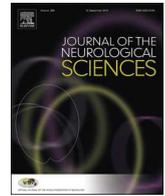




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General anesthesia vs local anesthesia during mechanical thrombectomy in acute ischemic stroke

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ABSTRACT

Objective: To investigate the effect of general anesthesia (GA) on functional outcomes and complications rates in acute ischemic stroke (AIS) patients treated with mechanical thrombectomy (MT) compared to the use of local anesthesia (LA) at the puncture site.

Methods: This observational study was based on a prospectively registry study. AIS patients underwent MT with GA or LA from January 2013 to October 2017 were included. The primary outcome was the modified Rankin Scale (mRS) score at 90 days post-intervention. Furthermore, we assessed the long-term outcome of these patients. Multivariable logistic regression analysis was conducted to adjust for confounders.

Results: We enrolled 187 AIS patients in this study, patients in GA group had a similar mRS score compared to LA group at 90 days (2 [IQR, 1–4] vs 2.5 [IQR, 1–4], $P = .917$). No differences were found in the rates of functional independence (mRS 0–2), no or minimal disability (mRS 0–1), and mortality (mRS 6) between the 2 groups at 90 days post-intervention as well as long-term follow-up. The procedure-related complications and serious adverse events were similar between the LA group and GA group ($P > .05$ each). In multivariable analysis, GA use was not associated with functional outcomes.

Conclusion: AIS patients who received GA during MT had similar functional outcomes and complications rates compared to patients received LA.

1. Introduction

Several clinical trials have demonstrated the safety and efficacy of mechanical thrombectomy (MT) in acute ischemic stroke (AIS) patients due to proximal anterior circulation occlusions [1–3]. Timely and successful vessel recanalization with MT is now considered the standard treatment and is a critical determinant of favorable outcomes after large vessel occlusion in AIS patients [4,5]. However, there is continued debate regarding the procedural approach, including the type of anesthesia [6].

The purpose of anesthesia during MT is to minimize patient movement, decrease surgical risks and shorten procedure time. Generally, there are 3 types of anesthesia available for MT: general anesthesia (GA), conscious sedation (CS), and local anesthesia (LA). In recent

years, most observational studies have focused on the comparison between GA and CS with most studies suggesting better outcomes with CS [7–9]. However, three randomized clinical trials of anesthesia during MT have not confirmed the superiority of CS over GA [10–12]. On the other hand, a recently published study indicated that CS was of no benefit compared to LA [13]. A few studies have also compared the functional outcomes between AIS patients with LA and GA. A multicenter retrospective registry study demonstrated that clinical outcomes and survival were significantly better in AIS patients treated with LA than GA [14]. Data from The Interventional Management of Stroke III trial showed a similar result that GA was associated with worse neurological outcomes and increased mortality compared to LA [15]. However, considering that these studies were heavily biased, it was difficult to validate the applicability of these studies to others. In other

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words, the best anesthesia approach remains an area of uncertainty. The current study aimed to investigate the effect of GA on functional outcomes and complications rates in AIS patients treated with MT compared to the use of LA.

2. Methods

2.1. Standard protocol approvals, registrations, and patient consents

This study was based on a registry study in Xuanwu Hospital, Capital Medical University in Beijing, China. All consecutive AIS patients receiving revascularization therapy (i.e. intravenous thrombolysis and endovascular treatment) in our center are registered in this prospectively collected registry which had been approved by the Ethics Committee of Xuanwu Hospital of Capital Medical University. Written informed consent was provided at admission by patients or their legal representatives.

2.2. Study population

In our center, AIS patients with large vessel occlusion were treated with MT in accordance with the guidelines as soon as possible after symptoms onset [4,5]. For the present study, we enrolled the AIS patients who underwent MT from January 2013 to October 2017. The inclusion criteria for this study were as follows: 1) diagnosis of AIS; 2) large vessel occlusion in the anterior circulation confirmed by computed tomographic angiography, magnetic resonance angiography or digital subtraction angiography; 3) MT initiated within 6.5 h after symptoms onset. We excluded patients with prestroke modified Rankin Scale (mRS) score of > 2 points and those who were lost to follow-up. To improve the quality of the current study, we reported our results in keeping with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [16].

2.3. Interventions

Based on the regulations in our center, only the neurointerventionists who are trained in the technique of performing extracranial and intracranial stents can be qualified for MT. During the procedure, heparin is given intravenously to maintain the activated coagulation time between 250 and 300 s, except for the AIS patients who received intravenous thrombolysis prior to MT. The specific intervention strategies, the type of stent retrievers, and other devices were chosen at the discretion of the neurointerventionists.

Per institutional protocol, the only anesthesia options available for the interventional procedure are LA and GA. The decision of whether to perform LA or GA was made in inter-disciplinary fashion by neurointerventionists, anesthesiologists, and neurologists according to the level of patient cooperation and physical status. LA was achieved by subcutaneous injection of anesthetic at the puncture site. GA was achieved with etomidate, rocuronium, sufentanil and then maintained with propofol, sevoflurane, remifentanyl. The specific dosages of these drugs were calculated based on patient weight and age and were adjusted according to the actual conditions during the procedure. Reasons influencing the choice for GA include uncontrollable agitation, respiratory abnormality, nausea/vomiting, and hypoxemia/hypercarbia. Patients under GA received endotracheal intubation and mechanical ventilation until the end of the procedure. FiO_2 was titrated to maintain $\text{SpO}_2 > 92\%$ and $\text{PaO}_2 > 60 \text{ mmHg}$. Ventilation was adjusted to maintain normocapnia (PaCO_2 , 35 to 45 mmHg). Considering the potential risk of hypotension and blood pressure (BP) variability associated with anesthesia, fluids and vasopressor agents were on standby to maintain the BP strictly. In brief, systolic BP was maintained between 140 and 180 mmHg and diastolic BP < 105 mmHg during the procedure according to the recommendation of the Society for Neuroscience in Anesthesia and Critical Care Expert Consensus Statement [17].

After MT, patients were transferred to the neurological intensive care unit for further treatments. For patients with successful recanalization which was defined as the modified Thrombolysis in Cerebral Infarction (mTICI) perfusion score $\geq 2b$, postoperative systolic BP was maintained between 100 and 140 mmHg to avoid hyperperfusion as well as intracranial hemorrhage. However, for those not achieving successful recanalization, the systolic BP was maintained between 140 and 180 mmHg to protect the collateral circulation. Other therapeutic regimens followed the recommendation of guidelines [4,5].

The data we collected from the database and described below contained demographics, comorbidities, pathogenesis of stroke, stroke severity assessed by National Institutes of Health Stroke Scale (NIHSS) score, baseline Alberta Stroke Program Early Computed Tomography Score (ASPECTS) on computed tomography (CT) scan, vital signs, time intervals, details of interventional procedure, recanalization condition and outcomes. NIHSS score is a neurologic examination stroke scale with a full score of 42. A higher NIHSS score means a more severe disability [18]. ASPECTS is a quantitative CT score with a full score of 10. A lower ASPECTS indicates more early ischemic changes detected on CT scan [19].

2.4. Outcome assessments

The primary outcome was the mRS score at 90 days post-intervention. The mRS is a 7-point scale ranging from 0 (no symptoms) to 6 (dead). Secondary outcomes contained the clinical outcomes and safety outcomes. Clinical outcomes included the rates of functional independence (mRS 0–2), no or minimal disability (mRS 0–1) and mortality (mRS 6) at 90 days as well as long-term follow-up. Safety outcomes included the procedure-related complications (vessel perforation, dissection, new emboli, distal thrombus, vasospasm, and any hemorrhage) and serious adverse events (symptomatic intracranial hemorrhage, new ischemic stroke, progression of stroke, pneumonia, other infections, myocardial ischemia, and allergic reaction). Outcomes were assessed by an independent investigator who did not know the type of anesthesia used during MT. Patient status was followed up by telephone interviews or clinic visits when possible.

2.5. Statistical analysis

Baseline characteristics and outcomes were compared between the patients received LA and GA during the procedure. In accordance with the intention-to-treat principle, patients converted from LA to GA were regarded as patients in the LA group. We presented the descriptive statistics as mean (standard deviation [SD]) for normally distributed continuous variables or medians (interquartile range [IQR]) for non-normally distributed continuous variables and as percentages for categorical variables. Kolmogorov-Smirnov test was performed for the normality assessment of data. For the integrity of data, single imputation was used to compensate for missing values that counted for < 5% of all. Comparisons between the LA group and GA group were conducted with the Student *t*-test or the Mann-Whitney *U* test for continuous variables and chi-square test or Fisher's exact test for categorical variables. To minimize the potential bias and adjust for confounders, we performed the multivariable logistic regression analysis with functional outcomes at 90 days as the dependent variable and with age, NIHSS, ASPECTS, atrial fibrillation, previous stroke, time from symptoms onset to reperfusion, recanalization condition, and symptomatic intracranial hemorrhage as the covariates. Furthermore, Kaplan-Meier survival analysis was performed to compare the survival probability at long-term follow-up between the LA group and GA group with the log-rank test. The significance level was set at $P \leq .05$ (2-sided). Statistical analyses were performed with SPSS 23.0 (IBM Corp).

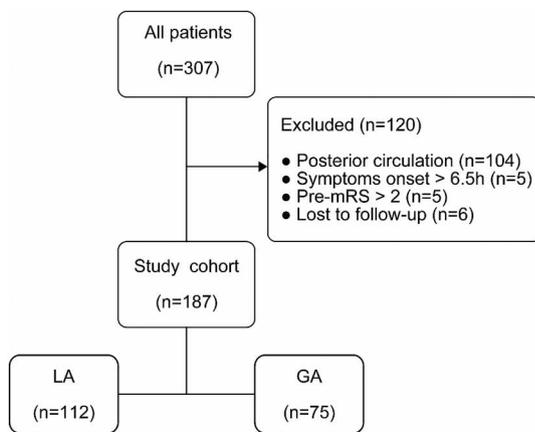


Fig. 1. Flow diagram.

This figure shows the enrollment information of patients, including the reasons for exclusion and the grouping situation.

Abbreviations: LA = local anesthesia; GA = general anesthesia; mRS = modified Rankin scale

3. Results

3.1. Demographic characteristics

Of 307 enrolled patients between January 2013 and October 2017, 120 patients were excluded (104 patients with posterior circulation stroke, 5 patients with the time of symptoms onset to MT > 6.5 h, 5 patients with pre-stroke mRS > 2 and 6 patients were lost to follow-up). The final study cohort consisted of 187 patients. 112 patients received LA at the puncture site and 75 patients received GA during the procedure (Fig. 1).

The mean age was 64.5 (SD, 10.7) years in the LA group and 63.5 (SD, 11.3) years in the GA group ($P = .525$). The median NIHSS score were 15 (IQR, 10–18) and 15 (IQR, 9–19) in the 2 groups ($P = .959$), respectively. Baseline characteristics including patient characteristics, comorbidities, and pathogenesis were well balanced between the LA group and GA group (Table 1).

3.2. Time intervals and details of interventional procedure

We found no significant difference in time from symptoms onset to admission emergency department (ED) between the LA group and GA group (200 [IQR, 140–260] vs 202 [IQR, 106–260], $P = .971$). Time from admission ED to groin puncture was 8 min shorter for patients received LA, although there was no statistically significant difference between the 2 groups (86 [IQR, 70–105] vs 94 [IQR, 78–120], $P = .282$). Time from groin puncture to reperfusion was 5 min longer in the LA group, without significant difference (70 [IQR, 50–86] vs 65 [IQR, 50–87], $P = .649$). Ultimately, time from symptoms onset to reperfusion did not differ between the LA group and GA group (356 [290–410] vs 360 [307–417], $P = .504$).

There was no difference in the distribution of occlusion sites between the 2 groups. In addition, successful recanalization was achieved in 81.3% of LA group versus 82.7% of GA group, without difference ($P = .806$).

3.3. Outcome

The median mRS was 2.5 (IQR, 1–4) in the LA group and 2 (IQR, 1–4) in the GA group at 90 days post-intervention ($P = .917$). Of all patients, 96 patients (51.3%) had functional independence, 48 patients (25.7%) achieved no or minimal disability and 31 patients (16.6%) died

Table 1
Baseline characteristics.

	LA (n = 112)	GA (n = 75)	P value
Patient characteristics			
Age, y, mean (SD)	64.5 (10.7)	63.5 (11.3)	0.525
Male, n (%)	73 (65.2)	54 (72)	0.327
BMI, mean (SD)	25.4 (3.2)	25.1 (2.6)	0.585
NIHSS, median (IQR)	15 (10–18)	15 (9–19)	0.959
ASPECTS, median (IQR)	8 (7–9)	8 (7–9)	0.733
Intravenous alteplase, n (%)	40 (35.7)	28 (37.3)	0.822
Systolic BP, median (IQR)	136 (123–155)	135 (123–154)	0.880
Diastolic BP, median (IQR)	80 (70–86)	80 (73–90)	0.230
Heart rate, median (IQR)	80 (70–85)	78 (68–90)	0.954
Comorbidities, n (%)			
Hypertension	60 (53.6)	37 (49.3)	0.570
Diabetes mellitus	27 (24.1)	19 (25.3)	0.849
Hyperlipidemia	25 (22.3)	14 (18.7)	0.547
Atrial fibrillation	31 (27.7)	22 (29.3)	0.806
Previous stroke	14 (12.5)	8 (10.7)	0.703
Smoking	46 (41.1)	33 (44)	0.691
Pathogenesis, n (%)			
Large artery atherosclerosis	71 (63.4)	45 (60.0)	0.639
Cardioembolism	33 (29.5)	24 (32.0)	0.712
Other	8 (7.1)	6 (8.0)	0.827
Time intervals			
From symptoms onset to admission ED, min, median (IQR)	200 (140–260)	202 (106–260)	0.971
From admission ED to groin puncture, min, median (IQR)	86 (70–105)	94 (78–120)	0.282
From symptoms onset to groin puncture, min, median (IQR)	286 (237–348)	294 (224–358)	0.561
From groin puncture to reperfusion, min, median (IQR)	70 (50–86)	65 (50–87)	0.649
From symptoms onset to reperfusion, min, median (IQR)	356 (290–410)	360 (307–417)	0.504
Details of interventional procedures			
Occlusion site, n (%)			
MCA	66 (58.9)	40 (53.3)	0.449
ICA	43 (38.4)	32 (42.7)	0.559
ACA	3 (2.7)	3 (4.0)	0.937
Hemisphere, n (%)			
Left	56 (50.0)	37 (49.3)	0.929
Right	56 (50.0)	38 (50.7)	0.929
Number of device passes			
1	56 (50.0)	42 (56.0)	0.421
2	24 (21.4)	18 (24.0)	0.680
≥ 3	32 (28.6)	15 (20.0)	0.185
Recanalization, n (%)			
mTICI ≥ 2b	91 (81.3)	62 (82.7)	0.806
mTICI 3	54 (48.2)	34 (45.3)	0.699

Abbreviations: LA = local anesthesia; GA = general anesthesia; SD = standard deviation; BMI = body mass index; NIHSS = National Institutes of Health Stroke Scale; IQR = interquartile range; ASPECTS = Alberta Stroke Program Early Computed Tomography Score; BP = blood pressure; ED = emergency department; MCA = middle cerebral artery; ICA = internal carotid artery; ACA = anterior cerebral artery; mTICI = modified thrombolysis in cerebral infarction.

at 90 days. The rates of functional independence, no or minimal disability, and mortality were not significantly different between patients received LA and GA during MT ($P > .05$ each). As for the long-term follow-up, the median follow-up time was 16.5 (IQR, 5–25) months in the LA group and 15 (IQR, 3–27) in the GA group ($P = .731$). Similarly, no differences were found in the rates of functional independence, no or minimal disability, and mortality between the 2 groups at long-term follow-up ($P > .05$ each). The details of clinical outcomes and the distribution of the mRS categories were presented in Table 2 and Fig. 2.

Besides, Kaplan-Meier survival analysis showed that there was no

Table 2
Primary and secondary outcomes.

	LA (n = 112)	GA (n = 75)	P value
Primary outcome, median (IQR) mRS at 90 d	2.5 (1–4)	2 (1–4)	0.917
Secondary outcomes, clinical			
90 d follow-up			
Functional independence, n (%)	56 (50.0)	40 (53.3)	0.655
No or minimal disability, n (%)	29 (25.9)	19 (25.3)	0.932
Mortality, n (%)	17 (15.2)	14 (18.7)	0.530
Long-term follow-up			
Time, median (IQR), months	16.5 (5–25)	15 (3–27)	0.731
mRS, median (IQR)	2 (1–5)	2 (1–6)	0.949
Functional independence, n (%)	60 (53.6)	39 (52.0)	0.833
No or minimal disability, n (%)	40 (35.7)	26 (34.7)	0.883
Mortality, n (%)	23 (20.5)	19 (25.3)	0.441
Secondary outcomes, safety, n (%)			
Procedure-related complications	34 (30.4)	22 (29.3)	0.881
Serious adverse events			
sICH	8 (7.1)	7 (9.3)	0.589
New ischemic stroke	3 (2.7)	2 (2.7)	1
Progression of stroke	7 (6.3)	6 (8.0)	0.645
Pneumonia	21 (18.8)	12 (16.0)	0.629
Other infections	4 (3.6)	3 (4.0)	1
Myocardial ischemia	1 (0.9)	0	1
Allergic reaction	0	0	–

Abbreviations: LA = local anesthesia; GA = general anesthesia; IQR = interquartile range; mRS = modified Rankin Scale; sICH = symptomatic intracranial hemorrhage.

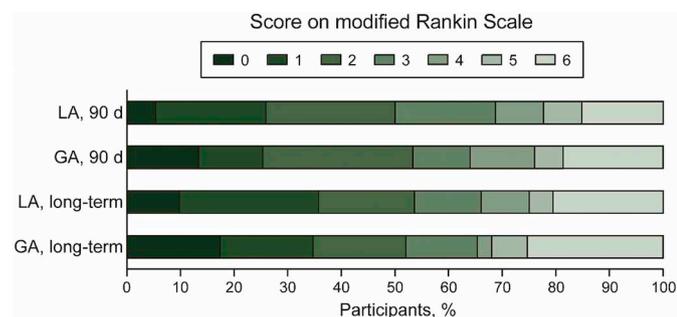


Fig. 2. Distribution of the modified Rankin Scale at 90 days and long-term follow-up.

The percentages are shown in each cell according to the distribution of modified Rankin Scale. We found that there was no difference in the distribution of modified Rankin Scale between LA and GA at either 90 days ($P = .917$) or long-term follow-up ($P = .949$).

Abbreviations: LA = local anesthesia; GA = general anesthesia

difference in the long-term survival probability between the 2 groups (log-rank, $P = .432$, Fig. 3).

Also, the safety outcomes including procedure-related complications and serious adverse events were similar between the LA group and GA group ($P > .05$ each, Table 2).

In the multivariable logistic regression analysis, NIHSS, time from symptoms onset to reperfusion, recanalization condition, and symptomatic intracranial hemorrhage were associated with functional outcomes at 90 days post-intervention. However, GA use was not associated with functional independence (OR 1.45 [95% CI 0.58–3.62], $P = .426$), no or minimal disability (OR 1.52 [95% CI 0.56–4.14], $P = .418$), and mortality (OR 1.75 [95% CI 0.52–5.87], $P = .366$). The results of the multivariable regression analysis were summarized in Table 3.

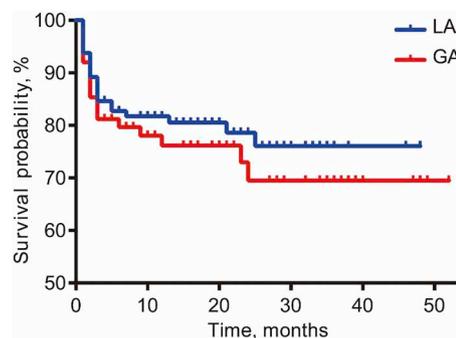


Fig. 3. Kaplan-Meier curves for the long-term survival probability. There was no difference between the LA group and GA group in survival probability at long-term follow-up (log-rank, $P = .432$). Abbreviations: LA = local anesthesia; GA = general anesthesia.

4. Discussion

In the present study, we found that in AIS patients treated with MT, GA use did not influence the 90 days and long-term functional outcomes compared to LA. Furthermore, there were no differences between the LA group and GA group in time intervals, recanalization rates as well as the safety outcomes including procedure-related complications and serious adverse events.

The issue of which type of anesthesia is the best has been debated for a long time [20]. Over the past decade, a large number of observational studies have indicated that AIS patients under GA have worse outcomes compared to non-GA patients [7–9,14,15,21,22]. However, it should be recognized that, in most studies, there was an imbalance in stroke severity between patients with different anesthesia types as measured by NIHSS suggesting that patients who received GA were clinically sicker than those with non-GA [14,15,21,22]. In our study, the stroke severity was well balanced between groups with the median NIHSS score of 15 at baseline. This suggests that our result that GA use did not influence the functional outcomes of AIS patients under MT is not confounded by baseline differences.

Moreover, previous studies showed that time delays were common in patients with GA, especially the time from symptoms onset to groin puncture [21,23]. However, in our study, although GA took more time than LA numerically, the difference was not statistically significant. More importantly, the longer time spent on GA prior to MT was offset by the shorter intraoperative time during MT in GA group, finally, the time from symptoms onset to reperfusion did not differ between the 2 groups. While anesthesia induction and endotracheal intubation required for GA are more time-consuming, patient immobilization under GA allows the procedure to proceed more expeditiously with shorter intraoperative time during MT. Based on the evidence that each 1-h delay to reperfusion would reduce the likelihood of functional independence by 19% [24], any time delays due to anesthesia should be avoided. According to the protocol in our institution, a skilled anesthesia team is in-house at all times and arrives to the neurointervention suite prior to patient arrival in order to minimize the time spent on anesthesia. However, this resource may not be available at all centers. One study reports that 37% of the anesthesia departments cannot guarantee an immediate response, irrespective of time of day [25]. In the absence of the local guidelines on anesthesia for AIS patients in most anesthesia departments, the personal experience of the anesthesiologist is particularly important. An experienced anesthesiologist can administer anesthesia in a short time and work in parallel with neurointerventionist, which may further accelerate the interventional procedure.

During the stroke, ischemic brain tissue becomes more sensitive to

Table 3
Predictors of outcome at 90 days (multivariable analysis).

	Functional independence		No or minimal disability		Mortality	
	Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value
Age	0.97 (0.93–1.02)	0.211	0.98 (0.94–1.02)	0.325	0.99 (0.94–1.04)	0.679
NIHSS	0.87 (0.79–0.95)	0.001	0.79 (0.70–0.88)	< 0.001	1.22 (1.10–1.36)	< 0.001
ASPECTS	1.33 (0.94–1.89)	0.106	1.24 (0.85–1.81)	0.273	0.87 (0.56–1.36)	0.544
Atrial fibrillation	1.50 (0.52–4.39)	0.455	0.75 (0.23–2.44)	0.637	3.03 (0.85–10.87)	0.088
Previous stroke	2.18 (0.49–9.70)	0.305	1.26 (0.27–6.00)	0.771	0.89 (0.15–5.17)	0.895
Time from symptoms onset to reperfusion	0.99 (0.99–1.00)	0.007	0.99 (0.99–1.00)	0.052	1.01 (1.00–1.01)	0.027
Recanalization condition	5.50 (1.11–27.34)	0.037	4.93 (0.72–33.95)	0.105	0.27 (0.07–1.08)	0.065
sICH	0.10 (0.02–0.57)	0.010	0.12 (0.01–1.12)	0.062	10.59 (2.37–47.34)	0.002
GA	1.45 (0.58–3.62)	0.426	1.52 (0.56–4.14)	0.418	1.75 (0.52–5.87)	0.366

Abbreviations: NIHSS = National Institutes of Health Stroke Scale; ASPECTS = Alberta Stroke Program Early Computed Tomography Score; sICH = symptomatic intracranial hemorrhage; GA = general anesthesia. NIHSS, time from symptoms onset to reperfusion, recanalization condition and sICH are associated with functional independence. NIHSS is associated with no or minimal disability. NIHSS, time from symptoms onset to reperfusion and sICH are associated with mortality.

BP because of the impaired cerebrovascular autoregulation. Thus, maintaining BP stability is crucial to protect the ischemic penumbra and collateral circulation, and is therefore of great significance to AIS patients [26]. Hypotension is frequent during the induction of GA, which may contribute to GA related poor outcomes [27]. A recent study demonstrated that patients who received GA had a lower minimum systolic BP than patients with CS during induction (115 ± 23 mmHg vs 139 ± 23 mmHg; $P = .0003$) [28]. In the present study, although there was a lack of data on BP during the procedure, we selected medications with less impact on hemodynamics for AIS patients (such as etomidate) [29] and prepared fluids and vasopressor agents in advance to minimize the risk of BP fluctuations. Furthermore, whether different types of anesthesia will affect the safety of MT is another matter of concern. Theoretically, patient movement during the procedure increases the risks of complications such as perforation, dissection, and hemorrhage. However, we found no significant difference in the safety outcomes between the LA group and GA group. Furthermore, there is currently no evidence that GA is safer than LA for AIS patients treated with MT [14,15,30].

Our study has several limitations. First, the decision to perform LA or GA during MT was not randomized, which may introduce the possibility of selection bias. However, the observational design of our study reflects real world experience. Second, although we used the multivariable regression analysis to adjust for relevant variables, the possibility of unmeasured and residual confounding remained. Additionally, as mentioned above, intraoperative BP readings were not available, especially during the induction of GA. Another limitation is that the support from the anesthesia team varies from center to center. For example, we have an experienced anesthesia team readily available for MT, but such a resource may not be universally available. In consideration of these issues, a multicenter randomized clinical trial to promote generalizability is warranted.

5. Conclusion

In conclusion, in this study, AIS patients received GA during MT had similar 90 days and long-term functional outcomes and complications rates compared to patients received LA. It is reasonable that the choice of anesthesia type should be based on the patient's individual condition as well as the support from the anesthesia team.

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Declarations of interest

None.

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