RESEARCH ARTICLE

Thrombectomy Outcomes With General vs Nongeneral Anesthesia

A Pooled Patient-Level Analysis From the EXTEND-IA Trials and SELECT Study

Amrou Sarraj, MD, Gregory W. Albers, MD, Peter J. Mitchell, MMed, Ameer E. Hassan, DO, Michael G. Abraham, MD, Spiros Blackburn, MD, Gagan Sharma, MS, Nawaf Yassi, PhD, Timothy J. Kleinig, PhD, Darshan G. Shah, MBBS, Teddy Y. Wu, PhD, Muhammad Shazam Hussain, MD, Wondwoseen G. Tekle, MD, Santiago Ortega Gutierrez, MD, MS, Amin Nima Aghaebrahim, MD, Diogo C. Haussen, MD, Gabor Toth, MD, Deep Pujara, MBBS, MPH, MS, Ronald F. Budzik, MD, William Hicks, MD, Nirav Vora, MD, Randall C. Edgell, MD, Sabreena Slavin, MD, Colleen G. Lechtenberg, MD, Laith Maali, MD, Abid Qureshi, MD, Lee Rosterman, MD, Mohammad Ammar Abdulrazzak, MD, Tareq AlMaghrabi, MD, Faris Shaker, MBChB, Osman Mir, MD, Ashish Arora, MD, Sheryl Martin-Schild, MD, Clark W. Sitton, MD, Leonid Churilov, PhD, Rishi Gupta, MD, Maarten G. Lansberg, MD, PhD, Raul G. Nogueira, MD, James C. Grotta, MD, Geoffrey Alan Donnan, MD, Stephen M. Davis, MD, and Bruce C. V. Campbell, MBBS, PhD, on behalf of the SELECT, EXTEND-IA, EXTEND-IA TNK, and EXTEND-IA TNK Part-II Investigators

Correspondence
Dr. Sarraj
Amrou.Sarraj@uhhospitals.org

Neurology® 2023;100:e336-e347. doi:10.1212/WNL.0000000000201384

MORE ONLINE

Class of Evidence
Criteria for rating therapeutic and diagnostic studies
NPub.org/coe

Infographic
NPub.org/ig1003

Abstract

Background and Objectives

The effect of anesthesia choice on endovascular thrombectomy (EVT) outcomes is unclear. Collateral status on perfusion imaging may help identify the optimal anesthesia choice.

Methods

In a pooled patient-level analysis of EXTEND-IA, EXTEND-IA TNK, EXTEND-IA TNK part II, and SELECT, EVT functional outcomes (modified Rankin Scale score distribution) were compared between general anesthesia (GA) vs non-GA in a propensity-matched sample. Furthermore, we evaluated the association of collateral flow on perfusion imaging, assessed by hypoperfusion intensity ratio (HIR) – Tmax > 10 seconds/Tmax > 6 seconds (good collaterals – HIR < 0.4, poor collaterals – HIR ≥ 0.4) on the association between anesthesia type and EVT outcomes.

Results

Of 725 treated with EVT, 299 (41%) received GA and 426 (59%) non-GA. The baseline characteristics differed in presentation National Institutes of Health Stroke Scale score (median [interquartile range] GA: 18 [13–22], non-GA: 16 [11–20], $p < 0.001$) and ischemic core volume (GA: 15.0 mL [3.2–38.0] vs non-GA: 9.0 mL [0.0–31.0], $p < 0.001$). In addition, GA was associated with longer last known well to arterial access (203 minutes [157–267] vs 186 minutes [138–252], $p = 0.002$), but similar procedural time (35.5 minutes [23–59] vs 34 minutes [22–54], $p = 0.51$). Of 182 matched pairs using propensity scores, baseline characteristics were similar. In the propensity score–matched pairs, GA was independently associated with worse functional outcomes (adjusted common odds ratio [adj. cOR]: 0.64, 95% CI: 0.44–0.93, $p = 0.021$) and higher neurologic worsening (GA: 14.9% vs non-GA: 8.9%, aOR: 2.10, 95% CI: 1.02–4.33, $p = 0.045$). Patients with poor collaterals had worse functional

From the Case Western Reserve University (A.S.), Neurology; University Hospitals Cleveland Medical Center (A.S., D.P.), Neurology, OH; Stanford University (G.W.A., M.G.L.), Neurology, CA; The Royal Melbourne Hospital – University of Melbourne (P.J.M.), Radiology, Parkville, Victoria, Australia; University of Texas Rio Grande Valley - Valley Baptist Medical Center (A.E.H., W.G.T.), Harlingen; University of Kansas Medical Center (M.G.A., S.S., C.G.L., L.M., A.Q., L.R.), Neurology and Radiology; UTHealth McGovern Medical School (S.B., F.S.), Neurosurgery, Houston TX; The Royal Melbourne Hospitals (G.S., N.Y., L.C., G.A.D., S.M.D., B.C.V.C.), University of Melbourne, Neurology; The Walter and Eliza Hall Institute of Medical Research (N.Y.), Population Health and Immunity, Parkville, Victoria; Royal Adelaide Hospital (T.J.K.), Neurology, Adelaide, South Australia; Gold Coast University Hospital (D.G.S.), Neurology, Southport, Queensland, Australia; Christchurch Hospital (T.Y.W.), Neurology, Christchurch, Canterbury, New Zealand; Cleveland Clinic (M.S.H., G.T., M.A.A.), Cerebrovascular Unit, OH; University of Iowa Hospitals (S.O.G.), Neurosurgery; Baptist Health (A.N.A.), Lyerly Neurosurgery, Jacksonville, FL; Emory University (D.C.H., R.G.N.), Neurology, Atlanta, GA; Riverside Methodist Hospital (R.F.B., W.H., N.V.), Colombia, OH; Saint Louis University (R.C.E.), Neurology, MO; University of Tabuk (T.A.), Neurology, KSA; Baylor Scott & White Health (O.M.), Neurology, Dallas, TX; Greensboro | Cone Health (A.A.), Neurology, Greensboro, NC; Touro Infirmary and New Orleans East Hospital (S.M.-S.), Neurology, LA; UTHealth McGovern Medical School (C.W.S.), Diagnostic and Interventional Radiology, Houston, TX; WellStar Health System (R.G.), Neurology, Marietta, GA; and Memorial Hermann Hospital Texas Medical Center (J.C.G.), Neurology, Houston, TX.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

SELECT, EXTEND-IA, EXTEND-IA TNK, and EXTEND-IA TNK Part-II coinvestigators are listed at links.lww.com/WNL/C448.

outcomes with GA (adj. cOR: 0.47, 95% CI: 0.29–0.76, $p = 0.002$), whereas no difference was observed in those with good collaterals (adj. cOR: 0.93, 95% CI: 0.50–1.74, $p = 0.82$), $p_{interaction}$: 0.07. No difference was observed in infarct growth overall and in patients with good collaterals, whereas patients with poor collaterals demonstrated larger infarct growth with GA with a significant interaction between collaterals and anesthesia type on infarct growth rate ($p_{interaction}$: 0.020).

Discussion
GA was associated with worse functional outcomes after EVT, particularly in patients with poor collaterals in a propensity score–matched analysis from a pooled patient-level cohort from 3 randomized trials and 1 prospective cohort study. The confounding by indication may persist despite the doubly robust nature of the analysis. These findings have implications for randomized trials of GA vs non-GA and may be of utility for clinicians when making anesthesia type choice.

Classification of Evidence
This study provides Class III evidence that use of GA is associated with worse functional outcome in patients undergoing EVT.

Trial Registration Information
EXTEND-IA: ClinicalTrials.gov (NCT01492725); EXTEND-IA TNK: ClinicalTrials.gov (NCT02388061); EXTEND-IA TNK part II: ClinicalTrials.gov (NCT03340493); and SELECT: ClinicalTrials.gov (NCT02446587).

Endovascular thrombectomy (EVT) improves clinical outcomes for patients with ischemic stroke with a proximal large vessel occlusion (LVO) in the anterior circulation.[1] Optimizing the variables that affect EVT outcome is crucial. Whether the choice of anesthesia can affect the outcomes of EVT is still unclear.

Data on the effect of anesthesia choice on EVT outcomes have conflicting results. There have been 3 single-center randomized trials[2-4] and an individual-level meta-analysis of those randomized controlled trials (RCTs)[5] that showed that EVT outcomes were better with general anesthesia (GA). Conversely, post hoc analyses from the MR CLEAN RCT[6] and from the HERMES individual-level meta-analysis[7] showed better EVT outcomes with non-GA. A subsequent analysis of the MR CLEAN registry suggested that local anesthesia was associated with better outcomes than conscious sedation or GA.[8] In addition, an updated meta-analysis of randomized controlled trials and nonrandomized studies identified non-GA to be associated with better functional outcomes and improved mortality.[9] However, substantial heterogeneity within results was identified as a sensitivity analysis including data from randomized trials demonstrated worse functional outcomes with non-GA, with no difference in mortality between the 2 groups.

Treating patients without the use of general anesthetic (non-GA), using either conscious sedation or local anesthesia without sedation, is less invasive, permits monitoring the clinical status, and is less likely to cause hypotension that may impair collateral blood flow to the ischemic brain. However, inability to control patient movement and protect the airway may pose a risk for procedural complications and yield a longer procedure. GA may delay the start of EVT,[7] and there is potential hyper- and hypoventilation, increased hemodynamic variability,[5] and, at least theoretically, increased risk of respiratory infections with GA.[10]

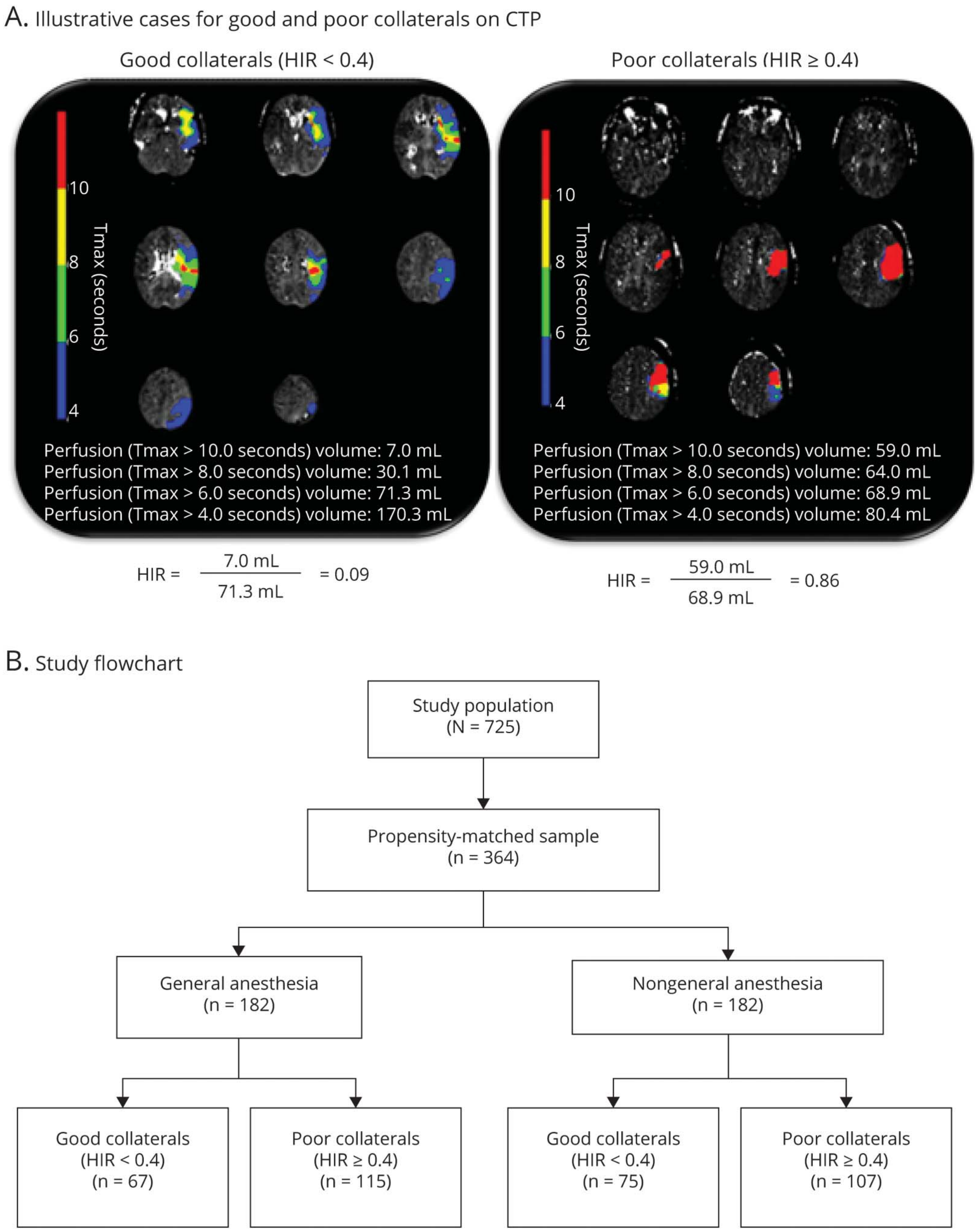
The effect of anesthesia choice on EVT outcomes may be modulated by other factors within the studied population including collateral status that may interact with the hemodynamic effects of GA. It is plausible that patients with worse collaterals may be more sensitive to GA-related hemodynamic changes, which could result in larger infarct growth and subsequently worse functional outcomes compared with those with non-GA. These baseline stroke-imaging characteristics have not been examined in previous studies.

We sought to evaluate whether use of GA is associated with worse functional outcomes in patients undergoing EVT and whether this association is modified by collateral status on perfusion imaging. We hypothesized that GA may be associated with worse outcomes after EVT compared with non-GA, particularly in patients with worse collaterals.

Methods

Study Population
This is a pooled patient-level analysis from 3 randomized controlled trials (EXTEND-IA, EXTEND-IA TNK, and EXTEND-IA TNK part II) and a prospective cohort study (SELECT).[11-14] The details regarding the inclusion and exclusion criteria for these studies have been published previously. Briefly, all patients with anterior circulation LVOs (in the intracranial internal carotid artery or proximal segments of the middle cerebral artery [MCA-M1 and M2]) receiving EVT in the aforementioned studies were included in this analysis. Additional study-level characteristics of participating studies are provided in eTable 1 (links.lww.com/WNL/C449) in the Supplement. In each study, the use of an anesthetic approach for endovascular treatment was at the discretion of the local neurointerventionalists and neuroanesthesia team, who may have determined the choice of

Figure 1 Illustrative Cases for Good and Poor Collaterals and Study Flowchart



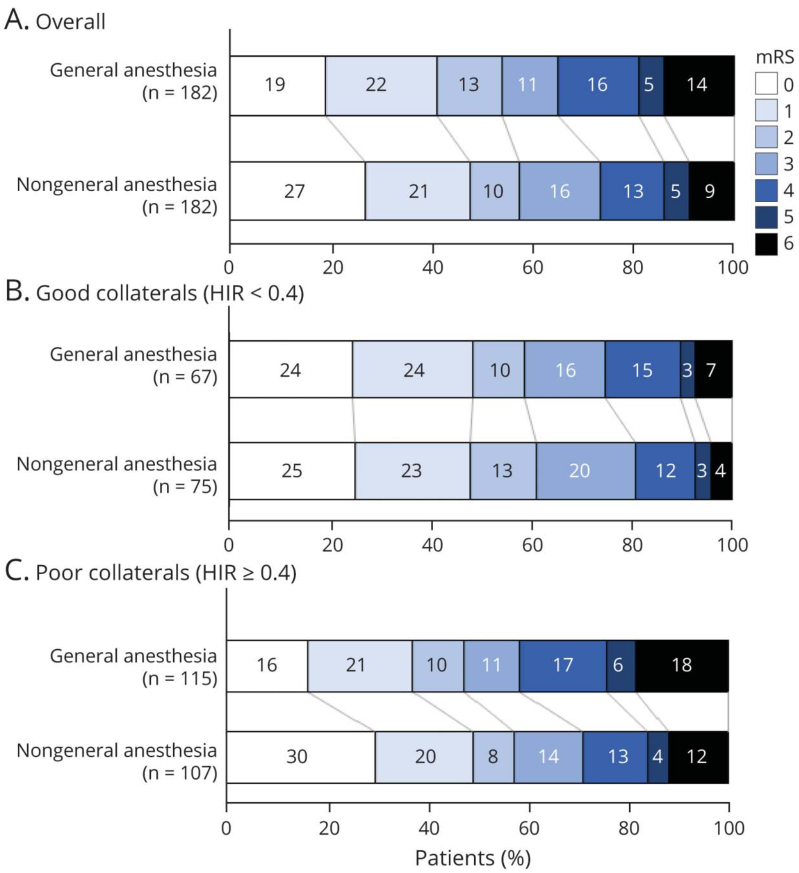
(A) Illustrative cases for good and poor collaterals on perfusion imaging. Patient 1 demonstrated Tmax >10 seconds volume of 7.0 mL and Tmax > 6 seconds volume of 71.3 mL, resulting in an HIR of 0.09, which is considered a marker for good collaterals, whereas patient 2 demonstrated Tmax > 10 seconds volume of 59.0 mL and Tmax > 6 seconds volume of 68.9 mL, resulting in an HIR of 0.86, which is considered a marker for poor collaterals. (B) Study flowchart. HIR = hypoperfusion intensity ratio.

anesthesia based on patient-specific characteristics. The study cohort was stratified, based on the type of anesthesia, into GA vs non-GA. The non-GA approach included patients who received conscious sedation and those receiving local anesthesia without sedation. They were prospectively followed for the next 90 days after admission, and modified Rankin Scale (mRS) score assessment at 90 days was performed by investigators blinded to both the core laboratory reading and treatment assignment.

Imaging Evaluation

All patients received noncontrast CT, CT angiogram, and CT perfusion imaging processed using iSchemaView RAPID before EVT. Acquired images were not reprocessed for this study. Individual study-reported imaging evaluation parameters were used to complete the analyses provided in the article. Collateral flow on perfusion imaging was obtained using hypoperfusion intensity ratio (HIR), a ratio of Tmax > 10 seconds and Tmax > 6 seconds tissue volumes on time to

Figure 2 Distribution of Functional Outcomes by 90-Day mRS Score in the Propensity-Matched Cohort



(A) Illustrates EVT outcomes in patients based on their anesthesia type, demonstrating an overall shift toward better functional outcomes in patients treated with non-GA. (B) Illustrates EVT outcomes in patients based on their anesthesia type in patients with HIR < 0.4. (C) Illustrates EVT outcomes in patients based on their anesthesia type in patients with HIR ≥ 0.4. Patients with poor collaterals (HIR ≥ 0.4) demonstrated a clear shift in the functional outcomes with non-GA, whereas the distribution of functional outcomes was similar for GA and non-GA approaches for patients with good collaterals (HIR < 0.4). EVT = endovascular thrombectomy; GA = general anesthesia; HIR = hypoperfusion intensity ratio; mRS = modified Rankin Scale.

maximum intensity residue function. Patients with an HIR < 0.4 were considered to have good collaterals, whereas an HIR ≥ 0.4 was considered indicative of poor collaterals on perfusion imaging (Figure 1A).[15]

Outcomes

The primary outcome was the distribution of the 90-day mRS score. Functional independence (mRS score of 0–2) at 90-day follow-up was a secondary outcome. Safety outcomes included mortality at 90-day follow-up, symptomatic intracerebral hemorrhage (sICH), defined as worsening of the National Institutes of Health Stroke Scale (NIHSS) score of ≥4 with evidence of parenchymal hemorrhage type 2 on follow-up imaging,[16] and neurologic worsening, defined as increase of ≥4 points in the NIHSS score within 24 hours from hospital admission. Infarct growth, defined as the volumetric difference between ischemic core at presentation and infarct volume measured by manual delineation of the infarct tissue on follow-up imaging (diffusion weighted imaging preferred/CT if not available) were also evaluated.

Standard Protocol Approvals, Registrations, and Patient Consents

The protocols for individual trials were approved at sites' local institutional review boards, and all studies were registered at clinicaltrials.gov. All participants and/or their legally authorized representatives provided informed consent before enrollment in the individual studies.

Data Availability

The data that support the findings of this study are available from the corresponding author, A.S., on reasonable request.

Statistical Analysis

Patients were stratified into GA vs non-GA. Baseline clinical and imaging characteristics and outcomes were described and compared between the 2 groups using the Pearson χ^2 test or Fisher's exact test for categorical variables and the Student t test or Wilcoxon rank-sum test for continuous variables, where appropriate.

Propensity score matching was used to address the baseline differences. A propensity score was calculated across the study sample using age, NIHSS score at presentation, IV thrombolytic administration, transfer status, serum glucose at presentation, occlusion location, time from last known well to procedure, ischemic core, HIR (<0.4 vs ≥ 0.4), and study design being randomized controlled trial vs prospective cohort, accounting for balancing of characteristics across propensity score blocks. Visual examination of propensity score distribution was undertaken to assess common support. A 1:1 matching was conducted using the nearest neighbor method. Balancing of 2 groups was ensured by calculating standardized mean differences of key baseline characteristics. The association of the type of anesthesia on functional outcome was assessed using multivariable ordinal logistic regression models adjusting for age (≥65—prespecified dichotomy), presentation NIHSS score, IV thrombolytic status, clot location, time from last known well to procedure, volumes for ischemic core and critically hypoperfused tissue, and successful reperfusion status (modified thrombolysis in cerebral ischemia [mTICI] grade 2b-3) at the end of the procedure. To account for individual participating studies being prospective cohorts vs randomized trials, the design of the individual participating study (randomized controlled trial vs prospective cohort) was incorporated as a fixed effect. The adjusted common odds ratio (adj. cOR) with 95% CI and *p* values were reported. The proportional odds assumption for ordinal regression was examined using the approximate likelihood ratio test. A sensitivity analysis, using study design as a random effect in a mixed-effects ordinal logistic regression, was also conducted.

Data regarding hemodynamic changes were available for the SELECT study. Changes in systolic blood pressure (BP) between arrival and minimum intraprocedure readings were calculated, and patients were stratified based on the change in systolic BP into <20, 20–39, 40–59, and ≥60 mm Hg drop. We compared the magnitude of change between subgroups with good and poor collaterals on perfusion imaging. The effect of BP drop on infarct growth was also evaluated using a multivariable linear regression model, adjusting for aforementioned covariates. Furthermore, we assessed the effect of anesthesia type on the correlation with collateral status on perfusion imaging by stratifying the patients based on the HIR of <0.4 vs ≥ 0.4.

In addition, we evaluated infarct growth volumes in the propensity-matched sample overall and in HIR strata using a linear regression model, adjusting for age (≥65), presentation NIHSS score, IV thrombolytic status, clot location, time from last known well to procedure, volumes for ischemic core and critically hypoperfused tissue, and successful reperfusion status (mTICI 2b-3) at the end of the procedure. To account for individual participating studies being prospective cohorts vs randomized trials, the design of the individual participating study (randomized controlled trial vs prospective cohort) was incorporated as a fixed effect. A sensitivity analysis, using study design as a random effect in a mixed-effects regression, was also conducted.

STATA 15 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC.) was used for statistical analyses. All *p* values were 2 sided, and $p < 0.05$ was considered statistically significant. Missing data were not imputed.

Results

Baseline Characteristics—Overall Cohort

A total of 725 patients receiving EVT were included in this pooled analysis. Figure 1B describes the flow diagram of the cohort based on the type of anesthesia received and stratified by collateral flow status. The baseline characteristics demonstrated significant differences between patients who received GA and non-GA, including presentation NIHSS score (GA: 18 [13–22], non-GA: 16 [11–20], $p < 0.001$) and ischemic core volume (GA: 15.0 [3.2–38.0] vs non-GA: 9.0 [0.0–31.0], $p < 0.001$). In addition, GA was associated with longer last known well (LKW) to arterial puncture times (GA 203 [157–267] minutes vs non-GA 186 [138–252], $p = 0.002$). However, time from arterial puncture to reperfusion/end of the procedure was not significantly different between GA (35.5 [23–59] minutes) and non-GA (34 [22–54] minutes), $p = 0.51$. eTable 2 (links.lww.com/WNL/C449) provides a comparison of different baseline clinical and imaging characteristics between patients with GA vs non-GA.

Baseline Characteristics in the Propensity-Matched Cohort

Using propensity scores, 182 matched pairs of patients receiving GA vs non-GA for EVT were identified. Table 1 describes similar baseline clinical and imaging characteristics of matched pairs stratified based on the type of anesthesia, including age (GA: 70.5 [61–79] vs non-GA: 70 [61–78], $p = 0.66$), NIHSS score at presentation (GA: 17 [13–21] vs non-GA: 16 [12–20], $p = 0.40$), ischemic core (GA: 13.0 [0.0–32.0] mL vs non-GA: 11.5 [0.0–32.0], $p = 0.83$), or times from last known well to arterial puncture (GA: 195 [151–248] minutes vs non-GA: 190 [140–258] minutes, $p = 0.67$).

Functional, Safety, and Imaging Outcomes for GA vs Non-GA in the Propensity-Matched Cohort

There was a significant shift (cOR: 0.66, 95% CI = 0.46–0.96, $p = 0.028$), demonstrating worse 90-day mRS scores in patients who received GA in the univariable analysis as demonstrated in Figure 2A. After adjustment for potential confounders, GA was independently associated with worse functional outcomes (adj. cOR: 0.64, 95% CI: 0.44–0.93, $p = 0.021$). Importantly, improved outcomes with non-GA were sustained in a model that adjusted for HIR (adj. cOR: 0.64, 95% CI: 0.44–0.93, $p = 0.019$).

Furthermore, GA was associated with higher rates of neurologic worsening (GA: 14.9% vs non-GA: 8.9%, aOR: 2.08, 95% CI: 1.01–4.29, $p = 0.048$) and numerically higher mortality (GA: 14.3% vs non-GA: 8.8%, aOR: 2.15, 95% CI: 0.97–4.76, $p = 0.06$), whereas symptomatic ICH (GA: 4.9% vs non-GA: 5.5%, aOR: 0.94, 95% CI: 0.34–2.56, $p = 0.90$) did not differ.

Table 1 Baseline Clinical and Imaging Characteristics in the Propensity-Matched Cohort Based on the Type of Anesthesia

	Non-GA N = 182	GA N = 182	*p* Value
Age (y)	70 (61–78)	70.5 (61–79)	0.66
Sex			
Females	84 (46.2%)	83 (45.6%)	0.92
Males	98 (53.8%)	99 (54.4%)	
Serum glucose (mg/dL)	122.5 (104.5–155)	118.9 (105–150)	0.35
H/o hypertension	125 (68.7%)	126 (69.6%)	0.85
H/o congestive heart failure	9 (10.0%)	5 (6.0%)	0.34
H/o ischemic heart disease	43 (25.4%)	36 (20.7%)	0.30
H/o atrial fibrillation	59 (32.4%)	57 (31.5%)	0.85
H/o diabetes mellitus	44 (24.2%)	35 (19.3%)	0.26
H/o hyperlipidemia	94 (51.9%)	96 (53.0%)	0.83
H/o stroke/TIA	20 (11.8%)	31 (17.8%)	0.11
Smoking status			
Nonsmoker	108 (62.1%)	118 (65.9%)	0.27
Current smoker	21 (12.1%)	27 (15.1%)	
Past smoker	45 (25.9%)	34 (19.0%)	
Occlusion location			
ICA	44 (24.2%)	39 (21.4%)	0.67
MCA-M1	104 (57.1%)	103 (56.6%)	
MCA-M2	34 (18.7%)	40 (22.0%)	
Transfer status			
Direct to EVT center	137 (75.3%)	138 (75.8%)	0.90
Transferred to EVT center	45 (24.7%)	44 (24.2%)	
Time from last known well to arterial puncture (min)	190 (140–258)	195 (151–248)	0.67
Time from last known well to arrival (min)	89 (53–151)	83 (55–141)	0.52
Time from arrival to puncture (min)	89 (62–122)	97 (73–121)	0.12
Baseline NIHSS score	16 (12–20)	17 (13–21)	0.40
ASPECTS on baseline CT	9 (7–10)	8 (7–9)	0.46
Ischemic core (rCBF <30%) volume (mL)	11.5 (0.0–32.0)	13.0 (0.0–32.0)	0.83
Tissue volume with Tmax >6 s (cc)	124.5 (87.0–166.0)	120.2 (89.0–170.0)	0.87
Tissue volume with Tmax >10 s (cc)	55.0 (25.0–97.0)	54.0 (28.4–90.0)	0.82
HIR	0.47 (0.31–0.60)	0.47 (0.33–0.60)	0.55
Successful reperfusion (mTICI 2b-3)	157 (87.7%)	159 (87.8%)	0.97

Abbreviations: EVT = endovascular thrombectomy; GA = general anesthesia; HIR = hypoperfusion intensity ratio; ICA = internal carotid artery; MCA = middle cerebral artery; NIHSS = National Institutes of Health Stroke Scale; rCBF = relative cerebral blood flow.

Infarct growth from baseline ischemic core (GA: 11.1 [0.0–54.5] mL vs non-GA: 7.0 [−2.4 to 34.7] mL, adj. coeff: 14.59, 95% CI: −2.40 to 31.59, p = 0.092) did not demonstrate significant difference between GA and non-GA approaches. Sensitivity analysis using mixed-effects models also demonstrated similar results (Table 2).

Table 2 Clinical Outcomes in the Propensity-Matched Cohort, Stratified by Anesthesia Type

	Total N = 364	Non-GA N = 182	GA N = 182	Adjusted estimates (95% CI), *p* value—fixed-effects model	Adjusted estimates (95% CI), *p* value—mixed-effects model
90-d mRS score[a]	2 (1–4)	2 (0–3)	2 (1–4)	0.64, 95% CI: 0.44–0.93, *p* = 0.021	0.64, 95% CI: 0.44–0.93, *p* = 0.021
Mortality at 90-d follow-up[b]	42 (11.5%)	16 (8.8%)	26 (14.3%)	2.15, 95% CI: 0.97–4.76, *p* = 0.06	2.20, 95% CI: 0.99–4.87, *p* = 0.05
Neurologic worsening[b]	43 (11.9%)	16 (8.9%)	27 (14.9%)	2.08, 95% CI: 1.01–4.29, *p* = 0.048	2.10, 95% CI: 1.02–4.33, *p* = 0.045
Symptomatic intracranial hemorrhage[b]	19 (5.2%)	10 (5.5%)	9 (4.9%)	0.94, 95% CI: 0.34–2.96, *p* = 0.90	0.90, 95% CI: 0.33–2.43, *p* = 0.84
Infarct growth (mL)[c]	8.7 (−0.8 to 45.0)	7.0 (−2.4 to 34.7)	11.1 (0.0–54.5)	14.59, 95% CI: −2.40 to 31.59, *p* = 0.092	14.11, 95% CI: −2.58 to 30.80, *p* = 0.097

Abbreviations: GA = general anesthesia; mRS = modified Rankin Scale.
[a] Assessed using ordinal logistic regression.
[b] Assessed using logistic regression.
[c] Assessed using linear regression.

General vs Non-GA Based on Collateral Status in the Propensity-Matched Cohort

There were 142 patients (67 GA and 75 non-GA) with favorable collaterals on perfusion imaging (HIR <0.4). Baseline characteristics were similar between the 2 groups, eTable 3 (links.lww.com/WNL/C449). Baseline characteristics were also largely similar in 222 patients (115 GA and 107 non-GA) with poor collaterals on perfusion imaging (HIR ≥0.4), except for shorter LKW to puncture times with non-GA (170 [137–249] vs GA: 195 [159–260] minutes, $p = 0.029$; eTable 4).

Tables 3 and 4 represent the clinical outcomes in patients with good and poor collaterals on perfusion imaging, respectively. With good collaterals, no difference was observed in the distribution of mRS scores at 90-day follow-up (adj. cOR: 0.93, 95% CI: 0.50–1.74, $p = 0.82$), whereas in patients demonstrating poor collaterals on perfusion (HIR ≥ 0.4), GA was associated with significantly worse functional outcomes (adj. cOR: 0.47, 95% CI: 0.29–0.76, $p = 0.002$), with interaction of thrombectomy outcomes by anesthesia type approaching, but not reaching statistical significance ($p_{interaction}$: 0.07).

Furthermore, no differences in safety outcomes including death, neurologic worsening, or symptomatic ICH were observed between GA and non-GA approaches in patients with good collaterals. While with poor collaterals, neurologic worsening (GA: 19.3% vs 8.6%, aOR: 3.07, 95% CI: 1.21–7.77, $p = 0.018$) was significantly higher and mortality (GA: 18.3% vs non-GA: 12.1%, fixed aOR: 2.26, 95% CI: 0.91–5.59, $p = 0.078$) was numerically higher with GA, whereas sICH (GA: 7.8% vs non-GA: 5.6%, aOR: 1.60, 95% CI: 0.48–5.36, $p = 0.45$) did not demonstrate a difference between choice of anesthesia technique.

In regard to imaging outcomes, infarct growth did not differ with anesthesia technique (GA: 6.5 [−1.5 to 18.4] mL vs non-GA: 11.5 [2.8–32.9] mL, adj. coeff: −11.20, 95% CI: −27.47–5.07, $p = 0.18$) in patients with good collaterals, whereas we observed larger infarct growth with GA (GA: 18.8 [3.5–83.5] mL vs non-GA: 2.5 [−5.2 to 39.4] mL, adj. coeff: 30.13, 95% CI: 4.38–55.88, $p = 0.022$) in those with poor collaterals. Importantly, there was an interaction between infarct growth and anesthesia technique ($p_{interaction}$: 0.020). Sensitivity analyses using mixed-effects models also represented similar results, as detailed in Tables 3 and 4. Additional sensitivity analyses are provided in eResults and eTable 5 (links.lww.com/WNL/C449), demonstrating similar results with use of time from LKW to door and door to puncture instead of LKW to puncture and continuous age instead of dichotomized age, respectively.

Hemodynamic Changes in Relation to Anesthesia Type

In 264 SELECT cohort patients with available hemodynamic measures, GA was associated with larger drop in systolic BP (30 [7–57] mm Hg vs non-GA: 16 [5–45] mm Hg, $p = 0.025$). Furthermore, the proportion of patients with <20, 20–39, 40–59, and ≥60 mm Hg drop in systolic BP was 36%, 25%, 17%, and 22% for patients receiving GA and 57%, 13%, 18%, and 11% in patients receiving non-GA, respectively ($p = 0.002$). Furthermore, we observed an association toward significantly increased infarct volume with larger SBP drop (for each mm Hg drop in BP – reg. coeff: 0.32, 95% CI: −0.06 to 0.71, $p = 0.099$), which approached but did not reach statistical significance.

Classification of Evidence

The study provides Class III evidence that use of GA is associated with worse functional outcome in patients undergoing EVT, especially with poor collaterals on perfusion imaging.

Discussion

Our results, based on the analysis of a propensity-matched cohort from pooled patient-level data from 3 randomized trials and a prospective cohort study, demonstrate worse thrombectomy functional outcomes and higher mortality rates in patients undergoing EVT with GA. This difference was primarily driven by patients with poor collaterals on perfusion imaging, in contrast to those with good collaterals

Table 3 Clinical Outcomes in the Propensity Score–Matched Cohort in Patients With HIR <0.4 Based on the Type of Anesthesia Received

	Total N = 142	Non-GA N = 75	GA N = 67	Adjusted estimates (95% CI), *p* value—fixed-effects model	Adjusted estimates (95% CI), *p* value—mixed-effects model
90-d mRS score[a]	2 (1–3)	2 (0–3)	2 (1–4)	0.93, 95% CI: 0.50–1.74, $p = 0.82$	0.93, 95% CI: 0.50–1.74, $p = 0.82$
Mortality at 90-d follow-up[b]	8 (5.6%)	3 (4.0%)	5 (7.5%)	2.44, 95% CI: 0.20–29.59, $p = 0.48$	3.95, 95% CI: 0.37–42.06, $p = 0.26$
Neurologic worsening[b]	12 (8.5%)	7 (9.5%)	5 (7.5%)	0.67, 95% CI: 0.14–3.34, $p = 0.63$	0.67, 95% CI: 0.14–3.33, $p = 0.63$
Symptomatic intracranial hemorrhage[b]	4 (2.8%)	4 (5.3%)	0 (0.0%)	N/A	N/A
Infarct growth (mL)[c]	8.3 (0.1–27.2)	11.5 (2.8–32.9)	6.5 (−1.5 to 18.4)	−11.20, 95% CI: −27.47 to 5.07, $p = 0.18$	−11.90, 95% CI: −27.39 to 3.58, $p = 0.13$

Abbreviations: GA = general anesthesia; HIR = hypoperfusion intensity ratio; mRS = modified Rankin Scale.
[a] Assessed using ordinal logistic regression.
[b] Assessed using logistic regression.
[c] Assessed using linear regression.

where no difference in thrombectomy outcomes based on the anesthesia type was observed. Our findings shed light on potential baseline imaging parameters identifying subpopulations who may have worse outcomes with GA.

Current randomized evidence assessing the effect of anesthesia choice on EVT outcomes is ambiguous, suggesting no benefit of non-GA vs GA in some trials,[3,4] whereas another trial[2] and the pooled patient-level meta-analysis[5] demonstrated the superiority of GA in terms of functional outcomes after EVT. Criticisms of these trials include their single-center nature and limited enrollment. The single-center design with strict protocols regarding the choice of anesthetic agents and intraprocedural hemodynamic management make the findings less generalizable. The wide range of functional independence rates observed across these trials suggests significant population heterogeneity.

On the other hand, the analysis from the MR CLEAN trial and a patient-level meta-analysis of the Highly Effective Reperfusion Using Multiple Endovascular Devices [HERMES] collaboration demonstrated improved outcomes in patients treated without GA.[6,7] Furthermore, the significance of EVT treatment effect was shown to be lost in patients treated with GA in the MR CLEAN trial.[17] Although these trials were not randomized on the basis of anesthesia strategy, the data reflect standard practice patterns at multiple centers across the world, suggesting greater generalizability of the findings. The contrasting findings have resulted in continued equipoise in the choice of anesthesia before EVT. Some ongoing thrombectomy trials discourage the use of GA.[18]

It is plausible that the effect of anesthesia choice on EVT outcomes may be related to specific clinical and imaging factors within the studied population. None of the prior RCTs or patient-level meta-analyses evaluated the association of the various baseline imaging characteristics and severity with the effect of anesthesia approach. Our study population was uniquely positioned to evaluate these imaging parameters; the results support the hypothesis that the association of GA with worse functional outcomes may be limited to patients with poor collateral flow on perfusion imaging. To that end, our results showed significantly larger infarct growth with GA in patients with poor collaterals, whereas no association with infarct growth and anesthesia technique was observed in those with good collaterals. Overall infarct growth was limited in our study population, which can be attributed to the high successful reperfusion rate and limited occurrence of significant cerebral edema and hemorrhagic transformation. Still, the largest infarct growth (18.8 [3.5–83.5] mL) was observed in patients with poor collaterals who received GA. These results support the hypothesis that the association of GA with worse functional outcomes may be limited to patients with poor collateral flow and highlight larger infarct growth as a biologically plausible mechanism.

GA and associated sedation is known to cause significant hypotension,[19,20] which may affect the collaterals preserving ischemic penumbra. This effect may be accentuated in patients with poor collaterals. The hemodynamic data in our cohort suggested higher rates of significant BP drop in patients who received GA, which may have contributed to the infarct growth in this group. These findings support the plausibility of our hypothesis.

Prior analysis has demonstrated potential effect modification of collateral status on GA-associated hypotension and infarct growth.[21] Our analysis supports the hypothesis and explores perfusion imaging parameters to potentially guide anesthesia choice. Although HIR may have shown good correlation with collaterals flow on CT angiogram,[15,22,23] variations within good and poor grades of HIR may have contributed to some of our findings.

The effect of successful reperfusion through EVT may be so robust that the overall effect of modifiers such as type of anesthesia technique may be insignificant in patients with

Table 4 Clinical Outcomes in the Propensity Score–Matched Cohort in Patients With HIR ≥0.4 Based on the Type of Anesthesia Received

	Total N = 222	Non-GA N = 107	GA N = 115	Adjusted estimates (95% CI), *p* value—fixed-effects model	Adjusted estimates (95% CI), *p* value—mixed-effects model
90-d mRS score[a]	2 (1–4)	2 (0–4)	3 (1–4)	0.47, 95% CI: 0.29–0.76, $p = 0.002$	0.47, 95% CI: 0.29–0.76, $p = 0.002$
Mortality at 90-d follow-up[b]	34 (15.3%)	13 (12.1%)	21 (18.3%)	2.27, 95% CI: 0.91–5.59, $p = 0.08$	2.26, 95% CI: 0.92–5.59, $p = 0.08$
Neurologic worsening[b]	31 (14.2%)	9 (8.6%)	22 (19.3%)	3.07, 95% CI: 1.21–7.77, $p = 0.018$	3.08, 95% CI; 1.22–7.77, $p = 0.017$
Symptomatic intracranial hemorrhage[b]	15 (6.8%)	6 (5.6%)	9 (7.8%)	1.60, 95% CI: 0.48–5.36, $p = 0.45$	1.59, 95% CI: 0.47–5.30, $p = 0.45$
Infarct growth (mL)[c]	9.8 (−2.5 to 62.4)	2.5 (−5.2 to 39.4)	18.8 (3.5–83.5)	30.13, 95% CI: 4.38–55.88, $p = 0.022$	29.90, 95% CI: 5.01–54.79, $p = 0.019$

Abbreviations: GA = general anesthesia; HIR = hypoperfusion intensity ratio; mRS = modified Rankin Scale.
[a] Assessed using ordinal logistic regression.
[b] Assessed using logistic regression.
[c] Assessed using linear regression.

limited ischemic changes, slow infarct progression, and preserved collaterals. On the other hand, patients with compromised collaterals would have lower likelihood of benefit with reperfusion achieved through EVT; thus, the effect of anesthesia technique may become much more prominent. This potential differential effect of anesthesia in these patient groups has not been evaluated before, with only 43/368 (12%) patients with ASPECTS <6 in the pooled patient-level meta-analysis of anesthesia RCTs.[5] The SELECT2 (NCT03876457) trial of thrombectomy for patients with large core and fast progression will examine the effect of anesthesia in a prespecified secondary analysis.[18]

Although some of the patients scheduled to undergo EVT need GA for reasons such as airway protection in severe stroke or to control agitation threatening patient safety, anesthesia choice still is based on the preference of interventionalist/anesthetist in most of the cases, as confirmed by the variation in the proportion of patients treated under GA in pivotal EVT trials.[11,17,24-26] Underlying imaging considerations may help guide physicians where anesthesia may truly be a matter of choice. Furthermore, as BP drop after GA is associated with worse clinical outcomes, this can serve as a potentially modifiable mechanism that should be further explored in clinical research.

Our analysis has several limitations. This was a post hoc analysis with the inherent limitations of such analyses. The study protocol was not preregistered at PROSPERO or other similar registries. The patients were not randomized by anesthesia strategy in either RCTs or SELECT cohort. Details regarding the approach of non-GA (conscious sedation vs local anesthesia without sedation) were not available; thus, we could not perform an analysis comparing these groups. Despite propensity matching, residual confounding by the indication for GA in more severely unwell patients may persist. Our study is hypothesis generating, and further validation through future studies is warranted.

GA was associated with worse EVT outcomes, and this effect was driven by those patients with worse collateral flow. There was no significant association of anesthetic strategy with EVT outcomes in patients with good collaterals. These findings may contribute to the design of future randomized trials assessing the question of choice of anesthesia for EVT to enrich such populations.

Study Funding

The SELECT trial was funded by Stryker Neurovascular through a grant to UT McGovern Medical School. EXTEND-IA trials were funded by the National Health and Medical Research Council of Australia. The pooled analysis efforts received no funding. The funding source was not involved in study design, monitoring, data collection, statistical analyses, interpretation of results, or manuscript writing.

Disclosure

A. Sarraj reports serving as the principal investigator of the SELECT and SELECT2 trials through a grant from Stryker Neurovascular to University of Texas–Houston and as a consultant, speaker bureau member, and advisory board member for Stryker. G.W. Albers has an ownership interest in the iSchemaView and is a consultant or on advisory boards for iSchemaView. Dr. P. Mitchell reports receiving grant support, paid to his institution, from Medtronic, Stryker, and Codman Johnson and Johnson (now Codman Neuro), serving as an unpaid consultant to Codman Johnson and Johnson, and receiving travel support from Stryker and MicroVention and institutional research support from Stryker and Medtronic. A.E. Hassan is a consultant, speaker bureau member, and proctor for Medtronic and MicroVention and a consultant and speaker bureau member for Stryker, Penumbra, and Balt and reports personal funding from VizAI. M.G. Abraham is a consultant for Stryker Neurovascular and Penumbra Inc. S.L. Blackburn reports receiving a grant from the NIH. Dr. D.G. Shah reports receiving personal fees and travel support from Boehringer

Ingelheim and personal fees from Bayer and Medtronic. W.J. Hicks reports receiving personal fees and other funding from Medtronic. S. Ortega-Gutierrez reports serving as a consultant for Stryker and Medtronic. M.G. Lansberg reports personal fees from Novo Nordisk, Genentech, Biogen, Moleac, and NuvOx. R. Gupta is the principal investigator of the ASSIST Registry sponsored by Stryker Neurovascular and for Tiger Study sponsored by RAPID Medical. C.W. Sitton has served as the core lab for the SELECT trial. Dr. G.A. Donnan reports receiving grants from the Australian National Health and Medical Research Council and personal fees from Allergan, Amgen, Bayer, Boehringer Ingelheim, Pfizer, and Servier. Dr. S.M. Davis reports receiving lecture fees from Medtronic, personal fees from Bayer, Boehringer Ingelheim, Tide Pharmaceuticals, and Medtronic, and grants from the National Health and Medical Research Council of Australia. Dr. B.C.V. Campbell reports grant support from the National Health and Medical Research Council of Australia, the National Heart Foundation of Australia, the Royal Australasian College of Physicians, and the Royal Melbourne Hospital Home Lottery and grant and non-financial support from Covidien. The other authors report no relevant disclosures. Go to Neurology.org/N for full disclosures.

Publication History

Received by *Neurology* February 24, 2022. Accepted in final form August 24, 2022. Submitted and externally peer reviewed. The handling editor was José Merino, MD, MPhil, FAAN.

Appendix 1 Authors

Name	Location	Contribution
Amrou Sarraj, MD	University Hospitals Cleveland Medical Center, Neurology, Cleveland, OH, USA	Design or conceptualization of the study, major role in the acquisition of data, and drafting or revising the manuscript for intellectual content
Gregory W. Albers, MD	Stanford University, Neurology, Stanford, CA, USA	Drafting or revising the manuscript for intellectual content
Peter J. Mitchell, MMed	The Royal Melbourne Hospital – University of Melbourne, Radiology, Parkville, Victoria, Australia	Drafting or revising the manuscript for intellectual content
Ameer E. Hassan, DO	University of Texas Rio Grande Valley - Valley Baptist Medical Center, Harlingen, TX, USA	Drafting or revising the manuscript for intellectual content
Michael G. Abraham, MD	University of Kansas Medical Center, Neurology and Radiology, Kansas City, KS, USA	Drafting or revising the manuscript for intellectual content
Spiros L. Blackburn, MD	UTHealth McGovern Medical School, Neurosurgery, Houston TX, USA	Drafting or revising the manuscript for intellectual content
Gagan Sharma, MS	The Royal Melbourne Hospitals, University of Melbourne, Neurology, Parkville, Victoria, Australia	Drafting or revising the manuscript for intellectual content and analysis or interpretation of the data

Appendix 1 *(continued)*

Name	Location	Contribution
Nawaf Yassi, PhD	The Royal Melbourne Hospitals, University of Melbourne, Neurology, Parkville, Victoria, Australia	Drafting or revising the manuscript for intellectual content
Timothy Kleinig, PhD	Royal Adelaide Hospital, Neurology, Adelaide, South Australia, Australia	Drafting or revising the manuscript for intellectual content
Darshan Shah, MBBS	Gold Coast University Hospital, Neurology, Southport, QLD, Australia	Drafting or revising the manuscript for intellectual content
Teddy Y. Wu, PhD	Christchurch Hospital, Neurology, Christchurch, Canterbury, New Zealand	Drafting or revising the manuscript for intellectual content
Muhammad Shazam Hussain, MD	Cleveland Clinic, Cerebrovascular Unit, Cleveland, OH, USA	Drafting or revising the manuscript for intellectual content
Wondwossen G. Tekle, MD	University of Texas Rio Grande Valley - Valley Baptist Medical Center, Harlingen, TX, USA	Drafting or revising the manuscript for intellectual content
Santiago Ortega-Gutierrez, MD, MS	University of Iowa Hospitals, Neurosurgery, Iowa City, IA, USA	Drafting or revising the manuscript for intellectual content
Amin Nima Aghaebrahim, MD	Baptist Health, Lyerly Neurosurgery, Jacksonville, FL, USA	Drafting or revising the manuscript for intellectual content
Diogo C. Haussen, MD	Emory University, Neurology, Atlanta GA, USA	Drafting or revising the manuscript for intellectual content
Gabor Toth, MD	Cleveland Clinic, Cerebrovascular Unit, Cleveland, OH, USA	Drafting or revising the manuscript for intellectual content
Deep K. Pujara, MBBS, MPH, MS	University Hospitals Cleveland Medical Center, Neurology, Cleveland, OH, USA	Drafting or revising the manuscript for intellectual content and analysis or interpretation of the data
Ronald F. Budzik, MD	Riverside Methodist Hospital, Colombia, OH, USA	Drafting or revising the manuscript for intellectual content
William J. Hicks II, MD	Riverside Methodist Hospital, Colombia, OH, USA	Drafting or revising the manuscript for intellectual content
Nirav Vora, MD	Riverside Methodist Hospital, Colombia, OH, USA	Drafting or revising the manuscript for intellectual content
Randall C. Edgell, MD	Saint Louis University, Neurology, St. Louis, MO, USA	Drafting or revising the manuscript for intellectual content
Sabreena J. Slavin, MD	University of Kansas Medical Center, Neurology, Kansas City, KS, USA	Drafting or revising the manuscript for intellectual content
Colleen G. Lechtenberg, MD	University of Kansas Medical Center, Neurology, Kansas City, KS, USA	Drafting or revising the manuscript for intellectual content

Continued

Appendix 1 *(continued)*

Name	Location	Contribution
Laith Maali, MD	University of Kansas Medical Center, Neurology, Kansas City, KS, USA	Drafting or revising the manuscript for intellectual content
Abid Y. Qureshi, MD	University of Kansas Medical Center, Neurology, Kansas City, KS, USA	Drafting or revising the manuscript for intellectual content
Lee Rosterman, MD	University of Kansas Medical Center, Neurology, Kansas City, KS, USA	Drafting or revising the manuscript for intellectual content
Mohammad Ammar Abdulrazzak, MD	Cleveland Clinic, Cerebrovascular Unit, Cleveland, OH, USA	Drafting or revising the manuscript for intellectual content
Tareq AlMaghrabi, MD	University of Tabuk, Neurology, Tabuk, KSA, USA	Drafting or revising the manuscript for intellectual content
Faris Shaker, MBChB	UTHealth McGovern Medical School, Neurosurgery, Houston TX, USA	Drafting or revising the manuscript for intellectual content
Osman Mir, MD	Baylor Scott & White Health, Neurology, Dallas, TX, USA	Drafting or revising the manuscript for intellectual content
Ashish Arora, MD	Greensboro | Cone Health, Neurology, Greensboro, NC, USA	Drafting or revising the manuscript for intellectual content
Sheryl Martin-Schild, MD	Touro Infirmary and New Orleans East Hospital, Neurology, New Orleans, LA, USA	Drafting or revising the manuscript for intellectual content
Clark Sitton, MD	UTHealth McGovern Medical School, Diagnostic and Interventional Radiology, Houston TX, USA	Drafting or revising the manuscript for intellectual content
Leonid Churilov, PhD	The Royal Melbourne Hospitals, University of Melbourne, Neurology, Parkville, Victoria, Australia	Drafting or revising the manuscript for intellectual content and analysis or interpretation of the data
Rishi Gupta, MD	WellStar Health System, Neurology, Marietta, GA, USA	Drafting or revising the manuscript for intellectual content
Maarten G. Lansberg, MD, PhD	Stanford University, Neurology, Stanford, CA, USA	Drafting or revising the manuscript for intellectual content
Raul G. Nogueira, MD	Emory University, Neurology, Atlanta GA, USA	Drafting or revising the manuscript for intellectual content
James C. Grotta, MD	Memorial Hermann Hospital Texas Medical Center, Neurology, Houston TX	Drafting or revising the manuscript for intellectual content
Geoffrey A. Donnan, MD	The Royal Melbourne Hospitals, University of Melbourne, Neurology, Parkville, Victoria, Australia	Drafting or revising the manuscript for intellectual content
Stephen M. Davis, MD	The Royal Melbourne Hospitals, University of Melbourne, Neurology, Parkville, Victoria, Australia	Drafting or revising the manuscript for intellectual content

Appendix 1 *(continued)*

Name	Location	Contribution
Bruce C.V. Campbell, MBBS, MD	The Royal Melbourne Hospitals, University of Melbourne, Neurology, Parkville, Victoria, Australia	Major role in the acquisition of data and drafting or revising the manuscript for intellectual content

Appendix 2 Coinvestigators

Coinvestigators are listed at links.lww.com/WNL/C448.

References

1. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2019;50(12): e344-e418. doi: 10.1161/STR.0000000000000211
2. Schönenberger S, Uhlmann L, Hacke W, et al. Effect of conscious sedation vs general anesthesia on early neurological improvement among patients with ischemic stroke undergoing endovascular thrombectomy: a randomized clinical trial. *JAMA* 2016; 316(19):1986-1996. doi: 10.1001/jama.2016.16623
3. Simonsen CZ, Yoo AJ, Sørensen LH, et al. Effect of general anesthesia and conscious sedation during endovascular therapy on infarct growth and clinical outcomes in acute ischemic stroke: a randomized clinical trial. *JAMA Neurol.* 2018;75(4):470-477. doi: 10.1001/jamaneurol.2017.4474
4. Löwhagen Hendén P, Rentzos A, Karlsson J-E, et al. General anesthesia versus conscious sedation for endovascular treatment of acute ischemic stroke: the AnStroke trial (anesthesia during stroke). *Stroke* 2017;48(6):1601-1607. doi: 10.1161/ STROKEAHA.117.016554
5. Schönenberger S, Hendén PL, Simonsen CZ, et al. Association of general anesthesia vs procedural sedation with functional outcome among patients with acute ischemic stroke undergoing thrombectomy: a systematic review and meta-analysis. *JAMA* 2019;322(13):1283-1293. doi: 10.1001/jama.2019.11455
6. Berkhemer OA, van den Berg LA, Fransen PSS, et al. The effect of anesthetic management during intra-arterial therapy for acute stroke in MR CLEAN. In: Dippel D, Roos Y, van Oostenbrugge R, et al., editors., Vol 87; 2016:656-664. doi: 10.1212/ WNL.0000000000002976. *Neurology*7.
7. Campbell BCV, van Zwam WH, Goyal M, et al. Effect of general anaesthesia on functional outcome in patients with anterior circulation ischaemic stroke having endovascular thrombectomy versus standard care: a meta-analysis of individual patient data. *Lancet Neurol.* 2018;17(1):47-53. doi: 10.1016/S1474-4422(17)30407-6
8. Goldhoorn R-JB, Bernsen MLE, Hofmeijer J, et al. Anesthetic management during endovascular treatment of acute ischemic stroke in the MR CLEAN Registry. *Neurology* 2020;94(1):e97-e106. doi: 10.1212/WNL.0000000000008674
9. Goyal N, Malhotra K, Ishfaq MF, et al. Current evidence for anesthesia management during endovascular stroke therapy: updated systematic review and meta-analysis. *J NeuroInterventional Surg.* 2019;11(2):107-113. doi: 10.1136/neurintsurg-2018-013916
10. Hassan AE, Chaudhry SA, Zacharatos H, et al. Increased rate of aspiration pneumonia and poor discharge outcome among acute ischemic stroke patients following intubation for endovascular treatment. *Neurocrit Care* 2012;16(2):246-250. doi: 10.1007/s12028-011-9638-0
11. Campbell BCV, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med.* 2015;372(11):1009-1018. doi: 10.1056/NEJMoa1414792
12. Campbell BCV, Mitchell PJ, Churilov L, et al. Tenecteplase versus alteplase before thrombectomy for ischemic stroke. *N Engl J Med.* 2018;378(17):1573-1582. doi: 10.1056/NEJMoa1716405
13. Campbell BCV, Mitchell PJ, Churilov L, et al. Effect of intravenous tenecteplase dose on cerebral reperfusion before thrombectomy in patients with large vessel occlusion ischemic stroke: the EXTEND-IA TNK Part 2 randomized clinical trial. *JAMA* 2020; 323(13):1257-1265. doi: 10.1001/jama.2020.1511
14. Sarraj A, Hassan AE, Grotta J, et al. Optimizing patient selection for endovascular treatment in acute ischemic stroke (SELECT): a prospective, multicenter cohort study of imaging selection. *Ann Neurol.* 2020;87(3):419-433. doi: 10.1002/ana.25669
15. Guenego A, Marcellus DG, Martin BW, et al. Hypoperfusion intensity ratio is correlated with patient eligibility for thrombectomy. *Stroke* 2019;50(4):917-922. doi: 10.1161/STROKEAHA.118.024134
16. Wahlgren N, Ahmed N, Davalos A, et al. Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study. *The Lancet* 2007;369(9558):275-282. doi: 10.1016/S0140-6736(07)60149-4
17. Berkhemer OA, Fransen PSS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med.* 2015;372(1):11-20. doi: 10.1056/ NEJMoa1411587

18. Sarraj A, Hassan AE, Abraham M, et al. A randomized controlled trial to optimize patient's selection for endovascular treatment in acute ischemic stroke (SELECT2): study protocol. *Int J Stroke* 2022;17(6):689-693. doi: 10.1177/17474930211035032
19. Talke PO, Sharma D, Heyer EJ, Bergese SD, Blackham KA, Stevens RD. Society for neuroscience in anesthesiology and critical care expert consensus statement: anesthetic management of endovascular treatment for acute ischemic stroke*: endorsed by the society of NeuroInterventional surgery and the neurocritical care society. *J Neurosurg Anesthesiology* 2014;26(2):95-108. doi: 10.1097/ana.0000000000000042. journals.lww.com/jnsa/Fulltext/2014/04000/Society_for_Neuroscience_in_Anesthesiology_and.1.aspx
20. Rasmussen M, Schönenberger S, Hendèn PL, et al. Blood pressure thresholds and neurologic outcomes after endovascular therapy for acute ischemic stroke: an analysis of individual patient data from 3 randomized clinical trials. *JAMA Neurol.* 2020;77(5):622-631. doi: 10.1001/jamaneurol.2019.4838
21. Raychev R, Liebeskind DS, Yoo AJ, et al. Physiologic predictors of collateral circulation and infarct growth during anesthesia - detailed analyses of the GOLIATH trial. *J Cereb Blood Flow Metab.* 2020;40(6):1203-1212. doi: 10.1177/0271678X19865219
22. Lyndon D, van den Broek M, Niu B, Yip S, Rohr A, Settecase F. Hypoperfusion intensity ratio correlates with CTA collateral status in large-vessel occlusion acute ischemic stroke. *AJNR Am J Neuroradiol* 2021;42(8):1380-1386. doi: 10.3174/ajnr.A7181
23. Wang C-M, Chang Y-M, Sung P-S, Chen C-H. Hypoperfusion index ratio as a surrogate of collateral scoring on CT angiogram in large vessel stroke. *J Clin Med.* 2021;10(6):1296. doi: 10.3390/jcm10061296
24. Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med.* 2015;372(24):2285-2295. doi: 10.1056/NEJMoa1415061
25. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med.* 2015;372(24):2296-2306. doi: 10.1056/NEJMoa1503780
26. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med.* 2015;372(11):1019-1030. doi: 10.1056/NEJMoa1414905