ISSN: 3049-7361

Review Article

Journal of Clinical Surgery and Anesthesia

Anesthetic Preconditioning and Myocardial Protection in Coronary Artery Bypass Grafting: A Review of Mechanisms and Clinical Outcomes

Vedhsai Thiriveedi

Nashua High School South, Nashua, New Hampshire, USA

Corresponding author
Vedhsai Thiriveedi, Nashua High School South, Nashua, New Hampshire, USA.

Received: July 28, 2025; **Accepted:** August 04, 2025; **Published:** August 10, 2025

ABSTRACT

Coronary artery bypass grafting (CABG) carries a high risk of perioperative myocardial injury due to ischemia-reperfusion insult. Volatile anesthetics, including sevoflurane and isoflurane, have been found to mimic ischemic preconditioning and provide myocardial protection by activating mitochondrial and anti-inflammatory signaling pathways. This review examines peer-reviewed clinical trials, meta-analyses, and mechanistic studies to assess the evidence supporting anesthetic preconditioning in CABG. Mechanistically, volatile anesthetics act via mitochondrial KATP channel activation, modulation of apoptosis-related proteins, and suppression of systemic inflammation. Clinically, they are associated with reduced postoperative troponin levels, improved ventricular function, and shorter ICU stays compared to total intravenous anesthesia (TIVA). Although large-scale trials such as the MYRIAD study report mixed mortality outcomes, short-term cardioprotective effects are consistently observed. These findings support the strategic use of volatile anesthetics during CABG to enhance myocardial preservation and motivate further targeted research.

Introduction

Coronary artery bypass grafting (CABG) is a widely performed surgical procedure for ischemic heart disease. Despite its clinical benefits, CABG exposes the myocardium to ischemia-reperfusion injury (IRI), a process associated with oxidative stress, inflammation, and myocardial apoptosis. These injuries often manifest as postoperative cardiac dysfunction and contribute to increased morbidity and mortality.

Anesthetic preconditioning refers to the use of volatile anesthetics to simulate the protective effects of ischemic preconditioning. Agents like isoflurane and sevoflurane have been shown to enhance myocardial tolerance to ischemia. This review explores the cellular and molecular pathways implicated in anesthetic preconditioning and critically evaluates clinical evidence comparing volatile anesthetics to total intravenous anesthesia (TIVA) in the context of CABG, with a focus on myocardial protection and patient outcomes. Refining anesthetic protocols to improve postoperative outcomes is central to perioperative cardiovascular care. Therefore, understanding the pharmacologic basis and translational application of anesthetic preconditioning is essential for optimizing perioperative cardiovascular care.

Mechanisms of Anesthetic Preconditioning

Volatile anesthetics activate mitochondrial ATP-sensitive potassium (KATP) channels, stabilizing mitochondrial membranes and reducing calcium overload. This mechanism prevents the opening of the mitochondrial permeability transition pore (mPTP), a critical mediator of cell death during reperfusion. Additionally, anesthetics generate low levels of reactive oxygen species (ROS), which activate cardioprotective signaling cascades involving protein kinase C (PKC) and phosphatidylinositol 3-kinase (PI3K)/Akt pathways. These cascades promote anti-apoptotic effects and improve myocardial recovery after ischemia.

Experimental studies suggest that anesthetic preconditioning shares many similarities with ischemic preconditioning, involving a priming phase where protective molecular pathways are activated before a major ischemic event. Notably, volatile

Citation: Vedhsai Thiriveedi. Anesthetic Preconditioning and Myocardial Protection in Coronary Artery Bypass Grafting: A Review of Mechanisms and Clinical Outcomes. J Clin Surg Anesth. 2025. 3(3): 1-3. DOI: doi.org/10.61440/JCSA.2025.v3.35

anesthetic preconditioning has been shown to modulate oxidative stress and nitric oxide bioavailability in patients undergoing CABG, suggesting enhanced endothelial function and cytoprotective signaling [1]. This modulation likely contributes to the preservation of vascular tone and myocardial oxygen delivery during reperfusion. Additionally, the modulation of calcium homeostasis by volatile anesthetics help preserve intracellular signaling and contractile function in cardiomyocytes under stress. For example, sevoflurane has been shown to reduce myocardial injury by inhibiting cyclooxygenase-2 (COX-2) through a caveolin-3–dependent pathway, reinforcing its role in modulating inflammatory signaling [2].

Anesthetics also modulate apoptosis-related proteins, decreasing pro-apoptotic Bax and increasing anti-apoptotic Bcl-2 expression. Furthermore, volatile agents reduce systemic inflammation by suppressing cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α). Preservation of endothelial function, partly via enhanced nitric oxide (NO) production, improves coronary perfusion and limits microvascular damage during reperfusion. These anti-inflammatory effects may also mitigate endothelial activation and leukocyte adhesion, two key contributors to microvascular injury during and after CPB.

Clinical Evidence in CABG Patients

Several studies have evaluated the impact of anesthetic technique on myocardial protection during CABG. One randomized controlled trial found that patients receiving sevoflurane had significantly lower postoperative troponin I levels compared to those receiving propofol, suggesting reduced myocardial injury [3]. A comprehensive meta-analysis that reviewed over 1,900 patients concluded that volatile anesthetics decreased cardiac enzyme release, shortened ICU stay, and lowered in-hospital mortality [4]. Improvements in left ventricular function have also been documented. A study comparing sevoflurane with a sevoflurane-propofol combination observed differences in postoperative renal function, highlighting how anesthetic choice may influence not only myocardial preservation but also multiorgan protection, including renal outcomes [5]. These results lend support to the hypothesis that volatile anesthetics facilitate myocardial recovery.

Evidence from inflammatory biomarker analysis further supports the cardioprotective role of volatile anesthetics. A study observed that patients receiving sevoflurane during CABG had reduced levels of IL-6 and TNF-α, which were associated with improved postoperative hemodynamics and fewer complications [6]. Additionally, perioperative use of volatile anesthetics has been associated with better microcirculatory flow, reduced incidence of arrhythmias, and shorter time to extubation in select patient populations. Several observational studies have even suggested a reduced incidence of postoperative atrial fibrillation, though this effect remains controversial and merits more rigorous, large-scale investigation to establish clinical relevance and consistency of outcomes.

Nevertheless, this consensus is not universal, as evidenced by the MYRIAD trial-a large multicenter RCT with over 5,400 participants, found no significant difference in one-year mortality between volatile anesthetic and TIVA groups [7]. Still, subgroup analyses indicated possible benefit among patients with impaired cardiac function. Furthermore, differences in anesthetic protocols, including agent type, exposure duration, and timing relative to cardiopulmonary bypass, may account for some of the heterogeneity in outcomes observed across studies.

Comparison: Volatile Anesthetics vs. TIVA

Volatile anesthetics consistently outperform TIVA in reducing cardiac enzyme release and improving short-term cardiac function. They offer anti-inflammatory effects and preserve endothelial function better than propofol-based regimens. However, TIVA offers superior hemodynamic stability and remains preferred in some patient populations, particularly those with contraindications to volatile agents. Propofol's antioxidant properties and its potential role in modulating GABAergic signaling and mitochondrial protection should also not be overlooked, though its lack of preconditioning effects limits its cardioprotective capacity.

Comparative trials emphasize the importance of individualizing anesthetic plans. While volatile agents confer myocardial benefits, their use must be balanced against risks such as myocardial depression, vasodilation, and delayed emergence in hemodynamically unstable patients. TIVA, with its favorable recovery profile and predictable pharmacokinetics, may be more appropriate in patients with significant left ventricular hypertrophy, severe aortic stenosis, or other structural cardiac abnormalities. Ultimately, the decision should incorporate patient-specific factors, surgical complexity, and institutional experience.

Limitations and Confounding Factors

Interpretation of the data is complicated by heterogeneity in patient populations, surgical techniques, and anesthetic protocols. Factors such as cardiopulmonary bypass time, cross-clamp duration, and baseline cardiac function influence outcomes independently of anesthetic choice. Moreover, short-term biochemical markers like troponin may not reliably predict long-term cardiac health. The timing, concentration, and duration of anesthetic exposure also vary between studies, reducing comparability.

Many of the studies assessing anesthetic preconditioning rely on surrogate endpoints such as enzyme release or LVEF, rather than hard outcomes like survival or major adverse cardiovascular events (MACE). Additionally, perioperative factors like fluid management, vasoactive medication use, and temperature control further complicate the isolation of anesthetic effects. The complex interplay between surgery-induced inflammation and anesthesia-mediated protection underscores the need for mechanistic studies using advanced imaging, biomarker profiling, and genomic tools.

Discussion

Volatile anesthetic preconditioning, by engaging mechanisms such as COX-2 inhibition through caveolin-3 and ferroptosis modulation, represents a biologically targeted approach to myocardial protection during CABG. Volatile anesthetics should be considered as part of a comprehensive myocardial protection strategy during CABG, especially for patients at higher risk of IRI. Standardization of volatile anesthetic protocols may improve consistency in clinical outcomes. Future trials should focus on

identifying which subgroups derive the most benefit and on establishing long-term outcome data. Integration of anesthetic preconditioning with pharmacologic agents and other surgical techniques could further enhance myocardial protection.

The use of multimodal cardioprotection strategies, combining anesthetic preconditioning with

ischemic postconditioning, beta-blockers, statins, and antioxidant supplementation, may further reduce perioperative myocardial damage. Enhanced recovery after surgery (ERAS) protocols should consider incorporating volatile anesthetic regimens when appropriate. In addition, anesthesiologists should engage in shared decision-making with surgical teams to optimize the intraoperative plan and post-CPB myocardial reperfusion strategies.

Conclusion

Anesthetic preconditioning represents a promising, non-invasive approach to reduce myocardial injury during CABG. Volatile anesthetics like sevoflurane and isoflurane exert protective effects through mitochondrial stabilization, anti-inflammatory signaling, and improved coronary perfusion. While short-term benefits such as lower cardiac enzyme levels and improved ventricular function are well supported, long-term survival advantages remain inconclusive.

Given the high volume of CABG procedures globally, optimizing anesthetic strategies holds significant implications for patient outcomes. Future investigations should seek to clarify the patient populations and intraoperative conditions under which anesthetic preconditioning provides maximal benefit [8].

References

1. Dharmalingam SK, Amirtharaj GJ, Ramachandran A, Korula M. Volatile anesthetic preconditioning modulates oxidative stress and nitric oxide in patients undergoing coronary artery bypass grafting. Ann Card Anaesth. 2021. 24: 319-326.
2. Zhao J, Wang F, Zhang Y, Jiao L, Lau WB, et al. Sevoflurane preconditioning attenuates myocardial ischemia/reperfusion injury via caveolin-3-dependent cyclooxygenase-2 inhibition. Circulation. 2013. 128: 121-129.
3. Hou T, Ma H, Wang H, Chen C, Ye J, et al. Sevoflurane preconditioning attenuates hypoxia/reoxygenation injury of H9c2 cardiomyocytes by activation of the HIF-1/PDK-1 pathway. PeerJ. 2020. 8: 10603.
4. Bonanni A, Signori A, Alicino C, Mannucci I, Grasso MA, et al. Volatile Anesthetics versus Propofol for Cardiac Surgery with Cardiopulmonary Bypass: Meta-analysis of Randomized Trials. Anesthesiology. 2020. 132: 1429-1446.
5. Jose RL, Damayanathi D, Unnikrishnan KP, Suneel PR. A comparison of sevoflurane versus sevoflurane-propofol combination on renal function in patients undergoing valvular heart surgery-A prospective randomized controlled pilot study. Ann Card Anaesth. 2021. 24: 172-177.
6. Cardoso TA, Kunst G, Neto CN, de Ribamar Costa Júnior J, Silva CG, et al. Effect of sevoflurane on the inflammatory response during cardiopulmonary bypass in cardiac surgery: the study protocol for a randomized controlled trial. Trials. 2021. 22: 25.
7. Landoni G, Lomivorotov VV, Nigro Neto C, Monaco F, Pasyuga VV, et al. Volatile Anesthetics versus Total Intravenous Anesthesia for Cardiac Surgery. N Engl J Med. 2019. 380: 1214-1225.
8. Sheng H, Xiong J, Yang D. Protective Effect of Sevoflurane Preconditioning on Cardiomyocytes Against Hypoxia/Reoxygenation Injury by Modulating Iron Homeostasis and Ferroptosis. Cardiovasc Toxicol. 2023. 23: 86-92.