ORIGINAL RESEARCH ARTICLE

# The Effect of High and Low Dose Methylprednisolone on Systemic Inflammatory Response to Cardiopulmonary Bypass and Clinical Outcome in Coronary Artery Bypass Graft

Alireza Mahoori[1], Ebrahim Hassani[1], Shahyad Salehi[2], Tahereh Hajizadeh[1], Hossein Khosravi[1,3]

Published: 25 December 2025


## Abstract

**Background** Cardiopulmonary bypass during coronary artery bypass grafting is associated with activation of systemic inflammatory pathways that may contribute to postoperative complications. Corticosteroids have been used to attenuate cardiopulmonary bypass -induced inflammatory responses; however, the optimal dosing strategy for methylprednisolone remains controversial. This study aimed to compare the effects of high-dose versus low-dose methylprednisolone on systemic inflammatory response and postoperative clinical outcomes in patients undergoing elective coronary artery bypass grafting with cardiopulmonary bypass.

**Methods** In this double-masked randomized trial, 40 adult patients undergoing elective coronary artery bypass grafting with cardiopulmonary bypass were assigned to two equal groups. All patients received methylprednisolone at 30 mg/kg in the cardiopulmonary bypass priming solution before initiation of cardiopulmonary bypass. The high-dose group additionally received intravenous methylprednisolone 30 mg/kg after cardiopulmonary bypass separation, while the low-dose group received placebo. Serum tumor necrosis factor-alpha, C-reactive protein, polymorphonuclear leukocyte count, creatine kinase-MB, and blood glucose were measured preoperatively and two hours postoperatively. Clinical outcomes evaluated included mechanical ventilation duration, inotropic support requirement, and ICU stay.

**Results** Baseline demographic and intraoperative variables were comparable. Postoperative tumor necrosis factor-alpha, C-reactive protein, creatine kinase-MB, and blood glucose increased in both groups without significant intergroup differences ($p > 0.05$). However, postoperative polymorphonuclear leukocyte counts were significantly lower in the high-dose group compared with the low-dose group ($8447.35 \pm 2932.47$ vs. $11398.90 \pm 4730.71$; $P=0.02$). No significant differences were observed in mechanical ventilation duration ($6.58 \pm 2.60$ vs. $7.85 \pm 4.12$ hours; $p = 0.25$), ICU stay ($2.70 \pm 0.73$ vs. $2.92 \pm 0.59$ days; $p = 0.29$), or postoperative inotropic support requirements.

**Conclusion** High-dose methylprednisolone during coronary artery bypass grafting with cardiopulmonary bypass significantly reduced postoperative polymorphonuclear leukocyte counts, suggesting partial inflammatory response attenuation. However, no significant improvement was observed in other inflammatory markers or short-term clinical outcomes compared with the low-dose regimen. Routine high-dose methylprednisolone use for coronary artery bypass grafting patients undergoing cardiopulmonary bypass may therefore not provide substantial additional clinical benefit.

**Keywords** Cardiopulmonary bypass; Coronary artery bypass; Methylprednisolone; Systemic inflammatory response syndrome; Tumor necrosis factor-alpha

✉ Hossein Khosravi
hossein1356khosravi@gmail.com

1. Department of Anesthesiology, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran
2. Department of Cardiology, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran
3. Department of Anesthesiology, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran

Received: 19 October 2025 / Revised: 17 November 2025 / Accepted: 16 December 2025

## 1 Introduction

Cardiopulmonary bypass (CPB) remains an indispensable component of modern coronary artery bypass grafting (CABG); however, it is strongly associated with activation of systemic inflammatory pathways that may contribute to postoperative organ dysfunction and adverse clinical outcomes. Despite significant advances in surgical techniques, perfusion technology, and perioperative management, CPB-induced systemic inflammatory response syndrome (SIRS) continues to represent a major challenge in cardiac surgery.[1]

The inflammatory response during CPB is multifactorial and results from contact of blood with artificial extracorporeal surfaces, ischemia–reperfusion injury, endotoxemia, oxidative stress, surgical trauma, and activation of the complement and coagulation cascades. These processes lead to the activation of neutrophils, monocytes, endothelial cells, and platelets, followed by the release of pro-inflammatory cytokines, including tumor necrosis factor-α (TNF-α), interleukin (IL)-6, and IL-8.[2,3] Excessive inflammatory activation has been associated with pulmonary dysfunction, myocardial injury, acute kidney injury, vasoplegia, prolonged mechanical ventilation, and increased intensive care unit (ICU) stay following cardiac surgery.[4]

Among inflammatory mediators, TNF-α plays a central role in initiating the inflammatory cascade after CPB. Elevated circulating levels of TNF-α and IL-6 have been correlated with postoperative morbidity and severity of inflammatory response.[5] Therefore, attenuation of perioperative inflammation has become an important therapeutic target in cardiac anesthesia and perioperative medicine.

Corticosteroids have long been investigated as potential modulators of CPB-associated inflammation because of their potent anti-inflammatory and immunosuppressive properties. Methylprednisolone suppresses transcription of pro-inflammatory cytokines, reduces leukocyte activation, stabilizes lysosomal membranes, and inhibits complement-mediated inflammatory pathways.[6] Several randomized trials and meta-analyses have evaluated perioperative corticosteroid administration in cardiac surgery; however, their clinical efficacy remains controversial.

Recent systematic reviews and meta-analyses have shown conflicting findings regarding the benefits of corticosteroids in adult cardiac surgery. A 2024 Cochrane review involving more than 17,000 patients reported that prophylactic corticosteroids may slightly reduce pulmonary complications but have little or no effect on mortality and may increase certain cardiac complications.[7] Similarly, a contemporary meta-analysis published in 2024 demonstrated that although corticosteroids attenuate inflammatory responses, their effects on major postoperative outcomes remain inconsistent across studies.[8] On the other hand, some recent investigations suggested that corticosteroids may reduce vasoactive inotropic requirements and improve postoperative recovery in selected patient populations undergoing CPB.[9]

An additional unresolved issue is the optimal dosing strategy for methylprednisolone during cardiac surgery. While high-dose corticosteroid regimens may theoretically provide greater suppression of inflammatory mediators, they may also increase adverse effects such as hyperglycemia, impaired wound healing, infection, and myocardial complications. Previous studies comparing high-dose and low-dose methylprednisolone protocols have yielded inconsistent results, and evidence supporting the superiority of one regimen over another remains insufficient.[10]

Current European guidelines for CPB in adult cardiac surgery also emphasize that, although modulation of the inflammatory response is clinically important, routine administration of high-dose corticosteroids cannot yet be universally recommended due to limited evidence of meaningful improvement in clinical outcomes.[11]

Given the ongoing controversy surrounding perioperative corticosteroid administration and the lack of consensus regarding the optimal methylprednisolone dose, the present study aimed to compare the effects of high-dose versus low-dose methylprednisolone on systemic inflammatory response and postoperative clinical outcomes in patients undergoing CABG with CPB. We specifically evaluated perioperative TNF-α levels, inflammatory biomarkers, biochemical changes, duration of mechanical ventilation, inotropic support requirements, and ICU length of stay.

## 2 Methods

This double-blind randomized clinical trial was conducted on 40 adult patients with ischemic heart disease who were candidates for elective CABG with CPB at Seyed Al-Shohada Educational and Medical Center, affiliated with Urmia University of Medical Sciences.

Patients aged over 18 years with left ventricular ejection fraction (LVEF) ≥ 45% who were scheduled for elective isolated CABG surgery using CPB were included in the study. Patients with a history of corticosteroid therapy, diabetes mellitus, active pulmonary infection, gastrointestinal bleeding, severe systemic disorders, including hepatic or renal disease, autoimmune disorders, emergency surgery, reoperation, or combined cardiac procedures were excluded from the study.

Following induction of anesthesia and before initiation of CPB, patients were randomly assigned to two equal

groups using a computer-generated randomization table and sealed opaque envelopes. Both patients and investigators responsible for postoperative evaluations and laboratory analyses were blinded to group allocation throughout the study period.

All patients underwent standardized anesthetic and surgical management. Standard intraoperative monitoring included electrocardiography, invasive arterial blood pressure monitoring, pulse oximetry, central venous pressure monitoring, end-tidal carbon dioxide monitoring, and urinary output monitoring. CPB was established using a standard extracorporeal circulation system with non-pulsatile flow and moderate systemic hypothermia. Myocardial protection was achieved using cold cardioplegia in accordance with institutional protocols. The CPB circuit, priming solution composition, and operative conditions were identical in both groups.

Patients were randomly assigned to one of two study groups. In both groups, methylprednisolone 30 mg/kg was added to the CPB priming solution before initiation of CPB. Following separation from CPB and stabilization of hemodynamic status, patients in the high-dose methylprednisolone group received an additional intravenous dose of methylprednisolone 30 mg/kg. In contrast, patients in the low-dose group received an equal volume of normal saline placebo prepared in an identical syringe.

The study was designed as a double-masked trial. Patients, surgeons, anesthesiologists responsible for postoperative management, ICU staff, laboratory personnel, and investigators analyzing study outcomes were all blinded to treatment allocation. Preparation of methylprednisolone and placebo solutions was performed by an independent anesthesia technician who was not involved in data collection or patient evaluation. Both intervention protocols were prepared in identical syringes and infusion containers, with the same volume and appearance, to maintain blinding throughout the study period. Group allocation codes remained concealed until completion of statistical analysis.

Demographic and intraoperative variables, including age, sex, duration of CPB, aortic cross-clamp time, number of grafts, duration of surgery, and requirement for inotropic support during CPB weaning, were recorded for all patients. Blood samples were collected immediately after induction of anesthesia as baseline values and again two hours after surgery. Serum tumor necrosis factor-alpha (TNF-α), C-reactive protein (CRP), polymorphonuclear leukocyte (PMN) count, creatine kinase-MB (CK-MB), and blood glucose levels were measured in all patients. Postoperative clinical outcomes, including duration of mechanical ventilation, time to tracheal extubation, requirement for inotropic support, and length of ICU stay, were also documented.

All laboratory analyses were performed under identical conditions using the same assay kits and standardized laboratory techniques. In cases of withdrawal or development of confounding clinical conditions during the study period, patients were replaced to maintain the required sample size.

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software version 25 (IBM Corp., Armonk, NY, USA). Quantitative variables were expressed as mean ± standard deviation (SD), and categorical variables were presented as frequency and percentage. The Kolmogorov–Smirnov test was used to assess the normality of the data. An independent-samples t-test was applied for comparison of continuous variables between groups, while a chi-square test or Fisher's exact test was used for categorical variables where appropriate. A p-value less than 0.05 was considered statistically significant.

## 3 Results

A total of 40 patients undergoing elective CABG with CPB were enrolled in this double-masked randomized clinical trial. All patients completed the study protocol and were included in the final statistical analysis. The study population consisted of 33 male patients (82.5%) and 7 female patients (17.5%). The overall mean age of the participants was 63.57 ± 10.76 years.

Patients were randomly allocated to two equal groups: the high-dose methylprednisolone group (n=20) and the low-dose methylprednisolone group (n=20). Baseline demographic characteristics and intraoperative variables were comparable between the two groups, and no statistically significant differences were observed regarding age, sex distribution, duration of CPB, or aortic cross-clamp time (Table 1).

**Table 1** Baseline demographic and intraoperative characteristics of the study population

| Variable | High-dose MP (n = 20) | Low-dose MP (n = 20) | P-value |
|---|---|---|---|
| Age (years) | 64.10 ± 10.80 | 63.05 ± 10.83 | 0.76** |
| Male sex, n (%) | 17 (85%) | 16 (80%) | 0.50* |
| Female sex, n (%) | 3 (15%) | 4 (20%) | |
| CPB duration (min) | 133.40 ± 23.96 | 123.35 ± 24.40 | 0.10** |
| Aortic cross-clamp time (min) | 94.30 ± 22.07 | 87.15 ± 18.16 | 0.20** |

* Fisher's exact test

** Independent-samples t-test

Assessment of inflammatory and biochemical markers demonstrated that serum TNF-α levels increased postoperatively in both study groups. Baseline TNF-α levels were 0.10 pg/mL in the high-dose

methylprednisolone group and 0.33 ± 0.17 pg/mL in the low-dose group (p = 0.32). Two hours after surgery, TNF-α levels increased to 0.24 ± 0.18 pg/mL and 1.76 ± 0.49 pg/mL in the high-dose and low-dose groups, respectively, without a statistically significant difference between groups (p = 0.43). Similarly, serum CRP levels were elevated postoperatively in both groups. Baseline CRP levels were 5.84 ± 4.19 mg/L in the high-dose group and 5.55 ± 5.26 mg/L in the low-dose group (p = 0.55). Two hours after surgery, CRP levels increased to 7.77 ± 2.57 mg/L in the high-dose group and 3.54 ± 0.80 mg/L in the low-dose group, with no statistically significant intergroup difference (p = 0.12). Polymorphonuclear leukocyte (PMN) counts increased significantly after surgery in both groups. Baseline PMN counts were 4089 ± 1394.90 in the high-dose group and 3393.90 ± 1076.07 in the low-dose group (p = 0.19). However, postoperative PMN counts measured two hours after surgery were significantly lower in the high-dose methylprednisolone group compared with the low-dose group (8447.35 ± 2932.47 vs. 11398.90 ± 4730.71, respectively; p = 0.02) (Table 2). Serum CK-MB concentrations increased postoperatively in both groups without significant intergroup differences. Baseline CK-MB levels were 27.55 ± 17.82 U/L in the high-dose group and 24.50 ± 20.11 U/L in the low-dose group (p = 0.61). Two hours after surgery, CK-MB levels increased to 66.10 ± 20.10 U/L in the high-dose group and 53.65 ± 12.11 U/L in the low-dose group (p = 0.53). Blood glucose levels also increased following surgery in both groups. Baseline glucose levels were 123.40 ± 38.35 mg/dL in the high-dose methylprednisolone group and 105.35 ± 23.13 mg/dL in the low-dose group (p = 0.07). Postoperative glucose levels increased to 168.40 ± 36.32 mg/dL and 151.10 ± 19.84 mg/dL in the high-dose and low-dose groups, respectively, with no statistically significant difference observed between the groups (p = 0.069) (Table 2).

Postoperative clinical outcomes were comparable between the two study groups. The mean duration of mechanical ventilation and time to tracheal extubation was 6.58 ± 2.60 hours in the high-dose methylprednisolone group and 7.85 ± 4.12 hours in the low-dose group, with no statistically significant difference between groups (p = 0.25). Similarly, the mean length of stay in ICU was 2.70 ± 0.73 days in the high-dose group and 2.92 ± 0.59 days in the low-dose group, without a statistically significant difference (p = 0.29) (Table 3).

Requirement for inotropic support during postoperative management was observed in 5 patients (25%) in the high-dose methylprednisolone group and one patient (5%) in the low-dose group, whereas 15 patients (75%) in the high-dose group and 19 patients (95%) in the low-dose group did not require inotropic support (Table 3).

Overall, the administration of high-dose methylprednisolone was not associated with a significant advantage over low-dose methylprednisolone in reducing the systemic inflammatory response or improving postoperative clinical outcomes in patients undergoing CABG with CPB. The only statistically significant finding was a lower postoperative PMN count in the high-dose group.

**Table 3** Comparison of postoperative clinical outcomes between study groups

| Variable | High-dose MP (n = 20) | Low-dose MP (n = 20) | P-value |
|---|---|---|---|
| Need for inotropic support, n (%) | 5 (25%) | 1 (5%) | 0.91* |
| Extubation time (h) | 6.58 ± 2.60 | 7.85 ± 4.12 | 0.25** |
| ICU stay (days) | 2.70 ± 0.73 | 2.92 ± 0.59 | 0.29** |

* Fisher's exact test
** Independent-samples t-test

**Table 2** Comparison of inflammatory and biochemical markers

| Variable | High-dose MP | Low-dose MP | P-value* |
|---|---|---|---|
| Baseline TNF-α (pg/mL) | 0.10 ± 0.27 | 0.17 ± 0.33 | 0.32 |
| Postoperative TNF-α (pg/mL) | 0.18 ± 0.24 | 0.49 ± 1.76 | 0.43 |
| Baseline CRP (mg/L) | 4.19 ± 5.84 | 5.26 ± 5.55 | 0.55 |
| Postoperative CRP (mg/L) | 2.57 ± 7.77 | 0.80 ± 3.54 | 0.12 |
| Baseline PMN count | 4089 ± 1394.90 | 3393.90 ± 1076.07 | 0.19 |
| Postoperative PMN count | 8447.35 ± 2932.47 | 11398.90 ± 4730.71 | 0.02 |
| Baseline CK-MB (U/L) | 27.55 ± 17.82 | 24.50 ± 20.11 | 0.61 |
| Postoperative CK-MB (U/L) | 66.10 ± 20.10 | 53.65 ± 12.11 | 0.53 |
| Baseline blood glucose (mg/dL) | 123.40 ± 38.35 | 105.35 ± 23.13 | 0.07 |
| Postoperative blood glucose (mg/dL) | 168.40 ± 36.32 | 151.10 ± 19.84 | 0.069 |

* Independent-samples t-test

## 4 Discussion

The present double-masked randomized clinical trial evaluated the effects of high-dose versus low-dose methylprednisolone on systemic inflammatory response and postoperative clinical outcomes in patients undergoing CABG with CPB. The principal finding of this study was that administration of an additional high dose of methylprednisolone after CPB significantly reduced postoperative polymorphonuclear leukocyte (PMN) counts compared with the low-dose regimen. However, no statistically significant differences were observed between the groups regarding serum TNF-α levels, CRP concentrations, CK-MB levels, blood glucose changes, duration of mechanical ventilation, ICU length of stay, or requirement for inotropic support. These findings suggest that although intensified corticosteroid therapy may attenuate certain components of the inflammatory cascade, this effect may not necessarily translate into clinically meaningful improvements in short-term postoperative outcomes.

Cardiopulmonary bypass is known to induce a complex systemic inflammatory response through several mechanisms, including contact of blood with artificial extracorporeal surfaces, ischemia–reperfusion injury, complement activation, oxidative stress, endotoxemia, and the release of pro-inflammatory cytokines.[12,13] Among these mediators, TNF-α plays a pivotal role in initiating and amplifying postoperative inflammation and has been associated with organ dysfunction and adverse outcomes after cardiac surgery.[12, 14, 15] In the present study, postoperative TNF-α levels increased in both groups, although the increase appeared numerically lower in the high-dose methylprednisolone group. Nevertheless, this difference did not reach statistical significance. This finding may be related to the relatively small sample size, interindividual variability in cytokine response, and the limited timing of postoperative cytokine measurements.

In contrast, postoperative PMN counts were significantly lower in patients receiving high-dose methylprednisolone. This observation is biologically plausible because corticosteroids inhibit neutrophil activation, endothelial adhesion, and migration into inflamed tissues.[16,17] Activated neutrophils are considered major contributors to endothelial injury, pulmonary dysfunction, and tissue damage following CPB. Therefore, suppression of neutrophilic inflammatory activity may indicate partial attenuation of the CPB-induced inflammatory response with higher corticosteroid exposure.

The findings of the present study are generally consistent with previous investigations evaluating corticosteroid administration during cardiac surgery.[8,17,18] Varan et al. demonstrated that high-dose methylprednisolone reduced inflammatory activation during pediatric cardiac surgery; however, this reduction was not consistently associated with improved clinical outcomes.[10] Similarly, recent meta-analyses have shown that corticosteroids may attenuate inflammatory markers without providing definitive benefits regarding mortality or major postoperative complications.

The recent 2024 Cochrane systematic review involving more than 17,000 adult cardiac surgery patients concluded that prophylactic corticosteroids may slightly reduce pulmonary complications but have little or no effect on mortality and may increase the risk of certain cardiovascular adverse events.[18] Likewise, the meta-analysis by Losiggio et al. in 2024 reported that although corticosteroids may reduce vasoactive inotropic requirements in selected populations, evidence supporting improvement in major clinical outcomes remains inconsistent.[8] Chen et al. also demonstrated that perioperative corticosteroids may reduce inflammatory responses but do not consistently shorten ICU stay or mechanical ventilation duration.[9]

An important finding of the current study was the absence of significant differences in postoperative clinical recovery parameters between groups. Although extubation time was numerically shorter in the high-dose methylprednisolone group, the difference was not statistically significant. Similarly, ICU stay was comparable between groups. These observations support the growing evidence that suppression of biochemical inflammatory markers alone may not necessarily improve overall postoperative recovery.[8,9,18] Multiple perioperative factors, including surgical technique, myocardial preservation, duration of CPB, fluid management, preoperative patient status, and postoperative critical care, likely play a greater role in determining clinical outcomes.

Although corticosteroids are effective in attenuating certain inflammatory pathways activated during CPB, improvements in postoperative clinical outcomes, such as duration of mechanical ventilation, time to tracheal extubation, requirement for inotropic support, and ICU length of stay, are influenced by multiple perioperative factors. These outcomes are determined not only by the degree of systemic inflammatory suppression but also by myocardial function, preoperative clinical status, pulmonary reserve, fluid balance, transfusion burden, duration of CPB, surgical complexity, and postoperative critical care management. Therefore, the reduction in PMN counts observed in the high-dose methylprednisolone group may not have been sufficient to translate into measurable improvements in early postoperative recovery. This interpretation is consistent with previous studies showing that corticosteroids may reduce inflammatory markers without producing consistent benefits in ventilation time, ICU stay, or vasoactive inotropic requirements.[8,9,16-19]

Another clinically relevant observation was the postoperative increase in blood glucose levels in both groups, with a tendency toward higher glucose levels in the high-dose methylprednisolone group. Although this difference did not reach statistical significance, corticosteroid-induced hyperglycemia remains an important concern in cardiac surgery patients because it may contribute to impaired wound healing, increased infection risk, and adverse cardiovascular events. Previous studies have similarly reported increased insulin requirements and postoperative hyperglycemia with higher corticosteroid doses.[9,19]

The findings of the present trial are also aligned with contemporary European recommendations regarding inflammatory modulation during CPB.[11] The 2024 EACTS/EACTAIC/EBCP Guidelines emphasize that despite the pathophysiological rationale for corticosteroid administration, current evidence remains insufficient to universally recommend routine high-dose corticosteroid therapy for adult cardiac surgery patients.[11] Therefore, corticosteroid administration should likely be individualized according to patient characteristics, inflammatory risk profile, and institutional practice.

Several limitations of the present study should be acknowledged. First, the relatively small sample size may have limited the statistical power to detect modest but clinically relevant differences between groups. Second, only a limited number of inflammatory biomarkers were measured, whereas other important mediators, such as IL-6, IL-8, IL-10, and complement activation markers, were not evaluated. Third, inflammatory biomarkers were measured only during the early postoperative period, which may not fully reflect the dynamic inflammatory response following CPB. In addition, long-term postoperative outcomes, including atrial fibrillation, acute kidney injury, infection, and mortality, were not assessed.

Despite these limitations, the present study has several strengths, including its randomized double-masked design, standardized anesthetic and surgical management, and simultaneous assessment of laboratory and clinical outcomes. The study provides additional evidence on the ongoing controversy over optimal corticosteroid dosing strategies during cardiac surgery with CPB.

## 5 Conclusion

In conclusion, administration of high-dose methylprednisolone in patients undergoing CABG with CPB significantly reduced postoperative PMN counts, suggesting partial attenuation of the inflammatory response. However, high-dose therapy did not produce significant improvements in serum TNF-α levels, CRP concentrations, duration of mechanical ventilation, ICU stay, or postoperative inotropic requirements compared with the low-dose regimen.

These findings indicate that although higher doses of methylprednisolone may suppress certain cellular inflammatory pathways, this effect does not necessarily translate into superior short-term clinical outcomes. Considering the potential adverse effects associated with high-dose corticosteroid therapy, including hyperglycemia and metabolic complications, routine administration of high-dose methylprednisolone during CABG cannot currently be strongly recommended.

Further large-scale, multicenter, randomized trials with comprehensive inflammatory profiling and long-term follow-up are needed to determine the optimal corticosteroid dosing strategy and identify patient subgroups that may derive the greatest benefit from perioperative corticosteroid administration.

## Declarations

**Acknowledgments**
We want to express our gratitude to Urmia University of Medical Sciences for their support in conducting this research. We also thank all those who contributed to the successful completion of this study.

**Artificial Intelligence Disclosure**
During the preparation of this work, the authors did not use any AI-assisted technologies in the writing process, data analysis, or generation of this manuscript.

**Authors' Contributions**
All authors contributed significantly to the work and approved the final version of the manuscript. Alireza Mahoori and Ebrahim Hassani supervised the project, provided clinical interpretation of the findings, critically revised the manuscript, and gave final approval. Shahyad Salehi and Tahereh Hajizadeh were responsible for data collection from medical records, study design, supervision of data collection, data analysis and interpretation, drafting the manuscript, and critical revision. Hossein Khosravi handled conceptualization and data curation, participated in critical revision, and provided final approval.

**Availability of Data and Materials**
The datasets generated and/or analyzed in the current study are not publicly available due to restrictions imposed by the institutional ethics committee and hospital data privacy regulations that protect patient confidentiality. However, de-identified data may be made available from the corresponding author upon reasonable request and with permission from the Ethics Committee of Urmia University of Medical Sciences.

**Conflict of Interest**
hh The authors declare that they have no competing interests or conflicts of interest related to this work, including financial, personal, or professional relationships that could potentially influence (or be perceived to influence) the work.

**Consent for Publication**
Not applicable.

**Ethical Considerations**

The study protocol was approved by the Ethics Committee of Urmia University of Medical Sciences, Urmia, Iran, under the Code of Ethics IR.UMSU.REC.1392.231. All procedures were performed in accordance with the ethical standards of the institutional research committee and with the 1964 Declaration of Helsinki and its later amendments, or comparable ethical standards. Given the retrospective, observational nature of the study using anonymized data, the ethics committee waived the requirement for informed consent.

**Funding**

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The study was conducted as part of routine academic activities at Urmia University of Medical Sciences with no external financial support.



## References

1. Banerjee D, Feng J, Sellke FW. Strategies to attenuate maladaptive inflammatory response associated with cardiopulmonary bypass. Front Surg. 2024;11:1224068. doi:10.3389/fsurg.2024.1224068.
2. Ferreira LO, Vasconcelos VW, Lima JdS, Vieira Neto JR, da Costa GE, Esteves JdC, et al. Biochemical changes in cardiopulmonary bypass in cardiac surgery: new insights. J Pers Med. 2023;13(10):1506.doi:10.3390/jpm13101506.
3. Yan Y, Kamenshchikov N, Zheng Z, Lei C. Inhaled nitric oxide and postoperative outcomes in cardiac surgery with cardiopulmonary bypass: A systematic review and meta-analysis. Nitric Oxide. 2024;146:64-74. doi:10.1016/j.niox.2024.03.004.
4. Paparella D, Yau T, Young E. Cardiopulmonary bypass-induced inflammation: pathophysiology and treatment. An update. Eur J Cardiothorac Surg. 2002;21(2):232-44. https://doi.org/10.1016/S1010-7940(01)01099-5.
5. Steinberg JB, Kapelanski DP, Olson JD, Weiler JM. Cytokine and complement levels in patients undergoing cardiopulmonary bypass. J Thorac Cardiovasc Surg. 1993;106(6):1008-16.doi: 1016/S0022-5223(19)33971-6.
6. M Dieleman J. Corticosteroids for the inflammatory response to cardiopulmonary bypass: an update. Curr Pharm Des. 2013;19(22):3979-91.
7. Group CH, Abbasciano RG, Olivieri GM, Chubsey R, Gatta F, Tyson N, et al. Prophylactic corticosteroids for cardiopulmonary bypass in adult cardiac surgery. Cochrane Database Syst Rev. 1996;2024(3).doi:10.1002/14651858.CD005566.pub4.
8. Losiggio R, Lomivorotov V, Ursoleo JDA, Kotani Y, Monaco F, Milojevic M, et al. The effects of corticosteroids on survival in pediatric and nonelderly adult patients undergoing cardiac surgery: a meta-analysis of randomized studies. J Cardiothorac Vasc Anesth. 2024;38(11):2783-91. https://doi.org/10.1053/j.jvca.2024.07.001.
9. Chen L, Xiang F, Hu Y. Corticosteroids in patients undergoing cardiac surgery: A meta-analysis of 12,559 patients. Perfusion. 2023;38(4):853-9. doi:10.1177/02676591221106324.
10. Varan B, Tokel K, Mercan S, Dönmez A, Aslamaci S. Systemic inflammatory response related to cardiopulmonary bypass and its modification by methyl prednisolone: high dose versus low dose. Pediatr Cardiol. 2002;23(4):437-41. doi:10.1007/s00246-002-0118-3.
11. Wahba A, Kunst G, De Somer F, Agerup Kildahl H, Milne B, Kjellberg G, et al. 2024 EACTS/EACTAIC/EBCP Guidelines on cardiopulmonary bypass in adult cardiac surgery. Interdiscip Cardiovasc Thorac Surg. 2025;40(2):ivaf002. doi:10.1093/icvts/ivaf002.
12. Squiccimarro E, Stasi A, Lorusso R, Paparella D. Narrative review of the systemic inflammatory reaction to cardiac surgery and cardiopulmonary bypass. Artif Organs. 2022;46(4):568-77. doi: 10.1111/aor.14171.
13. Warltier DC, Laffey JG, Boylan JF, Cheng DC. The systemic inflammatory response to cardiac surgery: implications for the anesthesiologist. Anesthesiology. 2002;97(1):215-52.
14. Wang Y, Bellomo R. Cardiac surgery-associated acute kidney injury: risk factors, pathophysiology and treatment. Nat Rev Nephrol. 2017;13(11):697-711. doi:10.1038/nrneph.2017.119.
15. Ortega-Loubon C, Fernández-Molina M, Carrascal-Hinojal Y, Fulquet-Carreras E. Cardiac surgery-associated acute kidney injury. Ann Card Anaesth. 2016;19(4):687-98. doi:10.4103/0971-9784.191578.
16. Whitlock RP, Devereaux P, Teoh KH, Lamy A, Vincent J, Pogue J, et al. Methylprednisolone in patients undergoing cardiopulmonary bypass (SIRS): a randomised, double-blind, placebo-controlled trial. The Lancet. 2015;386(10000):1243-53. https://doi.org/10.1016/S0140-6736(15)00273-1.
17. Dieleman JM, Nierich AP, Rosseel PM, Van Der Maaten JM, Hofland J, Diephuis JC, et al. Intraoperative high-dose dexamethasone for cardiac surgery: a randomized controlled trial. JAMA. 2012;308(17):1761-7. doi:10.1001/jama.2012.14144.
18. Chubsey R, Tyson N, Zakkar M. Prophylactic corticosteroids for cardiopulmonary bypass in adult cardiac surgery. 2024;3:CD005566. doi:10.1002/14651858.CD005566.pub4.
19. Herbst RA, Telford OT, Hunting J, Bullock WM, Manning E, Hong BD, et al. The effects of perioperative dexamethasone on glycemic control and postoperative outcomes. Endocr Pract. 2020;26(2):218-25. doi:10.4158/EP-2019-0252.