Archives of Anesthesiology and Critical Care (In Press); x(x): xx-xx.

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Review Article

A Review of the Effect of Sevoflurane Versus Propofol for Maintenance of General Anesthesia during Cardiopulmonary Bypass

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ARTICLE INFO

Article history:
Received 01 January 2025
Revised 22 January 2025
Accepted 05 February 2025

Keywords:
Cardiac surgical procedures;
Cardiopulmonary bypass;
Cognitive dysfunction;
Inflammation;
Sevoflurane

ABSTRACT

Background: In cardiopulmonary bypass (CPB), there is a need to better maintain appropriate anesthesia due to the physiological and hemodynamic alterations induced by CPB. This review aimed to explore the effects of sevoflurane versus propofol in the management of patients undergoing cardiac surgeries with CPB.
Methods: The literature search was conducted in the international databases, including Cochrane, Science-Direct, Scopus, PubMed, and Google Scholar, from January 2012 to July 2024.
Results: According to the studies, sevoflurane was associated with a significantly shorter time to extubation, eye-opening, and command compliance with better intraoperative hemodynamic stability. It was superior in reducing oxygen demand and may be associated with less hypoxia in the aortic cross-clamp phase. In addition, sevoflurane produces more prominent myocardial protection, attenuates inflammatory response, and has a lower impact on cognitive function. On the other hand, propofol decreased the incidence and intensity of acute kidney injury and may be preferred over sevoflurane in patients at risk of postoperative nausea.
Conclusion: It seems in adults undergoing cardiac surgery with CPB, the class of sevoflurane is superior to propofol with regard to many perioperative and postoperative outcomes. However, more studies with larger sample sizes are needed to clarify this issue.

Introduction

It is estimated that 1 to 1.5 million heart surgeries are performed annually [1]. Most of the cases of cardiac surgery require the use of cardiopulmonary bypass (CPB) with cardioplegic arrest of the heart [2]. When Gibbon performed the first successful cardiac operation using the CPB circuit in 1953, it became a standard medical practice worldwide [3]. Studies have shown many changes in the microcirculation during cardiac surgery, especially when CPB is used [4]. Despite major advances in the past decades, CPB is still associated with an adverse inflammatory response affecting the brain, kidneys, liver, lungs, and heart, as well as postoperative cognitive dysfunction (POCD) and changes in hormone secretion and blood glucose levels [3, 5-7]. In cardiac surgery, inhalation anesthesia and propofol-based total intravenous anesthesia (TIVA) are two common anesthesia methods [5, 8]. Anesthetic agents may have protective effects against ischemia-reperfusion injury not only in the electrical phase but also during the inflammatory phase [7]. Several meta-analyses [9-14] and narrative review studies [15-17] have evaluated the

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effect of anesthesia methods on mortality and complications caused by cardiac surgery with different results. However, there is no conclusive review on the efficacy of propofol or inhalation anesthesia in the management of patients undergoing cardiac surgeries. In order to evaluate the most recent available anesthesia methods, we performed an updated review of randomized clinical trials (RCTs) to compare and summarize all available evidence and enable informed decision-making on the use of inhalational anesthetic sevoflurane versus propofol-based TIVA during CPB.

Methods

The literature search was conducted in the international databases, including Cochrane, Science-Direct, Scopus, PubMed, and Google Scholar. The relevant keywords and their combination for this research are as follows: "[(Sevoflurane [MeSH Terms]) AND (Propofol [MeSH Terms]) AND (Cardiac Surgical Procedures [MeSH Terms]) OR (Cardiopulmonary Bypass [MeSH Terms])]." We incorporated RCTs involving adults aged 18 years and older who underwent cardiac surgery with CPB and received anesthesia maintenance using either volatile anesthetic (sevoflurane) or propofol. The studies selected were published in English and were available in full text from January 2012 to July 2024.

Results

(Table 1) summarizes characteristics and results of RCTs done on adults (aged 18 years and above) who underwent cardiac surgery with CPB and were maintained under anesthesia using either the volatile anesthetic sevoflurane or propofol-based TIVA, comparing the clinical outcomes and adverse events of these two anesthesia methods. Biedrzycka et al. [18] conducted a study to evaluate the impacts of propofol and sevoflurane anesthesia on tissue saturation. In this manner, 60 subjects were divided into two groups. One group was administered intravenous propofol (n = 30), while the other group received inhaled sevoflurane (n = 30). Propofol anesthesia during cardiac surgery with CPB led to a more significant decrease in tissue saturation throughout the ischemic phase of the vascular occlusion test (VOT) in comparison to that of sevoflurane (P = 0.018).

Another investigation was conducted to examine cognitive function and delirium following sevoflurane or propofol anesthesia during valve replacement surgery. [5]. In this RCT, a total of 289 patients were randomly allocated to receive sevoflurane or propofol for anesthesia. The incidence of cognitive dysfunction was evaluated using four cognitive assessments prior to surgery and 7 to 14 days following the procedure. The occurrence of POCD in the sevoflurane group was considerably less than that in the TIVA group (P value = 0.044). In addition, the Katz index on the third day post-surgery showed a notable difference between the two groups (P value = 0.01). According to the results, sevoflurane anesthesia had a milder impact on cognitive abilities and daily living activities compared to propofol anesthesia. Nevertheless, the occurrence of delirium was similar in patients who received sevoflurane and those who underwent TIVA. Similarly, Jiang et al. [19] evaluated the impact of volatile anesthesia versus TIVA on postoperative delirium in adults undergoing valve surgery on the heart. In this research, 684 subjects were randomly allocated to receive anesthesia maintenance with either a volatile agent (sevoflurane or desflurane) (n = 341) or propofol-based TIVA (n = 343). There was no notable difference in the occurrence of delirium among the groups (within the first 7 days post-surgery), the length of delirium, the types of delirium, the 30-day mortality rate, pain scores, instances of major morbidity, the duration of mechanical ventilation, or the lengths of stay in intensive care unit (ICU) and the hospital.

The effects of sevoflurane and propofol on the duration of hospitalization and mortality rate have also been evaluated in another study. In this way, Landoni et al. [20] examined the effects of volatile anesthesia and TIVA in patients undergoing high-risk cardiac surgery. There was no significant difference between the two groups in prolonged ICU stay, mortality, or both.

Some studies evaluated the protective or detrimental effects of propofol and sevoflurane on body organs. Yang et al. [21] performed an RCT to evaluate sevoflurane and propofol for their myocardial protecting effects during cardiac valve replacement surgery with CPB. Seventy-three patients were randomly assigned to the propofol (n = 37) or sevoflurane (n = 36) group. To evaluate myocardial damage, cardiac troponin I (cTnI) and creatine kinase-myocardial band (CK-MB) levels were assessed prior to induction (T0), 30 minutes (T1), and 3 hours (T2) following aortic unclamping, as well as 24 hours (T3) and 48 hours (T4) post-surgery. The interleukin (IL)-6 and IL-10 levels as systemic inflammatory and anti-inflammatory markers were also measured at the aforementioned time points. CK-MB and cTnI from T1 to T4 and the levels of IL-6 and IL-10 from T1 to T2 were significantly lower in the sevoflurane group (P value < 0.05). Moreover, a higher ratio of automatic heart rate recovery, a shorter length of ICU or hospital stay, and less duration of mechanical ventilation were shown in the sevoflurane group (P < 0.05). Another study examined the impact of two anesthetics on the occurrence of acute kidney injury (AKI) after valvular cardiac surgery with CPB [22]. In this study, 112 patients were randomized to receive either propofol or sevoflurane anesthesia. In the propofol group, the

incidence of AKI, the postoperative levels of cystatin C at 24 and 48 hours, IL-6 measured 6 hours after the removal of the aortic cross-clamp, C-reactive protein (CRP) on the first postoperative day, and segmented neutrophil counts on the third postoperative day were notably reduced (P value < 0.05). The incidence of severe renal impairment was notably greater in the sevoflurane group than in the propofol group (P value < 0.05).

O'Gara et al. [23] conducted an RCT in order to assess the preventive effects of anesthetics on lung injury in cardiac surgery. A total of 40 patients were randomized in a 1:1 ratio to receive anesthetic maintenance with sevoflurane or propofol. According to the results, IL-8 plasma concentration was significantly lower (P value = 0.04), and there was a significantly smaller increase in the receptor for advanced glycation end products (RAGE) in the sevoflurane group compared with propofol (P value = 0.03) after bypass. In addition, there was no significant difference between the groups in the concentration of tumor necrosis factor alpha (TNFα) in bronchoalveolar lavage, postoperative pulmonary complications, and hypoxemia.

Maintaining hemodynamic stability is an important consideration during anesthesia. In a study, the effect of sevoflurane and propofol on the hemodynamics of patients during cardiac surgery was evaluated [24]. A total of 40 patients were assigned randomly into two groups to receive propofol (n = 20) or sevoflurane (n = 20). The mean arterial pressure (MAP), oxygen demand, energy consumption, cardiac index, and total peripheral resistance were significantly lower in the sevoflurane group compared with the propofol group (P value < 0.05).

Nausea and vomiting, an important complication after surgery, have always been challenging. Aykut et al. [25] compared propofol and sevoflurane anesthesia in terms of postoperative nausea-vomiting (PONV) in cardiac surgery. Sixty-two patients undergoing coronary artery bypass graft (CABG) surgery were included in the study. After standard induction of anesthesia, the incidence of PONV between 0-6 hours (early) and 6-24 hours (late) after extubation was compared as the primary outcome. The incidence of delirium was analyzed as a secondary outcome for similar periods. Postoperative nausea (PN) in the early post-extubation period was significantly higher in the sevoflurane group (P value = 0.031). The incidence of delirium was similar between the groups in both periods.

Flinspach et al. [26] investigated sevoflurane versus propofol after cardiac valve surgery in terms of time to extubation and postoperative care. A significantly earlier extubation (P value < 0.001), eye opening (P value < 0.001), and command compliance (P value < 0.001) was shown in the application of sevoflurane sedation. However, there were not any significant differences between the two groups in terms of complications and CPB time.

Table 1- Overview of RCTs

Year	Reference	Location	Type of volatile for maintenance (number of patients)	Type of TIVA for maintenance (number of patients)	Outcomes	Limitations
2014	Landoni et al. [20]	Italy	Sevoflurane (100)	Propofol (100)	• Postoperative cardiac troponin release (P value = 0.6) • Mortality during one year (P value > 0.05) • Re-hospitalizations (P value > 0.05) • Adverse cardiac events (P value > 0.05)	• The study may have been underpowered due to overly optimistic assumptions about the expected effect size • The study was not powered to detect differences in mortality at 30 days and 1 year • The inclusion of patients with valve surgery may have diluted any potential benefits of sevoflurane, and this study does not rule out the possibility that sevoflurane may be effective in the broader

						cardiac surgery population
2014	Yoo et al. [22]	Korea	Sevoflurane (56)	Propofol (56)	• A decrease in the occurrence of AKI was observed in the propofol group, along with lower postoperative levels of cystatin C at 24 and 48 hours, IL-6 measured six hours post-removal of the aortic cross-clamp, CRP levels on the first day after surgery, and segmented neutrophil counts on the third day following the operation (P value < 0.05) • More severe renal dysfunction in the sevoflurane group (P value < 0.05)	• Lack of blinding for the anesthesiologist • Small sample size and lower than expected incidence of AKI • Single-center design • Limited generalizability to high-risk patients for AKI
2016	Biedrzycka et al. [18]	NA	Sevoflurane (30)	Propofol (30)	• Lower tissue saturation during ischemia in the propofol group (P value = 0.01)	• Lack of standardization in muscle oximetry measurements • Lack of cardiac output measurements • Failing to examine the impact of extended ischemia on muscle saturation
2017	Yang et al. [21]	China	Sevoflurane (36)	Propofol (37)	• Reduced consumption of vasoactive medications, an increased ratio of automatic heart rate recovery, a shorter duration of ICU or hospital stay, as well as a decreased length of mechanical ventilation was found in the sevoflurane group (P value < 0.05) • CK-MB and cTnI from T1 to T4 and the levels of IL-6 and IL-10 from T1 to T2 were significantly lower in the sevoflurane group (P value < 0.05)	• Lack of blinding for the anesthesiologists • Small sample size • Lack of clinically important positive outcomes • Short CPB time, need for further study on longer CPB times and multi-valve replacements
2022	O'Gara et al. [23]	United States	Sevoflurane (18)	Propofol (22)	• No significant difference between the groups in the concentration of TNFα	• Small sample size • Lack of protocolization for induction and postoperative sedation

					in bronchoalveolar lavage (P value > 0.05) • Lower post-bypass concentration of plasma IL-8 in the sevoflurane group (P value = 0.04) • Smaller increase in the receptor for advanced glycation end products in the sevoflurane group after bypass (P value = 0.03)	• Lack of blinding • Limited sampling time points to capture the peak pulmonary inflammatory response
2023	Baiterek et al. [24]	Kazakhstan	Sevoflurane (20)	Propofol (20)	• Lower oxygen consumption in the sevoflurane group (P value < 0.05)	• Single-center study • Small sample size
2023	Duan et al. [5]	China	Sevoflurane (144)	Propofol (145)	• Lower POCD in the sevoflurane group (P value = 0.04). • Lower Katz index on day 3 after surgery in the sevoflurane group (P = 0.01) • Delirium occurrence (P value > 0.05)	• The estimated incidence of POCD used for power calculation was higher than the actual incidence • There was a high rate of loss to follow-up for the 3-month POCD assessment • The study only included patients undergoing aortic valve replacement surgery
2023	Jiang et al. [19]	China	Sevoflurane or desflurane (337)	Propofol (339)	• Delirium occurrence (P value > 0.05)	• The study did not assess the severity of delirium • Single-center study
2024	Flinspach et al. [26]	Germany	Sevoflurane (47)	Propofol (47)	• Shorter time until eye opening (P value < 0.001), command compliance (P value < 0.001), and extubation (P value < 0.001) in the sevoflurane group • Delirium occurrence (P value > 0.05) • The time to discharge to the normal ward (P value > 0.05) • CPB time (P value> 0.05)	• Single-center study • Expertise of the research center may not generalize to other institutions • Limited to elective heart valve surgery patients • Unable to assess for pneumonia due to short duration of sedation • Small sample size as a pilot study
2024	Aykut et al. [25]	Turkey	Sevoflurane (31)	Propofol (31)	• More PN in the early post-extubation period in the sevoflurane group (P value = 0.031)	• Single-center study • PONV was only evaluated as present/absent, not graded

	• Delirium occurrence (P value > 0.05)	• Hypoactive delirium may have been overlooked • The sample size and patient risk profile differed from the reference study

AKI: acute kidney injury; CK-MB: creatine kinase isoenzyme; CPB: cardiopulmonary bypass; cTnI: cardiac troponin I; ICU: intensive care unit; IL: interleukin; N/A: not available; PN: postoperative nausea; POCD: postoperative cognitive dysfunction; PONV: postoperative nausea-vomiting; RCT: randomized clinical trial; TIVA: total intravenous anesthesia; TNFα: tumor necrosis factor alpha.

Discussion

This review provides an overview of the effectiveness of propofol-based TIVA or inhalational anesthetic sevoflurane in the management of patients undergoing cardiac surgery with CPB. Several studies reported that sevoflurane appears to offer some advantages [5, 18, 21, 23-24, 26]. According to the findings, sevoflurane is associated with a significantly shorter time to extubation, eye-opening, and command compliance [26], and better intraoperative hemodynamic stability with superiority in reducing oxygen demand and energy expenditure [24]. While CPB, especially the aortic cross-clamp phase, is accompanied by reduced tissue oxygenation and microvascular reactivity in the thenar muscle, sevoflurane anesthesia may be associated with less tissue hypoxia [18] and a lower impact on cognitive function and independence in daily life activities [5]. Furthermore, sevoflurane produces more prominent myocardial protection and attenuates inflammatory response, resulting in shorter duration of mechanical ventilation and hospitalization [21]. In addition, sevoflurane has been found to decrease the levels of two plasma biomarkers involved in lung inflammation and postoperative pulmonary complications [23], compared with propofol-based TIVA in patients undergoing cardiac surgery with CPB.

On the other hand, propofol may be selected as an anesthetic in specific patient contexts. According to the results, the use of propofol for anesthesia maintenance decreases both the incidence and severity of AKI in patients undergoing cardiac surgery with CPB when compared to sevoflurane anesthesia [22]. Furthermore, propofol may be preferred over sevoflurane in cardiac surgery patients at risk of PN [25].

The use of the volatile anesthetic sevoflurane for maintaining anesthesia, when compared to propofol-based TIVA, did not result in a reduction in the occurrence of postoperative delirium in adult patients undergoing cardiac surgery with CPB [5,19]. Also, sevoflurane did not demonstrate any positive impact on the combined outcome of extended ICU duration and mortality in patients undergoing high-risk cardiac surgery [20].

Few studies were included in this review; some studies had limited sample sizes and failed to implement suitable blinding techniques. The main strength of this review is that we included RCTs evaluating the effects of inhalation (sevoflurane) versus intravenous anesthesia with a special focus on propofol during CPB.

Conclusion

It seems in adults undergoing cardiac surgery with CPB, the class of sevoflurane is superior to propofol with regard to many perioperative and postoperative outcomes. However, more studies with larger sample sizes are needed to clarify this issue, and it should be noted that the selection of an appropriate anesthetic agent depends on the medical status of the patient.

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