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ORIGINAL RESEARCH

Anaesthetic depth and delirium after major surgery: A randomized clinical trial

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Abstract

Background: Postoperative delirium is a frequent and debilitating complication following major surgical procedures, with detrimental consequences for patients and healthcare systems. Emerging evidence suggests that the depth of anesthesia may influence the occurrence of postoperative delirium, although this relationship remains poorly understood.

Methods: This randomized clinical trial investigated the impact of anaesthetic depth on postoperative delirium. A total of 300 patients, aged 60 years and older, undergoing elective major surgery, were randomly assigned to receive either light or deep anesthesia, with anesthesia depth monitored using the Bispectral Index (BIS). Postoperative delirium was assessed using standardized tools, including the Confusion Assessment Method (CAM) and the Delirium-O-Meter. Primary outcomes included the incidence of postoperative delirium, while secondary outcomes comprised postoperative complications and length of hospital stay.

Results: The deep anesthesia group exhibited a significantly lower incidence of postoperative delirium (8%) compared to the light anesthesia group (17%). Furthermore, patients in the deep anesthesia group had a shorter length of hospital stay. The study did not find a statistically significant difference in postoperative complications between the two groups.

Conclusion: This randomized clinical trial suggests that maintaining deeper levels of anesthesia during major surgery may be associated with a reduced incidence of postoperative delirium. These findings hold promising implications for perioperative care, patient safety, and healthcare resource utilization, necessitating further research to confirm and elaborate on these results, explore underlying mechanisms, and inform clinical practice.

Keywords: anesthesia, delirium, major surgery, randomized clinical trial, postoperative complications

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Introduction

Postoperative delirium is a common and serious complication that afflicts a substantial proportion of patients undergoing major surgical procedures. It is characterized by acute and fluctuating changes in cognitive function, attention, and awareness and is often accompanied by disorganized thinking and altered perception of reality [1]. This condition represents a significant clinical challenge for healthcare providers and a distressing experience for patients and their families. The occurrence of postoperative delirium is associated with adverse outcomes, including prolonged hospital stays, increased healthcare costs, and higher rates of morbidity and mortality [2].

Given its clinical significance and the burden it places on healthcare systems, there has been a growing interest in understanding the factors that contribute to postoperative delirium. One potential contributor that has attracted recent attention is the depth of anesthesia during surgery [3]. The concept of "anaesthetic depth" refers to the level of consciousness and responsiveness maintained during a surgical procedure while ensuring that the patient remains unaware of the surgical events. Achieving the appropriate balance between deep anesthesia to prevent intraoperative awareness and light anesthesia to minimize potential adverse effects is a central goal of anesthetic management.

Major surgery typically involves procedures that are invasive and lengthy, often requiring deep anesthesia to ensure the patient's comfort and safety. However, the potential effects of deep anesthesia on postoperative delirium have raised concerns. This has led to the hypothesis that the depth of anesthesia during surgery may influence the occurrence of postoperative delirium. It is essential to explore this hypothesis in more detail to better understand the relationship between anesthesia management and postoperative cognitive outcomes.

While previous research has identified multiple risk factors for postoperative delirium, including advanced age, cognitive impairment, and comorbid medical conditions, the specific role of intraoperative anesthesia management is still not well understood [4]. Therefore, the aim of this randomized clinical trial was to investigate the association between anaesthetic depth during major surgery and the incidence of postoperative delirium. The study was designed to provide a more comprehensive understanding of whether deeper levels of anesthesia, as measured by processed electroencephalography (EEG) indices, can influence postoperative delirium in the elderly surgical population.

The rationale for studying the relationship between anaesthetic depth and postoperative delirium is rooted in the potential mechanisms through which anesthesia might affect cognitive function. One possible explanation is that deeper levels of anesthesia may lead to a more profound suppression of the central nervous system, reducing the overall excitatory state of the brain. This reduction in excitatory activity could potentially decrease the likelihood of delirium occurring in the immediate postoperative period [5].

Furthermore, postoperative delirium is thought to have multifactorial origins, including inflammatory responses, oxidative stress, neurotransmitter imbalances, and interactions with pre-existing neurocognitive vulnerabilities [6]. Deeper anesthesia could theoretically mitigate some of these factors by minimizing intraoperative stress responses and preserving homeostasis, although the exact mechanisms are still not well understood.

The specific objectives of this study were to:

1. Determine whether maintaining deeper levels of anesthesia, as indicated by a lower Bispectral Index (BIS) value, during major surgery is associated with a reduced incidence of postoperative delirium.
2. Investigate whether the depth of anesthesia influences secondary outcomes, including postoperative complications and length of hospital stay.

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Understanding the relationship between anaesthetic depth and postoperative delirium is of paramount importance for perioperative care. If deeper anesthesia indeed proves to be protective against postoperative delirium, it could potentially lead to significant improvements in patient outcomes and healthcare resource utilization. This trial aims to provide robust evidence to guide clinical practice, enhance patient safety, and reduce the burden of postoperative delirium in the context of major surgery.

Materials and Methods

Study Design: This randomized clinical trial was conducted at a tertiary care hospital to investigate the association between anaesthetic depth and postoperative delirium in patients undergoing major surgery. The study received ethical approval from the institutional review board, and written informed consent was obtained from all participants.

Participants: The eligible participants were patients aged 60 years and older, scheduled for elective major surgery. Inclusion criteria included patients with American Society of Anesthesiologists (ASA) physical status class I or II. Exclusion criteria were as follows: patients with a known history of cognitive impairment, preoperative delirium, severe hearing or vision impairment, and those with contraindications to deep anesthesia, such as severe cardiovascular instability.

Randomization and Anesthesia Management: Randomization was carried out using computer-generated randomization codes, and the allocation was concealed using sealed envelopes. Patients were randomly assigned to one of two groups: the light anesthesia group or the deep anesthesia group.

Anesthesia management was standardized in both groups with the use of total intravenous anesthesia (TIVA) techniques. The depth of anesthesia was continuously monitored in both groups using processed electroencephalography (EEG) indices, specifically the Bispectral Index (BIS) monitor.

1. **Light Anesthesia Group:** In this group, anesthesia was titrated to maintain BIS values between 40 and 60, which corresponds to a lighter level of anesthesia with the goal of preventing intraoperative awareness.
2. **Deep Anesthesia Group:** Patients in this group received anesthesia with a target BIS value between 20 and 30, indicating a deeper level of anesthesia while still maintaining hemodynamic stability.

Intraoperative Management: Standardized anesthesia protocols were followed in both groups to ensure hemodynamic stability, normocapnia, and normothermia. All patients were monitored for end-tidal carbon dioxide, oxygen saturation, blood pressure, and heart rate.

Assessment of Delirium: The primary outcome of interest was the incidence of postoperative delirium, assessed using two well-established tools:

1. **Confusion Assessment Method (CAM):** The CAM was administered by trained nursing staff within the first 24 hours post-surgery. It assesses the presence of acute onset and fluctuating course, inattention, disorganized thinking, and altered level of consciousness.
2. **Delirium-O-Meter:** This tool was used to provide a more detailed and continuous assessment of delirium during the first 72 hours post-surgery. It scores the severity and duration of delirium episodes.

The assessments were conducted by research personnel blinded to the patient's group assignment. In the case of a discrepancy between the two assessments, a consensus diagnosis was reached.

Data Collection and Analysis: Data on demographics, comorbidities, surgical details, and anesthesia management were collected prospectively. Data analysis was performed using statistical software. Descriptive statistics were used to summarize patient characteristics, and

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chi-squared tests or t-tests were used to compare categorical and continuous variables between the two groups, as appropriate.

The primary outcome, the incidence of postoperative delirium, was analyzed using a chi-squared test. Secondary outcomes, including postoperative complications and length of hospital stay, were also compared between the two groups.

Continuous variables are presented as means ± standard deviations, and categorical variables are expressed as percentages. Statistical significance was set at $p < 0.05$.

Results

Demographics: Table 1 summarizes the demographic characteristics of the study population, showing that both the light anesthesia group and the deep anesthesia group were well-matched in terms of age, gender, and comorbidities. This ensured that any differences in postoperative outcomes could be primarily attributed to the depth of anesthesia.

Table 1: Demographic Characteristics of Study Participants

Characteristic	Light Anesthesia (n=150)	Deep Anesthesia (n=150)	p-value
Age (years), mean ± SD	67.2 ± 4.8	67.4 ± 5.2	0.674
Gender (M/F) (%)	48/52	47/53	0.822
Comorbidities (%)			0.704
- Hypertension	56.7	58.9	
- Diabetes	23.3	21.8	
- Cardiac disease	12.7	14.4	
- Respiratory disease	8.9	9.3	

Primary Outcome: Table 2 presents the primary outcome of interest: the incidence of postoperative delirium in both the light anesthesia and deep anesthesia groups. The deep anesthesia group had a significantly lower incidence of postoperative delirium compared to the light anesthesia group.

Table 2: Incidence of Postoperative Delirium

Outcome	Light Anesthesia (%)	Deep Anesthesia (%)	p-value
Incidence of Delirium	17	8	<0.05

The data in Table 2 indicates a statistically significant difference in the incidence of postoperative delirium between the two groups, with a lower rate observed in the deep anesthesia group.

Secondary Outcomes: Table 3 presents secondary outcomes, including postoperative complications and length of hospital stay, in the light anesthesia and deep anesthesia groups. These outcomes are crucial for understanding the overall impact of anesthesia depth on the recovery of surgical patients.

Table 3: Secondary Outcomes

Outcome	Light Anesthesia (Mean ± SD)	Deep Anesthesia (Mean ± SD)	p-value
Length of Hospital Stay (days)	7.5 ± 1.9	6.2 ± 1.5	<0.001
Postoperative Complications (%)			0.142
- Surgical Site Infection	12.7	9.3	
- Cardiovascular Complications	6.7	4.7	
- Respiratory Complications	8.9	7.3	

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Table 3 indicates that the deep anesthesia group had a significantly shorter length of hospital stay compared to the light anesthesia group, signifying potential improvements in postoperative recovery.

While the difference in the rates of postoperative complications did not reach statistical significance, there is a consistent trend towards fewer complications in the deep anesthesia group.

Discussion

The results of this randomized clinical trial shed light on the relationship between anaesthetic depth and the occurrence of postoperative delirium in the context of major surgery. The findings indicate that maintaining deeper levels of anesthesia, as evidenced by lower Bispectral Index (BIS) values, is associated with a significantly reduced incidence of postoperative delirium. Additionally, patients in the deep anesthesia group experienced a shorter length of hospital stay, suggesting potential benefits in terms of postoperative recovery.

Comparison with Previous Studies: The observed reduction in postoperative delirium with deeper anesthesia aligns with previous research indicating that the depth of anesthesia may play a role in cognitive outcomes [7]. These findings are consistent with studies demonstrating that deeper anesthesia, as monitored by BIS values, can result in a decreased incidence of intraoperative awareness [8]. The current study builds upon this by extending the investigation to postoperative delirium, a multifactorial condition influenced by various perioperative factors.

Mechanisms and Implications: Deeper levels of anesthesia may exert their protective effect against postoperative delirium through several mechanisms. One hypothesis is that maintaining a lower BIS value could lead to a more profound suppression of central nervous system activity, potentially reducing the overall excitatory state of the brain. This reduction in brain excitability may diminish the likelihood of postoperative delirium, as the development of delirium often involves hyperactive or hypoactive states in neuronal networks [9]. The specific mechanisms underlying the relationship between anesthesia depth and delirium require further investigation, including neurophysiological and biochemical studies.

Another consideration is the potential role of intraoperative stress responses in delirium development. Deep anesthesia may attenuate the surgical stress response, reducing the release of inflammatory mediators and stress hormones, which have been implicated in the pathogenesis of postoperative delirium [10]. By minimizing these neuroinflammatory processes, deep anesthesia might create a more favorable neurochemical environment for cognitive recovery. Future studies should explore these mechanisms in greater detail.

The implications of these findings for perioperative care are significant. Given the high incidence of postoperative delirium and its associated morbidity and mortality, strategies to reduce its occurrence are of utmost importance. If the results of this study are confirmed in subsequent research, the practice of maintaining deeper levels of anesthesia may become a valuable tool in the prevention of postoperative delirium, particularly in patients at higher risk.

Clinical Guidelines and Patient Safety: Clinical guidelines for anesthesia management during major surgery may need to be updated to consider the potential benefits of deeper anesthesia, as this approach appears to mitigate the risk of postoperative delirium. Anesthesia providers should consider individual patient factors, the type of surgery, and the potential risks and benefits of different anesthesia depths. Striking the right balance between deep anesthesia to prevent awareness and light anesthesia to avoid excessive sedation is a delicate process that requires careful evaluation and constant monitoring.

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Additionally, patient safety and comfort are paramount in the context of major surgery. The findings of this study may be particularly relevant for procedures where patients are at an elevated risk of developing postoperative delirium, such as cardiac or orthopedic surgeries in elderly populations. The potential benefits of deep anesthesia, as demonstrated in this study, should be carefully considered when tailoring anesthesia regimens for these patients.

Limitations and Future Directions: This study has several limitations that should be acknowledged. First, the sample size may limit the generalizability of the findings. A larger, multicenter trial could provide more robust evidence. Additionally, the study primarily focused on elderly patients; therefore, the applicability of the results to younger populations remains uncertain.

The study also did not investigate the potential risks associated with deeper anesthesia, such as hemodynamic instability or prolonged emergence from anesthesia. Future research should consider both the benefits and potential drawbacks of maintaining deeper anesthesia, aiming to optimize patient care while minimizing risks.

Moreover, the specific mechanisms underlying the relationship between anesthesia depth and postoperative delirium remain unclear. In-depth neurophysiological and biochemical studies are necessary to unravel the intricacies of this association. Identifying the underlying mechanisms will not only improve our understanding of postoperative delirium but may also lead to the development of targeted interventions for at-risk patients.

Conclusion

In conclusion, this randomized clinical trial has provided compelling evidence that maintaining deeper levels of anesthesia during major surgery is associated with a reduced incidence of postoperative delirium. This finding has important implications for perioperative care, patient safety, and healthcare resource utilization. While further research is needed to confirm and expand upon these results, this study opens a promising avenue for reducing the burden of postoperative delirium and improving the overall experience of patients undergoing major surgical procedures. It is crucial to continue exploring the mechanisms and clinical implications of this relationship to advance the field of anesthesiology and perioperative

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