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Anaesthesia modality on endovascular therapy outcomes in patients with large infarcts: a post hoc analysis of the ANGEL-ASPECT trial

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ABSTRACT

Objectives Endovascular therapy (EVT) now penetrates the once obscure realm of large infarct core volume acute ischaemic stroke (LICV-AIS). This research aimed to investigate the potential correlation between different anaesthetic approaches and post-EVT outcomes in LICV-AIS patients.

Methods Between October 2020 and May 2022, the China ANGEL-Alberta Stroke Programme Early CT Score (ASPECT) trial studied patients with LICV-AIS, randomly assigning them to the best medical management (BMM) or BMM with EVT. This post hoc subgroup analysis categorised subjects receiving BMM with EVT into general anaesthesia (GA) and non-GA groups based on anaesthesia type. We applied multivariable logistic regression to evaluate the relationship between anaesthesia during EVT and patient functional outcomes, as measured by the modified Rankin scale (mRS), in addition to the occurrence of complications. Further adjustment for selection bias was achieved through propensity score matching (PSM).

Results In total, 230 patients with LICV-AIS were enrolled (GA 84 vs Non-GA 146). No significant difference was observed between the two groups in terms of the proportion of patients who achieved an mRS score of 0–2 at 90 days (27.4% for the GA group vs 31.5% for the non-GA group, p=0.51). However, the GA group had significantly longer median surgical times (142 min vs 122 min, p=0.03). Furthermore, GA was associated with an increased risk of postoperative pneumonia (adjusted OR 2.03, 95% CI 1.04 to 3.98). The results of PSM analysis agreed with the results of the multivariate regression analysis. No significant difference in intracranial haemorrhage incidence or mortality rate was observed between the groups.

Conclusion This post hoc analysis of subgroups of the ANGEL-ASPECT trial suggested that there may be no significant association between the choice of anaesthesia and neurological outcomes in LICV-AIS patients. However, compared with non-GA, GA prolongs the duration of EVT and is associated with a greater postoperative pneumonia risk.

Trial registration number NCT04551664.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ While there is an emerging accumulation of research into the choice of anaesthesia during endovascular treatment (EVT) for acute ischaemic stroke (AIS), scientific evidence is scant regarding anaesthetic management specific to large infarct core volume AIS (LICV-AIS). This paucity is attributed to the exclusion of these patients—who are potentially more vulnerable to the effects of anaesthesia—from the majority of clinical trials.

WHAT THIS STUDY ADDS

⇒ It is plausible that the choice of anaesthetic technique does not significantly impact neurological prognosis in LICV-AIS patients following EVT. Employing anaesthesia techniques other than general anaesthesia might contribute to shorter operative times and lower rates of pneumonia related to intubation.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ For the majority of such patients, non-general anaesthesia is appropriate. When general anaesthesia is used, vigilant monitoring for postoperative pneumonia is advised.

INTRODUCTION

The sequential reporting of positive results from the RESCUE-Japan LIMIT,[1] SELECT2,[2] ANGEL-Alberta Stroke Programme Early CT Score (ASPECT)[3] and TENSION[4] studies established that endovascular therapy (EVT) significantly improved the prognosis of large infarct core volume acute ischaemic stroke (LICV-AIS) patients compared with those who received standard medical care alone. This evidence strongly promises to update clinical treatment guidelines.

Guidelines do not provide formal recommendations regarding the choice of anaesthesia for EVT.[5] Expert panels strongly recommend considering local anaesthesia (LA) or conscious sedation (CS) as the priority in patients without posterior circulation occlusion, with a National Institutes of Health Stroke Scale (NIHSS) score ≥15 and agitation or ventilatory concerns.[6] Over the years, there has been a substantial

accumulation of research in this field.[7–14] However, even meta-analyses based on randomised controlled trials (RCTs) do not always yield consistent conclusions. After pooling the results of seven RCTs, Campbell *et al* emphasised that standardised intraoperative management may be a potential contributing factor to the superiority of general anaesthesia (GA).[15] In contrast, Jia *et al*, following supplemental analysis of the AMETIS study, reported contradictory findings.[16] Although patients who underwent GA had a greater rate of successful vessel recanalisation, no significant differences were observed compared with non-GA patients in terms of functional outcomes, mortality rates or NIHSS scores. Despite the use of standardised haemodynamic management protocols in these RCTs, more than 53% of patients in the GA group experienced intraoperative hypotensive events.[16]

Prior to this, the LICV-AIS has been consistently used as an exclusion criterion in conventional RCTs involving EVT intervention. Notably, due to ethical considerations and participant safety, these RCTs often excluded patients who had lost their airway protective reflexes, with a conversion rate from non-GA to GA ranging between 6% and 16%.[17] Patients with large core infarcts in AIS generally present with poor overall health conditions, and currently published studies indicate that the majority of patients have an initial NIHSS score greater than 15.[1–4] The size of the infarct core and the ischaemic penumbra is constrained by the brain's ischaemic tolerance and cerebral hemodynamics, which are often inversely related.[18] Prereperfusion hypotension is associated with impaired collateral blood flow, larger infarct volumes and worse functional outcomes.[19] Anaesthesia-induced decreases in blood pressure (BP) negatively impact cerebral collateral circulation during EVT and cannot be reversed by vasopressor administration.[20] Moreover, dynamic BP fluctuations, other than severe hypertension and hypotension, are considered detrimental.[21] Therefore, it can be inferred that LICV-AIS patients may experience heightened sensitivity to different anaesthesia modalities, posing advanced considerations for anaesthetic management in the clinical setting. Nevertheless, to date, evaluations of different anaesthesia approaches during thrombectomy for LICV-AIS patients have not been performed.

The ANGEL-ASPECT study is a multicentre RCT in which patients with radiologically confirmed large ischaemic core volume strokes in the anterior circulation were randomised to undergo EVT following a standardised workflow. The main anaesthetic modalities employed during the intervention included GA, LA and CS, with a particular focus on GA and LA. This research aimed to conduct a post hoc analysis of the original data from the trial to explore the effects of different anaesthesia strategies (GA vs non-GA) during EVT on the recovery outcomes of patients with LICV-AIS, thereby providing a preliminary evidence base for clinical decision-making.

METHODS

Study design and participants

The ANGEL-ASPECT trial is a multicentre, prospective, open-label, endpoint-blinded design RCT that aimed to evaluate whether the combination of best medical management (BMM) with EVT improved the neurofunctional prognosis of patients with acute anterior circulation large vessel occlusion and a significant infarct core present within 24 hours of symptom onset compared with that of patients with BMM alone (NCT04551664). Our post hoc analysis was based on the intention-to-treat (ITT) population of the ANGEL-ASPECT trial, excluding those who received only BMM. Patients who underwent EVT were divided into GA or non-GA groups, the latter of which included the CS and LA groups. The anaesthesia induction method was selected based on the patient's characteristics at admission and the outcomes of close consultation with the neurointerventionalist rather than being randomised.

The specific trial protocol, inclusion/exclusion criteria and primary outcomes have been published.[3 22] Briefly, in this study, patients with LICV-AIS due to occlusions in the M1 segment of the middle cerebral artery (MCA) or the intracranial segment of the internal carotid artery were enrolled from 46 Chinese medical institutions. The LICV is defined as an admission ASPECTS of 3–5. For patients with an ASPECTS less than 3 or greater than 5, the infarct core volume must be between 70 mL and 100 mL. The ASPECTS is based on non-contrast CT (NCCT) assessment, whereas the infarct core is determined using CT perfusion imaging (CTP) or MRI diffusion-weighted imaging.

The reporting of this post hoc analysis adheres to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Outcome measures

The primary outcome was the percentage of patients who attained a favourable functional status at 90±7 days postrandomisation, defined as a score of 0–2 on the modified Rankin scale (mRS), which ranges from 0 to 6, with 6 indicating death. The secondary outcomes included the following: (1) the distribution of mRS scores at 90±7 days; (2) the percentage of patients with an mRS score of 0–3 at 90±7 days; (3) the change in NIHSS score from baseline to 36±12 hours postrandomisation, labelled 36-hour ΔNIHSS; (4) the change in infarct volume as assessed by NCCT at 7±1 day or at discharge and by MRI at 36±12 hours relative to baseline and (5) the rate of successful recanalisation following EVT, defined as an mTICI grade of 2b or higher.

The safety outcomes included the following: (1) the incidence of postoperative pneumonia; (2) the probability of symptomatic intracranial haemorrhage (sICH) within 48 hours postrandomisation, as defined by the Heidelberg bleeding classification; (3) the probability of any ICH within 48 hours postrandomisation; (4) the probability of decompressive hemicraniectomy during hospitalisation;

(5) mortality at 90±7 days postrandomisation and (6) any procedural complications, including arterial dissection, arterial perforation, vasospasm requiring treatment and embolisation in a new territory.

In the ANGEL-ASPECT study, as intraoperative BP was not continuously recorded, we only measured systolic BP (SBP) postpuncture and postfinal angiography. Scoring was conducted by well-trained personnel. Imaging data relevant to the study were interpreted centrally by the research centre.

Statistical analysis

In this study, continuous variables are summarised using the median (IQR), while categorical variables are presented as frequencies and percentages. To compare baseline characteristics between the GA group and the non-GA group, the χ^2 test and Fisher's exact test were used for categorical variables, whereas the Mann-Whitney U test was employed for continuous variables. Given the completeness of the primary outcome data in the ANGEL-ASPECT trial, no data imputation was performed; however, exhaustive documentation and reporting of missing data for the variables of interest were conducted.

In the analysis exploring the association between anaesthetic techniques and dichotomous outcomes, ORs and 95% CIs were estimated using binary logistic regression models. On testing the proportional odds assumption, ordinal logistic regression was applied to evaluate the relationship between anaesthetic methods and mRS scores to estimate cORs and 95% CIs. Additionally, linear regression analyses were employed to examine the association between anaesthetic techniques and variations in the 36-hour NIHSS score (ΔNIHSS score), as well as changes in infarct volume. The covariates adjusted for in the multivariate model included age, prestroke mRS score, baseline NIHSS score, baseline ASPECTS, core infarct volume, time from onset to puncture and receipt of intravenous thrombolysis (Model 1). Furthermore, subgroup analyses were conducted to assess the potential impacts of specific variables on the risk of the following primary outcome: (1) age less than 70 years vs 70 years or older; (2) time from stroke onset to randomisation less than 6 hours vs 6 hours or more; (3) baseline NIHSS score less than 16 vs 16 or more; (4) ASPECTS less than 3 vs 3 or more; (5) core infarct volume less than 70 mL vs 70 mL or more and (6) whether the patient received intravenous thrombolysis or not.

To ascertain the robustness of our findings, several sensitivity analyses were undertaken. First, we constructed various multivariate models. Model 2 was constructed with data from the per-protocol analysis, adjusting for the same covariates used in the primary analysis. Model 3 was developed by adjusting for operation time on the basis of model 1. Subsequently, propensity score matching (PSM) analysis was conducted. The matching variables included age, admission NIHSS score, prestroke mRS score, ASPECTS, infarct core volume and penumbra volume. The nearest neighbour matching method was used with a calliper set at 0.2 times the SD of the PS score and a matching ratio of 1:1. All the statistical analyses were performed using R software (V.4.3.1) and SAS software (V.9.4), with a p value less than 0.05 (two-tailed) set as the predetermined significance threshold.

RESULTS

Patient characteristics

The selection process for the study population is delineated in figure 1. Of the 456 LICV-AIS patients enrolled in the ANGEL-ASPECT trial, 231 were randomised to receive EVT combined with BMM, and 1 patient withdrew informed consent. Consequently, the remaining 230 patients were included in this post hoc analysis. GA agents were administered to 84 patients, whereas 146 patients received non-GA agents. The demographic data, medical history, clinical characteristics on admission, site of occlusion and temporal variables related to stroke onset were comparable between the two groups (table 1). The proportion of patients receiving intravenous thrombolysis was similar between the GA group and the non-GA group (27.4% vs 28.8%, p=0.82). The core infarct volume tended to be greater in the GA group than in the non-GA group (median (IQR): 67.5 (28.5–94) mL vs 56 (30–79) ml, p=0.09). The only significant difference observed was a longer operative time in the GA group than in the non-GA group (median (IQR): 142 (110–182) min vs 121 (85–172) min, p=0.03).

The PSM cohort included 130 patients whose baseline characteristics are detailed in online supplemental table 1, and the group balance is shown in online supplemental figure 1. The SBP recorded postpuncture and postfinal angiography in the GA group was significantly lower than that in the non-GA group (figure 2, online supplemental figure 2).

Neurological outcomes

All 230 LICV-AIS patients completed the mRS assessment at 90 days. Figure 3 illustrates that at 90 days, the distribution of mRS scores was similar between the GA group and the non-GA group, with median scores of (4 (IQR 2–6) vs 3.5 (IQR 2–5), p=0.23). Within the GA group, 27.4% of patients had a favourable 90-day functional outcome (mRS 0–2), whereas 31.5% of the patients in the non-GA group achieved this outcome. According to multivariate logistic regression analysis, the distribution of 90-day mRS 0–2 did not significantly differ (adjusted OR 0.97; 95% CI 0.51 to 1.86), nor did the 90-day mRS 0–3 distribution (adjusted OR 0.88; 95% CI 0.48 to 1.60) between the GA and non-GA groups (table 2). During the in-hospital follow-up, the group administered GA exhibited a slightly greater increase in the NIHSS score within the first 36 hours than did the non-GA group (adjusted β −2.68; 95% CI −5.03 to −0.33). However, there were no significant differences between the groups regarding the change in infarct volume from baseline during the follow-up period (adjusted β 1.28; 95% CI −26.06 to 28.62). The results of

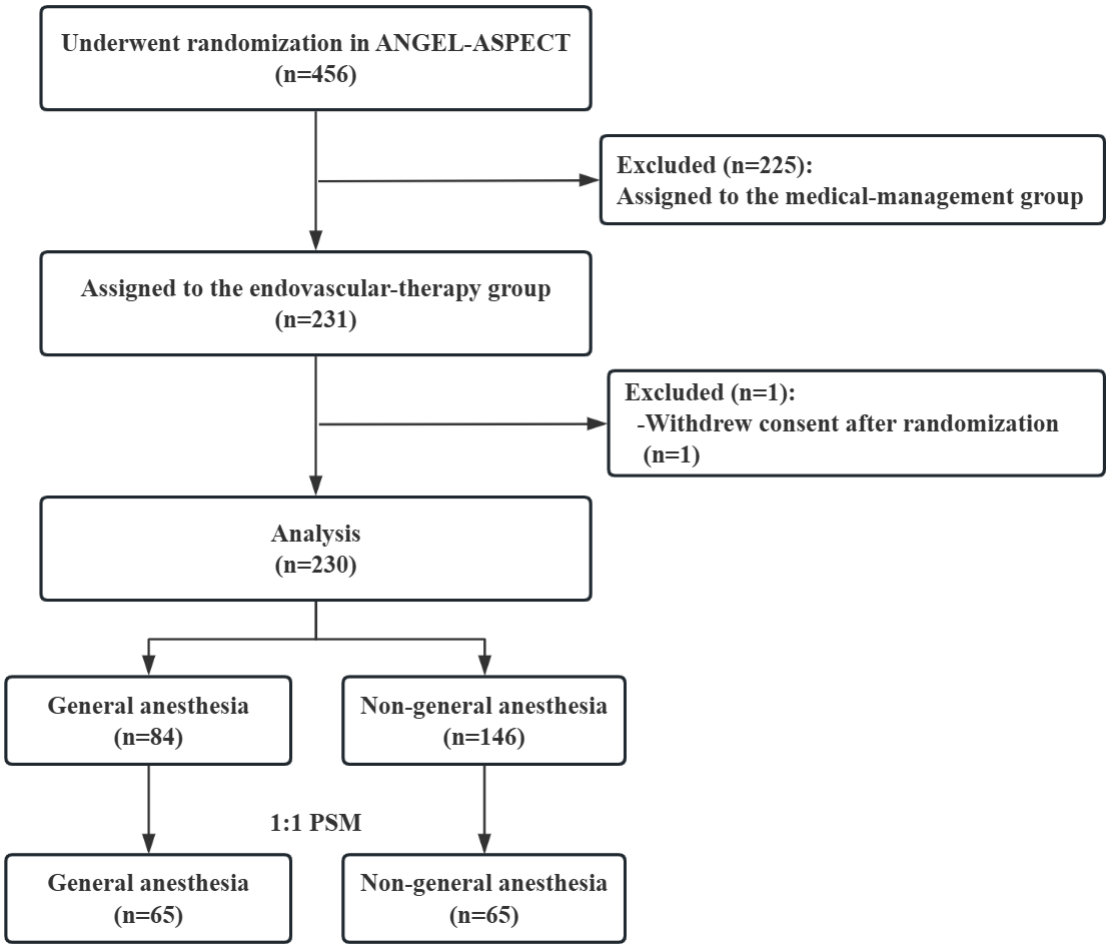

Figure 1 Anaesthesia technique-based analysis of the participant screening flow chart from the ANGEL-ASPECT Trial. ASPECT, Alberta Stroke Programme Early CT Score; PSM, propensity score matching.

the multivariate regression analysis were confirmed in the PSM analysis (table 2).

According to our subgroup analysis focused on the primary outcome (90-day mRS 0–2), no significant discrepancies were noted between any of the subgroups (figure 4). Furthermore, the sensitivity analysis yielded results consistent with those of the primary analysis (online supplemental table 2), suggesting that the anaesthesia method had no significant impact on long-term functional prognosis, as measured by the mRS.

Procedural and safety outcomes

Similarly, following EVT, the rate of successful reperfusion was high and did not significantly differ between the anaesthetic approaches, with more than 80% of the patients in both groups (82.1% in the GA group and 80.3% in the non-GA group; p=0.73). In addition, both groups experienced low and statistically similar rates of procedure complications (GA group, 8.3%; non-GA group, 6.8%; p=0.73) (table 2). Subsequent adjustment using logistic regression models revealed no significant differences between the GA and non-GA groups in terms of any ICH within 48 hours (adjusted OR 1.18, 95% CI 0.37 to 3.77), sICH (adjusted OR 0.94, 95% CI 0.54 to 1.65), mortality within 90 days (adjusted OR 1.50, 95% CI 0.75 to 2.97) or the necessity for decompressive hemicraniectomy during hospitalisation (adjusted OR 1.51, 95% CI 0.53 to 4.36). However, compared with the non-GA group, the GA group had an increased risk of pneumonia (adjusted OR 2.03, 95% CI 1.04 to 3.98), as detailed in table 2. The sensitivity analyses were consistent with the primary analysis results, which revealed a greater risk of pneumonia in the GA group—a finding that remained stable across the different models (model 2 adjusted OR 2.13, 95% CI 1.06 to 4.27; model 3 adjusted OR 2.03, 95% CI 1.03 to 3.98), as shown in online supplemental table 2.

DISCUSSION

In this post hoc analysis of the ANGEL-ASPECT trial, we found that although GA extended the duration of the procedure, there was no significant difference in 90-day neurological outcomes between the GA group and the non-GA group. The only two positive outcomes were as follows: relative to baseline, the improvement in the NIHSS score at 36 hours was less pronounced in the GA group, and the incidence of pneumonia during hospitalisation was greater.

LIVC lesions exceed one-third of the cerebral territory supplied by the MCA. The LICV-AIS is usually identified

Table 1 Baseline characteristics

Characteristics	General anaesthesia (N=84)	Non-general anaesthesia (N=146)	P value	Missing, n
Age, median (IQR), year	69 (60–74)	68 (61–73)	1.00	0
Male sex, no. (%)	47 (56.0)	88 (60.3)	0.52	0
Medical history, no. (%)				
Hypertension	49 (58.3)	87 (60.0)	0.85	0
Diabetes mellitus	16 (19.1)	27 (18.5)	0.92	0
Hyperlipidaemia	4 (4.8)	9 (6.2)	0.66	0
Atrial fibrillation	23 (27.4)	34 (23.3)	0.49	0
Ischaemic stroke	14 (16.7)	24 (16.4)	0.96	0
Coronary heart disease	13 (15.5)	24 (16.4)	0.85	0
NIHSS score (IQR)	17 (14–20)	16 (13–19)	0.12	0
ASPECTS value based on CT				
Median value (IQR)	3 (3–4)	3 (3–4)	0.53	0
Distribution, no. (%)			0.91	0
0–2	13 (15.5)	18 (12.3)		
3	36 (42.9)	63 (43.2)		
4	22 (26.2)	42 (28.8)		
5	13 (15.5)	23 (15.8)		
Infarct-core volume, median (IQR), mL	67.5 (28.5–94)	56 (30–79)	0.09	0
Penumbra volume, median (IQR), mL	183 (144–236)	168 (120–219)	0.28	28
Prestroke mRS, no. (%)			0.99	0
0	76 (90.5)	132 (90.4)		
1	8 (9.5)	14 (9.6)		
Baseline SBP, median (IQR), mm Hg	147 (133–168.5)	143 (128–165)	0.26	0
Admission glucose, median (IQR), mmol/L	7.3 (6.4–8.6)	7.1 (6.0–9.2)	0.51	45
Intravenous thrombolysis, no. (%)	23 (27.4)	42 (28.8)	0.82	0
Occlusion site, no. (%)			0.73	0
ICA	33 (39.3)	51 (34.9)		
M1 segment	50 (59.5)	94 (64.4)		
M2 segment	1 (1.2)	1 (0.7)		
Stroke classification, no. (%)			0.61	0
Atherothrombotic	22 (26.2)	39 (26.7)		
Cardioembolic	37 (44.1)	72 (49.3)		
Undetermined and others	25 (29.8)	35 (24.0)		
Interval between onset and hospital arrival, median (IQR), min	330 (187–649)	348 (205–627)	0.86	0
Interval between onset and first imaging, median (IQR), min	433 (239–700)	391 (252–659)	0.95	0
Onset to randomisation				
Median (IQR), min	472 (275–746)	427 (306–710)	0.91	0
Distribution, no. (%)			0.56	0
< 6 hours	32 (38.1)	50 (34.3)		
6–24 hour	52 (61.9)	96 (65.8)		
Interval between onset and puncture, median (IQR), min	519 (321–786)	455 (328–774)	0.78	4
Interval between onset and recanalisation, median (IQR), min	620 (395–890)	558 (426–835)	0.80	4
Interval between puncture and recanalisation, median (IQR), min	78 (51.5–104.5)	72.5 (43-115)	0.48	3
Operative time*, median (IQR), min	142 (110–182)	121 (85–172)	0.03	3

*Operative time is defined as the difference between 'the time the patient arrives at the catheterisation room' and 'the time the patient leaves the catheterisation room'.
ASPECTS, Alberta Stroke Programme Early CT score; ICA, internal carotid artery; M, middle cerebral artery; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure.

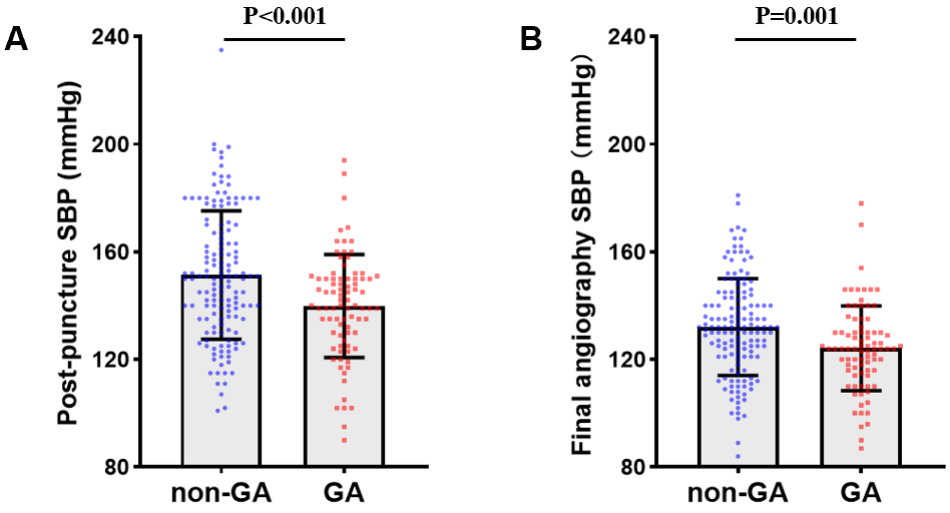

Figure 2 Systolic blood pressure (SBP) at critical time points. (A) After groin puncture. (B) After final angiography. GA, general anaesthesia.

on the basis of an NCCT ASPECTS of less than six points or by a quantitative measurement of the infarct core volume of more than 50 or 70 mL on CTP/MRI.[23] No difference in prognosis was noted between LICV patients identified by either imaging modality.[24] The optimal choice of anaesthesia for EVT following substantial brain infarction depends on regional differences, patient characteristics and physician preferences. Of the patients with LICV-AIS who underwent mechanical thrombectomy, 36.7%, 44.0% and 58.4% received GA in the ANGEL-ASPECT, TENSION and SELECT2 trials, respectively. The ANGEL-ASPECT trial protocol suggested that LA can expedite the initiation of EVT, with CS and GA subsequently considered based on patient condition, cooperation level and airway status.[22] Although not significantly, our study revealed that the baseline NIHSS score and infarct volume were greater in the GA group than in the non-GA group, consistent with the findings of the HERMES Collaboration.[25] This study employed PSM analysis to simulate the randomisation process, significantly enhancing the balance between the two groups of patients and achieving conclusions similar to those of previous RCTs.

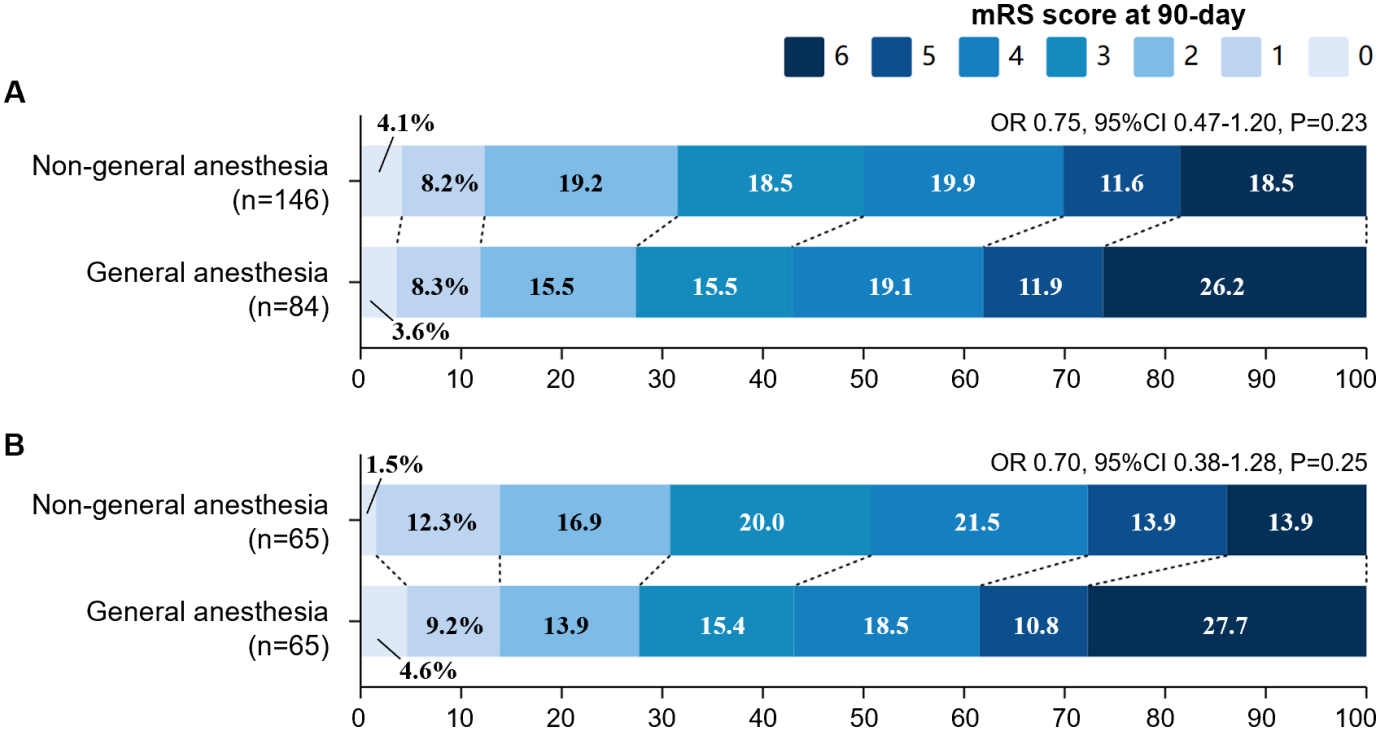

Figure 3 Distribution of 90-day mRS scales between the general and non-general anaesthesia groups. (A) Initial cohort. (B) Propensity score matching cohort. mRS, modified Rankin scale.

Table 2 Association between anaesthetic techniques and outcomes of interest: general anaesthesia versus non-general anaesthesia

	Unadjusted			Adjusted model 1*	PSM	
	General anaesthesia	Non-general anaesthesia	Effect size (95% CI)†	Effect size (95% CI)†	Effect size (95% CI)†	
N	84	146	230	230	130	Missing, n
Primary outcome						
mRS of 0–2 at the 90-day follow-up	23 (27.4)	46 (31.5)	0.82 (0.45 to 1.48)	0.97 (0.51 to –1.86)	0.86 (0.40 to –1.84)	0
Secondary outcomes						
mRS score at the 90-day follow-up	4 (2-6)	3.5 (2-5)	0.75 (0.47 to 1.20)	0.83 (0.51 to 1.35)	0.70 (0.38 to –1.28)	0
mRS of 0–3 at the 90-day follow-up	36 (42.9)	73 (50.0)	0.75 (0.44 to 1.29)	0.88 (0.48 to 1.60)	0.73 (0.37 to –1.46)	0
36-hour ΔNIHSS	0 (-5–3.5)	1 (-1–4)	–2.78 (-5.11 to –0.45)	–2.68 (-5.03 to –0.33)	–2.42 (–5.68 to 0.85)	0
Change from baseline in infarct volume	65.1 (29.0–143.4)	57.3 (30.8–128.7)	2.85 (–24.15 to 29.86)	1.28 (–26.06 to 28.62)	15.25 (–19.71 to 50.21)	3
Successful reperfusion (mTICI 2b-3)	69 (82.1)	114 (80.3)	1.13 (0.56 to 2.26)	1.11 (0.54 to 2.27)	0.90 (0.37 to 2.22)	4
Safety outcomes						
Pneumonia	26 (31.0)	25 (17.1)	2.17 (1.15 to 4.08)	2.03 (1.04 to 3.98)	2.42 (1.08 to 5.42)	0
sICH within 48 hours	6 (7.1)	8 (5.5)	1.33 (0.44 to 3.96)	1.18 (0.37 to 3.77)	1.27 (0.33 to 4.96)	0
Any ICH within 48 hours	41 (48.8)	72 (49.3)	0.98 (0.57 to 1.68)	0.94 (0.54 to 1.65)	1.21 (0.60 to 2.41)	0
Death within 90-day	22 (26.2)	27 (18.5)	1.56 (0.82 to 2.97)	1.50 (0.75 to 2.97)	2.38 (0.98 to 5.80)	0
Decompressive hemicraniectomy during hospitalisation	8 (9.5)	9 (6.2)	1.60 (0.59 to 4.32)	1.51 (0.53 to 4.36)	4.42 (0.90 to 21.69)	0
Any procedural complications‡	7 (8.3)	10 (6.8)	1.19 (0.44 to 3.26)	1.32 (0.47 to 3.71)	1.25 (0.32 to 4.88)	5

*Adjusted for age, prestroke mRS score, baseline NIHSS score, baseline ASPECTS, core infarct volume, time from onset to puncture and receipt of intravenous thrombolysis in the intention-to-treat population.
†The results of the binary logistic regression are reported as ORs with 95% CIs, those of the linear regression are reported as β values with 95% CIs and those of the ordinal logistic regression are reported as cORs with 95% CIs.
‡Procedural complications include arterial dissection, arterial perforation, vasospasm requiring treatment and embolisation in a new territory.
ASPECTS, Alberta Stroke Programme Early CT Score; cOR, crude OR; ICH, intracranial haemorrhage; mRS, modified Rankin scale; mTICI, modified thrombolysis in cerebral infarction; NIHSS, National Institutes of Health Stroke Scale; PSM, propensity score matching; sICH, symptomatic ICH.

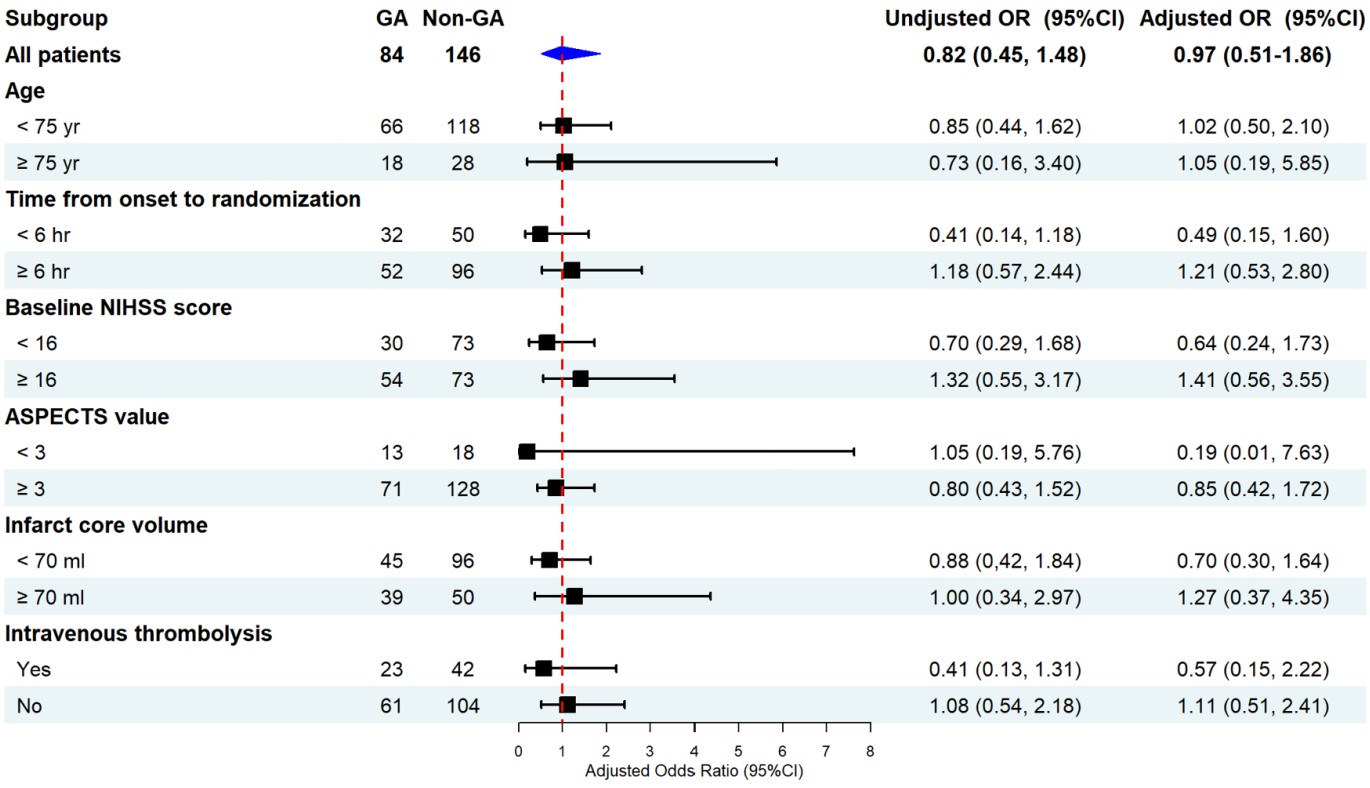

Figure 4 Exploratory subgroup analysis of the primary outcome. ASPECTS, Alberta Stroke Programme Early CT score; GA, general anaesthesia; NIHSS, National Institutes of Health Stroke Scale.

Patients with LICV-AIS typically suffer from severe neurological impairment, with a higher incidence of coma and confusion, leading to high disability and mortality rates.[26] The advantages of GA include maintaining patient immobility, ensuring adequate oxygenation, preventing aspiration, and providing comprehensive airway protection. An individual patient data meta-analysis derived from the ITT population of RCTs indicated that GA may lead to better functional outcomes due to higher reperfusion rates.[27] However, the beneficial outcomes associated with GA were not statistically significant after excluding patients for whom CS had to be emergently converted to GA. Published reports indicate a markedly poorer prognosis for patients requiring emergency conversion from CS to GA during EVT than for those who undergo the entire procedure under CS.[17] In our study, the recanalisation rates and neurological outcomes were similar between the two groups.

LICV-AIS results in a more extensive infarct core. Damage to cerebral arterioles impairs autoregulation, leading to pressure-dependent cerebral perfusion, which forms the basis for permissible hypertension treatment prior to successful recanalisation.[28 29] Data from a secondary analysis of the General or Local Anaesthesia in Intra-Arterial Therapy trial indicate that hypotension induced by GA/CS during EVT is a predictor of collateral circulation deterioration, and this adverse effect is difficult to counteract with vasopressors.[20] Maintaining appropriate haemodynamic stability is a prerequisite for the safe application of GA during EVT. In this study, the SBP in the GA group slightly decreased but remained within the acceptable range following the completion of the puncture procedure. Furthermore, preclinical evidence suggests that GA during periods of brain development (infancy) and degeneration (elderly) could lead to changes in neurodevelopment and cognitive behaviour.[30 31] However, the potential neurotoxicity of these agents is dose-dependent and time-dependent, and transient exposure to anaesthetic agents during EVT is unlikely to result in lasting brain damage.

The NIHSS score is an essential tool for assessing the severity of a stroke, and early neurological improvement (ENI) is closely related to patient-centred long-term functional outcomes.[32] Previous studies have suggested that a decrease in the NIHSS score by an absolute value of 4, 8 or 10 points or a score of 0–1 at 24 hours can effectively reflect the ENI score.[33] Consequently, in our investigation, while the increase in the NIHSS score at 36 hours was marginally lower for the GA group than for the non-GA group, this disparity was not clinically meaningful.

Although GA provides a stable operative environment conducive to medical procedures, the accompanying intubation process and its potential impact on pulmonary function may increase the risk of postoperative pneumonia. In the real-world clinical setting, immediate extubation post-EVT is uncertain, with many patients requiring continued airway support and further sedation after transfer to neurointensive care units. Studies have

shown that the longer a patient is intubated, the greater the risk of pneumonia during hospitalisation, with a lower likelihood of achieving functional independence and survival at 90 days.[34] Post hoc analysis of the Basilar Artery International Cooperation Study also suggested that the potential benefits of EVT may be mitigated by the indirect effects of early intubation.[35] Research by Nikoubashman *et al* revealed that overall, an extended ventilation time was associated with in-hospital pneumonia, adverse functional outcomes and mortality at follow-up; however, these associations were not present when ventilation did not exceed 24 hours.[36]

Advances in modern medicine have made technical issues no longer the main barrier to the treatment of LICV-AIS, yet there are challenges faced in perioperative management, such as reperfusion injury, malignant cerebral oedema, seizure activity and haemorrhagic transformation.[28] In our study, although the rate of successful recanalisation reached 80%, the percentage of patients who reached functional independence was 30%, which was significantly lower than the 46% for patients with small to medium infarcts who underwent EVT.[37] Furthermore, although the GA group experienced an approximately 20 min delay in surgery, this delay did not result in worsening of the functional prognosis, underscoring the importance of a standardised workflow to avoid time delays associated with intubation. The anaesthetic modality should be tailored to the patient's specific condition and the need for rapid treatment initiation in emergency situations, with an efficient GA process potentially maximising the treatment window. In the treatment of LICV-AIS, anaesthesiologists are an indispensable part of the interventional treatment team. Compared with the type of anaesthesia, perioperative management of vital parameters such as BP, oxygenation, ventilation, blood glucose and surgical complications is undoubtedly critical.[19 38] This difference may be particularly evident in LICV-AIS patients with more pronounced vascular fragility. Unless the patient is at high risk for agitation or aspiration, non-GA should be the preferred treatment.

Several limitations are inherent in this study. First, the ANGEL-ASPECT trial was designed to assess the optimal treatment strategy for LICV-AIS, not to compare anaesthetic techniques. The application of the two anaesthetic methods within the study was subject to selection bias, and the limited sample size could compromise the reliability of the findings. Additionally, the present study has incomplete data regarding the specific characteristics of GA, such as pharmacological details (inhalational or intravenous), airway management techniques, haemodynamic variables and ventilation parameters. There is an urgent need for prospective studies that comprehensively collect perioperative data to establish standardised anaesthesia management protocols, which could provide strong guidance for clinical decision-making. Third, as LA is typically administered by the interventional physicians themselves, we were unable to obtain detailed intraoperative monitoring data, particularly precise information on BP fluctuations. Fourth, the choice of anaesthetic technique is often based on the clinical assessment of the patient, with those in a generally worse condition being more likely to experience GA. Furthermore, patients who initially started with non-GA and were emergently converted to GA were categorised within the GA cohort, potentially diluting the positive impact of GA on the outcomes. Although we adjusted for various confounding factors, bias remains an inevitable issue. Fifth, the heterogeneity in the selection of the study population may also affect the results; therefore, sensitivity analyses were conducted to assess this impact. Sixth, while prolonged intubation time is a risk factor for nosocomial pneumonia, the distribution of post-EVT endotracheal tube retention times and the occurrence of reintubation in both groups are currently unclear. However, further research is warranted to clarify this issue.

CONCLUSION

It is tempting to speculate that, based on this post hoc analysis of the ANGEL-ASPECT trial, for patients with LICV-AIS who underwent EVT, there was no significant association between the type of anaesthesia and neurological functional recovery, despite the increased duration of the procedure in the GA group relative to the non-GA group. When GA is deemed necessary for intervention, it is imperative to closely monitor patients for the development of nosocomial pneumonia postoperatively and to provide vigilant care and treatment. However, further trials are warranted to explore the impact of anaesthesia methods on the outcomes of patients with LICV-AIS who undergo EVT.

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