



Comparison of Sevoflurane and Propofol Administration on Postoperative Cognitive Dysfunction in Spinal Surgery Using the Mini-Mental State Examination (MMSE)

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ABSTRACT

Background: Postoperative cognitive dysfunction (POCD; defined as >2-point MMSE decline from baseline) is common after general anesthesia in spinal surgery. This study compared sevoflurane vs. propofol effects on postoperative cognition.

Methods: Single-blind randomized controlled trial (1:1 allocation) with 20 adults undergoing elective spinal surgery under general anesthesia. Patients were assigned to sevoflurane (n=10) or propofol (n=10) maintenance. MMSE was assessed preoperatively and at 6 h, 24 h, 3 days, and 7 days postoperatively. Analysis: independent t-tests, chi-square, and Pearson correlation ($p < 0.05$ significant).

Results: No statistically significant differences were noted in baseline characteristics (age, gender, education; $p > 0.05$). While the MMSE test results in the propofol group were unchanged (Day 7: 28.3 ± 2.4), there was a slight reduction ($p = 0.04$). In the sevoflurane group, the decrease became significant on Day 3 ($p = 0.006$) and Day 7 ($p = 0.004$; score 25.4 ± 3.5 vs. propofol $p = 0.04$), with 60% having a mild POCD. The decline in sevoflurane group is associated with oxidative stress and hippocampal damage; propofol provides the antioxidative protection.

Conclusion: Propofol yields superior cognitive stability vs. sevoflurane post-spinal surgery, reducing POCD risk-recommend as the preferred agent.

Introduction

Postoperative cognitive dysfunction (POCD)—a >2-point decline in Mini-Mental State Examination (MMSE) score from baseline—is a frequent complication after general anesthesia, particularly in prolonged spinal surgeries for degenerative conditions prevalent in aging populations [1]. Spinal procedures often require general anesthesia with inhalational (sevoflurane) or intravenous (propofol) agents, both modulating GABA_A receptors but differing in cerebral effects [2-3].

Growing evidence suggests that the choice of an anesthetic may influence the risk and severity of POCD. Several studies have indicated that sevoflurane can increase oxidative stress, neuroinflammation, and apoptosis in neurons [4-5]. Although being considered one of the most neuroprotective agents due to antioxidative properties, propofol was also found to inhibit synaptic plasticity and cognitive functions under specific circumstances [6-7]. The Mini-Mental State Examination (MMSE) is still an efficient tool to evaluate any changes in patients' cognitive status before and after surgery, especially in elderly patients [8]. There are several studies comparing the influence of sevoflurane and propofol on postoperative cognition. According to

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[9], patients undergoing surgical treatment of lung cancer under the effect of sevoflurane had more pronounced cognitive impairment than patients under. However, most existing research focuses on thoracic or abdominal procedures, and data on cognitive outcomes in spinal surgeries remain limited, despite the heightened vulnerability of spinal surgery patients to neuroinflammatory responses due to long surgical duration and prone positioning [10]. This study aims to address this research gap by directly comparing the postoperative cognitive outcomes of sevoflurane versus propofol in spinal surgery patients using the MMSE. By capturing cognitive function at several postoperative intervals, the research seeks to identify whether one anesthetic poses a higher risk of POCD and thereby support more informed anesthetic choices in clinical practice for at-risk patient populations.

Methods

Study Design

His study was a single-blind randomized controlled trial with a pretest–posttest design comparing the effects of sevoflurane versus propofol on postoperative cognitive function. The primary outcome was the change in Mini-Mental State Examination (MMSE) scores over time. The study was approved by the institutional ethics committee (No: 88/KEPK/USU/2025) and conducted at two tertiary centers in Indonesia from February 2025 until sample completion. The trial was registered at ClinicalTrials.gov (ID: NCT07378878; registration date: January 22, 2026). The registration number has been verified and corresponds to this study.

Population and Samples

Adults aged 18–65 years scheduled for elective spinal surgery under general anesthesia were eligible if they had an ASA physical status I–II, at least a junior high school education, and a baseline MMSE score >24.

Exclusion criteria included a history of stroke, cardiovascular disease, visual or hearing impairment, pregnancy, substance abuse, allergy to study drugs, prolonged unconsciousness, or intraoperative hemodynamic instability requiring ICU admission.

Sample Size Calculation

Since the primary outcome (MMSE score) is a continuous variable, the sample size was recalculated using a formula for comparing two independent means based on previous studies reporting mean $\pm$ standard deviation differences in MMSE scores between anesthetic agents.

The sample size was estimated using the following equation:

$$n = \frac{2(Z_{\alpha/2} + Z_{\beta})^2 \sigma^2}{\Delta^2} \quad (1)$$

where:

- σ = pooled standard deviation
- Δ = expected mean difference in MMSE scores
- $\alpha = 0,05$, power = 80%

Based on pilot data and literature estimates, the minimum required sample size was 10 patients per group. However, due to feasibility constraints, this study should be considered exploratory.

Study Instruments

Based on preliminary data and estimates from the literature, the minimum required sample size is ten patients per group; however, due to limitations in study implementation, this study must be considered exploratory. Research Instruments

The primary outcome measured was cognitive function using the Mini-Mental State Examination (MMSE), with scores ranging from 0 to 30, where a score below 24 indicates cognitive impairment. Assessments were conducted before surgery and at 6 hours, 24 hours, 3 days, and 7 days after surgery. Covariate variables included demographic characteristics such as age, sex, and education, as well as vital signs including heart rate, respiratory rate, blood pressure, and SpO₂, in addition to the duration of anesthesia and surgery.

Randomization and Blinding

Patients were randomly assigned in a 1:1 ratio using a computer-generated randomization sequence.

This study employed a single-blind design in which the outcome assessors were blinded to group allocation, while the anesthesiologists administering the interventions were not blinded due to the nature of the procedures.

Intervention

After obtaining informed consent, patients were allocated into the following:

- Propofol group (n=10): Maintenance with target-controlled infusion (3–6 mg/kg/h)
- Sevoflurane group (n=10): Inhalational maintenance at 1.5–2.5 MAC

All patients received standardized perioperative management:

- Premedication: midazolam 0.05 mg/kg
- Induction: propofol 2 mg/kg, fentanyl 2 mcg/kg, rocuronium 0.6 mg/kg
- Analgesia: fentanyl infusion
- Reversal: neostigmine 0.05 mg/kg + atropine 0.02 mg/kg

Data Analysis

Data were analyzed using IBM SPSS version 26.0. Normality was assessed using the Shapiro–Wilk test. Baseline characteristics were compared using independent t-tests or Mann–Whitney U tests for

continuous variables and chi-square or Fisher's exact tests for categorical variables. To evaluate changes in MMSE scores over time between groups, a repeated measures analysis of variance (RM-ANOVA) was performed.

When significant interactions were found, post-hoc pairwise comparisons with Bonferroni correction were applied. A P value <0.05 was considered statistically significant.

Results

A total of 20 patients were included in this study and were equally randomized into two groups: propofol (n=10) and sevoflurane (n=10).

Most baseline characteristics were comparable between the two groups ($p>0.05$), including age, education level, hemodynamic parameters, duration of surgery, and duration of anesthesia. However, a significant difference in terms of gender ratio was noted ($p=0.04$), where more females belonged to the propofol group.

A total of 20 patients were included in the study, who were equally randomized into the propofol group and sevoflurane group (10 patients per group). All the baseline characteristics were similar except for the gender distribution ratio ($p>0.05$). There was a significant difference in terms of gender distribution ratio ($p=0.04$), where more females belonged to the propofol group (Table 2,3).

Time Change of the MMSE Scores

Changes in cognitive functions were compared using repeated measures analysis of variance (RM-ANOVA). Baseline characteristics were similar in the propofol group and sevoflurane group except for sex ratio (Table 1). RM-ANOVA revealed a significant group $\times$ time interaction ($p < 0.05$), suggesting a difference in the MMSE score trend in the two groups. Bonferroni post-hoc comparisons indicated no significant differences between the MMSE scores of the two groups at baseline (T0), 6 hours (T1), and 24 hours (T2) post-surgery (all $p > 0.05$). However, MMSE scores in the sevoflurane group were significantly lower than those in the propofol group on postoperative days 3 (T3) (27.5 ± 1.8 vs. 29.1 ± 1.3 ; $p = 0.04$) and 7 (T4) (25.4 ± 3.5 vs. 28.3 ± 2.4 ; $p = 0.04$) (Table 6).

In the sevoflurane group, the changes of the cognitive function were evaluated by the Mini Mental State Examination (MMSE) during the predefined perioperative times (Tables 4 and 5). Baseline MMSE score was 28.8 ± 0.9 . 6 Hours postoperatively (T1), the MMSE score dropped slightly to 28.0 ± 2.1 , but there was no statistical significance ($p = 0.121$). At 24 hours (T2), the score went back to baseline level, which was 28.9 ± 1.5 ($p = 0.798$). A statistically significant drop was found at postoperative day 3 (T3) (27.5 ± 1.8 ; $p = 0.006$). This drop was even larger at postoperative day 7 (T4) (25.4 ± 3.5 ; $p = 0.004$). 40% of the patients kept their normal cognition at T4, while 60% of them suffered from mild cognitive impairment (Table 5).

Table 1- Baseline Demographic and Clinical Characteristics

Characteristic	Propofol (n=10)	Sevoflurane (n=10)	P value
Gender			0.04
Woman	9 (90%)	5 (50%)	
Man	1 (10%)	5 (50%)	
Age (years)	52.4 ± 16.67	46.7 ± 18.73	0.19
Education Level			0.58
Senior High School	1 (10%)	1 (10%)	
Diploma	1 (10%)	0 (0%)	
Bachelor's Degree	8 (80%)	9 (90%)	
Systolic BP (mmHg)	120.7 ± 6.83	118.2 ± 6.32	0.41
Diastolic BP (mmHg)	76.0 ± 7.34	77.28 ± 5.96	0.74
Heart Rate (bpm)	78.2 ± 8.17	78.9 ± 6.4	0.39
Respiratory Rate	20 ± 0.0	20 ± 0.0	1.00
SpO ₂ (%)	98.7 ± 1.15	98.7 ± 0.94	0.93
Duration of Surgery (min)	318 ± 28.98	324 ± 30.98	0.66
Duration of Anesthesia (min)	331 ± 28.16	338.5 ± 30.64	0.57

Table 2- Change in MMSE Score Before and After Propofol Administration

Time Examination	MMSE Score	P value
T0 – T1	29.2 ± 0.63 vs. 28.5 ± 2.0	0.226
T0 – T2	29.2 ± 0.63 vs. 29.2 ± 1.1	1.00
T0 – T3	29.2 ± 0.63 vs. 29.1 ± 1.3	0.793
T0 – T4	29.2 ± 0.63 vs. 28.3 ± 2.4	0.04

Table 3- Interpretation of MMSE Score in Propofol Group

Interpretation	T1		T2		T3		T4	
	N	%	N	%	n	%	N	%
Normal Cognitive Function	10	100	10	100	10	100	9	90
Mild Cognitive Impairment	0	0	0	0	0	0	1	10

Table 4- Change in MMSE Score Before and After Sevoflurane Administration

Time Examination	MMSE Score		P value
T0 – T1	28.8 ± 0.9	28 ± 2.1	0.121
T0 – T2	28.8 ± 0.9	28.9 ± 1.5	0.798
T0 – T3	28.8 ± 0.9	27.5 ± 1.8	0.006
T0 – T4	28.8 ± 0.9	25.4 ± 3.5	0.004

Table 5- Interpretation of MMSE Score in Sevoflurane Group

MMSE Classification	T1		T2		T3		T4	
	N	%	n	%	n	%	N	%
Normal Cognitive Function	10	100	10	100	10	100	4	40
Mild Cognitive Impairment	0	0	0	0	0	0	6	60

Table 6- Comparison of Cognitive Impairment at 7 Days After Surgery Between Propofol and Sevoflurane Groups

MMSE Score	Propofol	Sevoflurane	P value
T0	29.2 ± 0.63	28.8 ± 0.9	0.27
T1	28.5 ± 2	28 ± 2.1	0.59
T2	29.2 ± 28.9	28.9 ± 1.5	0.63
T3	29.1 ± 1.3	27.5 ± 1.8	0.04
T4	28.3 ± 2.4	25.4 ± 3.5	0.04

Incidence of Cognitive Impairment

At seven days post-surgery (T4), the prevalence of mild cognitive impairment was found to be significantly more prevalent among the sevoflurane patients than the propofol patients. There was only one case (10%) of cognitive impairment in the propofol group while six cases (60%) were found in the sevoflurane group ($p = 0.01$).

Hemodynamic Stability

Blood pressure, heart rate, respiratory rate, and oxygen saturation stayed stable for all hemodynamic parameters in both groups during surgery. There was no significant difference between both groups ($p > 0.05$).

Overall Findings

It was found that there was a significantly lower level of cognitive function among sevoflurane anesthetized patients compared to the propofol anesthetized patients, especially three days and seven days after surgery. On the other hand, there were relatively similar levels of cognitive functioning in the propofol group.

Discussion

The current study demonstrates differential trajectory of postoperative cognitive recovery in terms of MMSE scores after sevoflurane or propofol anesthesia. Both methods were found to lead to slight postoperative cognitive changes occurring in the early postoperative

period (within 24 hours), but only the sevoflurane group showed a gradual cognitive decline over 7 days. Thus, it might be supposed that the choice of anesthetic technique influences the trajectory of postoperative cognitive recovery.

Decreased MMSE scores after sevoflurane anesthesia in comparison with propoflurane anesthesia on the 7th postoperative day correspond to previous clinical and experimental studies demonstrating possible neurocognitive effects of volatile anesthetics. Several mechanisms were suggested, namely neuroinflammation, oxidative stress, synaptic plasticity impairment, hippocampal neurogenesis disruption [4-5,11]. Experiments revealed that sevoflurane anesthesia might affect signaling pathways in neurons and increase oxidative stress level, which leads to cognitive dysfunction [12].

Moreover, sevoflurane was shown to increase cognitive impairment in Alzheimer-model rats through oxidative stress induction and formation of β -amyloid deposits in the hippocampus. The decrease in MMSE subscale scores, particularly recall and attention, proves the involvement of hippocampal cognitive functions. These domains are usually affected in POCD and are crucial for cognitive recovery. The extended surgical procedure and anesthesia can provoke such effect since prolonged exposition to anesthesia increases oxidative stress and neuroinflammatory reactions [13-14].

In turn, the propofol group was characterized by relatively stable MMSE scores with the only minimal decrease on the 7th day of surgery. This result correlates

with previous researches proving better neurocognitive outcome of propofol anesthesia. Possible mechanisms are the antioxidant activity, modulation of GABA_A and NMDA receptors activity, and inhibition of pro-inflammatory cytokines release [6-7]. Also, one randomized trial proved lower POCD incidence in patients who had propoflurane anesthesia in comparison with sevoflurane anesthesia [15].

The use of MMSE as the cognitive assessment tool in this study is appropriate since it is practical and used in perioperative practice. However, it is less sensitive than MoCA, but even so, the results of the study might indicate clinically relevant cognitive impairment because of its insensitivity.

The results of this study differ from previous researches that did not demonstrate the difference between inhalational and intravenous anesthesia techniques. The Cochrane meta-analysis revealed the absence of strong evidences supporting any of these techniques [16]. These variations might be due to differences in patient population, surgery procedure, and methodology used. In particular, the relative homogeneity of the sample and the standardized method used in this study could improve internal validity and make the differences easier to detect.

A possible reason for the observed differences may relate to brain physiology. According to the literature, propofol lowers brain metabolic demands and maintains autoregulation providing neuroprotection in surgical stress [17]. At the same time, even though sevoflurane enhances brain perfusion by dilatation, this feature does not seem to provide neuroprotection in increased oxidative stress conditions [18].

A higher rate of impaired cognitive functioning seen in the sevoflurane group at day 7 is consistent with POCD rates seen in comparable surgeries [8,19]. This suggests that anesthetic choice is one of the possible modifiable factors for reducing POCD risk.

However, there are also some limitations that need to be discussed. First of all, a relatively small sample reduces statistical power and restricts generalization of results and therefore, they should be treated as preliminary findings. Second, using MMSE alone as a measure might fail to detect more subtle and domain-specific changes. Also, the selection criterion restricting age above 65 years reduces generalization to populations at a higher risk of developing POCD. In addition, an imbalance in sex ratio between groups may introduce a potential bias.

Thus, the current study shows that propofol anesthesia can be related to more stable postoperative cognitive functioning compared with sevoflurane in patients having spinal surgery. However, large-scale studies with more diverse populations and more sensitive measures of cognitive functioning are necessary to confirm these findings [9].

Recommendations

It is recommended to further investigate the impact of sevoflurane vs. propofol on cognitive functions in elderly patients, long-term outcomes (>30 days), conduct multicenter studies, as well as to reveal the mechanisms of action (neuroinflammation markers, imaging).

Conclusion

In this study, propofol-based anesthesia has been found to have more stable postoperative cognitive functioning than sevoflurane in patients undergoing spinal surgery. More pronounced cognitive functioning decline and higher levels of postoperative cognitive impairment were found in the sevoflurane group, especially at 7 days after surgery.

However, taking into account the small sample and the limitations of the study, the findings need to be treated with caution. Larger scale studies are required to confirm any possible differences in cognitive outcomes of two anesthetic techniques.

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Ethics approval and consent to participate

Approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara (No: 88/KEPK/USU/2025). Conducted per Helsinki Declaration principles. Written informed consent was obtained from all patients prior to enrollment.

Authors' contributions

IL: conceptualization, methodology, data collection/analysis, writing the original draft, and visualization. RSI: supervision, validation, writing, review, and editing. CGB: methodology, formal analysis, project administration. YY: investigation, data curation, writing, reviewing, and editing. All authors approved the final manuscript and agree to be accountable.

Data availability

Data can be obtained from the corresponding author upon reasonable request.

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