



COMPARISON OF PROPOFOL- AND SEVOFLURANE-BASED GENERAL ANESTHESIA ON EARLY POST-OPERATIVE COGNITIVE DYSFUNCTION AND S100B LEVELS IN ELDERLY PATIENTS

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ABSTRACT: 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 53 patients (≥ 65 years) were divided into two groups of 26 and 27 each for this study at Fathima Institute of Medical Sciences, Kadapa and planned for elective Abdomianl surgeries under general anesthesia. Either propofol or sevoflurane was used to maintain anesthesia after it was induced. MMSE score, S100 β 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 S100 β level and MMSE score in early post-operative period.

Conclusion: This prospective randomized study demonstrates that propofol-based and sevoflurane-based general anesthesia have comparable effects on early post-operative cognitive function in elderly patients undergoing elective abdominal surgery. The incidence of early POCD did not differ significantly between the two anesthetic techniques. Both groups showed a similar post-operative rise in serum S100 β levels, suggesting comparable degrees of neuronal stress or blood–brain barrier alteration. A significant negative correlation between S100 β levels and MMSE scores highlights the potential role of S100 β as a biochemical marker of early cognitive decline. Hemodynamic stability was maintained equally with both anesthetic regimens. Overall, either propofol or sevoflurane may be safely used in elderly patients without differential impact on early post-operative cognition.

In terms of POCD, both propofol-based and sevoflurane-based anesthesia have the same effects on cognitive functions in early post-operative period.

KeyWords: Post-operative cognitive dysfunction; Elderly patients; General anesthesia; Propofol; Sevoflurane; S100 β ; Mini-Mental State Examination; Abdominal surgery; Perioperative neurocognitive disorders; Biomarkers

INTRODUCTION

Post-operative cognitive dysfunction (POCD) is a well-recognized neurocognitive complication observed after surgery, particularly in the elderly, and manifests as decline in memory, attention, and executive function relative to baseline cognitive status [1,2]. With increasing numbers of elderly patients undergoing major surgical procedures under general anesthesia, the clinical relevance of POCD has grown due to its association with delayed recovery, prolonged hospitalization, reduced functional independence, and increased healthcare costs [1,3]. Elderly patients are especially vulnerable to POCD owing to age-related declines in cerebral metabolic reserve, increased comorbidities, and diminished cognitive reserve, which render the aging brain more susceptible to perioperative stressors [2,3].

Anesthetic technique and choice of anesthetic agent have been extensively investigated as potential modulators of POCD incidence. Meta-analyses comparing intravenous anesthetics such as propofol with volatile anesthetics like sevoflurane in elderly non-cardiac surgical populations have generally found no significant differences in short-term POCD incidence, although volatile agents may be associated with higher early markers of neuronal injury [4]. Similar evidence suggests that anesthetic depth, as guided by tools such as Bispectral Index (BIS), can influence cognitive outcomes; optimized EEG-guided anesthetic titration appears to reduce short-term POCD by avoiding excessively deep anesthesia and minimizing hemodynamic fluctuations [5,6]. These findings underscore the multifactorial nature of perioperative neurocognitive outcomes, where anesthetic management interacts with physiological stress responses and individual patient risk profiles.

Neuroinflammation is increasingly implicated in the pathophysiology of POCD. Surgical trauma triggers systemic pro-inflammatory cytokines that can cross the blood–brain barrier, precipitating neuroinflammatory cascades and glial activation that contribute to acute postoperative cognitive decline [2,7]. Biomarkers reflective of neuronal injury and blood–brain barrier disruption, such as S100 β , have emerged as valuable indicators of cerebral insult in the perioperative period. Recent systematic syntheses report perioperative elevations in S100 β to be significantly associated with POCD, highlighting its potential role in early risk stratification and mechanistic understanding of neurocognitive changes after anesthesia and surgery [8]. Elevated S100 β levels have been linked with worse cognitive performance in elderly surgical patients, corroborating the biochemical underpinning of perioperative cognitive dysfunction [8].

While the choice between total intravenous anesthesia (TIVA) with agents such as propofol and inhalational anesthesia with agents like sevoflurane has been widely debated, current clinical evidence suggests that when anesthetic depth and hemodynamic parameters are adequately controlled, both techniques yield comparable early cognitive outcomes in elderly patients [4,5]. Additionally, multimodal perioperative strategies, including the use of neuroprotective adjuncts such as dexmedetomidine, have shown promise in attenuating inflammatory responses and reducing early postoperative cognitive decline, although definitive clinical consensus is pending [9]. Emerging literature also emphasizes the importance of comprehensive monitoring and personalized anesthetic regimens to mitigate POCD, including tailored anesthetic depth, effective analgesia, and hemodynamic optimization [5,6].

Despite advances in understanding perioperative neurocognitive disorders, heterogeneity in POCD definitions, timing of cognitive assessment, and variability in surgical and anesthetic contexts continue to challenge the development of standardized clinical guidelines [1,2]. Nonetheless, the integration of cognitive functional assessments with biochemical biomarkers holds promise for early identification of at-risk elderly patients and for developing targeted strategies to preserve cognitive integrity following surgery.

In this context, our study aimed to evaluate and compare the effects of propofol-based and sevoflurane-based general anesthesia on early postoperative cognitive dysfunction and serum S100 β levels in elderly patients undergoing elective abdominal surgery, thereby contributing to ongoing efforts to refine perioperative neurocognitive care in high-risk aging populations.

MATERIALS

Study Design and Setting

This study was conducted as a **prospective, randomized, interventional study** at **Fathima Institute of Medical Sciences, Kadapa**, after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants. The study period included patients scheduled for **elective abdominal surgeries under general anesthesia**.

Study Population

A total of **53 elderly patients aged 65 years and above** were enrolled. Patients belonging to **ASA physical status I–III** and planned for elective abdominal surgery under general anesthesia were included in the study.

Exclusion criteria included pre-existing cognitive impairment (MMSE <24), history of cerebrovascular disease, psychiatric illness, alcohol or substance abuse, severe hepatic or renal dysfunction, emergency surgeries, and refusal to participate.

Randomization and Group Allocation

Patients were randomly allocated into two groups using a computer-generated randomization table:

- **Group P (n = 26):** Propofol-based General anesthesia
- **Group S (n = 27):** Sevoflurane-based General anesthesia,

Allocation concealment was ensured using sealed opaque envelopes.

The following **elective abdominal surgeries**, were performed under general anesthesia in elderly patients.

- Open or laparoscopic **cholecystectomy**
- **Hernia repair** (inguinal, incisional, ventral)
- **Exploratory laparotomy**
- **Appendectomy**
- **Colorectal surgeries** (hemicolectomy, sigmoidectomy)
- **Gastrojejunostomy**
- **Small bowel resection**
- **Abdominoperineal resection**
- **Adhesiolysis**
- **Elective gastric surgeries** (e.g., antrectomy)

Anesthetic Technique

All patients were premedicated as per institutional protocol. General anesthesia was induced using standard agents, following which anesthesia was maintained either with **propofol infusion** (Group P) or **sevoflurane inhalation** (Group S), along with oxygen and air. Muscle relaxation and analgesia were provided using standard drugs in both groups. The Depth of anesthesia and ventilation parameters was maintained uniformly across both the groups.

Data Collection and Variables

Baseline demographic data including **age, sex, body mass index (BMI), educational status, ASA physical status, co-morbidities**, type and duration of surgery, duration of anesthesia, intra-operative blood loss, and peri-operative analgesic requirement were recorded.

Cognitive Function Assessment

Cognitive function was assessed using the **Mini-Mental State Examination (MMSE)**. MMSE scores were recorded:

- Pre-operatively (baseline)
- In the **early post-operative period (within 24 hours after surgery)**

A decline of **≥ 2 points from baseline MMSE score** was considered indicative of **post-operative cognitive dysfunction (POCD)**.

Biochemical Assessment

Venous blood samples were collected pre-operatively and in the early post-operative period for estimation of **serum S100 β levels**. Samples were analyzed using standard laboratory techniques. S100 β levels were used as a biochemical marker of neuronal injury and blood–brain barrier disruption.

Hemodynamic Monitoring

Hemodynamic parameters including **heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and oxygen saturation (SpO₂)** were monitored intra-operatively and recorded at regular intervals, as well as in the immediate post-operative period.

Outcome Measures

The **primary outcome** was the incidence of early post-operative cognitive dysfunction based on MMSE scores.

Secondary outcomes included correlation between serum S100 β levels and MMSE scores, and comparison of hemodynamic parameters between the two groups.

Statistical Analysis

Data were analyzed using appropriate statistical software. Continuous variables were expressed as **mean $\pm$ standard deviation**, while categorical variables were expressed as numbers and percentages. Intergroup comparisons were performed using **independent t-test or Mann–Whitney U test** for continuous variables and **Chi-square test** for categorical variables. Correlation between MMSE scores and S100 β levels was assessed using **Pearson or Spearman correlation analysis**. A p-value of **<0.05** was considered statistically significant.

RESULTS

Baseline Characteristics

A total of **53 patients aged ≥ 65 years** were included in the analysis. Patients were randomized into **Group P (Propofol, n = 26)** and **Group S (Sevoflurane, n = 27)**. There were **no statistically significant differences** between the two groups with respect to age, gender distribution, BMI, educational status, ASA physical status, type and duration of surgery, duration of anesthesia, baseline MMSE scores, or co-morbidities ($p > 0.05$), indicating comparability of the study groups.

Table 1 depicts the age-wise and gender-wise distribution of the study participants according to the anesthetic technique used. A total of 53 elderly patients were included, with 26 patients receiving propofol-based anesthesia and 27 patients receiving sevoflurane-based anesthesia. The majority of participants in both groups were within the 65–69 and 70–74 year age categories. Male patients constituted a slightly higher proportion in both anesthetic groups. The distribution of age and gender was comparable between the propofol and sevoflurane groups, indicating adequate randomization and demographic balance across the study population.

Table 1: Distribution of Study Participants by Age Group, Gender, and Anesthetic Technique (n = 53)

Age Group (years)	Male Propofol (n)	Female Propofol (n)	Total Propofol = 26)	Male Sevoflurane (n)	Female Sevoflurane (n)	Total Sevoflurane (n = 27)
65–69	6	4	10	5	5	10
70–74	5	3	8	6	4	10
≥ 75	4	4	8	4	3	7
Total	15	11	26	15	12	27

Table 2 outlines the classification of independent, dependent, confounding variables, and outcome measures assessed in the study. The independent variable was the type of maintenance anesthetic agent used—propofol or sevoflurane. Dependent variables included cognitive function assessed using the Mini-Mental State Examination (MMSE), biochemical evidence of neuronal injury measured by serum S100 β levels, and intra-operative hemodynamic stability assessed through heart rate, blood pressure parameters, mean arterial pressure, and oxygen saturation. Several confounding variables such as age, sex, educational status, body mass index, ASA physical status, surgical and anesthetic duration, blood loss, and co-morbidities were documented to minimize bias. The primary outcome was the incidence of post-operative cognitive dysfunction, defined as a decline of two or more points in MMSE score, while secondary outcomes included correlation analysis between S100 β levels and MMSE scores, as well as recovery parameters and hospital stay.

Table 2: Allocation of Study Variables and Outcome Measures

Category	Variable	Measurement / Scale
Independent Variable	Type of maintenance anesthetic	Propofol / Sevoflurane
Dependent Variables	Cognitive function	MMSE score (0–30)
	Neuronal injury	Serum S100 β (ng/L or pg/mL)
	Hemodynamic stability	HR, SBP, DBP, MAP, SpO ₂
Confounding Variables	Age	Years
	Sex	Male / Female
	Educational status	Literate / Illiterate
	BMI	kg/m ²
	ASA physical status	I–III
	Duration of surgery	Minutes
	Duration of anesthesia	Minutes
	Blood loss	mL
	Co-morbidities	HTN, DM, CVD
Primary Outcome	POCD	MMSE decline ≥ 2 points
Secondary Outcomes	Correlation	S100 β vs MMSE
	Recovery & hospital stay	Minutes / Days

Table 3: Assessment Tools and Time Points

Table 3 summarizes the assessment tools used in the study and their respective time points of evaluation. Cognitive function was assessed using the MMSE both pre-operatively and during the early post-operative period (6–24 hours after surgery). Serum S100 β levels were measured at the same time points to evaluate biochemical markers of neuronal injury. Hemodynamic parameters,

including heart rate, blood pressure, mean arterial pressure, and oxygen saturation, were monitored pre-operatively and in the early post-operative period to ensure hemodynamic stability and comparability between groups.

Table 3. Assessment Tools and Time Points

Assessment Tool	Parameter Measured	Pre-operative	Early Post-operative (6–24 h)
MMSE	Cognitive function	✓	✓
Serum S100 β	Neuronal injury	✓	✓
Hemodynamics	HR, BP, MAP, SpO ₂	✓	✓

Common Elective Abdominal Surgeries Included in the Study

The study included elderly patients undergoing a range of elective abdominal surgeries under general anesthesia. These procedures comprised open and laparoscopic cholecystectomy, various types of hernia repairs, exploratory laparotomy, appendectomy, colorectal resections, gastrojejunostomy, small bowel resection, abdominoperineal resection, adhesiolysis, and elective gastric surgeries. Inclusion of diverse abdominal procedures ensured a representative surgical population while maintaining uniformity in anesthetic management.

Incidence of Post-Operative Cognitive Dysfunction

POCD, defined as a **decline of ≥ 2 points in MMSE score**, was observed in:

- **Group P:** 7 patients (26.9%)
- **Group S:** 8 patients (29.6%)

The difference in incidence of POCD between the two groups was **not statistically significant** ($p = 0.81$).

Serum S100 β Levels

Cognitive Function (MMSE Scores)

The **baseline MMSE scores** were comparable between the two groups:

- **Group P:** 27.8 ± 1.2
- **Group S:** 27.6 ± 1.3

($p = 0.54$)

In the **early post-operative period (within 24 hours)**, both groups demonstrated a mild decline in MMSE scores:

- **Group P:** 26.5 ± 1.6
- **Group S:** 26.3 ± 1.7

($p = 0.62$)

The **mean reduction in MMSE score** from baseline was not statistically significant between the groups ($p > 0.05$).

Baseline serum **S100 β levels** were comparable between the two groups:

- **Group P:** 0.082 ± 0.021 ng/mL
- **Group S:** 0.085 ± 0.024 ng/mL

($p = 0.67$)

In the **early post-operative period**, a significant rise in S100 β levels was observed in both groups:

- **Group P:** 0.136 ± 0.032 ng/mL
- **Group S:** 0.139 ± 0.035 ng/mL

The intergroup difference was **not statistically significant** ($p = 0.74$).

Correlation Between MMSE Scores and S100 β Levels

A **statistically significant negative correlation** was observed between early post-operative MMSE scores and serum S100 β levels across the study population:

- **Correlation coefficient (r): -0.46**

- **p-value: < 0.01**

Higher S100 β levels were associated with lower MMSE scores, indicating a relationship between biochemical markers of neuronal injury and cognitive decline in the early post-operative period.

Hemodynamic Parameters

Intra-operative and post-operative **heart rate, systolic and diastolic blood pressure, mean arterial pressure, and oxygen saturation (SpO₂)** were comparable between the two groups at all measured time points. No clinically significant hemodynamic instability was observed in either group ($p > 0.05$).

Secondary Outcomes

- **Time to recovery from anesthesia and length of hospital stay** were similar between the two groups.
- No major post-operative complications related to anesthesia or cognition was reported.

Summary of Key Findings

- The incidence of **early POCD** was comparable between propofol- and sevoflurane-based anesthesia.
- **S100 β levels increased post-operatively** in both groups without significant intergroup differences.
- A **significant negative correlation** existed between S100 β levels and MMSE scores.
- Both anesthetic techniques demonstrated **similar cognitive and hemodynamic profiles** in the early post-operative period.

DISCUSSION

Post-operative cognitive dysfunction (POCD) remains a clinically relevant complication in elderly patients undergoing surgery under general anesthesia, with implications for recovery, quality of life, and healthcare utilization. The present prospective randomized study compared propofol-based and sevoflurane-based maintenance anesthesia with respect to early POCD and serum S100 β levels in elderly patients undergoing elective abdominal surgeries. The principal findings of this study indicate that the incidence of early POCD was comparable between the two anesthetic techniques, with no statistically significant intergroup differences in MMSE scores, serum S100 β levels, or hemodynamic parameters.

The observed incidence of early POCD in this study (approximately 27–30%) aligns with contemporary reports suggesting that early cognitive decline is common in elderly surgical patients, even after non-cardiac surgery. Recent reviews and cohort studies emphasize that POCD is multifactorial, influenced not only by anesthetic agents but also by patient-related factors such as age, baseline cognitive reserve, comorbidities, surgical stress, and inflammatory responses [9, 10]. The comparable incidence of POCD between propofol and sevoflurane groups in the present study supports the growing consensus that the choice of maintenance anesthetic alone may not be the dominant determinant of early cognitive outcomes.

Propofol has traditionally been considered potentially neuroprotective due to its antioxidant properties and ability to reduce cerebral metabolic rate, while volatile anesthetics such as sevoflurane have been implicated in neuroinflammation and amyloid-related pathways in experimental models. However, recent clinical studies and meta-analyses have reported conflicting results, with several demonstrating no significant difference in early cognitive outcomes between intravenous and inhalational anesthetic techniques [11, 12]. The findings of the present study are consistent with these reports, suggesting that when depth of anesthesia, ventilation, analgesia, and hemodynamic stability are uniformly maintained, both propofol and sevoflurane produce similar early cognitive effects in elderly patients.

An important contribution of this study is the evaluation of serum S100 β as a biochemical marker of neuronal injury and its relationship with cognitive function. The significant post-operative rise in S100 β levels observed in both groups corroborates earlier studies indicating transient blood–brain barrier disruption and neuronal stress following major surgery and anesthesia. Importantly, the lack of intergroup difference in S100 β levels suggests that both anesthetic techniques exert comparable effects on early neuronal injury. Recent anaesthesiology literature has increasingly highlighted the role of S100 β as a sensitive, albeit nonspecific, marker for perioperative neurocognitive disorders (PND), particularly in elderly patients [13, 14].

The statistically significant negative correlation between early post-operative MMSE scores and serum S100 β levels observed in this study reinforces the clinical relevance of biochemical markers in understanding POCD pathophysiology. Similar correlations have been reported in recent prospective studies, where elevated S100 β levels were associated with worse early cognitive performance following non-cardiac surgery [15]. This relationship supports the hypothesis that early POCD may reflect transient neuronal injury or neuroinflammatory responses rather than permanent neurodegeneration.

Hemodynamic stability is another critical determinant of cerebral perfusion and cognitive outcomes in elderly patients. In the present study, intra-operative and post-operative hemodynamic parameters were comparable between groups, and no episodes of clinically significant instability were recorded. Recent guidelines and expert consensus statements emphasize that avoidance of hypotension, hypoxia, and wide blood pressure fluctuations may be more important than the specific anesthetic agent in preventing perioperative neurocognitive disorders [16]. The uniform maintenance of hemodynamic parameters in this study likely contributed to the absence of differences in cognitive outcomes between the two anesthetic techniques.

The inclusion of a heterogeneous but representative range of elective abdominal surgeries strengthens the external validity of the study. Elderly patients undergoing abdominal surgery often experience significant surgical stress and inflammatory responses, which may predispose them to POCD. The comparable surgical profiles and anesthetic durations between groups minimized confounding and allowed for a focused evaluation of anesthetic technique on cognitive outcomes.

Despite its strengths, this study has certain limitations. The sample size was modest, which may limit the detection of subtle differences between anesthetic techniques. Cognitive assessment was limited to MMSE and the early post-operative period; longer-term cognitive follow-up and the use of more sensitive neuropsychological test batteries may provide additional insights. Furthermore, while S100 β is a useful biomarker, it is not specific to neuronal injury and may be influenced by extracerebral sources.

In conclusion, the findings of this study suggest that propofol-based and sevoflurane-based general anesthesia have comparable effects on early post-operative cognitive function and biochemical markers of neuronal injury in elderly patients undergoing elective abdominal surgery. The significant association between elevated S100 β levels and cognitive decline underscores the multifactorial nature of POCD and highlights the importance of comprehensive perioperative management. Future large-scale studies incorporating multimodal biomarkers and long-term cognitive follow-up are warranted to further elucidate strategies for preventing perioperative neurocognitive disorders in the aging surgical population.

CONCLUSIONS: This prospective randomized study demonstrates that propofol-based and sevoflurane-based general anesthesia have comparable effects on early post-operative cognitive function in elderly patients undergoing elective abdominal surgery. The incidence of early post-operative cognitive dysfunction did not differ significantly between the two anesthetic techniques. Both groups exhibited a similar post-operative rise in serum S100 β levels, indicating comparable degrees of transient neuronal injury or blood–brain barrier disruption. The significant negative correlation between S100 β levels and MMSE scores highlights the utility of biochemical markers in understanding early perioperative cognitive changes. Maintenance of stable hemodynamics and

uniform depth of anesthesia likely contributed to the similar cognitive outcomes observed. Overall, either propofol or sevoflurane may be safely employed for maintenance of general anesthesia in elderly patients without differential impact on early cognitive recovery, emphasizing the importance of comprehensive perioperative management over anesthetic choice alone.

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