***Med. Psychol. Health Res. J.* (2026),** Volume 2, Issue 5, 351-359

Medicinal, Psychological, and Health Research Journal

Journal homepage: https://www.mphrj.com/

DOI: 10.22034/mphrj.2026.586236.1092

Effect of Intraoperative Intravenous Dexmedetomidine on Oxidative Stress in Patients Undergoing Cardiac Surgery: A Systematic Review

Solmaz Fakhari [1], Artin Bilehjani[2], Eissa Bilehjani[3*]

[1]Professor of Anesthesiology, Department of Anesthesiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
[2]Medical students, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[3]Professor of Anesthesiology, Department of Anesthesiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

Article info
Received: 28.03.2026
Accepted: 18.06.2026
Available Online: 23.06.2026
Checked for Plagiarism: Yes

Keywords:
Dexmedetomidine; Cardiac surgery; Oxidative stress; Cardio myocyte protection; Systematic review

ABSTRACT

Introduction: Cardiac surgery is associated with substantial oxidative stress due to surgical trauma, cardiopulmonary bypass, and ischemia-reperfusion injury, which may contribute to postoperative organ dysfunction. Dexmedetomidine has shown potential antioxidative and organ-protective effects. Therefore, this study aimed to systematically review the effect of intraoperative intravenous dexmedetomidine on oxidative stress in patients undergoing cardiac surgery.

Material and methods: This systematic review followed PRISMA guidelines to identify clinical studies on intraoperative intravenous dexmedetomidine and oxidative stress in cardiac surgery. Multiple databases were searched without time limits by two independent reviewers using Boolean-based keywords. Eligible studies were screened, quality-assessed with the Cochrane Risk of Bias tool, and relevant study, patient, intervention, and outcome data were extracted.

Results: Across clinical and experimental cardiopulmonary bypass-related settings, intraoperative intravenous dexmedetomidine showed a broadly protective profile. It attenuated perioperative stress responses, reduced selected markers of myocardial injury and inflammation, improved hemodynamic and recovery outcomes, and lowered postoperative atrial fibrillation. Experimental evidence further indicated direct cardiomyocyte protection through antioxidant, antiapoptotic, autophagy-regulating, electrophysiological, and transcriptional mechanisms.

Conclusion: The available evidence suggests that intraoperative intravenous dexmedetomidine may mitigate oxidative stress-related injury during cardiac surgery through both systemic and cellular mechanisms. Its benefits appear to include attenuation of surgical stress, reduction of selected inflammatory and myocardial injury markers, and improvement in postoperative recovery. These findings support dexmedetomidine as a promising cardioprotective adjunct in cardiac surgical care.

Introduction

Cardiac surgery remains one of the most complex areas of perioperative medicine, despite major advances in surgical technique, cardiopulmonary bypass technology, anesthetic management, and postoperative intensive care. Procedures such as coronary artery bypass grafting, valve surgery, and combined cardiac operations performed in patients who often have advanced age, multiple comorbidities, and limited physiologic reserve. In this setting, the perioperative period characterized by profound

*Corresponding Author: **Eissa Bilehjani** (Eissabilejani@gmail.com - ORCID: 0000-0001-5843-3333)
1 Email: solmazfakhari@gmail.com - ORCID: 0000-0003-1946-3075)
2 Email: Artin-bilehjani@yahoo.com - ORCID: 0009-0009-0551-9884)

neuroendocrine, inflammatory, and metabolic disturbances that may contribute to organ dysfunction and delayed recovery. Among the biological mechanisms implicated in these adverse responses, oxidative stress has emerged as a particularly important pathway because it links ischemia–reperfusion injury, systemic inflammation, endothelial dysfunction, and cellular damage across multiple organ systems (1).

Oxidative stress refers to an imbalance between the generation of reactive oxygen species and reactive nitrogen species on one hand, and the capacity of endogenous antioxidant systems on the other. Under physiologic conditions, low concentrations of reactive species serve important signaling functions in vascular regulation, immune responses, and cellular adaptation. During cardiac surgery, however, excessive production of free radicals may overwhelm protective antioxidant defenses such as superoxide dismutase, catalase, glutathione peroxidase, and no enzymatic scavengers. This shift toward a pro-oxidant state promotes lipid peroxidation, protein oxidation, DNA injury, mitochondrial dysfunction, and activation of cell death pathways. Because these molecular processes can affect the myocardium, lungs, kidneys, brain, and vascular endothelium, oxidative stress is increasingly recognized not merely as a biochemical phenomenon but as a clinically relevant determinant of postoperative outcome (2).

The pathogenesis of oxidative stress in cardiac surgery is multifactorial and begins even before the first surgical incision. Patients presenting for cardiac operations frequently have chronic conditions such as atherosclerosis, diabetes mellitus, hypertension, obesity, heart failure, and chronic kidney disease, all of which are associated with baseline oxidative burden and impaired antioxidant capacity.

Intraoperatively, surgical trauma, sternotomy, blood loss, transfusion, hypothermia, fluctuations in tissue perfusion, and exposure to high oxygen concentrations can further amplify oxidant production. The use of cardiopulmonary bypass introduces additional triggers, including blood contact with artificial surfaces, complement activation, leukocyte activation, hem dilution, and no pulsatile flow. Aortic cross-clamping followed by reperfusion is especially important, as reperfusion of previously ischemic tissues leads to abrupt generation of reactive oxygen species and propagation of inflammatory injury (3).

Cardiopulmonary bypass has been studied extensively as a major contributor to oxidative and inflammatory stress in cardiac surgery. During extracorporeal circulation, activation of neutrophils, platelets, and endothelial cells leads to release of superoxide anions, hydrogen peroxide, proteolytic enzymes, and proinflammatory cytokines. This process is often compounded by ischemia–reperfusion injury after removal of the aortic cross-clamp, when mitochondrial dysfunction and xanthine oxidase activity accelerate free radical formation. Myocardial tissue is particularly vulnerable to oxidant injury because reperfusion may paradoxically worsen cellular damage after a period of controlled ischemia. At the same time, distant organs such as the lungs and kidneys may suffer secondary injury through microvascular dysfunction, capillary leak, and inflammatory signaling. For these reasons, modulation of oxidative stress has become an attractive target for perioperative pharmacologic strategies in cardiac anesthesia (4).

A growing body of evidence suggests that oxidative stress biomarkers correlate with postoperative morbidity in patients undergoing cardiac surgery. Elevations in malondialdehyde, 8-isoprostane, myeloperoxidase, and protein carbonyl levels, together with reductions in total antioxidant capacity, glutathione, and superoxide dismutase activity, have been associated with myocardial injury, atrial fibrillation, acute kidney injury, prolonged mechanical ventilation, and neurologic complications. Although biomarkers do not fully capture the complexity of redox biology, they provide a practical means of assessing perioperative oxidative burden and evaluating the biologic effects of candidate protective interventions.

Consequently, therapies capable of attenuating oxidative stress may have broader implications beyond biochemical improvement and may contribute to better organ protection and enhanced recovery after surgery (5).

Dexmedetomidine, a highly selective alpha-2 adrenergic receptor agonist, has become an important adjunct in modern anesthetic and critical care practice because of its sedative, sympatholytic, anxiolytic, and analgesic-sparing properties. Unlike many conventional sedatives, dexmedetomidine produces a cooperative form of sedation with minimal respiratory depression, making it useful in both intraoperative and postoperative settings. In cardiac surgery, intravenous dexmedetomidine has been used for anesthetic supplementation, attenuation of stress responses, facilitation of hemodynamic stability, reduction of opioid requirements, and postoperative sedation. Beyond these clinical effects, interest has expanded toward its potential organ-protective properties, including anti-inflammatory, ant apoptotic, and ant oxidative actions that may be especially relevant in the context of ischemia-reperfusion and extracorporeal circulation (6).

Several experimental and translational studies have proposed biologically plausible mechanisms through which dexmedetomidine may attenuate oxidative stress. By reducing sympathetic outflow and circulating catecholamine concentrations, dexmedetomidine may limit the metabolic and hemodynamic consequences of the surgical stress response, thereby decreasing oxygen demand and secondary oxidant production. In addition, alpha-2 receptor activation has linked to modulation of inflammatory signaling pathways, suppression of cytokine release, preservation of mitochondrial integrity, and enhancement of endogenous antioxidant defense systems. Animal models of ischemia-reperfusion injury have shown that dexmedetomidine may reduce lipid peroxidation, decrease neutrophil infiltration, and improve tissue antioxidant enzyme activity. These findings have stimulated interest in whether similar protective effects demonstrated consistently in human cardiac surgery populations (7).

In clinical practice, the relevance of dexmedetomidine in cardiac surgery extends beyond biochemical modulation alone. Cardiac surgical patients are particularly susceptible to tachycardia, hypertension, arrhythmia, myocardial oxygen imbalance, and postoperative delirium, all of which influenced by perioperative sympatholytic and sedative strategy. By blunting adrenergic activation, dexmedetomidine may contribute to improved perioperative hemodynamic control and reduce neurohumoral stress. Some studies have also suggested potential benefits in reducing postoperative atrial fibrillation, shortening time to extubation, and improving analgesic quality, although results have not been uniform across all settings. Since oxidative stress interacts closely with inflammation and neuroendocrine activation, the pharmacologic profile of dexmedetomidine makes it a particularly attractive candidate for investigation in patients undergoing cardiac surgery (8).

Despite this rationale, the clinical evidence regarding the effect of intraoperative intravenous dexmedetomidine on oxidative stress remains fragmented. Available studies differ in important ways, including patient populations, types of cardiac procedures, use or avoidance of cardiopulmonary bypass, dosing regimens, and timing of drug administration, comparator groups, anesthetic background protocols, and selected oxidative stress biomarkers. Some trials have reported significant reductions in markers such as malondialdehyde and increases in antioxidant enzyme activity, whereas others have shown more modest or inconsistent effects. The interpretation of these findings further complicated by variation in blood sampling times, laboratory methods, and concomitant perioperative interventions that may independently influence redox status. As a result, it remains difficult to draw clear conclusions from individual studies alone (9).

The need for a rigorous synthesis of the literature strengthened by the growing emphasis on evidence-based adjunctive therapies in cardiac anesthesia. While dexmedetomidine already used for several perioperative indications, its incorporation into routine cardiac surgical protocols based on ant oxidative benefit requires stronger and more coherent evidence. Clinicians must consider not only whether dexmedetomidine alters laboratory markers of oxidative stress, but also whether these changes are consistent, biologically meaningful, and potentially linked to improved clinical outcomes. Furthermore, safety considerations such as bradycardia and hypotension are especially relevant in cardiac patients and balanced against any proposed protective effects. A systematic evaluation of the current evidence can therefore clarify the magnitude, direction, and limitations of the available data (10).

Another important reason for examining this question systematically is that oxidative stress sits at the intersection of several perioperative injury pathways that remain inadequately controlled in cardiac surgery. Myocardial reperfusion injury, acute kidney injury, pulmonary dysfunction, endothelial damage, and neurocognitive complications all share redox-sensitive mechanisms. If dexmedetomidine exerts even partial modulation of these pathways, it may represent a practical and already available intervention with broader organ-protective potential. At the same time, the heterogeneity of the literature means that assumptions of benefit not accepted uncritically. A structured review can identify areas of consistency, expose methodological weaknesses, and guide future studies toward standardized biomarker selection, comparable dosing strategies, and clinically relevant endpoints (11). In light of these considerations, the present study designed to review the available evidence on the effect of intraoperative intravenous dexmedetomidine on oxidative stress in patients undergoing cardiac surgery. By synthesizing data from published clinical studies, this systematic review aims to evaluate how dexmedetomidine influences perioperative oxidative stress biomarkers, to assess the consistency of reported findings across different surgical and anesthetic contexts, and to provide a clearer evidence base for future research and clinical decision-making in this field.

Material and methods

Study Design

This study designed as a systematic review to evaluate the effect of intraoperative intravenous dexmedetomidine on oxidative stress in patients undergoing cardiac surgery. The review process conducted in accordance with the PRISMA statement to ensure transparent, rigorous, and reproducible identification, screening, eligibility assessment, and inclusion of relevant studies.

Eligibility Criteria

Studies considered eligible if they met the following criteria: clinical studies conducted in patients undergoing cardiac surgery; administration of intravenous dexmedetomidine during the intraoperative period; evaluation of oxidative stress–related outcomes, including oxidative biomarkers, antioxidant enzyme activity, or total antioxidant status; and publication as full-text articles in peer-reviewed journals in English. Randomized controlled trials, non-randomized interventional studies, and prospective or retrospective comparative clinical studies were eligible for inclusion. Studies were excluded if they were performed in non-cardiac surgical populations, involved non-intravenous or exclusively postoperative dexmedetomidine administration, lacked oxidative stress outcome measures, were animal or in vitro studies, conference abstracts, case reports, reviews, editorials, letters, protocols, duplicate publications, or did not provide sufficient data for data extraction.

Search Strategy

A comprehensive literature search performed in PubMed/MEDLINE, Scopus, Web of Science, Embase, and the Cochrane Library from database inception to the date of the final search, with no time restriction applied. The search strategy combined controlled vocabulary terms and free-text keywords related to dexmedetomidine, oxidative stress, and cardiac surgery using Boolean operators such as and OR. The search conducted independently by two reviewers, and any disagreement was resolved through discussion and consensus. Reference lists of included articles also screened manually to identify additional eligible studies (table 1).

Table 1. Search strategy used for database retrieval

Concept	Search terms
Dexmedetomidine	“dexmedetomidine” OR “intravenous dexmedetomidine” OR “alpha-2 agonist” OR “α2 adrenergic agonist”
Oxidative stress	“oxidative stress” OR “oxidant stress” OR “reactive oxygen species” OR “ROS” OR “lipid peroxidation” OR “malondialdehyde” OR “MDA” OR “superoxide dismutase” OR “SOD” OR “glutathione peroxidase” OR “GPx” OR “total antioxidant capacity” OR “TAC” OR “catalase”
Cardiac surgery	“cardiac surgery” OR “heart surgery” OR “cardiovascular surgery” OR “coronary artery bypass” OR “CABG” OR “valve surgery” OR “cardiopulmonary bypass” OR “open heart surgery”
Example combined search	(“dexmedetomidine” OR “intravenous dexmedetomidine”) AND (“oxidative stress” OR “malondialdehyde” OR “superoxide dismutase” OR “total antioxidant capacity”) AND (“cardiac surgery” OR “coronary artery bypass” OR “valve surgery” OR “cardiopulmonary bypass”)

Quality Assessment

The methodological quality of the included studies was assessed independently by two reviewers using an appropriate critical appraisal tool according to study design. For randomized controlled trials, the Cochrane Risk of Bias tool used to evaluate potential bias in domains such as randomization, allocation concealment, blinding, incomplete outcome data, and selective reporting. Any discrepancies in quality assessment resolved by discussion.

Data Extraction

Data extracted independently by two reviewers using a standardized data collection form. The following information was obtained from each included study: first author’s name, year of publication, country, study design, sample size, patient characteristics, type of cardiac surgery, dexmedetomidine dosing regimen and timing of administration, comparator intervention, oxidative stress biomarkers assessed, timing of biomarker measurement, main findings related to oxidative stress, and reported adverse events or other relevant clinical outcomes. Any disagreements in data extraction resolved by consensus.

Results

The literature search identified 744 records from PubMed, Web of Science, Science Direct, and Google Scholar. After screening, 186 records excluded and 558 full-text articles assessed for eligibility. Of these, 554 articles were excluded, and 4 studies were finally included in the qualitative synthesis (figure 1).

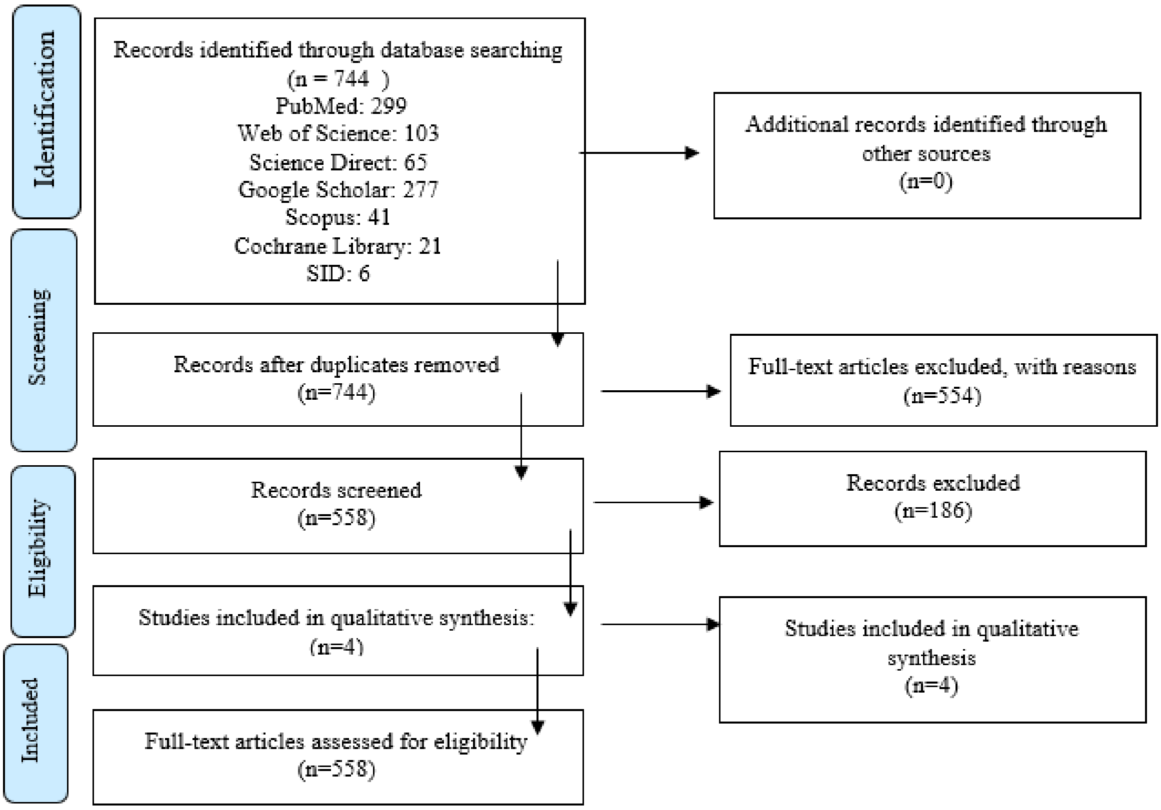

Figure 1. Flowchart depicting the selection process and stepwise inclusion and exclusion of studies in the present systematic review and meta-analysis2020

Across the included cardiopulmonary bypass-related studies, dexmedetomidine consistently demonstrated a protective perioperative profile, although the magnitude and domain of benefit varied across models and patient populations. In clinical valve and coronary bypass surgery, dexmedetomidine was associated with attenuation of the surgical stress response, reflected by lower circulating stress mediators, reduced postoperative cardiac troponin I, improved hemodynamic control at several perioperative time points, lower narcotic requirements, reduced incidence of postoperative atrial fibrillation, and shorter ICU and hospital stays. Some studies also suggested an anti-inflammatory effect, particularly through reduction of TNF-α, although this response was not uniform across all cytokines, as increases in IL-6 and IL-8 reported in one trial. In the aged rat cardiopulmonary bypass model, dexmedetomidine mitigated postoperative cognitive decline and reduced hippocampal expression of TNF-α, IL-6, and IL-1β, supporting a neuroprotective effect linked to suppression of inflammatory activation. Taken together, these findings indicate that dexmedetomidine may confer multi-system protection in the perioperative setting by moderating stress signaling, limiting selected inflammatory responses, improving postoperative recovery, and reducing certain complications, although the underlying mechanisms appear to be context-dependent and not uniformly demonstrated across all measured outcomes (table 2).

Table 2. Summary of Clinical and Experimental Studies Evaluating the Perioperative and Biological Effects of Dexmedetomidine in Cardiac Surgery and Cardiopulmonary Bypass-Related Models

Study	Model	Principal Findings	Proposed Mechanism
Wu et al. (2020) (12)	Randomized controlled trial in adults undergoing valve replacement with cardiopulmonary bypass	Dexmedetomidine reduced perioperative stress biomarkers, including cortisol, epinephrine, norepinephrine, and serotonin, and was associated with lower heart rate during surgical stimulation, shorter mechanical ventilation time, shorter ICU stay, and improved postoperative recovery.	Suppression of sympathetic and neuroendocrine stress responses during cardiac surgery.
Zhou et al.	Randomized double-blind placebo-	Dexmedetomidine lowered postoperative cardiac troponin I and reduced early TNF-α	Partial cardioprotection related to modulation of

(2019) (13)	controlled trial in adults undergoing elective valve replacement with cardiopulmonary bypass	release, suggesting attenuation of myocardial injury and early inflammatory activation, although changes in other inflammatory markers were not uniformly favorable.	perioperative inflammatory injury.
Dong et al. (2022) (14)	Aged rat cardiopulmonary bypass model of cardiac surgery	Dexmedetomidine improved postoperative learning and memory performance and reduced hippocampal levels and gene expression of TNF-α\alphaα, IL-6, and IL-1β, indicating mitigation of surgery-related neuroinflammation and cognitive dysfunction.	Neuroprotection mediated by suppression of postoperative inflammatory signaling in the hippocampus.
Hussien et al. (2025) (15)	Randomized controlled trial in adults undergoing elective on-pump coronary artery bypass grafting	Dexmedetomidine was associated with improved perioperative hemodynamic profile, lower narcotic requirements, reduced postoperative atrial fibrillation, and shorter ICU and hospital stay, while major adverse perioperative events were not significantly different between groups.	Clinical protection likely related to hemodynamic modulation, anesthetic-sparing effects, and reduced postoperative arrhythmic susceptibility.

Discussion

The studies included in this systematic review collectively indicate that intraoperative intravenous dexmedetomidine may exert a protective effect in patients undergoing cardiac surgery, although the extent and manifestation of this benefit vary according to the model, measured endpoint, and clinical context. Clinical studies in valve surgery and coronary artery bypass grafting showed that dexmedetomidine was associated with attenuation of the perioperative stress response, lower postoperative biomarkers of myocardial injury, reduced narcotic requirements, lower incidence of postoperative atrial fibrillation, and shorter ICU or hospital stay. At the same time, experimental and mechanistic studies demonstrated that dexmedetomidine can directly influence cardio myocyte biology by reducing oxidative injury, suppressing apoptosis, modulating inflammatory activity, enhancing autophagy adaptation, stabilizing ionic currents, and reshaping stress-responsive transcriptional programs under ischemic and oxygen-stress conditions (16-24).

One of the most consistent themes across the included studies is the capacity of dexmedetomidine to blunt the physiological stress response induced by cardiopulmonary bypass and surgical trauma. Cardiac surgery accompanied by substantial activation of the sympathoadrenal and neuroendocrine systems, leading to marked release of catecholamine's and cortisol, which can aggravate myocardial oxygen demand, vascular instability, inflammatory activation, and oxidative stress. Clinical evidence showing reductions in cortisol, epinephrine, norepinephrine, and serotonin suggests that dexmedetomidine attenuates this maladaptive response. This effect is highly relevant because excessive adrenergic stimulation contributes to mitochondrial reactive oxygen species production, calcium dysregulation, and ischemia–reperfusion-related myocardial injury. By dampening sympathetic activation, dexmedetomidine may therefore reduce the upstream drivers of oxidative damage and contribute to improved perioperative stability and postoperative recovery (16,19).

The reduction in postoperative myocardial injury markers observed in clinical studies further supports a cardio protective role for dexmedetomidine. In patients undergoing valve surgery, lower postoperative cardiac troponin I concentrations suggest reduced structural myocardial injury during the perioperative period. Although not all conventional oxidative stress markers changed significantly in that study, the decrease in troponin remains clinically meaningful because it reflects cumulative myocardial protection rather than isolated pathway modulation. Importantly, the inflammatory profile was not uniform, as early TNF-α\alphaα suppression accompanied by less favorable changes in some other cytokines in one trial. This mixed pattern indicates that dexmedetomidine is unlikely to act as a broad inhibitor of all inflammatory mediators and may instead exert selective or time-sensitive effects depending on the inflammatory milieu, duration of ischemia, and perioperative management strategy (17). The mechanistic studies offer a more detailed explanation for how dexmedetomidine may reduce oxidative injury at the cellular level. In hypoxia/reoxygenation-stressed cardio myocytes, dexmedetomidine activated the JAK2/STAT3/catalase pathway, with downstream attenuation of oxidative stress, endoplasmic reticulum stress, and apoptosis. This observation is highly relevant because catalase is a major antioxidant enzyme that detoxifies hydrogen peroxide, whereas STAT3 has implicated in mitochondrial preservation and cell survival during ischemia-reperfusion injury. Enhancement of this axis suggests that dexmedetomidine may strengthen endogenous antioxidant defenses rather than simply reducing oxidant production indirectly. In this context, the ant apoptotic effects observed in cardio myocyte models can reasonably be interpreted because of improved redox balance, reduced mitochondrial dysfunction, and interruption of stress-induced death signaling (20).

Additional evidence indicates that dexmedetomidine also promotes adaptive intracellular responses to metabolic stress. In human induced pluripotent stem cell-derived cardio myocytes, dexmedetomidine enhanced autophagy flux and limited ischemic injury through an α2-adrenergic receptor-dependent AMPK-mediated pathway. This finding is mechanistically important because autophagy plays a protective role in acute cellular stress by removing damaged mitochondria and misfolded proteins, thereby reducing reactive oxygen species accumulation and preserving energetic homeostasis. AMPK activation further supports a shift toward cellular adaptation under conditions of energy deprivation. These results suggest that dexmedetomidine may improve cardio myocyte resilience by facilitating stress adaptation rather than merely suppressing injury pathways, a property that is especially valuable in the setting of cardiac surgery, where transient ischemia, reperfusion, and mitochondrial dysfunction are central features (21).

The biological effects of dexmedetomidine also extend to electrophysiological regulation. One study showed that dexmedetomidine directly inhibited sodium and L-type calcium currents and prolonged action potential duration in human iPSC-derived cardio myocytes, apparently independent of classical adrenergic receptor signaling. Although this mechanism is not a direct antioxidant pathway, it remains highly relevant to myocardial protection because calcium overload is a major contributor to reperfusion injury, mitochondrial failure, and arrhythmogenesis. By limiting inward ionic currents, dexmedetomidine may reduce electrical instability and lessen calcium-dependent cellular stress. This interpretation may also help explain the lower incidence of postoperative atrial fibrillation observed in clinical coronary bypass patients who received dexmedetomidine, suggesting a translational link between direct cellular electrophysiology and perioperative rhythm outcomes (19, 22).

Dexmedetomidine may also exert cardio protection through anti-inflammatory and epigenetic regulation. In ischemia/reperfusion models, it shown to influence the TET1/Sirt1/NF-κ\kappaκB axis, thereby reducing inflammatory mediator production and limiting apoptosis. This finding broadens the mechanistic spectrum of dexmedetomidine because Sirt1 is closely associated with oxidative stress resistance, mitochondrial homeostasis, and suppression of inflammatory signaling, whereas NF-κ\kappaκB is a central transcriptional regulator of injury-related inflammation. The involvement of TET1 further suggests that dexmedetomidine may affect the epigenetic framework governing stress responses. Such a mechanism is particularly compelling in cardiac surgery, where oxidative stress and inflammation are tightly interconnected and where modulation at the transcriptional level could help explain improvements in both biochemical and recovery-related clinical outcomes (23).

A broader systems-level protective role suggested by studies evaluating dexmedetomidine under altered oxygen conditions. Under both hypoxic and hyperoxic stress, dexmedetomidine was found to modulate markers related to proliferation, apoptosis, autophagy, oxidative stress, extracellular matrix remodeling, and Hippo signaling. These data imply that dexmedetomidine does not act through a single isolated pathway but may instead coordinate a wider adaptive program that preserves cardio myocyte homeostasis during environmental stress. This is particularly relevant to cardiopulmonary bypass, where disturbed oxygen tension, reperfusion, inflammatory activation, and metabolic instability occur simultaneously. The convergence of antioxidant, ant apoptotic, autophagy, and remodeling-related effects supports the concept that dexmedetomidine functions as a pleiotropic stress-response modulator in the myocardium (24).

The neuroprotective findings from the aged rat cardiopulmonary bypass model further reinforce the systemic nature of dexmedetomidine-mediated protection. In that study, dexmedetomidine improved postoperative cognitive performance and reduced hippocampal levels of TNF-α\alphaα, IL-6, and IL-1β\betaβ. Although these observations are extra-cardiac, they are relevant to the present review because they indicate that dexmedetomidine can suppress inflammatory injury beyond the myocardium in the setting of bypass surgery. Since oxidative stress and inflammatory activation are closely interdependent in perioperative organ injury, the ability of dexmedetomidine to reduce neuroinflammation strengthens the broader hypothesis that it modulates common upstream stress pathways with multi-organ implications.

Despite these encouraging findings, several limitations acknowledged. The included studies were heterogeneous in terms of patient population, surgical procedure, dexmedetomidine dose and timing, comparator regimen, sample size, and endpoint selection. Moreover, not all studies directly assessed oxidative stress using the same biomarkers, and some focused primarily on inflammatory, electrophysiological, or clinical outcomes. Mechanistic evidence from cellular and animal models also extrapolated uncritically to human cardiac surgery. Nevertheless, the consistency of the overall direction of effect across multiple biological and clinical domains supports the view that dexmedetomidine has a meaningful protective role in the perioperative setting, even if the dominant mechanism differs across contexts (25).

In conclusion, the evidence synthesized in this review suggests that intraoperative intravenous dexmedetomidine may reduce oxidative stress-related injury during cardiac surgery through a combination of systemic and cellular mechanisms. These include attenuation of sympathetic over activation, enhancement of endogenous antioxidant defenses, suppression of selected inflammatory pathways, restoration of adaptive autophagy, stabilization of ionic homeostasis, and modulation of stress-responsive transcriptional signaling. Although the relative contribution of each mechanism likely varies according to the experimental and clinical setting, the available evidence supports dexmedetomidine as a multifunctional perioperative adjunct with potential relevance to myocardial protection in patients undergoing cardiac surgery (26).

Conclusion

Current evidence indicates that intraoperative intravenous dexmedetomidine may provide meaningful protection against oxidative stress-associated injury in patients undergoing cardiac surgery. Across clinical and experimental models, it was associated with suppression of perioperative stress responses, reduction of selected inflammatory and myocardial injury markers, improvement in hemodynamic stability and postoperative recovery, and lower arrhythmic burden. Mechanistic studies further suggest that these effects mediated through modulation of antioxidant defenses, apoptosis, autophagy, ion-channel activity, and stress-responsive signaling pathways. Although the magnitude of benefit varies across settings, dexmedetomidine appears to be a biologically plausible and clinically relevant adjunct in cardiac anesthesia.

Acknowledgments

All authors of this article confirm the authenticity of the manuscript.

Conflicts of interest

The authors declare that they have no competing interests.

Disclosure Statement

No potential conflict of interest reported by the authors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

References

[1] Featherstone, P. J., & Ball, C. M. (**2018**). The origins of cardiopulmonary bypass. *Anaesthesia and Intensive Care*, *46*(4), 351–353.

[2] Zakkar, M., Guida, G., Suleiman, M. S., & Angelini, G. D. (**2015**). Cardiopulmonary bypass and oxidative stress. *Oxidative Medicine and Cellular Longevity*, *2015*, Article 189863.

[3] Mauricio Del Rio, J., Nicoara, A., & Swaminathan, M. (**2017**). Neuroendocrine stress response: Implications for cardiac surgery-associated acute kidney injury. *Romanian Journal of Anaesthesia and Intensive Care*, *24*(1), 57–63.

[4] Gajarski, R. J., Stefanelli, C. B., Graziano, J. N., Kaciroti, N., Charpie, J. R., & Vazquez, D. (**2010**). Adrenocortical response in infants undergoing cardiac surgery with cardiopulmonary bypass and circulatory arrest. *Pediatric Critical Care Medicine*, *11*(1), 44–51.

[5] Winterhalter, M., Brandl, K., Rahe-Meyer, N., Osthaus, A., Hecker, H., Hagl, C., Adams, H. A., & Piepenbrock, S. (**2008**). Endocrine stress response and inflammatory activation during CABG surgery. A randomized trial comparing remifentanil infusion to intermittent fentanyl. *European Journal of Anaesthesiology*, *25*(4), 326–335.

[6] Ameli kalkhoran, S.M, Rabiei, K, Seyed Alizadeh, SM, Heravi, HM, Rouzpeykar, Y, (**2022**), Analyzing Impact of Intellectual Capital on Business Performance Using Structural Models Based on Customer Knowledge Management, *Discrete Dynamics in Nature and Society*, 7453565

[7] Fakhari, S., Pishghahi, A., Pourfathi, H., Farzin, H., & Bilehjani, E. (**2021**). A comparison between low-level laser therapy and intra-articular ozone injection in knee osteoarthritis treatment: A randomized clinical trial. *Journal of Lasers in Medical Sciences*, *12*, Article e44.

[8] Wijeysundera, D. N., Naik, J. S., & Beattie, W. S. (**2003**). Alpha-2 adrenergic agonists to prevent perioperative cardiovascular complications: A meta-analysis. *The American Journal of Medicine*, *114*(9), 742–752.

[9] Bulow, N. M., Colpo, E., Pereira, R. P., Correa, E. F., Waczuk, E. P., Duarte, M. F., & Rocha, J. B. (**2016**). Dexmedetomidine decreases the inflammatory response to myocardial surgery under mini-cardiopulmonary bypass. *Brazilian Journal of Medical and Biological Research*, *49*(4), Article e4646.

[10] Wang, X. W., Cao, J. B., Lv, B. S., Mi, W. D., Wang, Z. Q., Zhang, C., Wang, H. L., & Xu, Z. (**2015**). Effect of perioperative dexmedetomidine on the endocrine modulators of stress response: A

meta-analysis. *Clinical and Experimental Pharmacology and Physiology*, *42*(8), 828–836.

[11] Hashemian, M., Ahmadinejad, M., Mohajerani, S. A., & Mirkheshti, A. (**2017**). Impact of dexmedetomidine on hemodynamic changes during and after coronary artery bypass grafting. *Annals of Cardiac Anaesthesia*, *20*(2), 152–157.

[12] Wu, H., Tang, J., Pan, J., Han, M., Cai, H., & Zhang, H. (**2020**). Effects of dexmedetomidine on stress hormones in patients undergoing cardiac valve replacement: A randomized controlled trial. *BMC Anesthesiology*, *20*(1), Article 142.

[13] Zhou, H., Zhou, D., Lu, J., Wu, C., & Zhu, Z. (**2019**). Effects of pre-cardiopulmonary bypass administration of dexmedetomidine on cardiac injuries and the inflammatory response in valve replacement surgery with a sevoflurane post conditioning protocol: A pilot study. *Journal of Cardiovascular Pharmacology*, *74*(2), 91–97.

[14] Dong, W., Li, X., Wang, X., Cheng, X., Kong, L., Guo, Z., & Jing, H. (**2022**). Influence of dexmedetomidine on cognitive function and inflammatory factors in rats and analysis of its molecular mechanism after cardiac surgery under cardiopulmonary bypass. *Cellular and Molecular Biology (Noisy-le-Grand, France)*, *68*(2), 119–125.

[15] Hussien, R. M., El Shafei, M. N., Ahmed, M. M., Abdelmoneim, W., Ghoneim, M. A., & Tolba, M. A. (**2025**). Effect of dexmedetomidine on stress-induced changes in hemodynamic and left ventricular function in coronary artery bypass grafting surgery: A randomized controlled trial. *Journal of Cellular & Molecular Anesthesia*, *10*(10).

[16] Wald, E. L., Preze, E., Eickhoff, J. C., & Backer, C. L. (**2011**). The effect of cardiopulmonary bypass on the hypothalamic-pituitary-adrenal axis in children. *Pediatric Critical Care Medicine*, *12*(2), 190–196.

[17] Bilehjani, E., Fakhari, S., Farzin, H., Tajlil, A., & Nader, N. D. (**2024**). Diagnosis and treatment of cardiovascular manifestations of COVID-19: A narrative review. *Acta Cardiologica*, *79*(3), 267–273.

[18] Bekker, A., Haile, M., Kline, R., Didehvar, S., Babu, R., Martiniuk, F., & Urban, M. (**2013**). The effect of intraoperative infusion of dexmedetomidine on the quality of recovery after major spinal surgery. *Journal of Neurosurgical Anesthesiology*, *25*(1), 16–24.

[19] Hohl, C. M., Kelly-Smith, C. H., Yeung, T. C., Sweet, D. D., Doyle-Waters, M. M., & Schulzer, M. (**2010**). The effect of a bolus dose of etomidate on cortisol levels, mortality, and health services utilization: A systematic review. *Annals of Emergency Medicine*, *56*(2), 105–113.

[20] Albuzyad, S. S. and Jawad, M. K. (**2025**). A Systematic Review of Radiology and Radio Oncology Evaluations in Patients with Thoracic and Pelvic Cancers based on Radiological Images. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research*, *1*(1), 1-11.

[21] Agha Mohammadi, D., Bilehjani, E., Farzin, H., Fakhari, S., & Naderpour, M. (**2020**). Effect of pressure on the Yinmen point in relief of pain after middle ear surgery: A randomized clinical trial. *Anesthesiology and Pain Medicine*, *10*(5), Article e103328.

[22] Okuyama, K., Wada, K., Sakurada, S., Mizoguchi, H., Komatsu, H., Sora, I., Tamura, G., Ohkawara, Y., Takayanagi, M., & Ohno, I. (**2010**). The involvement of micro-opioid receptors in the central nervous system in the worsening of allergic airway inflammation by psychological stress in mice. *International Archives of Allergy and Immunology*, *152*(4), 342–352.

[23] NazarI, M. Akhlaghi, F. Pourfathi Nematabad, H. (**2025**), Comparison of Postoperative nausea and vomiting prevalence in patients with routine NPO and NPO with clear fluids 2 hours before cataract surgery, *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research*, *1*, 132-139

[24] Duncan, D., Sankar, A., Beattie, W. S., & Wijeysundera, D. N. (**2018**). Alpha-2 adrenergic agonists for the prevention of cardiac complications among adults undergoing surgery. *Cochrane Database of Systematic Reviews*, *2018*(3), Article CD004126.

[25] Park, J. W., Chung, H. W., Lee, E. J., Jung, K. H., Paik, J. Y., & Lee, K. H. (**2013**). Alpha2-adrenergic agonists including xylazine and dexmedetomidine inhibit norepinephrine transporter function in SK-N-SH cells. *Neuroscience Letters*, *541*, 184–189.

[26] Bilehjani, E., Nader, N., Farzin, H., Haghighate Azari, M., & Fakhari, S. (**2020**). The evaluation of factors affecting hemodynamic variability in mechanically ventilated patients after cardiac surgery. *Anesthesiology and Pain Medicine*, *10*(4), Article e101832.