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Research article

General anesthesia versus sedation for endovascular thrombectomy: Meta-analysis and trial sequential analysis of randomized controlled trials

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ABSTRACT

Background: The endovascular thrombectomy procedure has become an established standard of care in clinical practice for the management of acute ischemic stroke. However, the anesthesia modality on endovascular thrombectomy remains controversial. The aim of this meta-analysis was to investigate the impact of general anesthesia compared to sedation on immediate and 3-month neurological outcomes in patients undergoing endovascular thrombectomy.

Methods: PubMed, Scopus, and Embase databases were systematically searched to identify randomized controlled trials (RCTs) comparing general anesthesia with sedation in patients undergoing endovascular thrombectomy. The primary outcomes assessed were immediate and 3-month neurological function as well as the rate of successful recanalization. Additionally, secondary outcomes included pulmonary infection and symptomatic intracerebral hemorrhage.

Results: The analysis included eight randomized controlled trials with a total of 1352 patients (General Anesthesia group,N = 609; Sedation group,N = 743) for endovascular thrombectomy. Pooled data revealed that general anesthesia achieved successful reperfusion in 84.3 %, whereas the sedation group had a rate of 70.7 % (RR = 1.77, 95 % CI 1.33 to 2.35, $P < 0.0001$). Furthermore, Trial Sequential Analysis (TSA) confirmed the significant impact of general anesthesia on achieving successful reperfusion. The meta-analyses found no differences in the rates of favorable cerebral outcome, as evaluated by the National Institutes of Health Stroke Scale (NIHSS) at 24–48 h and the modified Rankin Scale (mRS) at 3 months, between the general anesthesia (GA) and sedation groups. However, The incidence of pulmonary infection was significantly higher in the GA group compared to the sedation group (RR = 1.86, 95 % CI 1.07 to 3.23; $P = 0.03$). The incidence of symptomatic intracranial hemorrhage did not differ between the groups receiving general anesthesia and sedation.

Conclusion: General anesthesia enhances the efficacy of recanalization without no improvement in cerebral function, while concurrently increasing the susceptibility to pulmonary infection among patients undergoing endovascular thrombectomy for acute ischemic stroke.

Non-standard abbreviations and acronyms

Acute Ischemic Stroke	AIS

(*continued on next page*)

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General Anesthesia	GA
modified Rankin Scale	mRS
National Institutes of Health Stroke Scale	NIHSS
Randomized Controlled Trial	RCT
Required information size	RIS
symptomatic intracerebral hemorrhage	sICH
Trial Sequential Analysis	TSA
Thrombolysis in cerebral infarction	TICI

1. Introduction

The presence of large vessel occlusion in acute ischemic stroke can lead to a significant prevalence of disability and mortality. The standard approach for managing patients with acute ischemic stroke involves the utilization of endovascular thrombectomy [1,2]. The correlation between the promptness of treatment and hemodynamic conditions has been demonstrated to be associated with a favorable outcome in patients with acute ischemic stroke [3,4]. The use of anesthetic modalities such as general anesthesia and sedation is widely prevalent in endovascular treatment. However, the impact of the chosen anesthetic modality on cerebral function remains a subject of debate. General anesthesia has been shown to offer advantages in terms of pain control, airway protection and immobilization. However, it should be noted that disadvantages such as hemodynamic fluctuations and intervention delays cannot be ignored [5–11]. The results of numerous investigations indicate that patients who undergo mechanical thrombectomy under general anesthesia experience unfavorable outcomes and increased mortality rates [12,13]. The use of local anesthesia or sedation ensures stable hemodynamics and reduces procedure time, despite the limitations of unprotected airways and potential patient movement [14]. The recent meta-analysis, comprising five randomized controlled trials (RCTs), has revealed that the utilization of general anesthesia is associated with higher rates of successful recanalization and improved functional outcomes compared to sedation [15]. Additionally, two recent multicenter randomized controlled trials (RCTs) have been published comparing the outcomes of patients undergoing general anesthesia versus sedation for mechanical thrombectomy [16,17]. The aim of this updated meta-analysis is to present the most recent and compelling evidence, thereby offering enhanced support for clinical decision-making.

2. Methods

2.1. Literature search and selection criteria

The present systematic review and meta-analysis was conducted and reported in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [18]. The protocol has been registered with the International Prospective Register of Systematic Reviews (PROSPERO identifier CRD42023485739). For further information, please refer to https://www.crd.york.ac.uk/PROSPERO/#myprospero.The literature search was conducted on October 24, 2023 using the keywords "general anesthesia," "sedation," "stroke," or "endovascular thrombectomy" and their respective synonyms through PubMed, Scopus, and Embase to explore the comparison between general anesthesia and sedation in patients undergoing endovascular thrombectomy. The English restriction was enforced. Two independent investigators (SH-J and WW-D) conducted the initial search, screened the titles and abstracts in accordance with the inclusion criteria: (1) Population:patients diagnosed with acute ischemic stroke; (2)Intervention: Endovascular thrombectomy; (3) Comparison:general anesthesia versus sedation; (4) Outcome:successful recanalization, symptomatic intracranial hemorrhage and pulmonary infection; (5) Design: randomized controlled trial.

2.2. Clinical data extraction

The clinical data extraction was conducted by SH-J and independently verified by other authors (WW-D and DD-L). The collected data included the following variables: first author; year of publication; country; number of patients; neurological outcome at 24–48 h post-procedure (evaluated by NIHSS score); favorable functional outcome after 3 months (recorded by modified Rankin Scale); successful recanalization (assessed by modified thrombolysis in cerebral infarction [TICI] grade of 2b or 3). The incidence of pulmonary infection and symptomatic intracerebral hemorrhage (sICH) was documented. The standardized excel file (Microsoft Corporation) was utilized for data arrangement. The disagreements were resolved through consensus or by engaging in discussions with a third author (YL-R).

2.3. Statistical analysis

The meta-analysis was conducted using RevMan (version 5.3, The Cochrane Collaboration, Copenhagen, Denmark). The difference was presented as relative risk (RR) along with a 95 % confidence interval (CI). The heterogeneity of the included studies was assessed utilizing the I^2 statistic. Revised Cochrane risk-of-bias tool for randomized trials was utilized by two independent authors (DD-L and SH-J) to assess the risk of bias in each study across five domains: randomization process, deviations from intended interventions, outcome measurement, missing outcome data, and selection of reported results. If I^2 exceeds 50 %, it indicates substantial

heterogeneity and necessitates the implementation of a random effects model [19]. Our analysis did not assess publication bias due to the inclusion of only eight studies. Meanwhile, The Trial Sequential Analysis (TSA) was performed using the TSA viewer version (0.9.5.10 beta, Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, available from http://www.ctu.dk/tsa)to evaluate the robustness of the primary outcomes against potential false-positive results arising from multiple testing. The necessary information size (NIS), trial sequential monitoring boundaries, cumulative Z curve, and TSA boundary were examined. For dichotomous outcomes, the NIS was determined based on type I error, power, and a relative risk reduction of 5 %, 80 %, and 10 % respectively. All statistical tests were two-tailed with a significance level set at $p < 0.05$.

3. Results

3.1. Study selection and characteristics of included studies

The screening process involved two investigators (SH-J and YL-R), who reviewed a total of 461 studies. Ultimately, eight randomized controlled trials (RCTs) were selected for inclusion in the systematic review and meta-analysis [16,17,20–25]. See Fig. 1 for study selection flow chart. The details of the included studies with primary and secondary outcomes are shown in Table 1. The risks of bias of individual studies are summarized in Fig. 2.

3.2. Primary outcomes

The forest plots found no difference in NIHSS scores within the first 24–48 h between the general anesthesia (GA) group and the sedation group (RR = −0.71, 95 % CI: 2.15 to 0.73, P = 0.33, $I^2 = 8$ %). (Fig. 3). Our analysis also found no difference in the functional outcome between the general anesthesia (GA) and sedation groups (RR = -0.05, 95 % CI: 0.26 to 0.16, $P = 0.64$, $I^2 = 0$ %) (Fig. 4).

The forest plots demonstrated a significantly higher rate of recanalization with general anesthesia compared to the sedation group

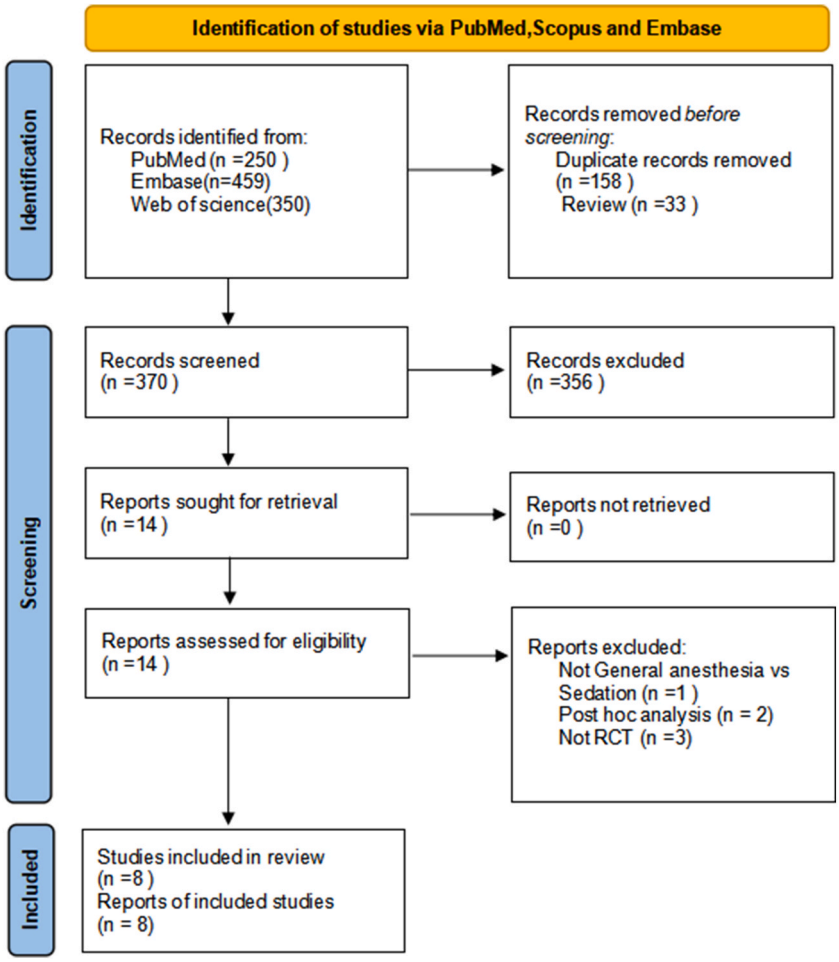

Fig. 1. Flow diagram for systematic review in our study.

Table 1
The characteristics of included studies.

Study/Year of publication	country	No.Patients (GA/Sedation)	Study Design	Comparison	outcomes
Silvia Schönenberger/2016 [20]	Germany	73/77	RCT	GA vs Sedation	NIHSS score, mRS after 3 months
Pia Löwhagen Hendén /2017 [21]	Sweden	45/45	RCT	GA vs Sedation	mRS score
Claus Z. Simonsen /2018 [22]	Denmark	65/63	RCT	GA vs Sedation	NIHSS score
Jian Sun /2020 [23]	China	20/20	RCT	GA vs Sedation	NIHSS score
Fa Liang /2022 [16]	China	43/44	RCT	GA vs Sedation	mRS after 3 months
Chun guang Ren /2020 [24]	China	42/48	RCT	GA vs Sedation	mRS after 3 months
R. Chabanne/2023 [25]	France	147/269	RCT	GA VS NO GA	mRS after 3 months
Axelle Maurice /2022 [17]	France	174/177	RCT	GA vs Sedation	mRS after 3 months

GA:General Anesthesia; RCT:Randomized Controlled Trial; mRS:modified Rankin Scale; NIHSS:National Institutes of Health Stroke Scale.

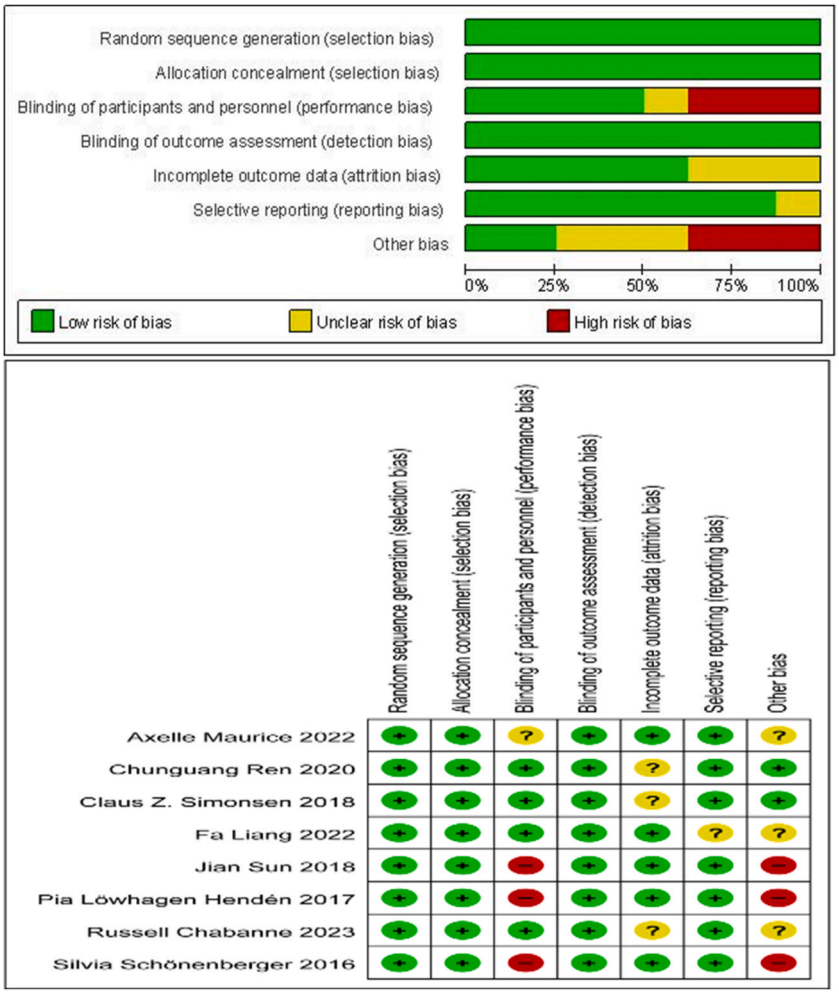

Fig. 2. Summary of the risk of bias of the included studies. Green: low risk of bias; yellow: moderate risk of bias; red: high risk of bias. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

(RR = 1.95, 95 % CI: 1.43 to 2.65, $P < 0.0001$, $I^2 = 0$). (Fig. 5A). Sensitivity analyses were not performed due to a low heterogeneity. Moreover, the crossing of the cumulative Z-curve over RIS on TSA provided substantial evidence to support a robust conclusion for this outcome. (Fig. 5B).

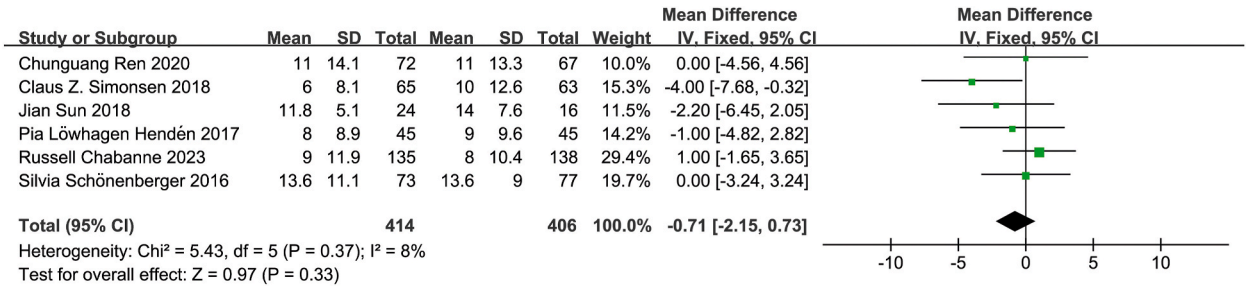

Fig. 3. NIHSS score at 24–48 h between GA group and sedation group.

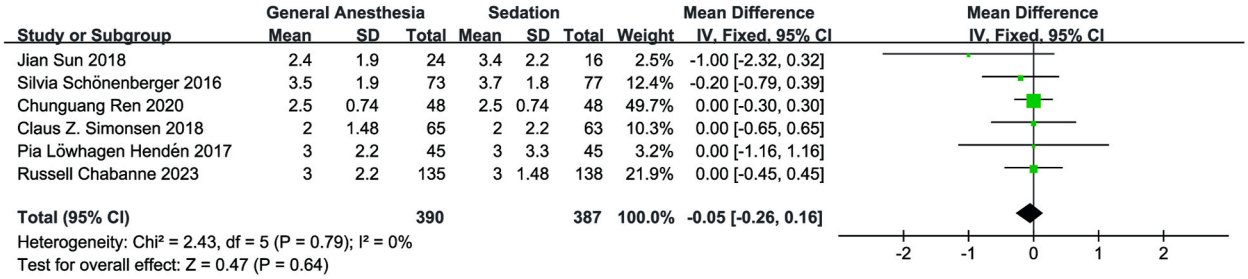

Fig. 4. Modified Rankin scale after 3 month between GA and sedation group.

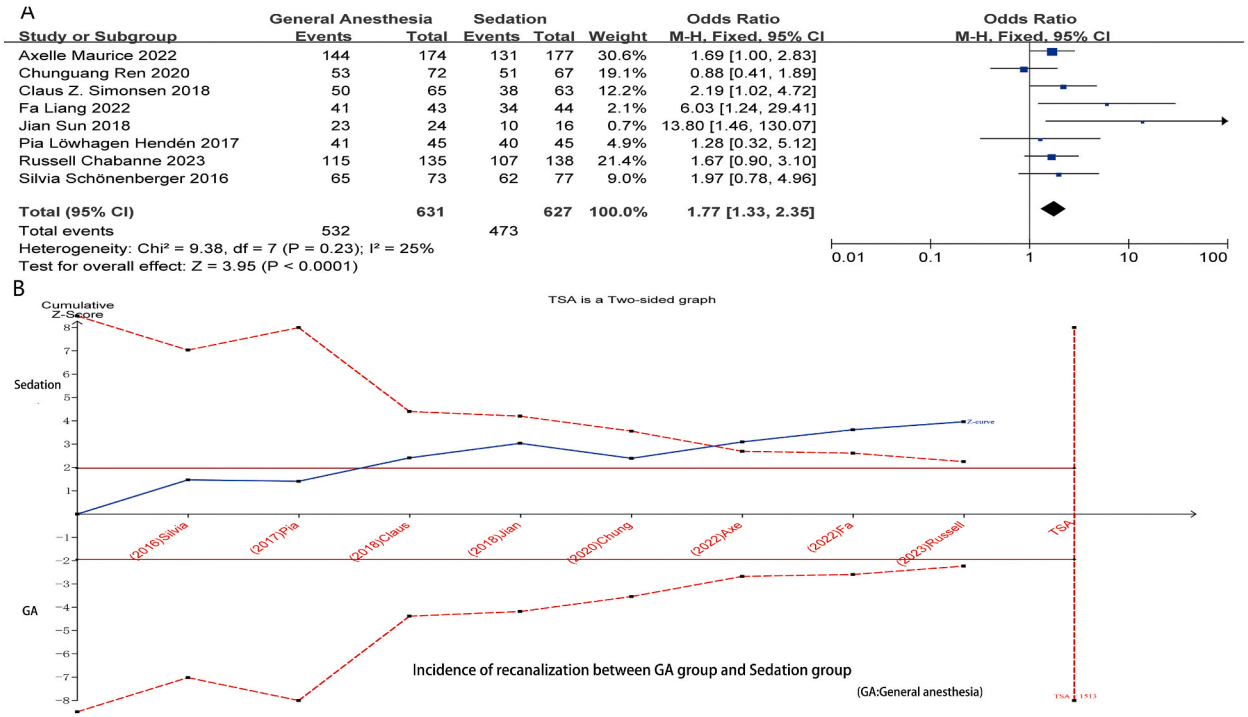

Fig. 5. Incidence of recanalization between GA group and sedation group.

3.3. Related complications

Forest plots demonstrated the rate of pulmonary infection was significantly increased in GA group, in contrast with sedation group (RR = 2.22, 95 % CI: 1.33 to 3.70 $P = 0.002$, $I^2 = 12$ %) (Fig. 6A); The incidence of symptomatic intracerebral hemorrhage was comparable between the GA and sedation groups (RR = 0.88, 95 % CI: 0.57 to 1.35 $P = 0.55$, $I^2 = 0$) (Fig. 6B).

4. Discussion

The present systematic review and meta-analysis, including 8 randomized controlled trials (RCTs), for endovascular thrombectomy in acute ischemic stroke patients, demonstrates that there is no immediate or 3-month neurological outcome advantage associated with general anesthesia compared to the sedation group. Interestingly, it is noteworthy that general anesthesia significantly enhances the rate of successful recanalization during the procedure. However, the risk of pulmonary infection is increased.

The results of numerous retrospective studies have consistently demonstrated a poorer neurological outcome following GA in comparison to sedation, even when accounting for potential selection bias [12,13,26]. However, a study conducted by Axelle Maurice and colleagues has demonstrated that the functional outcomes at 3 months following endovascular treatment were comparable between general anesthesia and sedation [17]. The recent literature indicates that general anesthesia yields comparable rates of functional independence and major complications in patients undergoing mechanical thrombectomy for acute ischemic stroke in the anterior circulation, when compared to procedural sedation [25]. The findings of our meta-analysis are consistent with previous literature, but contradict studies suggesting that patients undergoing general anesthesia experience a decrease in neurological recovery and an increase in morbidity and mortality compared to those receiving conscious sedation [6,14]. Previous study suggested that the administration of general anesthesia was correlated with a decreased reperfusion rate and inferior functional outcome [14]. Our meta-analysis found that the increased rate of recanalization under general anesthesia compared to sedation. Moreover, we have substantiated this conclusion for the first time through TSA analysis. The enhanced rates of recanalization logically correspond to improved neurological recovery. However, our study did not observe any changes in neurological outcomes between the two groups. These contradictory findings may be attributed to the specific characteristics of general anesthesia, such as hypotension, hyperventilation, and impairment of cerebral regulation that can compromise collateral perfusion in the penumbra region. Additionally, it is worth noting that general anesthesia was found to potentially delay procedure start times which could impact treatment outcomes related to recanalization. [12,13,20,27].

Our findings indicate a higher prevalence of pulmonary infection in the GA group, which aligns with previous studies [28]. The provision of adequate airway protection in patients with acute ischemic stroke may result in prolonged invasive ventilation, thereby contributing to this phenomenon. Furthermore, The likelihood of receiving general anesthesia was higher among patients with more severe illness, thereby increasing their vulnerability to pulmonary infection.

Our meta-analysis had several limitations. Firstly, the sample size of eight RCTs was insufficient to draw a robust conclusion. Additionally, the variation in sedation depth among the included studies contributed to potential heterogeneity that could impact the

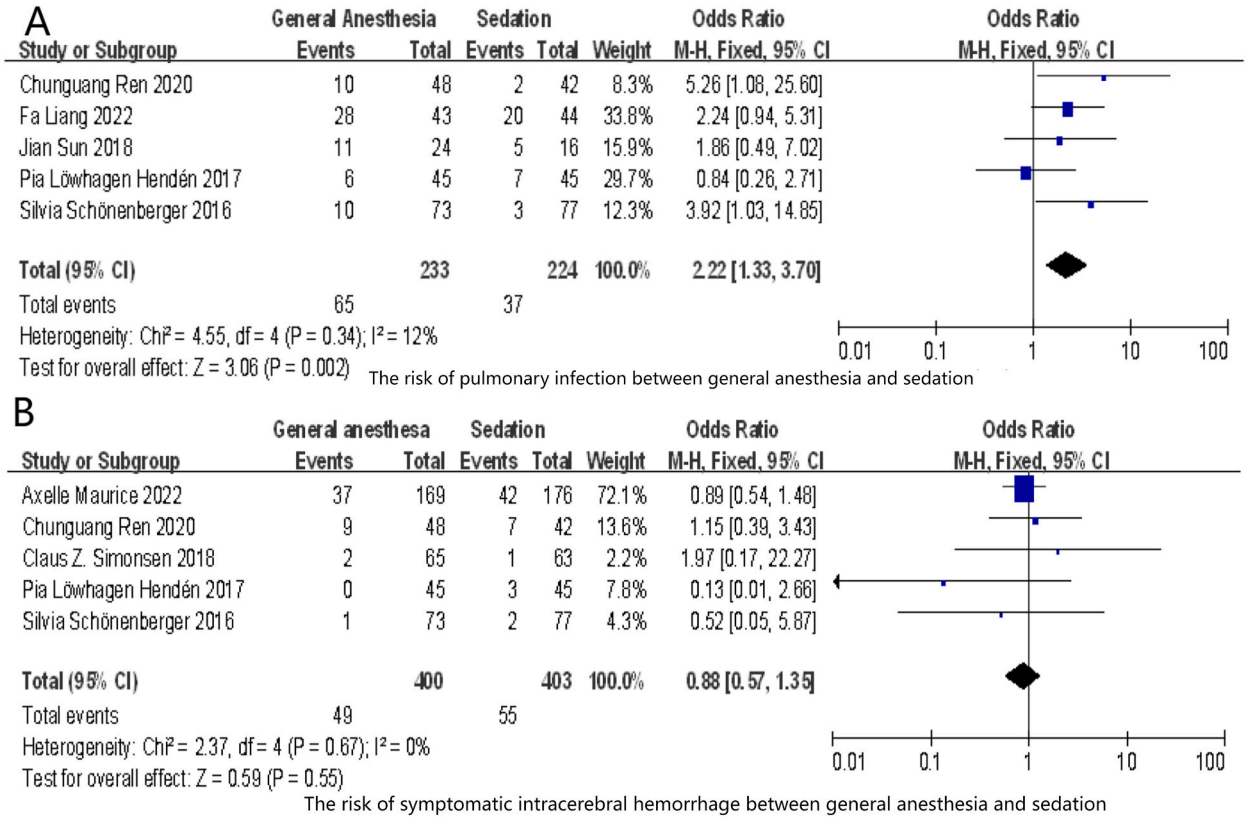

Fig. 6. The risk of pulmonary infection(A) and symptomatic intracerebral hemorrhage (B) between GA and sedation group.

results. Moreover, the utilization of different anesthetic agents may produce bias into our findings. Lastly, there is a possibility of selection bias as patients with severe illness who underwent endotracheal intubation are commonly treated with general anesthesia.

5. Conclusion

During endovascular thrombectomy, general anesthesia was associated with a higher rate of successful recanalization in patients and no improvement in cerebral function. However, it also increased the risk of pulmonary infection. Therefore, further comprehensive investigation is needed to determine whether the benefits of general anesthesia or sedation outweigh their risks.

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None.

CRediT authorship contribution statement

Jin Shenhui: Writing – original draft, Formal analysis, Conceptualization. **Du Wenwen:** Data curation, Conceptualization. **Liang Dongdong:** Supervision, Methodology, Data curation. **Ren Yelong:** Writing – review & editing, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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