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Original Article

BIS-Guided Anesthesia and Early Cognitive Recovery in Elderly: A Controlled Trial

Saba Arif[1], Muhammad Abdullah Shakeel[2], Aqeel Ahmad[3], Hafiz Muhammad Fawaad Bilal[4], Muhammad Imran Anjum[5], Dure Shahwar[6]

[1] Anesthetist, DHQ Hospital, Khanewal, Pakistan
[2] Post Graduate Trainee, Anaesthesia, KRL Hospital, Islamabad, Pakistan
[3] Assistant Professor, Anesthesiology, PGMI, Quetta, Pakistan
[4] Consultant Anesthesiologist, MS Anaesthesia, Primary and Secondary Health Care Department, District Khanewal, Pakistan
[5] Consultant Anesthetist, HOD Anesthesia/ICU, DHQ Hospital, Khanewal, Pakistan
[6] Services Hospital, Lahore, Pakistan

***Corresponding author: Saba Arif, sabaarifparacha@gmail.com**

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ABSTRACT

Background: Elderly patients undergoing general anesthesia are vulnerable to delayed cognitive recovery and postoperative delirium, partly because age-related physiological changes may increase sensitivity to excessive anesthetic depth. Objective: To compare BIS-guided anesthesia with standard anesthesia management for early postoperative cognitive recovery, delirium incidence, anesthetic consumption, and immediate recovery outcomes in elderly patients undergoing elective non-cardiac surgery. Methods: This parallel-group randomized controlled trial was conducted at a tertiary care teaching hospital in Central Punjab, Pakistan, from August 2025 to January 2026. Eighty patients aged 65–80 years undergoing elective non-cardiac surgery under general anesthesia were randomized to BIS-guided anesthesia or standard anesthesia management. In the BIS-guided group, anesthetic depth was maintained within a BIS range of 40–60. Cognitive recovery was assessed using MMSE and MoCA at baseline, 24 hours, and 72 hours postoperatively, while delirium was assessed using the Confusion Assessment Method. Final complete-case analysis included 73 participants. Results: At 72 hours, the BIS-guided group had higher MMSE scores than the standard anesthesia group (27.1 ± 1.5 vs 25.4 ± 1.9; mean difference, 1.7; 95% CI, 0.90–2.50) and higher MoCA scores (25.0 ± 1.8 vs 22.9 ± 2.1; mean difference, 2.1; 95% CI, 1.19–3.01). BIS-guided anesthesia also reduced sevoflurane consumption, extubation time, and recovery-room stay. Delirium occurred in 8.1% and 25.0% of participants, respectively, with exact testing indicating a clinically relevant but statistically non-definitive difference. Conclusion: BIS-guided anesthesia was associated with better early postoperative cognitive recovery and improved immediate recovery efficiency in elderly surgical patients. Keywords: Aged; Anesthesia; Bispectral Index; Cognitive Dysfunction; Delirium; Postoperative Complications; Randomized Controlled Trial.

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INTRODUCTION

Despite advancements made in perioperative monitoring and anesthetic and postoperative care, postoperative neurocognitive dysfunction remains an important issue in older adults who undergo surgery with general anesthesia. Older adults remain highly susceptible to such complications because aging leads to decreased cerebral reserve, changes in pharmacokinetics and pharmacodynamics, decreased ability to maintain homeostasis, and increased risk of drug-induced cortical depression. Consequently, aging is linked to the increased risk of delayed recovery of consciousness, postoperative delirium, prolonged time spent in recovery room, functional impairment, and greater use of medical services after surgery. Given this, optimal control of anesthesia level has become an important objective during perioperative period, particularly in elderly patients undergoing elective surgeries that are not performed on the heart, where unnecessary exposure to anesthetics can lead to early neurological impairment (1).

Traditional anesthesia management is usually based on clinical measures such as heart rate, blood pressure, oxygen saturation, autonomic measures, and patient movements. While these parameters can help to monitor the general state of patients, they do not directly estimate the degree of hypnosis caused by anesthetic medications. At the same time, this issue becomes important in case of elderly patients because identical doses of anesthetic drugs may cause a deeper than needed level of hypnosis because of changes in pharmacokinetics and pharmacodynamics and cerebral vulnerability that are related to the aging process. The excessive level of anesthesia has been suggested as a possible modifiable risk factor in development of postoperative delays in emergence, early cognitive impairment, and postoperative delirium, although the aforementioned effects have many different causes including pain, opioids, inflammation, hypoxia, hypotension, frailty of patients, and surgical stress (2).

The Bispectral Index is a quantitative measurement based on electroencephalography which determines anesthetic depth and enables real-time adjustment of hypnosis agents during general anesthesia. A BIS scale ranging from 40-60 is typically recommended to ensure sufficient anesthetic depth without excessive cortical depression. The use of BIS-based anesthesia has the potential to decrease anesthetic requirement, shorten awakening time and improve early postoperative recovery due to the more objective way of defining anesthetic hypnosis. Individualization of BIS-based anesthesia management can be especially effective in elderly patients requiring general anesthesia for their surgeries due to the disproportional effects of excessive anesthetic exposure on these patients' neurological functions (3).

Inconsistent results were previously obtained in various clinical trials and meta-analyses that aimed to examine the association between depth-of-anesthesia monitoring and neurocognitive outcomes after surgeries. In some researches, decreased anesthetic requirements, faster recovery, decreased rate of delayed neurocognitive recovery, and improved early cognitive scores have been demonstrated in patients who received anesthetics in the mode of electroencephalographic or BIS-based anesthetic titration. However, some studies have failed to show reduction in postoperative delirium or postoperative cognitive dysfunction. These contradictions can be explained by the differences in patient population, cognitive risk, anesthetic techniques, anesthetic depth, delirium measurement technique, follow-up period and cognitive tests used for determination of postoperative cognitive impairment (4).

Postoperative delirium is one of the most important early neurocognitive complications in elderly patients after surgeries. It is characterized by acute disturbances of attention, awareness, and cognition, and is associated with prolonged hospital stay, functional decline, institutionalization, and increased mortality. Although the etiology of delirium is complex and multifactorial, excessive anesthetic depth may contribute to it via prolonged cortical depression, hemodynamic instability, disturbed cerebral autoregulation and interaction with perioperative inflammatory and metabolic stressors. Therefore, approaches that minimize anesthetic exposure without affecting the surgical anesthesia may be helpful in prevention of neurological vulnerability after surgeries (5).

In addition to its potential neuroprotective effects, BIS-guided anesthesia can increase the efficiency of perioperative care due to decreased inhalation anesthetic use, shorter extubation time, and reduced length of stay in the recovery room. This is important from a clinical standpoint because of the possibility of improving the process of patient discharge and decreasing medication exposure among patients in high-volume surgical centers, especially those who belong to a geriatric population. At the same time, there is insufficient evidence to suggest that the use of BIS monitoring can have positive effects on early cognitive recovery and decrease the risk of delirium in geriatric patients under general anesthesia during elective non-cardiac surgery (6).

This particular randomized controlled trial was aimed at filling this gap in literature because of the need to compare the results of BIS-guided anesthesia and standard anesthesia management in geriatric patients aged 65-80 years undergoing elective non-cardiac surgery under general anesthesia. Through the use of MMSE and MoCA scores at baseline, 24 hours, and 72 hours after surgery and delirium assessment using Confusion Assessment Method, this study evaluated whether individualized anesthetic depth titration improved early cognitive recovery, decreased incidence of delirium, and the amount of anesthetics used. The main purpose of the study was to find out whether BIS-guided anesthesia improved early postoperative cognitive recovery compared with standard anesthetic dose, while secondary purposes were comparing postoperative delirium, sevoflurane consumption, extubation time, and recovery room stay between groups (7-10).

MATERIALS AND METHODS

A parallel-group randomized control trial was performed in the Department of Anesthesiology of a single-center tertiary care teaching hospital of Central Punjab, Pakistan. The trial screening and enrollment occurred from August 2025 to January 2026, with final follow-ups concluding in February 2026. The trial involved the comparison of BIS-guided anesthesia versus routine anesthesia management in elderly patients undergoing elective non-cardiac surgery under general anesthesia. The intervention involved the management of anesthetic depth intraoperatively only, while the postoperative neurocognitive follow-up was done in the first 72 hours following surgery. The design of the trial aimed to test the hypothesis that individualized anesthetic depth management using BIS monitoring improves early postoperative cognitive recovery and reduces the incidence of delirium compared to conventional clinical monitoring.

The sample size of the study was calculated using interventional evidence published before, regarding BIS-guided anesthesia and postoperative cognitive recovery in elderly patients undergoing surgery. Based on a moderate between-group effect on early postoperative cognitive recovery scores, 95% confidence level, and 80% statistical power, a minimum sample size of 68 participants was needed. To allow for attrition, incomplete postoperative evaluations, and postoperative exclusion, 80 participants were included and randomly assigned to two groups with 40 participants each in the BIS guided anesthesia and standard anesthesia groups respectively.

Adults aged 65-80 years old undergoing elective non-cardiac surgery under general anesthesia with an expected operative time greater than 90 minutes were screened for inclusion in the study. The inclusion criteria included ASA physical status II or III patients who could complete preoperative and postoperative neurocognitive evaluations. Patients with known cognitive deficits, psychiatric conditions, Parkinson's disease, history of cerebrovascular accidents, severe auditory or visual impairment limiting cognitive evaluations, alcohol dependence, chronic sedative usage, emergency surgery, and inability to complete MMSE, MoCA, and delirium evaluations were excluded. This was done to avoid neurocognitive and assessment-related confounding at baseline.

Eligible subjects were randomly assigned in a 1:1 allocation ratio based on a computer generated randomization schedule created by an independent investigator who had no role in subject enrollment, anesthesia delivery, postoperative assessment and statistical analyses. Concealment of allocation was done through sequential numbering of sealed opaque envelopes which were opened in the holding area immediately prior to transfer to the operating room. Owing to the nature of BIS guided anesthesia, it was impossible to blind anesthetists from group allocations but postoperative cognitive assessors and statistical analysts were kept blinded to reduce bias. Participants assigned to BIS guided anesthesia group were continuously monitored for anesthetic depth using a Bispectral Index monitor. Anesthesia was administered to maintain BIS readings within the target range of 40-60 during the maintenance phase of general anesthesia depending on BIS values, hemodynamics and clinical judgments. Participants allocated to the standard anesthesia group were administered conventional anesthesia depending on routine intraoperative clinical parameters like heart rate, blood pressure, oxygen saturation, ventilation status, autonomic responses and anesthetist judgments without visible BIS guided anesthesia. Participants in both groups were induced with propofol, fentanyl and atracurium and maintained on sevoflurane in an oxygen-air mixture. The hemodynamic data of each patient was collected every 15 minutes during the procedure and consumption of sevoflurane was recorded for each participant.

The main outcome measure was early postoperative cognitive recovery using the Mini-Mental State Examination and the Montreal Cognitive Assessment performed at three different time points: at baseline preoperatively, at 24 hours postoperatively, and at 72 hours postoperatively. These tools were selected to evaluate global cognitive performance, as well as orientation, attention, memory, language, executive function, and visuospatial skills postoperatively. Additional outcome measures included postoperative delirium measured with the use of Confusion Assessment Method, total consumption of sevoflurane, time to extubation, and recovery room stay. Time to extubation was determined by the period between stopping anesthetic drugs and removal of the endotracheal tube.

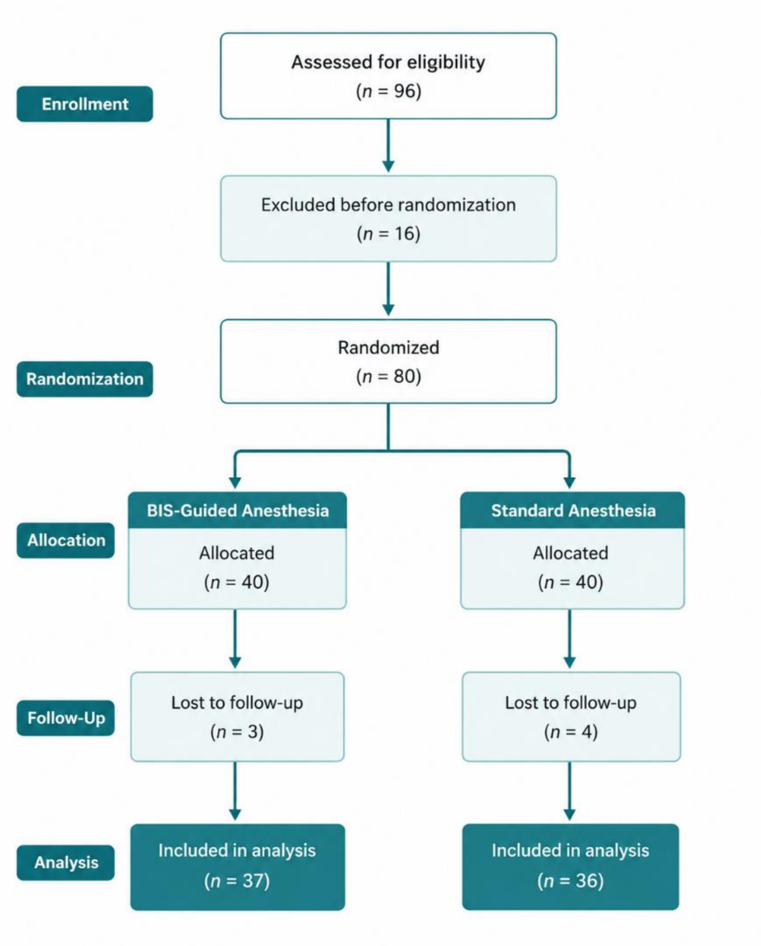

Figure 1 CONSORT Flowchart

Bias and confounding potential were controlled for using randomization, concealed assignment, standardized anesthetic induction and maintenance protocol, blinded postoperative outcome evaluation, and blinded data analyses. Baseline characteristics, such as age, gender, BMI, surgery duration, baseline MMSE score, and baseline MoCA score, were collected to test the comparability between groups. Patients with pre-existing neurological, psychological, sensory, and substance disorders were excluded from participation in order to minimize potential confounding in the assessment of the postoperative cognitive function. Post-randomization exclusion and incomplete follow-up assessment cases were tracked. Baseline data were analyzed using an Intention-to-Treat sample ($N = 80$) to reflect all randomized individuals, while primary and secondary outcome analyses utilized a complete-case approach based on patients with full postoperative outcome measurement data available.

The data were analyzed using SPSS v. 26.0. The normality of the continuous variable distribution was tested using the Shapiro–Wilk test, and normally distributed variables were presented as mean ± SD. The frequencies and percentages of the categorical variables were reported. Between-group comparisons of the normally distributed continuous variables were made using the independent samples t-test. Changes in normally distributed continuous variables from baseline to postoperative follow-up were evaluated using paired samples t-test. Repeated measures ANOVA was used to assess time, group, and time*group effects on the specific postoperative cognitive function recovery scores. Group differences in categorical outcomes, for example, incidence of postoperative delirium, were compared using appropriate categorical tests, and the exact testing was considered if expected cell counts were low. Sevoflurane consumption and postoperative cognitive function score were correlated using the Pearson correlation analysis. P-value below 0.05 was considered statistically significant.

RESULTS

In total, 96 elderly participants undergoing elective non-cardiac surgery were screened for eligibility from August 2025 to January 2026. Sixteen participants were excluded prior to randomization due to ineligibility or unwillingness to participate in the trial. The remaining 80 participants were randomly assigned equally between the BIS-guided anesthesia and control groups, with 40 participants assigned to each group. During the postoperative follow-up period, 3 participants from the BIS-guided group and 4 participants from the control group were unable to provide data at the final outcome evaluation point due to lack of postoperative cognitive evaluation or postoperative ICU admission. The outcome analysis was conducted on 73 participants who provided complete data including 37 participants from the BIS-guided group and 36 participants from the control group.

Table 1. Baseline Demographic and Clinical Characteristics of Randomized Participants (Intention-to-Treat Population)

Variable	Total Sample (N=80)	BIS-Guided Group (n=40)	Standard Anesthesia Group (n=40)	Mean Difference	95% CI	p-value
Age, years	71.2 ± 4.8	71.0 ± 4.6	71.4 ± 5.0	-0.4	-2.54 to 1.74	0.721
Male sex, n (%)	46 (57.5)	24 (60.0)	22 (55.0)	—	—	0.651
BMI, kg/m²	26.7 ± 3.1	26.5 ± 3.0	26.9 ± 3.2	-0.4	-1.78 to 0.98	0.588
Surgery duration, min	128.4 ± 21.7	126.8 ± 20.9	130.1 ± 22.4	-3.3	-12.94 to 6.34	0.497
Baseline MMSE score	27.8 ± 1.4	27.9 ± 1.3	27.7 ± 1.5	0.2	-0.43 to 0.83	0.544
Baseline MoCA score	25.9 ± 1.8	26.1 ± 1.7	25.8 ± 1.9	0.3	-0.50 to 1.10	0.463

All values are given as mean ± SD unless indicated otherwise. Mean difference indicates BIS-guided group – standard anesthesia group. BMI: Body Mass Index; BIS: Bispectral Index; CI: Confidence Interval; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment.

Baseline demographics, surgery, and cognition parameters were not significantly different between randomization groups. Mean age was 71.0 ± 4.6 years in the BIS-guided group, while it was 71.4 ± 5.0 years in the standard anesthesia group with mean difference of -0.4 years. Baseline MMSE and MoCA scores also did not differ between two randomization groups, being equal to 0.2 and 0.3 points respectively.

Table 2. Postoperative Cognitive Outcomes at 72 Hours in the Complete-Case Population

Outcome	BIS-Guided Group (n=37)	Standard Anesthesia Group (n=36)	Mean Difference	95% CI	Cohen's d	p-value
MMSE score	27.1 ± 1.5	25.4 ± 1.9	1.7	0.90 to 2.50	0.99	<0.001
MoCA score	25.0 ± 1.8	22.9 ± 2.1	2.1	1.19 to 3.01	1.07	<0.001

Values are expressed as mean ± SD. The mean difference is calculated as BIS-guided group minus standard anesthesia group. BIS: Bispectral Index; CI: confidence interval; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment.

At 72 hours after surgery, there were higher cognitive scores in the BIS-guided group than the standard anesthesia group. The between-group mean difference was 1.7 for MMSE and 2.1 for MoCA at 95% CI, which does not overlap zero. Thus, the values of Cohen's d of 0.99 for MMSE and 1.07 for MoCA suggest large standardized between-group differences for early postoperative cognitive performance.

Cognitive scores declined in both groups after 72 hours, but this decline was less pronounced in the BIS-guided group. The reduction of MMSE was –0.8 ± 0.7 in the BIS-guided group as opposed to –2.3 ± 1.1 in the standard anesthesia group. The reduction of MoCA was –1.1 ± 0.8 in the BIS-guided group as opposed to –2.9 ± 1.3 in the standard anesthesia group.

Table 3. Within-Group and Between-Group Changes in Cognitive Scores from Baseline to 72 Hours

Outcome	Group	Baseline	72 Hours	Mean Change	95% CI for Change	p-value
MMSE score	BIS-guided	27.9 ± 1.3	27.1 ± 1.5	-0.8 ± 0.7	-1.03 to -0.57	0.011
MMSE score	Standard anesthesia	27.7 ± 1.5	25.4 ± 1.9	-2.3 ± 1.1	-2.67 to -1.93	<0.001
MoCA score	BIS-guided	26.1 ± 1.7	25.0 ± 1.8	-1.1 ± 0.8	-1.37 to -0.83	0.008
MoCA score	Standard anesthesia	25.8 ± 1.9	22.9 ± 2.1	-2.9 ± 1.3	-3.34 to -2.46	<0.001

Values are presented as mean ± SD. Negative values indicate postoperative decline from baseline. BIS: Bispectral Index; CI: confidence interval; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment.

Table 4. Between-Group Differences in Cognitive Change from Baseline to 72 Hours

Outcome	BIS-Guided Mean Change	Standard Anesthesia Mean Change	Change Difference	95% CI	Cohen's d
MMSE score	-0.8 ± 0.7	-2.3 ± 1.1	1.5	1.07 to 1.93	1.63
MoCA score	-1.1 ± 0.8	-2.9 ± 1.3	1.8	1.29 to 2.31	1.67

Change difference is defined as BIS guided group minus standard anesthesia group. The positive values mean that there was less decrease in the BIS guided group post-operatively. BIS: Bispectral Index; CI: confidence interval; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment.

As observed from the between-group change analysis, there was smaller cognitive decline in BIS-guided anesthesia relative to baseline to 72 hours. The change difference was 1.5 for MMSE and 1.8 for MoCA with large effect sizes. This shows that the results of the primary outcome are supported by the results obtained.

Table 5. Repeated Measures Analysis of Cognitive Recovery (MMSE Metrics)

Outcome Domain	Effect	F	p-value
Postoperative cognitive recovery	Time	31.82	<0.001
Postoperative cognitive recovery	Group	7.64	0.007
Postoperative cognitive recovery	Time × group	9.27	0.002

Values are presented as reported in the manuscript data tracking sheets.

The repeated measures analysis found significant effects for time, group, and time × group in terms of postoperative cognitive recovery trends. The significant time × group interaction suggested that the longitudinal path of early cognitive recovery was different among the treatment groups.

Table 6. Secondary Recovery and Anesthetic Outcomes in the Complete-Case Population

Outcome	BIS-Guided Group (n=37)	Standard Anesthesia Group (n=36)	Mean Difference	95% CI	Cohen's d	p-value
Sevoflurane consumption, mL	18.7 ± 4.3	24.5 ± 5.1	-5.8	-8.01 to -3.59	-1.23	<0.001
Time to extubation, min	9.8 ± 2.6	14.2 ± 3.4	-4.4	-5.82 to -2.98	-1.46	<0.001
Recovery-room stay, min	41.6 ± 8.9	53.7 ± 10.5	-12.1	-16.65 to -7.55	-1.24	<0.001

The values were expressed as means ± SD. Difference in means refers to BIS-guided vs control anesthesia group. BIS: Bispectral Index; CI: Confidence Interval.

Recovery parameters during surgery were favorable for the BIS-guided group. Mean sevoflurane use was reduced by 5.8 mL in the BIS-guided group, while mean extubation time and recovery room stay was decreased by 4.4 minutes and 12.1 minutes, respectively. The effect sizes for these variables were large, suggesting that there were reductions in anesthetic use and postoperative recovery time.

Table 7. Postoperative Delirium in the Complete-Case Population

Outcome	BIS-Guided Group (n=37)	Standard Anesthesia Group (n=36)	Risk Difference	95% CI	Relative Risk	95% CI	Fisher's Exact p-value
Postoperative delirium, n (%)	3 (8.1)	9 (25.0)	-0.17	-0.34 to -0.00	0.32	0.10 to 1.10	0.064

The risk difference is the BIS-guided group value minus the standard anesthesia group value. BIS: Bispectral Index; CI: confidence interval.

Delirium after surgery was noted among 3 out of 37 patients in the BIS-guided group, compared to 9 out of 36 patients in the standard anesthesia group. The risk difference was -0.17, showing that the rate of delirium was low in the BIS-guided group. However, Fisher's exact p-value is 0.064, and the relative risk CI contained 1.00; therefore, this observation should be considered as a trend towards significance only.

Table 8. Association Between Sevoflurane Consumption and Postoperative Cognitive Score

Variable Pair	r	p-value
Sevoflurane consumption and postoperative MMSE score	-0.46	<0.001

r: Pearson correlation coefficient; MMSE: Mini-Mental State Examination.

A moderate negative correlation was found between sevoflurane use and the postoperative MMSE score, in which increased anesthesia use resulted in poorer postoperative cognitive function. As this relationship is unadjusted for treatment allocation, baseline cognition, age, ASA classification, length of surgery, or other possible perioperative confounding factors, it must be viewed as an exploratory relationship only.

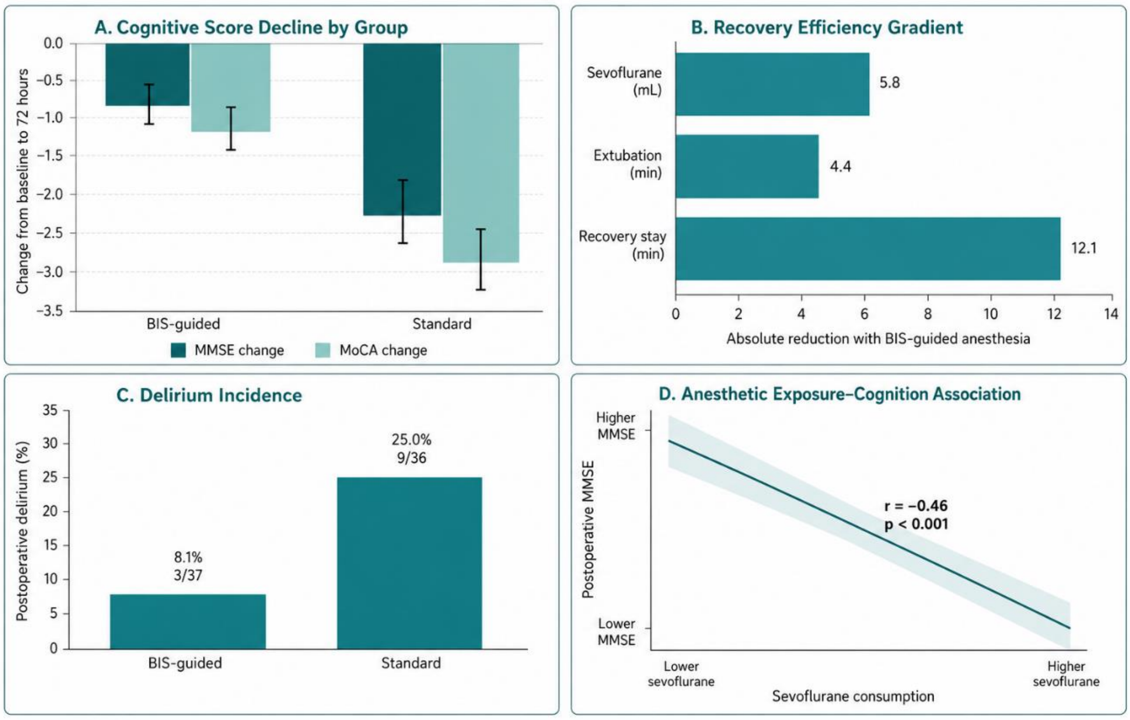

Figure 2 BIS-guided anesthesia showed smaller cognitive decline from baseline to 72 hours, with MMSE change of -0.8 versus -2.3 and MoCA change of -1.1 versus -2.9 compared with standard anesthesia. The BIS-guided group also showed lower sevoflurane consumption by 5.8 mL, shorter extubation time by 4.4 minutes, and shorter recovery-room stay by 12.1 minutes. Postoperative delirium occurred in 8.1% of BIS-guided participants compared with 25.0% of standard-anesthesia participants, while sevoflurane consumption showed a moderate inverse association with postoperative MMSE score (r = -0.46, p < 0.001).

Overall, the complete-case findings showed that BIS-guided anaesthesia was associated with better early postoperative cognitive scores, smaller decline from baseline, reduced sevoflurane consumption, shorter extubation time, and shorter recovery-room stay. The delirium proportion was lower in the BIS-guided group, but exact testing indicated that this result did not reach conventional statistical significance. These findings support the primary outcome that BIS-guided anesthetic titration may improve early postoperative cognitive recovery while reducing anesthetic exposure and immediate recovery burden in elderly patients undergoing elective non-cardiac surgery.

DISCUSSION

The current randomized control trial showed that BIS-guided anesthesia was linked to better cognitive recovery at 72 hours post-surgery in geriatric subjects having elective non-cardiac surgery using general anesthesia. Subjects undergoing BIS guidance during anesthesia administration had significantly higher scores in MMSE and MoCA tests compared to subjects in the control group, as well as the difference between pre-operative and post-operative scores was smaller for the BIS-guided group. Therefore, the individualized monitoring of depth of anesthesia may help maintain the cognitive function of elderly patients after the surgery since they have low brain reserve and increased sensitivity to anesthetics due to age. Moreover, the positive effects on both screening cognitive tests and executive-oriented cognitive function assessment make the findings clinically relevant because the early postoperative decline may influence patient orientation, mobilization, communication abilities, hospital discharge and functional recovery (11).

The current results are supported by the hypothesis about the link between minimizing the depth of anesthesia and lower postoperative neurocognitive dysfunction. Although the present study did not assess burst suppression of cortex, cerebral perfusion, inflammatory biomarkers, or neurophysiological connectivity, the use of BIS monitoring technique helped in maintaining hypnotic depth within a particular range. Lower sevoflurane consumption in the BIS-guided group suggests that standard clinical monitoring could lead to excessive anesthetic exposure in some elderly patients, even if their hemodynamic status is normal. There is previous clinical and systematic evidence about the reduction in the amount of anesthetics as a result of monitoring the depth of anesthesia (12,13).

The clinically significant differences in the amount of cognitive changes were identified in the immediate postoperative period. In particular, there was a decrease in MMSE score of -0.8 points in the BIS-guided anesthesia group compared to -2.3 points in the standard anesthesia group; MoCA scores decreased by -1.1 and -2.9 points in the BIS-guided anesthesia group and the standard anesthesia group, respectively. It should be noted that both groups have experienced the postoperative cognitive decline, and thus the obtained results cannot be explained in terms of complete prevention of postoperative neurocognitive impairment. It can be assumed that BIS-guided anesthesia had the ability to reduce the amount of cognitive decline in the postoperative period. The point is that postoperative cognition is affected by several factors, such as surgery-related stress, postoperative pain, opioids, disturbances in sleep and metabolism, hemodynamics, preexisting frailty, and inflammation. Therefore, in the current study, the use of BIS-guided anesthesia is seen as a way to reduce perioperative neurocognitive risks (14).

The study has also revealed a lower proportion of patients with delirium in the BIS-guided anesthesia group than in the standard anesthesia group. The incidence of delirium was 8.1% in the BIS-guided anesthesia group and 25.0% in the standard anesthesia group. However, after exact testing taking into account the number of events, the difference was not statistically significant, and the confidence interval of the relative risk included the value 1. Thus, this result may be considered as the trend to reduce delirium. Nevertheless, the direction of effect is important because delirium is a severe complication of elderly surgery, which increases the risk of prolonged hospital stay, disability, need for nursing home care, and even death. The results of larger studies will help understand whether this reduction is a replicable effect (15,16).

Secondary recovery effects serve even more to prove the clinical utility of individualized anesthetic depth assessment. Sevoflurane usage amount, extubation time, and recovery room time were decreased in the BIS-monitored group. This is clinically plausible as lower exposure to anesthesia can result in earlier recovery of consciousness and airway reflexes. In addition, smaller consumption of anesthetics, shorter extubation time, and reduced time in recovery room may be significant especially for highly operative facilities, where any changes can improve work process considerably. However, the results must be considered with respect to particular protocols of anesthetic administration, discharge criteria, staffing, and type of surgeries performed at each facility (17).

Negative correlation between sevoflurane consumption and postoperative MMSE score can be taken into account as another explorative evidence of connection between anesthetic exposure and early postoperative cognitive function. Greater sevoflurane consumption was associated with worse MMSE score, which can be considered as an indicator of cognitive dysfunction caused by higher anesthetic exposure. However, such relationship is not adjusted for treatment assignment, age, preoperative cognition, ASA status, surgery duration, intraoperative hemodynamics, analgesics exposure and many other possible confounders. Therefore, it should be used only for generating hypothesis for further research. Multivariate modeling or mediation approach could be applied to test the effect of anesthetic consumption on cognitive performance in further analysis (18).

The current study had several methodological advantages. The randomized parallel-group control trial minimized selection bias and ensured comparability between intervention groups. Allocation concealment using sealed opaque envelopes increased internal validity, while blinded postoperative cognitive assessment and blinded statistical analysis decreased the risk of outcome assessment and analytic biases. In addition, both MMSE and MoCA helped assess global cognition and more sensitive cognitive domains. The use of postoperative endpoints like extubation time, recovery room admission, and anesthetic usage provided clinically relevant postoperative outcomes. Induction and maintenance anesthesia agents were used as well to increase the consistency between groups.

A few limitations should be noted while interpreting the results of the study. Firstly, the trial was conducted at one tertiary care center; hence, the findings may lack generalizability across different patient population, anesthesia teams, and healthcare system. Secondly, the complete-case analysis was employed in the study since seven randomized patients were not evaluated for postoperative cognitive function or needed unexpected postoperative admission to intensive care unit. Even though the number of patients who were excluded from the analysis was numerically equal in both groups, the post-randomization exclusion may introduce bias, and future trials need to use prespecified strategy for handling of missing data. Thirdly, the follow-up period was only 72 hours; therefore, the current study does not provide information regarding the effect of bispectral index-guided anesthesia on persistent postoperative neurocognitive disorder or long-term functional impairment. Fourthly, anesthesiologists could not be blinded to BIS monitoring, which may have affected their intraoperative management even with the help of the standardized protocol. Lastly, the study did not evaluate the effects of frailty, pain scores, opioid intake, hypotensive burden during intraoperative period, burst suppression, inflammation markers, sleep disturbances, and postoperative complications (19).

Future multicenter randomized controlled trials with increased sample size, extended follow-up period, and predetermined delirium and neurocognitive outcomes are required to validate the results of the study. Such trials should have CONSORT compliant design with trial registration, complete management of missing data, longitudinal modeling for MMSE and MoCA scores and adjustment for perioperative confounders. More research concerning factors such as frailty, intraoperative EEG patterns, dose-response relationship between anesthetics and their effect, postoperative pain and opioids use, inflammation and neurobiological biomarkers may explain mechanisms through which depth-guided anesthesia affects cognition. Comparative trials of BIS and other EEG depth of anesthesia techniques may further personalize anesthetic regimen for elderly surgical patients (20).

In conclusion, the study findings suggest that BIS-guided anesthesia was related to better cognitive function recovery and higher recovery efficiency immediately after surgery for elderly patients. It is important to note the lower proportion of delirium in the BIS group, but one should be careful interpreting the results due to lack of statistical significance at exact testing. Within the limitations of complete case analysis and short follow-up period, this study shows that the use of BIS-guided anesthetics titration can be viewed as an effective perioperative strategy minimizing anesthetic exposure and postoperative cognitive decline.

CONCLUSION

BIS-controlled anesthesia showed better early postoperative cognition, lesser reduction in MMSE and MoCA scores, lower sevoflurane usage, shorter extubation time, and shorter stay in recovery room in elderly patients during elective non-cardiac surgeries requiring general anesthesia. However, the occurrence of postoperative delirium was lower in the BIS group, although this result must be taken into account with caution since actual test did not prove the presence of definite difference between groups. Thus, the obtained findings favor the use of personalized control of anesthetic depth as an effective tool to manage the anesthetic dose and promote early postoperative recovery in older surgical patients, but the large-scale multicenter trials are necessary to confirm its effects on delirium and long-term neurocognitive outcomes.

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