (2012)[15]	96 GA 50% LA 50% CV NA	2003–2009 Single center Retrospective	**mRS 0–2** GA 15, LA 60; $p = 0.001$	**Vessel perforation + SAH** GA 2.1, LA 0 **ICH** GA 2.1, LA 4.2	**3 months** RR 2.3 (1.1–3.7); $p = 0.039$	Increased good functional outcomes (RR 3.2) + lower mortality with LA c.w GA
Abou-Chebl (2014)[17]	281 GA 69.8% LA 30.2% CV NS	2012–2013 Multicentre Retrospective	**mRS 0–2** LA 52.6, GA 35.6; $p = 0.01$ **Recanalization (TICI 2b-3)** LA 72.9, GA 73.6	**SICH** LA 7.1, GA 11.2	LA 23.1, GA 34	Increased good functional outcomes with LA c.w GA
Abou-Chebl et al. (2015)[16]	434 LA 62% GA 33.9% UA 4% CV NS	2006–2013 Multicentre Retrospective	**mRS 0–2** LA 48, GA 30.6; $p = 0.0013$ **Recanalization (TICI 2–3)** GA 76.4, CS 72.8	**SICH** GA 8.2, CS 4.8	**In hospital** GA 23.1, CS 7.4; $p \leq 0.0001$	Increased good functional outcomes + reduced mortality with LA c.w GA
No difference in functional outcome for LA vs GA						
Bracard et al. (2017)[32]	141 GA 49% LA 52% CV NS	2010–2015 Multicentre Retrospective	**mRS 0–2** GA 52, CS/LA 49 **Recanalization (TICI 2b-3)** GA 76, CS/LA 62			No difference in functional outcomes or recanalization rates by anesthetic strategy
Wu et al. (2019)[33]	187 GA 40.1% LA 59.9% CV NS	2013–2017 Single center Prospective	**mRS 0–2** LA 50.0, GA 53.3 **Recanalization (TICI 2b-3)** LA 81.3, GA 82.7	**Periprocedural** LA 30.4, GA 29.3 **SICH** LA 7.1, GA 9.3 **Pneumonia** LA 18.8, GA 16.0	**3 months** LA 15.2, GA 18.7	No difference in functional outcomes, complications or mortality by anesthetic strategy
CS vs LA						
Improved functional outcome with LA vs CS						
Van de Graaf et al. (2018)[35]	146 CS 41.1% LA 58.9% CV NS	2014–2016 Single center Retrospective	**mRS 0–2** CS 22, LA 47; OR 0.4 (0.2–0.8) **Recanalization (TICI 2b-3)** CS 63, LA 78; OR 0.5 (0.2–1.0)	**SICH** CS 5, LA 3 **Pneumonia** CS 20, LA 10	**3 months** CS 35, LA 16; OR 2.3 (1.0–5.2)	Increased good functional outcomes, successful recanalization + reduced mortality with LA c.w CS
Improved functional outcome with CS vs LA						
Benvegnù et al. (2020)[34]	444 CS 50% LA 50% CV NA	2018 Multicentre Retrospective Propensity matched	**mRS 0–2** CS 52.0, LA 40.0 **Recanalization (TICI 2b-3)** CS 87.1, LA 76.6	**Vessel complications** CS 8.5, LA 10.2 **SICH** CS 8.3, LA 9.9	**3 months** CS 18.2, LA 24.3	Increased good functional outcomes + successful recanalization with CS c.w LA
No difference in functional outcome LA vs CS						
Marion et al. (2020)[39]	158 LA 70.3% CS 29.7% CV NS	2014–2018 Single center Retrospective	**mRS 0–2** LA 35.5, CS 40.9 **Recanalization (TICI 2b-3)** LA 81.1, CS 93.6	**Vessel dissection** LA 3.6, CS 4.3 **Vessel perforation** LA 1.8, CS 2.1 **SICH** LA 4.5, CS 8.5	**3 months** LA 20.7, CS 21.2	No difference in functional outcome or mortality by anesthetic strategy. Higher successful recanalization with CS c.w LA

Table 2. *Continued*

Author, year	N (patients)	Method	Outcomes (%)	Complications (%)	Mortality (%)	Summary
LA vs CS vs GA						
Improved functional outcome with LA vs CS/GA						
Goldhoorn et al. (2020)[36]	1376 LA 60% GA 28% CS 13% CV NS	2014–2016 Multicentre Retrospective	**mRS 0–2** LA 41, GA 35, CS 25; $p \leq 0.01$ CS vs LA adOR 0.35 (0.23–0.54) CS vs GA adOR 0.44 (0.27–0.71)	**SICH** LA 6, GA 6, CS 6 **Pneumonia** LA 11, GA 10, CS 20; $p \leq 0.001$ CS vs LA adOR 2.23 (1.44–3.48) CS vs GA adOR 2.51 (1.50–4.20)	**3 months** LA 27, GA 32, CS 36; $p = 0.04$ GA vs LA adOR1.39 (1.00–1.93) CS vs LA adOR1.96 (1.28–3.01)	Increased good functional outcomes with LA c.w CS + GA. Mortality lowest with LA
Improved functional outcome with LA/CS vs GA						
Cappellari et al. (2020)[37]	4429 GA 45.5% CS 29% LA 25.5% CV 5.5%	2011–2017 Multicentre Retrospective	**mRS 0–2** GA 42.5, CS 46.6, LA 52.4; $p \leq 0.001$ GA vs CS adOR 0.659 (0.538–0.807) GA vs LA adOR 0.769 (0.566–0.998) **Recanalization (TICI 2b-3)** GA 75.6 vs CS 73.4 vs LA 78.5; $p = 0.014$	**SICH** GA 2.2, CS 2.2, LA 3.3	**3 months** GA 21.5, CS 19.7, LA 14.8; $p \leq 0.001$ GA vs LA adOR 1.413 (1.095–1.823)	Increased good functional outcomes with LA + CS c.w GA. Reduced mortality with LA c.w GA
Nichols et al. (2009)[40]	75 53.3% LA 12% CS 34.7% GA CV NS	2003–2007 Multicentre Retrospective	**mRS 0–2** LA/CS 61.2, GA 23.1; $p \leq 0.01$ **Recanalization (TICI 2–3)** LA/CS 72.7, GA 35; $p = 0.01$	**SICH** LA/CS 8.2, GA 19.2 **Vessel complications** LA/CS 0, GA 3.9 **Infections** LA/CS 8.2, GA 30.8; $p = 0.02$	**3 months** LA/CS 8.2, GA 44.4; $p = 0.02$	Increased good functional outcomes, reduced complications + mortality with LA + CS c.w GA
Worsened functional outcomes with LA/CS versus GA						
Pop et al. (2021)[18]	194 GA 50% CS/LA 50% CV NA	2018 Multicentre Retrospective Propensity matched	**mRS 0–2** GA 52, CS/LA 36.1; $p = 0.039$ OR 0.53 (0.33–0.87) **Recanalization (TICI 2–3)** GA 95.8, CS/LA 70.1; $p \leq 0.001$ OR 0.13 (0.04–0.39)	**Procedural** GA 3.0, CS/LA 14.4; $p = 0.018$ **Vessel perforation** LA 3, GA 0; $p \leq 0.001$ **Embolization- new territory** GA 1, CS/LA 10.3; $p = 0.006$ **SICH** GA 7.5, CS/LA 10.6	**3 months** GA 21.8, CS/LA 26.6	Increased good functional outcomes + successful recanalization with GA c.w LA/CS. Higher procedural complications with LA/CS

adOR=adjusted odds ratio; CS=conscious sedation; CV=conversion from LA or CS to GA; GA=general anesthetic; ICH=intracranial hemorrhage; LA=local anesthesia; MAC=minimum alveolar concentration; mRS=modified Rankin scale; NA=nonapplicable – propensity matched; NS=not stated; OR=odds ratio; P-GA=planned GA; SICH=symptomatic intracranial hemorrhage; TICI=thrombolysis in cerebral infarction; UA=undetermined anesthesia; U-GA=unplanned GA.

mRS scores recorded at 3 months unless otherwise stated. Only significant p values provided.

*GA associated with lower rate of functional independence when mRS corrected for differences in baseline characteristics (OR 0.32; $p = 0.05$).

**These patients were excluded.

Table 3: Anesthesia-specific RCTs – baseline characteristics

	SIESTA[25] (2014–2016)		ANSTROKE[24] (2013–2016)		GOLIATH[21] (2015–2017)		CANVAS pilot[22] (2016–2017)		Ren et al.[23] (2017–2018)		HERMES[20] collaboration	
Primary outcome	**Change in NIHSS after 24 hours**		**mRS at 90 days**		**Infarct growth on MRI at 48–72 hours**		**Recruitment rate Conversion from CS to GA**		**mRS at 90 days**		**mRS at 90 days**	
Anesthetic	GA	CS	GA	CS	GA	CS	GA	CS	GA	CS	GA	No GA
N	73	77	45	45	65	63	20	20	48	42	236	561
Age (years)	71.8 (12.9)	71.2 (14.7)	73 (65–80)	72 (66–82)	71.0 (10.0)	71.8 (12.8)	67 (57–77)	60 (45–73)	69.19 ± 6.46	69.21 ± 5.78	63.8 (14.0)	66.3 (13.3)
Male (%)	65.8	54.5	58	51	55.4	47.6	65	65	57.1	54.1	57	51
mRS baseline 0–2 (%)	87.7	92.2	98	98	96.9	100	100	100	54.2	67.4	NS	NS
NIHSS baseline	17 (13–20)	17 (14–20)	20 (15–23)	17 (14–20)	18 (13–21)	17 (15–21)	14 (11–18)	13 (9–17)	14 (11–16)	14 (11–16)	18 (15–21)	17 (14–20)
ASPECTS (median)	8	8	10	10	NS	NS	NS	NS	9	9	7	8
Pretreated with TPA (%)	63.0	64.9	73.3	80	76.9	73.0	45	55	77.1	81.0	92	84

ANSTROKE=Anesthesia During Stroke Trial; ASPECTS=Alberta Stroke Programme Early CT Score; CANVAS=Choice of ANesthesia for EndoVAScular Treatment of Acute Ischemic Stroke; GOLIATH=General Or Local anesthesia in Intra Arterial Therapy; HERMES=Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke trials; mRS=modified Rankin scale; NIHSS=National Institutes of Health Stroke Scale; NS=not stated; SIESTA=Sedation versus Intubation for Endovascular Stroke Treatment; TPA=Tissue Plasminogen Activator.

Table 4: Anesthesia-specific RCTs – anesthetic protocols

	SIESTA[25] (2014–2016)	ANSTROKE[24] (2013–2016)	GOLIATH[21] (2015–2017)	CANVAS pilot[22] (2016–2017)	Ren et al.[23] (2017–2018)
CS	Propofol Remifentanil	Remifentanil	Fentanyl Propofol	Sufentanil Propofol	Propofol + DEX
GA Intubation/induction	Propofol Remifentanil	Propofol Remifentanil Suxamethonium/ Rocuronium	Suxamethonium Alfentanil Propofol	Sufentanil Propofol Rocuronium	Propofol Fentanyl Cisatracurium
GA Maintenance	Propofol Remifentanil	Sevoflurane Remifentanil	Propofol Remifentanil	Propofol Remifentanil	Propofol Remifentanil DEX Cisatracurium
BP target (mmHg)	SBP 140–160 (Limits 120–180)	SBP 140–180 prior to recanalization	SBP > 140 + MAP > 70 during procedure	SBP 140–180	NS
Respiratory target	ET CO_2 40–45 (Limits 35–45) SaO_2 95–98% (Limits 90–100)	Normoventilation	Normoventilation	NS	NS
Depth of sedation	RASS −3 to −2 (Limits −5 to −3)	NS	NS	CS: BIS > 70 GA: BIS 40–60	CS: RASS −2 to −3 GA: NS

BIS=bispectral index; CS=conscious sedation; DEX=dexmedetomidine; ET CO_2=end tidal carbon dioxide; GA=general anesthetic; MAP=mean arterial pressure; NS=not stated; RASS=Richmond Agitation Sedation Scale; SaO_2=arterial oxygen saturation; SBP=systolic blood pressure.

in the trial protocol. The primary outcome measure, infarct growth on MRI at 48–72 h, did not differ by anesthetic strategy (GA 8.2 ml (2.2–38.6), CS 19.4 ml (2.4–79.0), $p = 0.10$), although final infarct volume was lower in those managed with GA (GA 22.3 ml (8.1–64.5), CS 38.0 ml (16.7–128.0), $p = 0.04$), potentially as a result of higher successful recanalization rates (TICI 2b-3) with GA (GA 76.9%, CS 60.3%, $p = 0.04$). Those managed with GA had better functional outcomes at 3 months (mRS 0–2 GA 66.2%, CS 52.4%; median mRS GA 2 (1–3), CS 2 (1–4), $p = 0.04$).[21]

The CANVAS (Choice of ANesthesia for EndoVAScular Treatment of Acute Ischemic Stroke) trial assessed recruitment rates and rates of conversion from CS to GA to facilitate a larger trial evaluating the influence of anesthetic strategy on clinical outcomes (in progress). The target level of sedation in the CS group was a bispectral index of 70 or more, so that patients

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Table 5: Anesthesia-specific RCTs – outcomes

	SIESTA[25] (2014–2016)		ANSTROKE[24] (2013–2016)		GOLIATH[21] (2015–2017)		CANVAS pilot[22] (2016–2017)		Ren et al.[23]		HERMES[20] collaboration	
	GA	CS	GA	CS	GA	CS	GA	CS	GA	CS	GA	No GA
Workflow												
Groin/puncture to recanalization (min)	111.6 (62.5)	129.9 (62.5)	55 (38–110)	74 (37–104)	34 (21–51)	29 (16–51)	98 (75–123)	87 (66–101)	39.1 (±11.9)	47.0 (±15.8)	NS^	NS^
Outcomes												
Recanalization TICI 2b-3	89	80.5	91.1	88.9	76.9*	60.3*	95**	65**	87.5	85.7	75	76
Conversion to GA	–	14.3	–	15.6	–	6.3	–	18.2	–	9.5	–	NS
mRS 3 months (0–2%)	37*	18.2*	42.2	40	66.2	52.4	55	50	NS	NS	40*	50*
In hospital mortality (%)	6.8	7.8	13.3	13.3	NS	NS	NS	NS	12.5	11.9	NS	NS
Mortality 3 months (%)	24.7	24.7	13.3	24.4	7.7	12.7	5	30	18.8	20.9	17	13
Complications												
Occurrence of fall in MAP >20% baseline (%)	NS[#]	NS[#]	93**	60**	87.7**	34.9**	65*	30*	58.3	52.7	NS	NS
Time spent with fall in MAP >20% baseline (min)	NS[#]	NS[#]	22*	15*	NS[+]	NS[+]	NS	NS	9	9	NS	NS
Use of vasopressors	NS	NS	98*	79*	NS	NS	35	10	~	~	NS	NS
Vessel perforation (%)	1.4	2.6	6.7	2.2	0	0	0	10	NS	NS	1	2
Symptomatic ICH (%)	1.4	2.6	0	6.7	3.1	1.6	NS	NS	18.8	16.7	4	4
Pneumonia (%)	13.7*	3.9*	13.3	15.6	NS	NS	50	30	20.8*	4.8*	11	8

ANSTROKE=Anesthesia During Stroke Trial; CANVAS=Choice of ANesthesia for EndoVAScular Treatment of Acute Ischemic Stroke; GA=general anesthesia; GOLIATH=General Or Local anesthesia in Intra Arterial Therapy; HERMES=Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke trials; MAP=mean arterial pressure; mRS=modified Rankin scale; NS=not stated; SIESTA=Sedation versus Intubation for Endovascular Stroke Treatment; TICI=thrombolysis in cerebral infarction.

[*] $p \leq 0.05$, [**] $p \leq 0.001$.

[#]SIESTA reported critical hypo (SBP < 120 mmHg) and hypertension (SBP > 180 mmHg) rather than MAP values.[+]GOLIATH used time MAP < 70 mmHg as similar index.

^HERMES reported onset to randomization and randomization to reperfusion rather than puncture to recanalization.

~Ren et al. reported vasopressor use for each individual agent. For CS range 11.9%–23.8%. For GA range 6.25%–22.9%. No significant difference between groups.

maintained normal, purposeful responses to stimuli, and were able to protect their own airway. Only 31.4% of patients who presented to Beijing Tiantan Hospital Capital Medical University with LVO were enrolled in the trial (40 patients, GA 20, CS 20); the most common reason for exclusion was LVO of the posterior circulation. A fifth (18.2%) of CS patients were converted to GA. Functional outcomes at 3 months were similar across groups (mRS 0–2 GA 55%, CS 50%), although mortality was higher with CS (GA 5%, CS 30%).[22]

Most recently, Ren et al. randomized 90 patients (GA 48, CS 42), using the same depth of CS as SIESTA and demonstrated no difference in outcomes by anesthetic strategy (median mRS at discharge 2 for GA and CS, $p = 0.890$; mRS 3 months 2.5 for GA and CS, $p = 0.796$).[23]

Rates of symptomatic ICH (SICH) did not differ by anesthetic strategy in the anesthesia-specific RCTs, weakening the argument that GA is necessary to prevent excessive patient movement to reduce the risk of vessel perforation. With the exception of Ren et al., rates of SICH in the anesthesia-specific RCTs were comparable to results from the HERMES collaboration (SICH Ren et al. GA 18.8%, CS 16.7%; HERMES GA 4%, CS 4%).[20,23] GA was associated with higher rates of pneumonia in SIESTA (GA 13.7%, CS 3.9%, $p = 0.03$)[25] and the work by Ren et al. (GA 20.8%, CS 4.8%, $p = 0.031$).[23] Mortality rates were also similar to the HERMES collaboration results, ranging from 10% to 20% at 3 months.[20–24] SIESTA had the highest mortality rate at 24.7% in both groups.[25] There was a trend toward increased mortality in the CS arm in ANSTROKE, GOLIATH, and the CANVAS pilot; however, these differences were not statistically significant.[21,22,24]

Meta-Analyses

Campbell et al., summarized data using meta-analysis from SIESTA, ANSTROKE, GOLIATH, and CANVAS concluding that those managed with GA were more likely to achieve a favorable functional outcome at 3 months (mRS 0–2 GA 49.3%, CS 36.6%, OR 1.71 (CI 1.13–2.59), $p = 0.01$), a result which may have been partially attributable to higher recanalization rates in those managed with GA (GA 86.2%, CS 74.6%, OR 2.14 (CI 1.26–3.62), $p = 0.0050$). ICH rates were similar across groups (GA 2.5%, CS 4.9%, OR 0.61 (CI 0.2–1.85), $p = 0.38$).[44] Work by Zhang et al., following analysis of results from SIESTA, ANSTROKE, and GOLIATH, also demonstrated improved functional outcomes in those managed with GA (OR 1.87 (CI 1.15–3.03)). Increased successful recanalization (TICI 2b-3) was also seen with GA (OR 1.94 (CI 1.13–3.35)), with no difference in SICH or periprocedural complications.[45]

Findings from the anesthesia-specific RCTs and meta-analyses are in contrast to those from the HERMES collaboration. In HERMES, with the exception of MR CLEAN, anesthetic agents and protocols were not prespecified, and as such were more likely to reflect "real-world" practice. In HERMES, those managed without GA had significantly better functional outcomes compared to those managed under GA (covariate adjusted cOR 1.53 (CI 1.14–2.04), $p = 0.0044$), with 40% in the GA group achieving an independent functional outcome at 3 months compared with 50% in the no GA group (OR 1.65 (CI 1.14–2.38), $p = 0.0078$). An excellent functional outcome (defined as an mRS 0–1) was also more likely in those managed without GA (GA 23%, no GA 32%, OR 1.68 (CI 1.12–2.52, $p = 0.013$). These between-group differences were significant in that for every 100 patients managed with GA (rather than no GA), 18 would have poorer functional outcomes and 10 would not achieve functional independence.[20]

Validity and generalizability of results

Results from nonrandomized and randomized studies evaluating the influence of anesthetic strategy on clinical outcomes in patients with AIS managed with EVT are inconsistent. The outcomes from the nonrandomized studies suffer from selection bias and confounding by indication, but by how much is unknown and whether this is enough to account for differences between these cohort studies and the single center RCTs remains undetermined. There may also be residual confounding due to unmeasured sources of unknown bias. Those with more severe neurologic impairment on presentation (higher NIHSS scores, altered conscious state, agitation) or multiple preexisting comorbidities are more likely to be allocated to GA. This is supported by findings from a post hoc analysis of the International Management of Stroke III trial; patients with a medical indication for GA were less likely to have a good outcome (mRS 0–2 medically indicated GA 19.7%, LA 48%, adRR 0.49 (CI 0.30–0.81), $p = 0.005$) and had increased mortality (medically indicated GA 33.8%, LA 7.4%, adRR 3.93 (CI 2.18–7.10), $p \leq 0.0001$) compared with LA, while there was no difference in probability of good outcome (mRS 0–2 routine GA 40.8%, LA 48%, adRR 0.80 (CI 0.60–1.06), $p = 0.12$) and mortality (routine GA 13.2%, LA 7.4%, adRR 1.82 (CI 0.87–3.77), $p = 0.11$) between LA and routine intubation. Higher in-hospital mortality was also seen among the medically indicated GA compared with routine intubation cohort (medically indicated GA 33.8%, routine GA 13.2%, adRR 2.16 (CI 1.09–4.29), $p = 0.0274$).[16]

While findings from the anesthesia-specific RCTs suggest that GA is noninferior to CS or LA in patients with AIS undergoing EVT, there are a number of caveats which limit the applicability of these results to other EVT capable centers. Firstly, GA was the standard of care, and CS the intervention, in the majority of the anesthesia-specific RCTs, which may have made it more difficult to demonstrate a benefit of CS over GA. Anesthesia was provided by highly specialized neuroanesthesia and neurocritical care teams able to provide 24 hours in-hospital EVT coverage. Delays due to GA were minimal as teams were fast: arrival to puncture was only 11 minutes in the GA and CS group in the study by Ren et al.[23] and delays due to GA were 10 minutes or less in SIESTA, GOLIATH, and ANSTROKE,[21,24,25] in contrast to 20 minutes longer with GA in HERMES (GA 105 minutes (80–149 minutes) vs non-GA 85 minutes (51–118 minutes) $p \leq 0.0001$).[20] The type and depth of CS varied within and across trials, and a target depth for CS was not provided in some protocols (GOLIATH, ANSTROKE), making comparison across studies difficult. In some cases, the "noGA" group included those managed with both LA and CS (which could be deep), potentially masking a benefit of LA over GA. The small sample size used in each trial further limits the widespread applicability of these results; the largest anesthesia-specific RCT, SIESTA, enrolled only 150 patients.[25] Lastly, functional outcomes were only evaluated as a primary

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outcome measure in ANSTROKE and the study by Ren et al.[23,24] Taken together, these limitations suggest that the functionality and expertise of the team in highly experienced centers is a critical factor. Highly experienced, fast teams can use GA effectively and without loss of clinical efficacy of EVT, but this may not be generalizable.

Discussion

Pharmacology and Physiology Considerations

Different anesthetic agents have varying neurochemical, neurophysiologic, and systemic effects. Depending on the type and dose of anesthesia, increases or decreases in cerebral blood flow (CBF) and metabolic demand ($CMRO_2$) can confer both neuroprotective and neurotoxic effects. In general, inhaled or volatile agents (sevoflurane, isoflurane) uncouple $CMRO_2$ from CBF, reducing $CMRO_2$ while increasing CBF in a nonlinear manner; this becomes more apparent with increasing doses. GABAergic drugs (propofol, thiopental) decrease $CMRO_2$ and CBF in a dose-dependent manner. Opioids (fentanyl, sufentanil, remifentanil) result in variable effects on CBF and cerebral metabolic rate which are usually dose dependent and affected by the concomitant use of other anesthetic agents.[46] A reduction in $CMRO_2$ is theoretically beneficial for the ischemic penumbra.[47] Inhaled agents have been shown to increase CBF via cerebral vasodilatation,[48] although it has been hypothesized that this may result in an intracranial steal phenomenon resulting in reduced CBF to regions with impaired perfusion.[46,49] In contrast, propofol may have vasoconstrictive effects limited to the cerebral circulation reducing CBF.[50,51]

Inhaled anesthetic agents can be precisely titrated to effect by monitoring the end tidal anesthetic drug concentration. Propofol infusions cannot be monitored in the same way, and if not carefully titrated to clinical signs of anesthetic depth, can result in progressively higher brain and blood concentrations over time,[52] potentially with increasing risk for adverse hemodynamic effects. Importantly, ischemic stroke patients are commonly slightly hypovolemic at hospital arrival due to time incapacitated preventing fluid intake, predisposing them to hypotension even with slight sedation-associated increased venous compliance and arterial vasodilation. In the setting of hypotension, volatile anesthesia in particular may result in a substantial reduction in CBF while propofol may have a lesser effect.[53]

Propofol has been shown to reduce infarct size in animal models, potentially via redistribution of blood flow to the ischemic penumbra (a true Robin Hood syndrome) via cerebral vasoconstriction.[54] However other studies, including a meta-analysis of experimental stroke in rodents, have demonstrated that while anesthetic agents can reduce neurologic injury by up to 30% (26%–34%, $Z = 15$, $p \leq 0.001$), giving an estimated range of true effects from 3% to 58% ($Q = 250$, $p \leq 0.001$, $I^2 = 70\%$), the neuroprotective effect was not observed in females or in those with comorbidities such as hypertension or diabetes.[55] Such findings raise doubt as to whether anesthetic agents could truly exert a neuroprotective effect in the majority of patients presenting with stroke.

The anesthesia-specific RCTs, with the exception of ANSTROKE, utilized the same anesthetic agents in the GA and CS groups to minimize the potential impact of the specific type of drug on outcomes; different doses were used to achieve varying depths of anesthesia. Both SIESTA and GOLIATH reported improved outcomes with propofol GA compared with CS.[21,25] In SIESTA, those managed with propofol GA had improved clinical outcomes (mRS 0–2 GA 37%, CS 18.2%, $p = 0.01$),[25] although absolute rates of functional independence were substantially lower than in comparable trials.[20] GOLIATH also reported improved outcomes with propofol GA (mRS 0–2 GA 66.2%, CS 52.4%) despite longer times to recanalization (GA 34 minutes, CS 29 minutes, $p = 0.27$).[21] As propofol was used for CS in both of these trials, there may have been a beneficial, dose-dependent effect of propofol on outcomes. In ANSTROKE, sevoflurane was used for GA, and mRS at 3 months did not differ between groups (mRS 0–2 GA 42.2%, CS 40%, $p = 1.00$)[24] suggesting that different anesthetic agents may exert variable effects on outcomes. It may be that, through differing effects on cerebral autoregulation (via effects on $CMRO_2$ and CBF) and secondarily on the ischemic penumbra, the choice and dose of anesthetic agent impact outcomes following EVT.

Cerebral Autoregulation, Blood Pressure, and LVO

Prerecanalization

Under normal conditions, cerebral autoregulation ensures adequate blood flow to the brain despite variations in arterial blood pressure (BP) ranging between 60 and 150 mmHg systolic.[56,57] When mean arterial pressure (MAP) is within these limits, changes in arterial tone regulate CBF to meet demand.[58]

Cerebral autoregulation is impaired within hours of acute stroke.[59–62] An abrupt reduction in CBF in the setting of an occlusion impairs endothelial cell and receptor function and smooth muscle activation[63] resulting in maximally dilated arteries (pial collaterals) and arterioles which are unable to adjust their vasoconstrictive response to changes in CBF[58]; CBF becomes passively dependent on MAP.[64] In the setting of LVO, if MAP is low, as may occur during anesthetic induction, cerebral perfusion pressure falls leading to a reduction in CBF to the penumbra, and potentially extension of the core infarct and a less favorable clinical outcome. The downstream effects of anesthesia-induced hypotension are likely to be more pronounced in patients with baseline hypertension and an altered autoregulatory response (with an upward shift of lower and upper MAP thresholds[56]), particularly in the setting of poor pial collaterals (which are tightly correlated with lower ASPECTs score at baseline) and hyperglycemia on presentation.

During Recanalization/Postrecanalization

BP targets at the time of recanalization and during the early post-recanalization period are not well established. Targets are dependent on a number of factors including baseline ASPECTS, use of thrombolysis or other antithrombotic therapy, timing and extent of recanalization, presence and location of persistent occlusion, presence of mass effect or edema, location of infarction, and age. However, at least theoretically, and in contrast to the prerecanalization period, hypertension is not preferable during this time as it may be associated with an increased risk of reperfusion injury.

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Several hemodynamic parameters have been reported to influence clinical outcomes following stroke including a decrease in BP below specific thresholds,[15,65] the extent of BP reduction from baseline,[65,66] and BP variability.[10,67] In International Stroke Trial, a higher baseline BP and greater BP variability were both associated with a poorer prognosis. In contrast, an early (within 24 hours) decline in BP (OR 0.93 (CI 0.89–0.97) $p = 0.001$) and early initiation of antihypertensive therapy (0.78; CI 0.65–0.93; $p = 0.007$) were associated with improved outcomes,[68] although this may have been influenced by other factors such as baseline stroke severity, early recanalization, and the absence of ipsilateral carotid stenosis.

The anesthesia-specific RCTs targeted a systolic BP (SBP) of 140 mmHg or greater (see Table 4). BP targets were tightly controlled, although hemodynamic changes were still more common in the GA groups in ANSTROKE, GOLIATH, and CANVAS.[21,22,24] In ANSTROKE, MAP was lower with GA (GA 91 mmHg, CS 95 mmHg, $p = 0.0484$); a fall in MAP greater than 20 mmHg from baseline was also more common (GA 93%, CS 60%, $p = 0.003$), and more prolonged with GA (GA 22 minutes, CS 15 minutes, $p = 0.0432$). Those managed with GA required more inotropic support to maintain BP within range (GA 98%, CS 79%, $p = 0.0073$).[24] CANVAS reported similar results with a lower SBP in the GA group at the time of arterial puncture (GA 125 ± 26 mmHg, CS 159 ± 42 mmHg, $p = 0.004$) and for 10 minutes afterward (GA 123 ± 21 mmHg, CS 148 ± 33 mmHg, $p = 0.007$). A decrease in MAP more than 20% baseline was also more common with GA (GA 65%, CS 30%, $p = 0.027$), although the frequency of MAP decreases more than 40% were similar across groups (GA 15%, CS 10%, $p = 1.00$).[22]

In GOLIATH, average SBP (GA 143 mmHg, CS 155 mmHg, $p \leq 0.001$) and MAP were both lower with GA (GA 95 mmHg, CS 101 mmHg, $p \leq 0.001$). SBP (GA 94%, CS 62%, $p \leq 0.001$) and MAP were also more frequently below target (GA 91%, CS 46%, $p \leq 0.001$), resulting in increased inotrope use in patients managed with GA (phenylephrine and ephedrine, $p \leq 0.001$ for both agents). Variations in BP by anesthetic strategy in GOLIATH were not associated with differences in clinical outcome, potentially because neither the amount of time spent with a MAP below target nor MAP at time of reperfusion (GA 97 mmHg, CS 100 mmHg, $p = 0.12$) differed by anesthetic strategy.[21] In contrast, a post hoc analysis of MR CLEAN reported worse outcomes with a change in MAP in those managed with GA; a MAP 10 mmHg lower than baseline was associated with 1.67 times lower odds of a shift toward a good outcome on the mRS.[67] Whalin et al. also reported a 10% reduction in MAP from baseline as a risk factor for poor outcome (OR 4.38 (CI 1.53–12.56), $p = 0.01$).[65] It is possible that more pronounced or prolonged periods of hemodynamic variability occurred in MR CLEAN and the other HERMES trials as highly specified protocols (choice of anesthetic agent, method of administration, depth of sedation, and physiologic targets) were not a key component of the trial design. Aggressive treatment of BP to target, as per the anesthesia-specific RCTs (inotropes were administered to 98% of GA patients in ANSTROKE[24]), irrespective of the specific type of anesthesia administered, may reduce changes in CBF and its impact on the ischemic penumbra. This in turn may minimize, in part, any deleterious effect of GA on clinical outcomes seen in nonrandomized studies, in centers with ready access to teams able to implement the highly regulated BP protocols of the anesthesia-specific RCTs.

Conclusion

Findings from nonrandomized studies point towards improved functional outcomes without GA in patients with AIS due to LVO of the anterior circulation. This is in contrast to the results from the highly protocol-driven anesthesia-specific RCTs which report improved or no difference in outcomes with GA compared with CS. Strict BP monitoring and treatment to target, with avoidance of severe, prolonged hypotension, alongside fast anesthetic teams with short-time delays likely partially negated any negative impact GA can have on functional outcomes. Interestingly, rates of SICH did not differ by anesthetic strategy in the anesthesia-specific RCTs, weakening the argument that GA is necessary to prevent excessive patient movement to reduce the risk of vessel perforation, a major driver for routine GA use.

A number of outstanding questions remain. What is the optimal anesthetic strategy during EVT? Do different anesthetics and vasopressors with their various effects on brain oxygenation[69] have variable effects on clinical outcomes? Is their effect modulated by hemodynamic changes and/or collateral status? Do different anesthetics interact with neuroprotective agents such as nerinitide and alter outcomes? Several trials attempting to answer some of these questions are currently in progress including AMETIS, GASS, SEACOAST 1, and CANVAS.

Larger, multicenter RCTs, comparing three different anesthetic strategies (LA, CS, and GA) aimed at primarily assessing the effect on clinical outcomes are required. Ideally these trials will utilize the same anesthetic agent (i.e., propofol for example) across all three groups to minimize further confounding potentially caused by the anesthetic agent itself, standardize the vasopressor of choice to maintain BP within range and take collateral status into consideration. Further work should also consider the potential interaction of anesthesia with neuroprotective agents such as nerinitide.[70]

Statement of authorship

ELH wrote the draft and revised the manuscript. MDH edited and revised the manuscript.

Conflict of interest

Dr ELH has nothing to disclose.

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