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RESEARCH ARTICLE

Effect of sevoflurane versus propofol on early cognitive functions in elderly patients after lumbar disc surgery

Sherif Mohammed El-Hadi[a], Abd Alkader Zakria Abd Alkader[a], Reham Abdel Halem Abo Elwafa[b], Ehab Darwish Mohamed[a] and Rania Abo Elfetouh Abdel Azim[a]

[a]Anesthesia and Surgical Intensive Care, Faculty of Medicine, Alexandria University, Alexandria, Egypt; [b]Clinical and Chemical Pathology, Faculty of Medicine, Alexandria University, Alexandria, Egypt

ABSTRACT

Background: Post-operative cognitive dysfunction (POCD) is an important issue that is associated with substantial morbidity and increased mortality, especially in elderly patients who have undergone major surgical procedures under general anesthesia. The symptoms of POCD may last for several months after surgery, leading to extended hospital stays, a decline in life quality, an increased need for social assistance, and significant financial strain on the patients.
Settings and Design: It was a Prospective Randomized interventional study.
Methods: A total of 120 patients (≥65 years) were divided into two groups of 60 each for this study at Alexandria Main University Hospital and planned for elective lumbar disc surgery under general anesthesia. Either propofol or sevoflurane was used to maintain anesthesia after it was induced. MMSE score, S100β levels and hemodynamic measures were all evaluated.
Results: Incidence of POCD was not statistically significant different between the two studied groups. There was a statistical significant negative correlation between S100β level and MMSE score in early post-operative period.
Conclusion: In terms of POCD, both propofol-based and sevoflurane-based anesthesia have the same effects on cognitive functions in early post-operative period.

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Mini-mental state examination; cognitive dysfunction; S100 calcium binding beta protein; sevoflurane; propofol

1. Introduction

Postoperative cognitive dysfunction, or POCD, is a clinical syndrome with documented cases. In 1955, Bedford published the first description of it in the Lancet under the heading "adverse cerebral effects of anesthesia on old people" [1]. After surgery, POCD is characterized by a decline in cognitive function, particularly in memory and executive functions. This deterioration can last for up to a year or longer. After major operations, this medical condition may occasionally continue for many of years. POCD is not the same as emergence delirium. It frequently affects older people and those with pre-existing cognitive impairment [2].

POCD's causes remain uncertain. It does not seem to be caused by lack of oxygen or inadequate blood supply to the brain [3], and it is equally likely to occur under both general and regional anesthesia [2,4]. POCD's causes are unclear. It is believed that ischemia, hypoxemia, inflammatory response to surgery, or the production of stress hormones during surgery could be the cause [5]. POCD may render patients unable to recover from surgery, postpone hospital discharge, delay returning back to work after surgery, and affect their quality of life [5]. Although POCD may afflict individuals at any age, it is more prevalent in the elderly. After being admitted to the hospital for surgery, almost 40% of all patients over 60 had POCD on discharge [6].

Psychometric testing is necessary for both pre- and postoperative diagnosis of POCD. Depending on whether particular cognitive domains have been affected, it might show in a variety of subtle ways. The two most prevalent deficits are memory impairment and diminished intellectual functioning [7,8].

The incidence for POCD varies based on the group of patients investigated, the definition of POCD applied, the tests used to establish the diagnosis and their statistical evaluation, the timing of testing, and the selection of control group [9–11].

POCD's cause is yet unknown. However, many studies have been conducted on this subject over the past decade. There are several hypothesized pathways that contribute to POCD development. A systemic stress response caused by surgeries triggers neuroendocrine hormones release and an inflammatory response [12,13]. Adults over the age of 60 are more vulnerable to POCD. Aging-related physiological changes lead to a decreased ability to cope with the stress of surgery, anesthesia, and hospitalization.

CONTACT Ehab Darwish Mohamed ehabdarwish152@gmail.com Department of Anesthesia and Surgical Intensive Care, Faculty of Medicine, Alexandria University, Alexandria 21615, Egypt

Various pharmacokinetics and pharmacodynamics of medications are likewise altered by these physiological changes [14]. Moreover, a higher age is often associated with a higher prevalence of comorbidities and an increased probability of developing perioperative complications.

Mini-Mental State Examination was created to be a dementia screening tool. It includes questions about tasks related to retentiveness, spatial and temporal orientation, recall, attention and correctness, as well as tests of language and writing and drawing skills. It takes about 5 minutes to administer [15,16].

S-100β protein is a Calcium-binding protein. It is highly selective for central nervous system injuries. It is present in the glial cells cytoplasm. Multiple studies reported that S100β may be an effective indicator for dysfunction diagnosis [17–19]. Physiologically, S100β serum levels are low. During the early periods of brain injury, glial cells are activated, and following neuronal damage, S100β is released into the bloodstream. S100β appears to be a possible biochemical detector of POCD as a result [20].

The current study compared the effects of sevoflurane- and propofol-based anesthesia on early cognitive functions in elderly individuals undergoing general anesthesia for lumbar disc surgery. Evaluating the incidence of POCD 120 minutes and 24 hours after surgery was the primary aim.

2. Patients

A total of 120 cases (60 per group) (G.Power software Study population was used to calculate the sample size) patients admitted to neurosurgery department, Alexandria Main University Hospital and scheduled for elective lumbar disc surgery under general anesthesia.

Inclusion criteria: Patients with ASA score of I – II, of both sex, age 65 years or older, possess the necessary educational background to successfully finish neuropsychological testing, do not have serious hearing or vision impairment.

Exclusion criteria: Patient's refusal, ASA III/IV, MMSE score <26, severe hepatic, renal or cardiovascular disease, pre-existing neurological, dementia, current use of sedatives, antidepressants, history of brain surgery or recent stroke, history of alcohol abuse or drug addict, intraoperative events requiring interventions such as excessive blood loss and severe hypotension.

On the day of operation, all patients were randomized into one of 2 equal groups using a sealed opaque envelope method to receive either propofol-based anesthesia or sevoflurane-based anesthesia regimen.

Group P: 60 patients received propofol-based anesthesia.

Group S: 60 patients received sevoflurane-based anesthesia.

3. Methods

Study settings: This study was conducted in a tertiary spine surgery unit of the neurosurgery department, Alexandria Main University Hospital after obtaining the approval of the Institutional Review Board, Faculty of Medicine, University of Alexandria.

Study design: Prospective Randomized interventional study.

After informed written consent was taken from all patients and were evaluated through history taking, clinical examination, and laboratory investigations. Cognitive functions were evaluated with MMSE.

Anesthetic management: after attachment of standard monitoring through multichannel monitor (ECG, NIBP, and pulse oximetry for SPO_2, End-tidal Capnography, Gas analysis and nasopharyngeal core temperature) and Entropy monitoring for the depth of hypnosis.

- Before induction of anesthesia: A 3-mL venous blood sample was collected to determine S100β protein levels by (SEA567Hu ELISA Kit).
- After pre-oxygenation, fentanyl (1 μg/kg) and propofol (1–1.5 mg/kg) were given intravenously till loss of consciousness and loss of verbal communication (entropy at 40–60). To facilitate endotracheal intubation using a tracheal tube of the appropriate size, rocuronium at a dose of 0.8 mg/kg was injected.
- Ventilation done using 50% oxygen in air to keep EtCO2 (30–35 mmHg) and SPO_2 ≥98%.
- After turning to the prone position. Anesthesia was maintained according to one of the two group allocations: in group P with propofol infusion 6–8 mg/kg/h and in group S with sevoflurane 1.5–2%. Propofol infusion rate and Minimum Alveolar Concentration (MAC) of sevoflurane was adjusted according to the hemodynamic changes and entropy values maintaining entropy values between 40 and 60. Intermittent doses of rocuronium (0.1–0.2 mg/kg) will be given intravenously guided by TOF to maintain muscle relaxation.
- Strategies during anesthesia: to maintain core temperature (36–37°C), MAP within 20% of the baseline, plasma glucose concentration (5.0–7.8 mmol/L) and strict fluid replacement according to the standard fluid administration guidelines.
- An increase in MAP or heart rate by >20% from baseline was defined as insufficient analgesia and was treated with intermittent boluses of fentanyl 0.5 μg/kg IV if needed. No other opioids or sedatives were given during surgery.
- When the MAP was <20% from baseline, increase the infusion rate of crystalloid or colloid, or giving

bolus injection of vasoactive agent (5 mg ephedrine) when needed.

- Before closure the surgical wound, the subcutaneous tissue and the paraspinal musculature were infiltrated with 0.25% bupivacaine (30 ml) for postoperative pain control [21].
- After completion of surgery and repositioning of patient, discontinuation of anesthesia was done and neuromuscular block was reversed using sugammadex (2 mg/kg) to ensure adequate reversal of rocuronium action. After adequate awakening, the patient was extubated and observed in the recovery room for at least 40 minutes.
- For postoperative pain control, 15 mg/Kg paracetamol was infused intravenously and repeated every 6 hours. For patients with persistent pain (VAS ≥ 4), 0.05 mg/kg morphine was given intravenously and those were excluded from the study.
- Hemodynamic measurements were taken prior to induction, immediately following induction, after intubation, every 15 minutes till the end of surgery, and postoperatively every 10 minutes for 40 minutes.
- Duration of anaesthesia, intraoperative fentanyl consumption, preoperative and 24 hours postoperative values of hemoglobin, and estimated blood loss were recorded in both groups.
- Cognitive dysfunction assessment using Mini Mental State Examination (MMSE) test was recorded preoperatively (T0), 120 minutes (T1), and 24 hours postoperatively (T2).
- S-100 calcium binding beta protein levels (SEA567Hu ELISA Kit) (cloud-clone corp.) (Katy, Texas, USA) were recorded at T0 and T1.

3.1. Statistical procedures

The Medical Research Institute at Alexandria University in Egypt's department of statistics has determined that the sample size is sufficient.

4. Results

A total of 135 patients were screened for inclusion; 6 were disqualified due to problems during surgery, 9 were disqualified because their refusal to participate. The two groups' data were dispersed normally.

Regarding age, sex, ASA classification, BMI and education, No significant statistical difference was observed between the two groups (Table 1).

Regarding heart rate and MAP, no significant statistical difference was observed between the two groups before induction, after induction, after intubation.

Regarding heart rate and MAP, there was no significant statistical difference observed intraoperatively and postoperatively between the two groups.

Regarding the mean of duration of anesthesia and fentanyl consumption, no significant statistical difference observed between the two groups ($p = 0.827$ and 0.475 respectively).

Regarding hemoglobin level (g/dl), no significant statistical difference observed between the two groups preoperatively and postoperatively ($p = 0.472$ and 0.62 respectively).

Incidence of POCD according to MMSE score at (T1) was 26.7% (16 patients) in group P and 23.3% (14 patients) in group S. No significant statistical difference observed between the two groups ($p = 0.673$). (Table 2)

Incidence of POCD according to MMSE score at (T2) was 11.7% (7 patients) in group P and 11.7% (7

Table 1. Comparison between the two studied groups according to demographic data.

	Group P ($n = 60$)		Group S ($n = 60$)			
Demographic data	No.	%	No.	%	Test of sig.	*P*
Sex						
Male	29	48.3	30.0	50.0	$x^2 = 0.033$	0.855
Female	31	51.7	30	50.0		
Age (years)						
Median (Min. – Max.)	68.0 (65.0–74.0)		68.0 (65.0–74.0)		t = 0.753	0.453
Mean ± SD.	68.33 ± 2.48		68.0 ± 2.36			
BMI (k/gm2)						
Median (Min. – Max.)	29.2(24.40–34.30)		29.35(25.6–34.60)		t = 0.444	0.658
Mean ± SD.	29.24 ± 2.34		29.42 ± 2.13			
ASA						
I	14	23.3	14	23.3	x = 0.0	1.000
II	46	76.7	46	76.7		
Education						
Elementary	15	25.0	16	26.7		
Middle	17	28.3	16	26.7	$x^2 = 0.163$	1.000
High	22	36.7	21	35.0		
University	6	10.0	7	11.7		

SD: Standard deviation.
χ^2: Chi square test t: Student t-test.
p: *p* value for comparing between the two studied groups.

Table 2. Comparison between the two studied groups according to MMSE score.

MMSE	Group P ($n = 60$)	Group S ($n = 60$)	Test of sig.	p
T0				
Median (Min. – Max.)	27.0 (26.0–30.0)	27.0 (26.0–30.0)	t = 0.535	0.594
Mean ± SD.	27.23 ± 0.95	27.13 ± 1.10		
T1	**No. (%)**	**No. (%)**		
<24 (Abnormal)	16 (26.7%)	14 (23.3%)	$X^2 = 0.178$	0.673
≥24 (Normal)	44 (73.3%)	46 (76.7%)		
Median (Min. – Max.)	24.0 (16.0–28.0)	24.0 (16.0–28.0)	t = 0.072	0.943
Mean ± SD.	23.82 ± 2.70	23.78 ± 2.37		
T2	**No. (%)**	**No. (%)**		
<24 (Abnormal)	7 (11.7%)	7 (11.7%)	$x^2 = 0.0$	1.000
≥24 (Normal)	53 (88.3%)	53 (88.3%)		
Median (Min. – Max.)	26.0 (21.0–30.0)	26.0 (21.0–29.0)	t = 0.423	0.673
Mean ± SD.	25.97 ± 1.76	25.83 ± 1.70		

SD: Standard deviation χ^2: Chi square test t: Student t-test.
p: p value for comparing between the two studied groups.

patients) in group S. No significant statistical difference observed between the two groups ($p = 1.000$). (Table 2)

Regarding S100β (pg/ml), No significant statistical difference between the two groups at (T0) ($p = 0.051$). At T1, the mean of S100β level in group P was 412.50 ± 141.26 pg/ml, and in group S was 380.87 ± 133.43 pg/ml. No significant statistical difference observed between the two studied groups at (T1) ($p = 0.098$)

A statistically significant negative correlation was found between MMSE score and S100β level at T1 in both groups (Figure 1).

In group P, the mean of percentage of rise of S100β value (from T0 to T1) in patients developed POCD (MMSE < 24) was 86.47 ± 11.32 and in patients with normal cognitive function (MMSE ≥ 24) was 9.36 ± 3.05. Statistically significant relation (<0.001). (Table 3).

In group S, the mean of percentage of rise of S100β value (from T0 to T1) in patients developed POCD

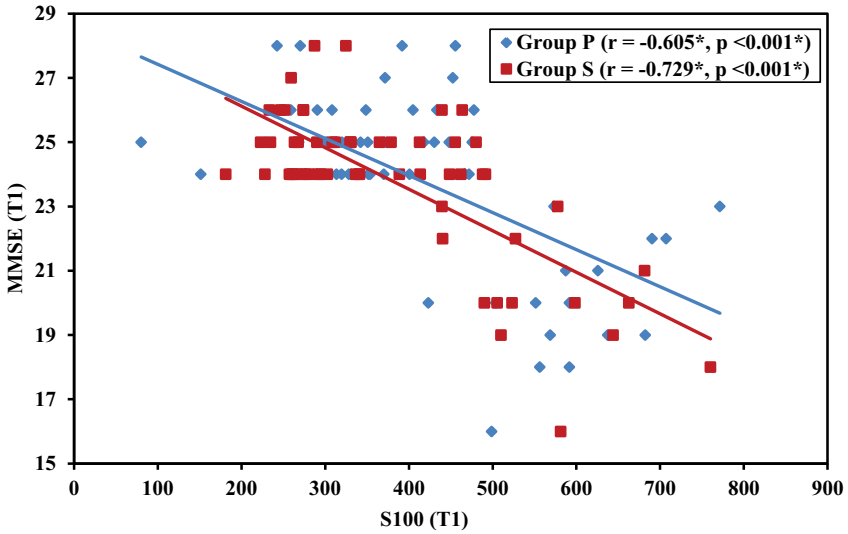

Figure 1. Correlation between MMSE (T1) and S-100 calcium binding beta protein level (pg/ml) (T1) in each group.

Table 3. Relation between MMSE (T1) and percentage of rise to S-100 calcium binding beta protein level in each group.

	MMSE (T1)			
	Group P ($n = 60$)		Group S ($n = 60$)	
	<24 (Abnormal) ($n = 16$)	≥24 (Normal) ($n = 44$)	<24 (Abnormal) ($n = 14$)	≥24 (Normal) ($n = 46$)
% of rise S100				
Min. – Max.	60.24–96.72	1.70–22.02	68.05–100.08	1.67–15.96
Mean ± SD.	86.47 ± 11.32	9.36 ± 3.05	88.15 ± 10.61	8.84 ± 2.66
Median	91.81	9.44	92.87	9.10
P	**<0.001***		**<0.001***	

SD: Standard deviation.
p: p value for Mann Whitney test for comparing between Abnormal and Normal in each group.
*: Statistically significant at $p \leq 0.05$.

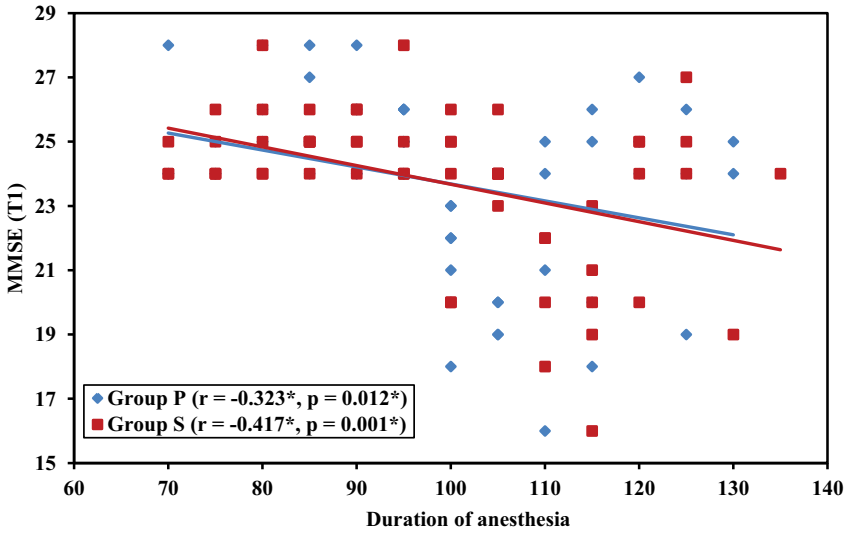

Figure 2. Correlation between MMSE (T1) and duration of anesthesia (minutes) in each group.

(MMSE < 24) was 88.15 ± 10.61 and in patients with normal cognitive function (MMSE ≥ 24) was 8.84 ± 2.66. Statistically significant relation (<0.001) (Table 3).

A statistically significant negative correlation was found between MMSE score at T1 and duration of anesthesia in both groups (Figure 2). Also, a statistically significant negative correlation found between MMSE score at T1 and age in both groups (Figure 3).

There was no statistically significant correlation observed between MMSE score at T1 and blood loss, also between MMSE score at T1 and education in both groups.

5. Discussion

POCD is a serious issue that has been linked to serious morbidity and increased mortality, particularly in older patients who have had major surgeries performed under general anesthesia. Following surgery, patients may experience more prolonged hospital stays, a decline in their quality of life, an increased need for social assistance, and significant financial burden due to the persistent symptoms of POCD [6,22].

In the present study, regarding the incidence of POCD according to MMSE score at (T1) and (T2) no significant statistical difference was observed between the two groups ($p = 0.673$ and 1.000 respectively). This agrees with Guo et al. who reported that, in elderly patients receiving sevoflurane-based or propofol-based general anesthesia, there was no significant statistical difference in the incidence of POCD [23]. Also, Konishi et al. discovered no statistically significant difference in terms of the occurrence of POCD at any timepoint between propofol and sevoflurane [24].

Sahoo et al. performed Montreal Cognitive Assessment (MOCA) test to evaluate the following cognitive domains – language, abstraction, recall,

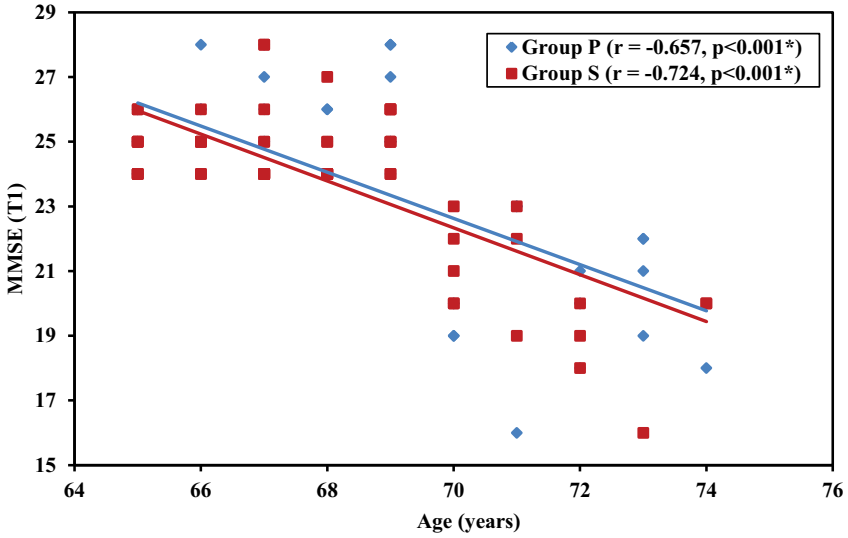

Figure 3. Correlation between MMSE (T1) and age (years) in each group.

orientation, naming, attention, and visuospatial/executive abilities. No signs of cognitive deterioration in postoperative period were found [6].

Contrary to the present study, when comparing sevoflurane and propofol for postoperative POCD, Qiao et al. employed MOCA test and found that, on the first, third, and seventh postoperative days, the sevoflurane group's scores were significantly less than those of the propofol group. That's may be due to POCD scoring systems were different and different assessment timing [25]. Similarly, Cao et al. concluded that, propofol-based anesthesia reduced the POCD incidence by a third compared with sevoflurane-based anesthesia [26].

Yang et al. indicated that adults who had abdominal, nasal, and ocular procedures showed reduced POCD incidence after receiving propofol-based anesthesia [27].

According to Goswami et al., during the early postoperative phase, sevoflurane improved cognitive functioning more than propofol [28]. Schoen et al. mentioned that individuals undergoing CABG showed significantly improved early memory cognitive functions when sevoflurane was administered instead of propofol [29].

The POCD incidence was greater in propofol group than in sevoflurane group when sevoflurane and propofol anesthesia were used with epidural anesthesia for cases of laparoscopic surgery lasting 3 hours or more [30]. The underlying mechanism may be due to long-term infusion lengthens propofol's terminal elimination half-life.

In the present study, as regard S100β level, No significant statistical difference observed between the two studied groups at (T1) ($P = 0.098$).

Early postoperative S100β levels showed a small increase, although it was not statistically significant (Sahoo et al.). The small rise in biomarker concentration seen in their study may have resulted from varying age groups and measurement times [6].

Qiao et al. showed that sevoflurane group had significantly higher postoperative S100β levels than propofol group [25].

In the current study, the MMSE score and S100β level at T1 in both groups showed a statistically significant negative correlation. According to Boos et al., after non-cardiac surgery, patients with lower preoperative MMSE scores had a greater prevalence of POCD [31]. Svenmarker et al. [32] studied the effects of S100β on memory functions following cardiopulmonary bypass; they found that, in comparison to neuron-specific enolase (NSE), S100β had a better correlation with the degree of hypoxic damage in the early period [33]. Following cardiac surgery, patients' serum levels of S100β and POCD found to correlate [34]. Thirty minutes postoperatively, patients with POCD have higher serum S100β concentrations than those without POCD, according to Linstedt et al. [17] Also, Peng et al. stated that high S100β concentrations are definitely correlated with the POCD [35].

Against the current study, Rappold et al. and Micha et al. concluded that POCD and S100β concentrations did not correlate with one another [36,37]. Also, Sahoo et al. could not find any association between levels of S100β with POCD in young patients undergoing spine surgery. This may be due to the different age group [6].

In the present study, a significant negative correlation was observed between MMSE score at T1 and age in both groups.

Guo et al., Monk et al., and Canet et al. showed that the POCD incidence was increased in elderly individuals compared to young or middle-aged individuals [23,38,39].

In the present study, no statistically significant relation observed between MMSE score at T1 and education in both groups. Unlike the current study, Geng YJ revealed that the level of education was a risk factor for POCD in elderly patients; however, the exact mechanism associated with this relation has yet to be explained [40].

6. Conclusions

In elderly patients undergoing lumbar disc surgery under general anesthesia, the use of either propofol or sevoflurane produced no significant differences between the two groups in terms of early cognitive outcomes or physiological parameters. The findings suggest that both propofol and sevoflurane anesthesia are safe and effective for elderly patients performing lumbar disc surgery.

7. Limitations

The present study was associated with several limitations. First, the long-term outcomes of patients were difficult to be monitored. Second, the sample size was small and limited to patients from a single center undergoing lumbar disc surgeries.

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Disclosure statement

The authors report no competing interests to declare.

ORCID

Ehab Darwish Mohamed http://orcid.org/0009-0001-6524-3973

Abbreviations

POCD	Post-Operative Cognitive Dysfunction
S100β	S-100 Calcium Binding Beta Protein
MMSE	Mini Mental State Examination
CABG	Coronary Artery Bypass Grafting
NSE	Neuron-Specific Enolase
VAS	Visual Analogue Scale
(T0)	Pre-Operative
(T1)	120 Minutes Post-operative
(T2)	24 Hours Post-operative

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