

Sevoflurane–Dexmedetomidine versus Propofol-based TIVA for Controlled Hypotension in Functional Endoscopic Sinus Surgery: Effects on Postoperative Cognitive Dysfunction

Faishal Arif Fathurrahman¹, Maulydia^{2,3}, Prananda Surya Airlangga^{2,3}, Christrijogo Sumartono Waloejo^{2,3}, and Agustina Salinding^{2,3}

¹Study Program of Anesthesiology and Intensive Care, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

²Department of Anesthesiology and Reanimation, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

³Department of Anesthesiology and Reanimation, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

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ABSTRACT

Background: Functional Endoscopic Sinus Surgery (FESS) often requires controlled hypotension to improve surgical visualization, which may increase the risk of postoperative cognitive dysfunction (POCD). Anesthetic agents differ in their neuroinflammatory and neuroprotective effects, potentially influencing POCD risk.

Objective: This study aim to compare the incidence of POCD between Sevoflurane–Dexmedetomidine (DEX-S) anesthesia and Propofol-based total intravenous anesthesia (PRO) in FESS patients undergoing controlled hypotension.

Methods: A prospective study was conducted on 32 adults (18–65 years) undergoing elective FESS. Patients were assigned to DEX-S or PRO groups. Cognitive function was assessed using the Mini-Mental State Examination (MMSE) preoperatively and at 24 and 72 hours after surgery. Perioperative hemodynamics, anesthesia duration, and blood loss were recorded. Statistical comparisons were made to evaluate cognitive outcomes and determine factors associated with POCD.

Results: Both groups demonstrated a significant MMSE decline at 24 hours, followed by recovery at 72 hours. The DEX-S group showed a greater early decline than the PRO group ($p < 0.05$), but the overall incidence of POCD remained low and did not differ significantly between groups at either postoperative interval ($p > 0.05$). Higher age and lower educational level were identified as stronger predictors of POCD than anesthetic technique or intraoperative parameters.

Conclusion: Sevoflurane–Dexmedetomidine and Propofol-based TIVA yield comparable effects on early postoperative cognitive function in FESS under controlled hypotension. Although DEX-S produced a greater transient cognitive decline, it did not increase POCD incidence. Patient characteristics—particularly age and education—play a more significant role in POCD development.

Keywords: Postoperative Cognitive Dysfunction (POCD), Sevoflurane, Dexmedetomidine, Propofol, Functional Endoscopic Sinus Surgery (FESS).

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INTRODUCTION

Functional Endoscopic Sinus Surgery (FESS) is one of the minimally invasive procedures in ENT to treat patients with chronic sinusitis. One of the main problems during FESS came from the excessive intraoperative bleeding, which in turn will obscure the view and may increase the risk of surrounding tissue damage.¹ Over time, clinicians developed a technique to overcome this issue called controlled hypotension by deliberately keeping the MAP between 50-65 mmHg to minimize blood loss and intraoperative bleeding, which will improve visibility of the surgical field and shorten operation time.^{2,3} There are two anesthetic methods commonly used to induce controlled hypotension, through inhalation anesthesia and total intravenous anesthesia (TIVA). The drug of choice for inhalation anesthesia in controlled hypotension is Sevoflurane and Desflurane, due to their small artery

dilatation effect. However, some studies show Desflurane to be less effective because it may increase heart rate and consequently MAP.⁴ Meanwhile, in TIVA, the drug of choice is usually Propofol since it gives stable hemodynamic control, suppressing sympathetic response and decreasing cardiac output, the best surgical field views.⁵ Though proven to provide benefits for surgery, controlled hypotension also comes with an increased risk of insufficient blood flow to the brain that may cause brain damage manifested as Postoperative Cognitive Dysfunction or POCD.⁶ POCD is characterized by impairments in memory, attention, orientation, and executive function, which may persist in both the short and long term.⁷ The global study shows that POCD incidence in the first week after non-cardiac operation is around 25.8-41.4%, and around 12-17% cases persist as long as 3 months post op with a 2 times increased risk in elderly patients, specifically

over 60 years old.^{8,9} In Indonesia, a study shows a 5.6–8.3% decreased in elderly patient's cognitive score evaluated using the MMSE and MoCA-Ina tests on 3 days post operation.¹⁰ In Dr. Soetomo General Hospital, 52% of all elective operation patients were found to experience POCD, and around 9.7% patients who underwent ENT surgery with controlled hypotension showed a significant decrease in MMSE score 2 hours post operation.^{11,12} Several factors were found to be contributing to the incidence of POCD, such as older age, lower education level, post operation pain level, type of anesthesia, as well as anesthesia and operation duration.^{13,14} A study shows individuals given anesthetic induction using Sevoflurane to have a higher concentration of S-100 β protein, TNF- α , IL-6 and increased Blood Brain Barrier (BBB) permeability, which contributed to POCD incidence in elderly patients.^{15,16} Another study on rats proved how Sevoflurane may induce inflammation and apoptosis to hippocampus neuron which disturbs the balance between neuroinflammation and neuron function.¹⁷ Dexmedetomidine as an adjuvant to Sevoflurane was found to reduce the incidence of POCD by attenuating the neurotoxic effect of Sevoflurane through decreasing plasma levels of IL-6 and TNF- α .¹⁸ On the other hand, Propofol based TIVA has already proven to have a better neuroprotective effect than Sevoflurane through suppressing microglia activation and reducing inflammation in the central nervous system.⁷ These findings raise the question of whether a Sevoflurane–Dexmedetomidine anesthetic combination is more effective than Propofol-based TIVA in preventing POCD among patients undergoing FESS under controlled hypotension, an issue this study aims to address.

MATERIAL AND METHODS

This prospective analytical experimental study was conducted at a tertiary referral center, Dr. Soetomo General Hospital, Surabaya, East Java, Indonesia, between September and November 2025. Ethical approval was obtained from the hospital's Ethics Committee (No. 1391/KEPK/VIII/2025).

A total of 32 patients scheduled for elective FESS with controlled hypotension participated in this study. Written informed consent was obtained from all patients who underwent elective FESS with controlled hypotension techniques age 18–65 years old, American Society of Anesthesiologists (ASA) physical status classes I to II and able to independently take cognitive tests before and after surgery that were included in this study. All participants are made aware of their rights and ability to withdraw consent and discontinue participation at any time. The exclusion criteria of this study were patients with history of neuropsychiatry illness affecting cognitive function (e.g. stroke, dementia, epilepsy, severe depression), allergy to dust, food or drugs including Dexmedetomidine or Propofol, cardiovascular disease (e.g. uncontrolled hypertension, heart failure), head trauma on the last 6 months, psychotropic drugs usage in the last 7 days, and severe kidney or liver dysfunction (total bilirubin > 3 mg/dl, GFR < 30 ml/min/1.73 m²). Patients showing severe

intraoperative complications (e.g. cardiac arrest, stroke, anaphylactic reaction), the needs to convert to other anesthetic methods and conditions hindering the ability to take the cognitive function test postoperatively, such as prolonged delirium or the use of a ventilator for more than 24 hours, were immediately dropped out of the study.

One day pre-operative, all 32 patients of this study underwent a cognitive function test using the Mini-Mental State Exam (MMSE). During surgery, both the DEX-S and PRO groups were monitored using identical standard modalities, including electrocardiography (ECG), peripheral pulse oximetry with an oxygen saturation target of $\geq 95\%$, non-invasive blood pressure (NIBP) monitoring with a mean arterial pressure (MAP) target of 60–65 mmHg, capnography with an end-tidal CO₂ (EtCO₂) target of 35–45 mmHg, Bispectral Index (BIS) maintained between 40 and 60, and body temperature maintained at 36–37°C. All patients received the same induction protocol consisting of fentanyl 2 mcg/kg, atracurium 0.5 mg/kg, and propofol 2 mg/kg. During the maintenance phase of anesthesia, patients were allocated into two groups. The first group (DEX-S) received inhaled sevoflurane at 0.8–1 minimum alveolar concentration (MAC) and a loading dose of dexmedetomidine at 1 mcg/kg/h for 10 minutes, followed by a maintenance infusion of 0.4 mcg/kg/h. The second group (PRO) received intravenous propofol at a rate of 50–200 mcg/kg/min. Both groups also received fentanyl at 20 mcg/h and atracurium at 5 mcg/kg/min for maintenance. Hemodynamic parameters were evaluated every 30 minutes. If controlled hypotension was not achieved, nicardipine was administered at 0.5 mcg/kg/min. In cases where the mean arterial pressure (MAP) decreased below 60 mmHg, norepinephrine 0.0125 mg was administered intravenously. If the heart rate decreased below 50 beats per minute, atropine sulfate 0.5 mg was administered intravenously. At the end of surgery, in the DEX-S group, the sevoflurane concentration was reduced to 1 vol% and the dexmedetomidine infusion was discontinued, whereas in the PRO group, the propofol infusion rate was reduced to 25 mcg/kg/min. In both groups, atracurium and fentanyl were discontinued. Following surgery, all patients received 100% oxygen and neuromuscular blockade reversal with atropine sulfate 0.75 mg and neostigmine 0.05 mg/kg. Lidocaine at a dose of 1 mg/kg was administered prior to extubation. Tracheal extubation was performed after patients achieved spontaneous, regular, and adequate respiration. Cognitive function was reassessed using the MMSE at 24 and 72 hours postoperatively.

DATA ANALYSIS

Data were analyzed using Microsoft Excel and IBM SPSS Statistics version 23. Descriptive statistics were used to summarize demographic and baseline characteristics, expressed as mean \pm standard deviation (SD) or median (interquartile range) as appropriate. Comparisons of continuous variables between study groups were performed using the independent t-test for normally distributed data and the Mann–Whitney U test for non-normally distributed data. Categorical variables were analyzed using the chi-

square test or Fisher’s exact test, as appropriate. A p-value < 0.05 was considered statistically significant.

RESULTS

The study included a total of 32 subjects, with no patients excluded or lost to follow-up throughout the data collection period. Participants were equally allocated to the DEX-S and PRO groups. The majority of participants were female (62.5%), with a mean age of 38.03 ± 11.17 years,

ranging from 18 to 60 years. Anthropometric measurements indicated a mean height of 159.19 ± 7.55 cm and a mean body weight of 64.09 ± 13.48 kg. Most participants had completed high school education (40.6%) or held a bachelor’s degree (40.6%), indicating a predominantly well-educated study population. Additional clinical characteristics are presented in Table 1.

Table 1. Demographic and Clinical Characteristics

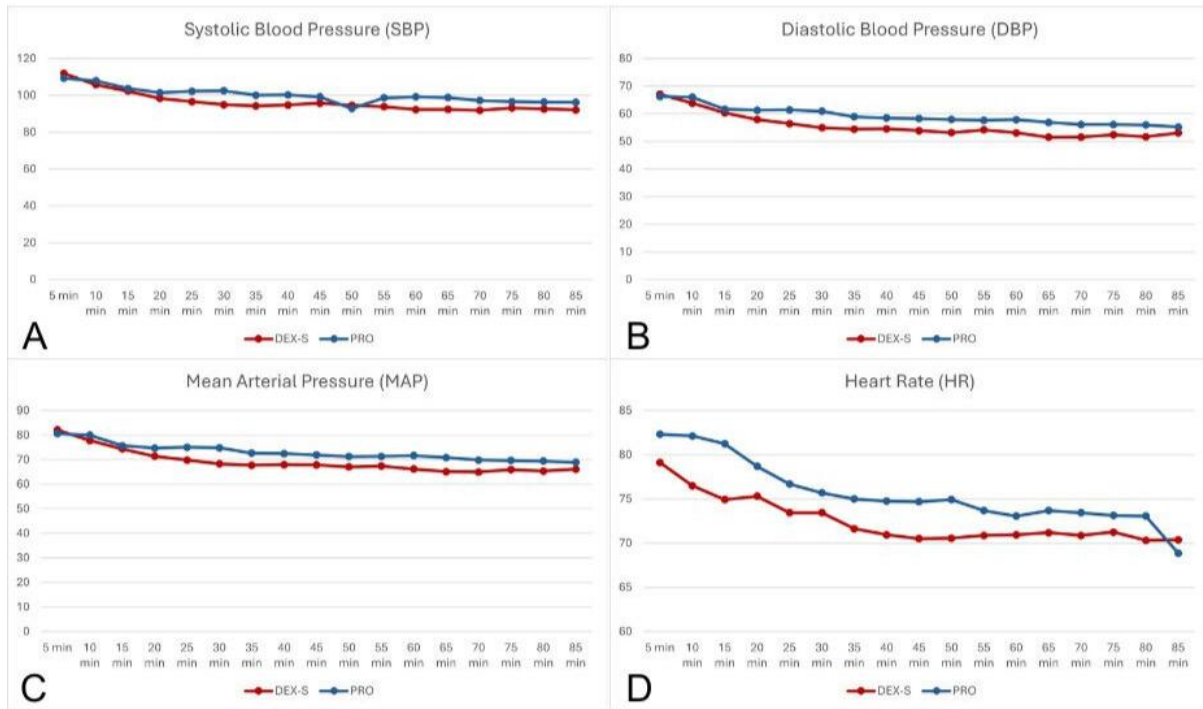
Characteristic	n	%
Gender		
Male	12	37.5
Female	20	62.5
Level of Education		
Elementary school	3	9.4
Middle School	3	9.4
High School	13	40.6
Bachelor	13	40.6
PS ASA Score		
I	9	28.1
II	23	71.9
	Mean \pm SD	Median (Min-Max)
Age (y.o.)	38.03 ± 11.17	38 (18-60)
Height (cm)	159.19 ± 7.55	159 (143-172)
Weight (kg)	64.09 ± 13.48	63 (40-92)
Baseline SBP (mmHg)	126.06 ± 9.62	125 (105-140)
Baseline DBP (mmHg)	74.47 ± 8.48	74 (60-92)
Baseline MAP (mmHg)	91.66 ± 8.27	90.67 (77.33-107.33)
Baseline HR (bpm)	80.94 ± 9.24	82 (65-108)
Baseline BIS	96.00 ± 1.32	96 (93-98)
Duration of Operation (min)	144.06 ± 40.66	140 (60-220)
Duration of Anaesthesia (min)	175.63 ± 41.49	167.5 (85-250)
Estimated Blood Loss (ml)	234.69 ± 200.15	180 (20-750)

Abbreviation: SBP=Systolic Blood Pressure, DBP=Diastolic Blood Pressure, MAP=Mean Arterial Pressure, HR=Heart Rate, BIS=Bispectral Index.

reduces sympathetic tone while preserving tissue perfusion, without inducing severe hypotension.

Intraoperative Hemodynamic Characteristics

Intraoperative hemodynamic assessment between the DEX-S and PRO groups demonstrated a relatively stable profile throughout the surgical and anesthetic periods, with observed physiological fluctuations remaining within clinically acceptable ranges (Fig. 1). The temporal trends were nearly parallel, indicating that both anesthetic agents exert comparable vasodilatory effects. Dexmedetomidine



*p < 0.05; **p < 0.001

Figure 1. Intraoperative Hemodynamic Parameters Comparison of (A) Systolic Blood Pressure, (B) Diastolic Blood Pressure, (C) Mean Arterial Pressure and (D) Heart Rate.

MMSE Score Changes and Comparison

Cognitive function was assessed at three time points using the MMSE: preoperatively as a baseline, and at 24 and 72 hours postoperatively. POCD was diagnosed based on an MMSE score below 24 or a decrease of ≥3 points from baseline. Both groups exhibited a significant decline in MMSE scores at 24 hours, followed by recovery at 72 hours. At all time points, the PRO group demonstrated higher MMSE scores than the DEX-S group (preoperative: 27.50 ± 1.59 vs. 27.13 ± 1.62; 24 hours postoperatively: 25.81 ± 1.87 vs. 24.56 ± 2.30; 72 hours postoperatively: 27.13 ± 1.92 vs. 26.00 ± 2.12), although the differences were minimal and did not reach a 2-point threshold.

Postoperative changes in MMSE scores were analyzed across the different time points and compared between the DEX-S and PRO groups. The results demonstrated that cognitive decline was more pronounced in the DEX-S group at both 24 and 72 hours postoperatively; however, statistically significant differences were observed only at 24 hours (Table 2). These findings suggest a transient early postoperative cognitive impact associated with DEX-S, which appears to attenuate by 72 hours.

POCD Incidence Comparison

Although earlier analyses indicated that the DEX-S group experienced a greater decline in MMSE scores compared with the PRO group, this did not translate into differences in POCD incidence between the groups at 24 and 72 hours postoperatively (Table 3). These results suggest that despite measurable early cognitive changes, the overall clinical impact on postoperative cognitive dysfunction was comparable between the two anesthetic regimens.

Table 2. Comparison of MMSE Score Changes

Δ MMSE Score	Groups	Mean SD	±	p-Value
Preoperative – 24h post op	DEX-S	2.56	± 1.36	0.036*
	PRO	1.69	± 0.94	
Preoperative – 72h post op	DEX-S	1.13	± 1.14	0.097
	PRO	0.38	± 1.14	
24h – 72h post op	DEX-S	-1.44	± 0.72	0.572
	PRO	-1.31	± 0.47	

Table 3. Comparison of POCD Incidence

POCD Incidence	Groups (n)		Total (n (%))	p-Value
	DEX-S	PRO		
24h post op				
POCD	4 (25)	2 (12.5)	6 (18.8)	0.654
Non-POCD	12 (75)	14 (87.5)	26 (81.3)	
72h post op				

POCD	3 (18.8)	1 (6.3)	4 (12.5)	0.600
Non-POCD	13 (81.3)	15 (93.8)	28 (87.5)	

*p <0.05; **p <0.001

Contributing Factors to POCD

Since the type of anesthesia was found to have no difference in the POCD incidence, other variables were further analyzed for their potential contribution to its development. From the various variables tested, it was found that patient’s age and education levels differs significantly in patients with POCD than with normal cognitive function, with p-value of < 0.001 and 0.004, respectively (Table 4). Other variables such as MAP, duration of anesthesia and estimated blood loss volume seems to have no role in the development of POCD in this study.

Table 4. Analysis of Demographic and Clinical Characteristics as Contributing Factors to POCD 72-hours After Surgery

Characteristic	POCD	Non-POCD	p-Value
	n = 4	n = 28	
Age (y.o.)	55.50 ± 3.41	35.54 ± 9.51	< 0.001**
MAP (mmHg)	69.79 ± 7.88	69.52 ± 4.63	0.393
Duration of Anaesthesia (min)	170.00 ± 36.74	176.43 ± 42.68	0.627
Estimated Blood Loss (ml)	320.00 ± 307.57	222.50 ± 185.08	0.587
Level of Education (n (%))	POCD	Non-POCD	0.004*
Elementary school	3 (75)	0 (0)	
Middle School	0 (0)	3 (10.7)	
High School	1 (25)	12 (42.9)	
Bachelor	0 (0)	13 (46.4)	

* p <0.05; **p <0.001

Discussion

The results of our study demonstrated no statistically significant difference in the incidence of POCD between the Sevoflurane–Dexmedetomidine combination and Propofol-based TIVA as anesthesia regimens. Previous studies have reported that Sevoflurane alone is associated with worse postoperative cognitive performance compared to Propofol within the first 48 hours, particularly in the domains of memory and processing speed.¹⁹ This effect may be attributed to Sevoflurane-induced neuroinflammation and

neural apoptosis, as demonstrated by Qiao et al in their experimental studies.¹⁵ Conversely, Propofol-based TIVA has been shown to exert superior anti-inflammatory effects compared with inhalation anesthesia, with lower levels of cytokines and other inflammatory mediators detected in the circulation of animals administered Propofol.²⁰ In our study, Dexmedetomidine was used as an adjuvant to Sevoflurane, which several studies have shown to significantly reduce POCD incidence compared to controls.^{21,22} Dexmedetomidine may have mitigated Sevoflurane-induced neurotoxicity through its role in inflammatory modulation and enhancement of glymphatic system function, facilitating the clearance of neurotoxic metabolites, resulting in cognitive outcomes comparable to Propofol-based TIVA.^{23,24}

Although the incidence of POCD was comparable between the two groups, the DEX-S group demonstrated a significantly greater reduction in MMSE scores at 24 hours postoperatively compared with the PRO group. Differences from baseline persisted at 72 hours, although they were no longer statistically significant. These findings may be attributed to differences in the pharmacokinetics and pharmacodynamics of the agents. Sevoflurane has a low blood–gas partition coefficient (0.69), allowing rapid elimination via the lungs and faster cognitive recovery compared with other inhalational agents.²⁵ However, Dexmedetomidine, administered as an adjuvant to Sevoflurane in this study, has sedative properties that mimic non-REM sleep by suppressing noradrenergic neurons in the locus coeruleus, such that drowsiness and reduced attention can persist even after the infusion has been stopped.²⁴ Because the MMSE is particularly sensitive to orientation and attention rather than executive function, these residual sedative effects are likely to contribute to lower scores.²⁶ In contrast, Propofol has a rapid onset and short half-life, resulting in rapid redistribution of the drug from the brain, and attention recovery tends to be better in the early phase.^{25,27} This may explain the relatively better MMSE scores observed in the first 24 hours with Propofol, which should not be interpreted as greater neuroprotective efficacy. Therefore, postoperative differences in MMSE scores are more likely a reflection of residual sedative effects on orientation and attention rather than a manifestation of organic cognitive dysfunction.

In terms of intraoperative hemodynamics, both the Sevoflurane–Dexmedetomidine combination and Propofol-based TIVA were able to achieve stable controlled hypotension, as reflected by the MAP trends observed in both groups throughout the surgical period. The MAP values generally remained around 70 mmHg, without abrupt decreases indicative of severe hypotension. Following the initial induction phase (5–15 minutes), MAP, SBP, and DBP in the DEX-S group tended to be slightly lower—by approximately 2–4 mmHg—than those in the PRO group; however, these differences remained within clinically safe limits and were consistent with the target range for controlled hypotension in FESS surgery. These findings are consistent with previous FESS studies reporting that both Propofol-based TIVA and Sevoflurane inhalation anesthesia

combined with vasodilator adjuvants or potent opioids were able to maintain MAP within the range 65–75 mmHg without increasing the incidence of cardiovascular complications.^{28,29} Heart rate was consistently lower in the DEX-S group compared with the PRO group at nearly all time points. This pattern reflects the sympatholytic effect of dexmedetomidine, an α_2 -adrenergic agonist that reduces sympathetic nervous system activity, thereby decreasing heart rate and slightly lowering blood pressure without compromising vital organ perfusion.²⁸ A recent meta-analysis also showed that, in modern FESS protocols using remifentanyl and controlled hypotension strategies, differences between TIVA and inhalational anesthesia on MAP, heart rate, intraoperative blood loss, and surgical field quality tended to be small and inconsistent.²⁸ Collectively, these findings suggest that the choice of anesthetic technique for FESS is primarily influenced by clinician preference, experience, and patient-specific factors, while from the aspect of hemodynamic stability, both Sevoflurane–Dexmedetomidine and Propofol-based TIVA can be considered equally safe and effective when appropriately titrated.

Further analysis of the other variables in this study shows that older age and educational level may contribute to the development of POCD. These findings are consistent with those reported by Wu and colleagues, who identified older age as an independent predictor of POCD in geriatric patients undergoing oral cavity tumor surgery.³¹ Increasing age is associated with greater cognitive vulnerability to surgical and anesthetic stress, thereby increasing the risk of POCD in the early postoperative period.^{32,33} Aging neural networks exhibit a reduced capacity for functional compensation when disrupted by inflammatory processes or alterations in cerebral perfusion. Furthermore, advanced age is associated with more severe neuroinflammation, reduced neuroplasticity, blood-brain barrier dysfunction, and accumulation of neurotoxic metabolites. This combination of structural and molecular changes makes the elderly brain more vulnerable to impairments in memory, attention, and executive function following surgery and general anesthesia.^{34,35} Several studies have also identified educational level as an important determinant of the brain's ability to preserve cognitive function after surgery.^{36,37} The concept of cognitive reserve explains that individuals with higher educational level have a more efficient neural network capacity (neural reserve) and the ability to recruit alternative pathways when the primary network is temporarily disrupted (neural compensation). These two mechanisms make the brain more resilient to acute post-surgical stress, including neuroinflammation and dysfunction of the frontoparietal network, which plays a critical role in attention and working memory.³⁸ Furthermore, several studies have shown that lifelong cognitive experiences, including formal education, result in a more stable network adaptability in the face of short-term metabolic or inflammatory insults.^{39,40} Overall, the findings of this study suggest that intrinsic patient-related factors exert a greater influence on the development of POCD than

variations in anesthetic technique or perioperative parameters.

This study has several limitations. Cognitive assessments were performed only up to 72 hours postoperatively, limiting insights into medium- and long-term outcomes. Additionally, the MMSE alone may be insufficiently sensitive to subtle deficits in executive function and working memory, commonly affected in POCD. Key factors potentially influencing POCD, such as inflammatory markers (IL-1 β , IL-6, TNF- α) and cerebral perfusion/oxygenation status (e.g., via NIRS), were not evaluated. Future studies incorporating comprehensive cognitive testing, longer follow-up, and monitoring of relevant physiological and inflammatory parameters are needed to better understand the mechanisms and determinants of POCD.

Conclusion

The incidence of POCD within 24 and 72 hours following FESS under controlled hypotension was low and was not significantly affected by the choice of anesthetic between Sevoflurane–Dexmedetomidine and Propofol-based TIVA. Patient-related factors, particularly age and cognitive reserve associated with educational level, appear to have a more critical influence on postoperative cognitive outcomes than intraoperative physiological variables such as MAP, anesthesia duration, or blood loss. These findings highlight the importance of personalized perioperative strategies to optimize cognitive recovery after surgery.

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Author Contribution

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work

Conflict of Interest

The authors declare that there are no conflicts of interest related to this study. All authors conducted the research independently, and no financial, personal, or professional relationships influenced the study design, data collection, analysis, interpretation, or the preparation of this manuscript.

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Ethical Approved

This study was conducted at a tertiary referral center, Dr. Soetomo General Hospital, Surabaya, East Java, Indonesia, between September and November 2025. Ethical approval was obtained from the hospital's Ethics Committee (Approval No. 1391/KEPK/VIII/2025). Written informed consent was obtained from all participants prior to their inclusion in the study.

Data Availability

All the data is available with the authors and shall be provided upon request

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