Volume 1, Issue 6

Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research

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

DOI: 10.22034/jampbr.2025.535549.1028

Evaluation of the Effects of Vitamin C Supplementation on the Incidence of Postoperative Complications Following Cardiac Surgery

Solmaz Fakhari[1]■, Aliakbar Ziyaazar[1]

[1]Department of Anesthesiology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

Article info

Received: 01.07.2025

Accepted: 06.08.2025

Available Online: 06.08.2025

Checked for Plagiarism: Yes

Keywords:

Vitamin C Supplementation, Postoperative Complications, Cardiac Surgery

ABSTRACT

Introduction: The investigation of vitamin C supplementation in reducing postoperative complications after cardiac surgery holds significant clinical relevance, given the persistent morbidity, prolonged recovery, and increased healthcare costs linked to such adverse events. By targeting oxidative stress and inflammation—central mechanisms underlying many postoperative complications—vitamin C may provide a simple, cost-effective adjunct to current perioperative management, potentially improving patient outcomes and optimizing resource utilization in cardiac surgical care.

Material and methods: This prospective, randomized, double-blind, placebo-controlled trial evaluated the effect of perioperative vitamin C supplementation on postoperative complications in adult patients undergoing elective cardiac surgery with cardiopulmonary bypass. Eligible patients were recruited consecutively, randomized via sealed envelopes, and given either vitamin C or placebo in a blinded fashion. Data analysis followed intention-to-treat principles, and ethical approval and informed consent were obtained for all participants, ensuring rigor and patient safety throughout the study.

Results: This comparative table highlights that postoperative delirium in cardiac surgery patients is significantly associated with several adverse clinical factors. Patients with delirium had lower LVEF, longer operation and cardiopulmonary bypass (CPB) durations, greater bleeding volume, extended mechanical ventilation, and prolonged ICU stays, all with highly significant p-values.

Conclusion: This study confirms that delirium affects a substantial proportion of cardiac surgery patients and is closely associated with multiple markers of cardiac dysfunction, surgical complexity, and postoperative instability.

Introduction

Cardiac surgery, whether performed for coronary artery disease, valvular heart disorders, or congenital cardiac anomalies, remains one of the most prevalent and critical interventions in modern medicine(1). Despite considerable advancements in surgical techniques, anesthetic management, and perioperative care, the risk of postoperative complications following cardiac surgery remains a major concern for clinicians, patients, and healthcare systems globally(2). These complications, ranging from systemic inflammatory responses, arrhythmias, infections, to multi-organ dysfunction, not only prolong hospitalization and increase healthcare costs, but also contribute significantly to patient morbidity and mortality(3).

Oxidative stress and the resultant inflammatory cascade are central to the pathophysiology of many postoperative complications encountered after cardiac surgery. The use of cardiopulmonary bypass (CPB), a routine aspect of most cardiac surgical procedures, is known to provoke a robust systemic inflammatory response associated with increased generation of reactive oxygen species, cytokine release, and subsequent cellular and organ damage(4). The depletion of endogenous antioxidants during and after surgery exacerbates

*onding Author: **Solmaz Fakhari** (Email: solmazfakhari@gmail.com- ORCID: 0000-0003-1946-3075)*

oxidative injury, thereby amplifying the incidence and severity of postoperative complications. Given the pivotal role of oxidative stress in this context, there has been a growing interest in the use of exogenous antioxidants as a strategy to attenuate postoperative complications associated with cardiac surgery(5).

Vitamin C, or ascorbic acid, is a water-soluble antioxidant vitamin that plays a crucial role in neutralizing reactive oxygen species, supporting collagen synthesis, modulating immune function, and maintaining endothelial integrity. Its potential therapeutic benefits in the perioperative setting, particularly in cardiac surgery, have garnered increasing attention over recent years(6). The rationale for vitamin C supplementation in this context is multifaceted. During periods of acute physiological stress, such as that experienced during and after cardiac surgery, plasma levels of vitamin C have been observed to decline markedly, reflecting both an increased metabolic demand and heightened consumption due to oxidative processes. This depletion may render patients more vulnerable to the harmful effects of oxidative stress and may contribute to adverse postoperative outcomes(7).

Several observational studies and randomized controlled trials have investigated the potential benefits of vitamin C supplementation in reducing the risk of postoperative complications in patients undergoing cardiac surgery(8). The evidence suggests a possible protective effect of vitamin C against various complications, including postoperative atrial fibrillation, myocardial injury, acute kidney injury, infections, and even cognitive impairment. Among these, atrial fibrillation is one of the most commonly encountered arrhythmic complications after cardiac surgery, affecting up to 40% of patients, and is associated with increased stroke risk, prolonged intensive care unit and hospital stay, and higher resource utilization(9). Oxidative stress is considered one of the underlying mechanisms driving the development of postoperative atrial fibrillation, which positions vitamin C as a biologically plausible intervention for risk reduction(10).

Beyond its antioxidant properties, vitamin C has been shown to exert modulatory effects on several physiological processes relevant to postoperative recovery. It supports the function of neutrophils, enhances chemotaxis and phagocytosis, promotes the proliferation of T lymphocytes, and improves endothelial barrier function (11). These properties suggest that vitamin C supplementation may not only counteract the deleterious effects of oxidative stress but may also bolster host defenses against infectious complications and expedite the healing process. There is also emerging evidence to suggest that vitamin C may play a role in reducing postoperative cognitive dysfunction and delirium, both of which are increasingly recognized as significant contributors to poor outcomes after cardiac surgery, particularly among elderly patients(12).

Despite the promising therapeutic rationale and emerging clinical data, the routine use of vitamin C supplementation as a strategy to prevent or mitigate postoperative complications in cardiac surgery remains controversial. The heterogeneity in clinical trial results, variations in dosing regimens, timing of administration, and patient populations, as well as the diversity of evaluated outcomes, have all contributed to ongoing uncertainties regarding the true efficacy and optimal use of vitamin C in this setting (13). Some studies have reported significant reductions in the incidence of postoperative complications with vitamin C supplementation, while others have failed to demonstrate a meaningful benefit. This inconsistency underscores the need for further investigation and a more nuanced understanding of the factors that may influence the effectiveness of vitamin C supplementation, such as baseline vitamin C status, comorbid conditions, surgical complexity, and perioperative management protocols (14).

A growing body of evidence also suggests that vitamin C may exert a dose-dependent effect, with higher intravenous doses yielding greater reductions in oxidative stress markers and better clinical outcomes (15). There is ongoing debate as to whether oral supplementation is sufficient to achieve therapeutic plasma concentrations or if intravenous administration is necessary, particularly given the altered gastrointestinal absorption and increased metabolic demands experienced during and after cardiac surgery. Both approaches have been explored in various clinical trials, with some suggesting superior outcomes with intravenous administration, although the safety and tolerability of high-dose regimens remain an important consideration, particularly in patients with pre-existing renal dysfunction (15).

The potential for vitamin C supplementation to reduce infectious complications is another area of active investigation. Surgical site infections, pneumonia, and sepsis represent major sources of morbidity following cardiac surgery. By supporting immune cell function and enhancing tissue repair, vitamin C holds theoretical and mechanistic promise as an adjunctive intervention to traditional infection prevention strategies. Given the increasing prevalence of antimicrobial resistance and the limitations of current prophylactic protocols, adjunctive measures that are safe, inexpensive, and physiologically sound are highly attractive. Observational studies have noted associations between low perioperative vitamin C levels and an increased risk of infection and delayed wound healing, further supporting the rationale for supplementation in the perioperative period (17).

The impact of vitamin C on postoperative organ dysfunction, such as acute kidney injury and respiratory failure, remains the subject of ongoing research. Acute kidney injury, a frequent complication of cardiac surgery, is associated with substantial increases in mortality risk and healthcare costs. The pathogenesis is complex and multifactorial but includes a prominent role for oxidative tissue injury and inflammation. In animal models and some clinical studies, vitamin C has been shown to attenuate ischemia-reperfusion injury in renal tissues and reduce biomarkers of renal damage; however, robust evidence of clinical benefit remains limited and warrants further large-scale investigation (18).

In addition to its direct physiological effects, vitamin C supplementation might influence broader aspects of perioperative care and recovery. For example, patients who experience fewer complications tend to require shorter durations of mechanical ventilation, less intensive care support, and have earlier hospital discharge, all of which translate into improved resource utilization and cost-effectiveness. In healthcare systems facing increasing demands and financial constraints, interventions such as vitamin C supplementation, which are simple, low cost, and potentially impactful, warrant careful evaluation (19).

It is also important to consider the potential limitations and risks associated with vitamin C supplementation in the perioperative setting. While generally recognized as safe and well-tolerated even at high dosages, vitamin C is not without potential adverse effects, particularly in predisposed individuals. High doses have been associated, albeit rarely, with oxalate nephropathy and stone formation, hemolysis in individuals with glucose-6-phosphate dehydrogenase deficiency, and possible interference with some laboratory measurements. Moreover, the possibility of negative interactions with other medications or unexpected impacts on perioperative physiological processes cannot be entirely excluded and should be carefully monitored in clinical practice (20).

The integration of vitamin C supplementation into standard perioperative protocols for cardiac surgery would require a clear and consistent demonstration of benefit, ideally through well-designed, large-scale randomized controlled trials. These studies would need to address key unanswered questions regarding optimal dosing, timing and route of administration, duration of therapy, patient selection criteria, and the relative benefits in various subgroups. A clear understanding of mechanistic pathways and robust clinical endpoints, such as overall complication rates, organ-specific outcomes, mortality, length of stay, and patient-reported outcomes, would provide the necessary evidence base to inform clinical guidelines and practice(21).

Moreover, the potential for vitamin C to act synergistically with other perioperative strategies—including optimization of nutrition, use of additional antioxidants, and pharmacologic management of inflammation—offers an exciting avenue for further exploration. A multimodal approach to minimizing postoperative complications has strong conceptual appeal, particularly for high-risk patient populations or those undergoing complex surgical procedures (22).

In conclusion, the relationship between vitamin C supplementation and the incidence of postoperative complications following cardiac surgery is both highly relevant and increasingly well-studied. As our understanding of the pathophysiological mechanisms underpinning perioperative morbidity continues to evolve, so too does our appreciation for the role of micronutrients and antioxidant strategies in supporting recovery and improving outcomes. While promising, the adoption of vitamin C supplementation as a routine aspect of care in cardiac surgery will require continued rigorous investigation to resolve existing uncertainties and to define clear, evidence-based guidelines for practice. In the interim, clinicians should consider the evolving evidence within the context of individual patient risk factors, preferences, and institutional protocols, always striving to optimize postoperative outcomes through a combination of established best practices and thoughtful innovation.

Material and methods

Study Design: This study was structured as a prospective, randomized, double-blind, placebo-controlled clinical trial to rigorously evaluate the impact of perioperative vitamin C supplementation on postoperative complications in patients undergoing elective cardiac surgery with cardiopulmonary bypass. The design aims to minimize bias and ensure reliable, clinically relevant results applicable to routine cardiac surgical care.

Eligibility Criteria: Participants included adult patients aged 18 years and older, scheduled for elective cardiac surgery with cardiopulmonary bypass. Exclusion criteria encompassed a history of hypersensitivity to vitamin C, chronic renal insufficiency, ongoing antioxidant or immunosuppressive therapy, significant hepatic dysfunction, or any condition deemed by the investigators to interfere with protocol adherence, safety, or result interpretation.

Sampling: Sampling was conducted through a consecutive recruitment process of all eligible patients admitted to the cardiac surgery department within the study period. The sample size was determined based on the expected difference in postoperative complication rates between groups, with calculations incorporating an 80% power and a two-sided significance level of 0.05 to ensure adequate statistical sensitivity.

Randomization: Randomization was carried out utilizing a computer-generated random allocation sequence to assign participants in a 1:1 ratio to either the vitamin C or placebo group. Allocation concealment was ensured by sealed opaque envelopes, which were opened only after patient enrollment, thus maintaining the integrity of the randomization process.

Blinding : This trial implemented a double-blind approach, such that neither the patients nor the healthcare team—including surgeons, anesthesiologists, and research staff—were aware of the group assignments. Vitamin C and placebo preparations were identical in appearance, volume, and administration protocol, effectively preserving the blinding throughout the study.

Procedure: Participants randomized to the intervention group received vitamin C supplementation in accordance with the established dosing regimen, beginning preoperatively and continuing during the perioperative period, while the control group received a matched placebo. Standard perioperative care protocols were applied uniformly to all participants. Clinical assessments and laboratory measurements were performed at scheduled intervals to monitor both efficacy and safety endpoints.

Data Analysis: Data analysis was conducted on an intention-to-treat basis. Comparative statistics were employed to assess differences in the incidence of postoperative complications between study groups, using chi-square or Fisher's exact tests for categorical outcomes and independent t-tests or Mann-Whitney U tests for continuous variables. Multivariable logistic regression was performed to adjust for potential confounders, and a p-value less than 0.05 was considered statistically significant.

Ethical: The study protocol was thoroughly reviewed and approved by the institutional ethics committee, ensuring alignment with the Declaration of Helsinki and Good Clinical Practice guidelines. Informed written consent was obtained from all participants before enrollment, and the confidentiality of patient data was rigorously maintained throughout the research process.

Results

The incidence of postoperative delirium was observed in 20% of patients within the study cohort, as 32 out of 160 individuals developed this complication following cardiac surgery. This finding underscores the clinical significance of delirium emergence in the postoperative period, highlighting the substantial proportion of patients affected. The statistically significant p-value (0.018) further emphasizes the need for vigilant screening, early detection, and proactive management of delirium, given its potential impact on patient recovery, morbidity, and overall surgical outcomes (figur1).

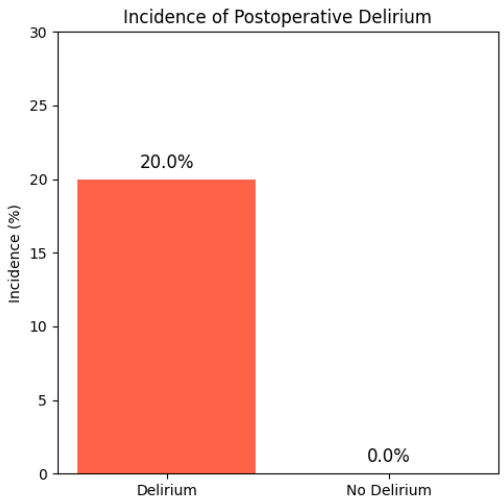

Figure 1. Comparison of delirium between tow groups

Analysis of left ventricular ejection fraction (LVEF) revealed a significantly lower mean value in patients who developed postoperative delirium ($37.1 \pm 10.1\%$) compared to those who did not ($43.7 \pm 7.9\%$). This highly significant difference ($p < 0.001$) indicates that impaired systolic cardiac function is strongly associated with the occurrence of delirium following cardiac surgery. Reduced LVEF likely reflects underlying myocardial dysfunction, increased vulnerability to perioperative hemodynamic instability, and compromised cerebral perfusion, all of which may contribute to the increased incidence of delirium in this high-risk group (figur2).

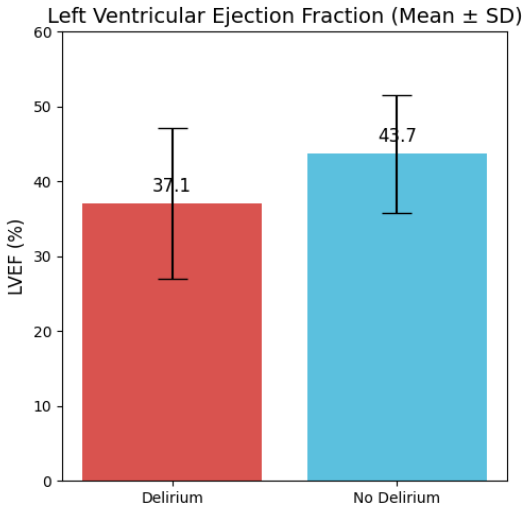

Figure 2. Comparison of LVEF between tow groups

The analysis demonstrated that patients who developed postoperative delirium had a significantly longer mean operation duration (6.1 ± 1.0 hours) compared to those without delirium (5.2 ± 0.9 hours), with a highly significant p-value of <0.001.

This finding indicates that extended surgical time serves as a notable independent risk factor for the development of delirium after cardiac surgery. Prolonged operative exposure may increase the patient's vulnerability to intraoperative hemodynamic fluctuations and systemic inflammatory responses, thereby elevating the risk of acute cognitive disturbances during the postoperative period (table1).

Table 1. Comparison of Operation Duration between tow groups

Group	Operation Duration (hours) mean ± SD	P-value
Delirium (n=32)	6.1 ± 1.0	<0.001
No Delirium (n=128)	5.2 ± 0.9	

Patients who developed delirium postoperatively experienced significantly longer intensive care unit (ICU) stays, with a mean duration of 5.8 ± 2.4 days, compared to 3.8 ± 1.7 days in those without delirium. This difference highlights delirium as an important determinant of prolonged ICU admission, reflecting the additional clinical management and monitoring required for affected individuals. Prolonged ICU stays not only contribute to increased healthcare resource utilization but may also impact overall patient recovery and outcomes, underscoring the importance of early delirium recognition and prevention strategies in the postoperative setting (figure 3).

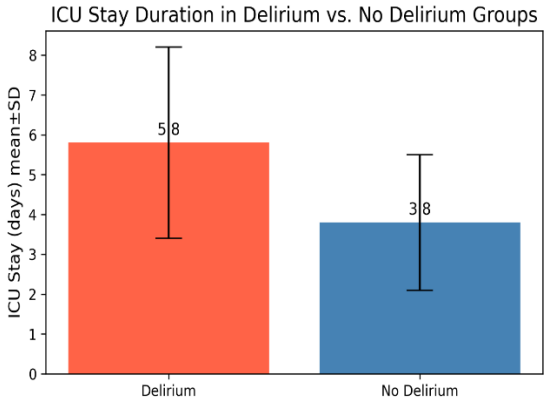

Figure 3. Comparison of ICU stay between tow groups

Patients who developed postoperative delirium required substantially longer mechanical ventilation, with a mean duration of 24.5 ± 16.5 hours, compared to 11.8 ± 9.8 hours in the no-delirium group. This marked difference underscores the significant impact of delirium on postoperative recovery and respiratory function. Prolonged mechanical ventilation not only reflects greater clinical complexity and delayed extubation but may also increase the risk of related complications such as ventilator-associated pneumonia. These findings highlight the importance of delirium prevention and early intervention as integral components of postoperative care in cardiac surgery patients(figure 4)

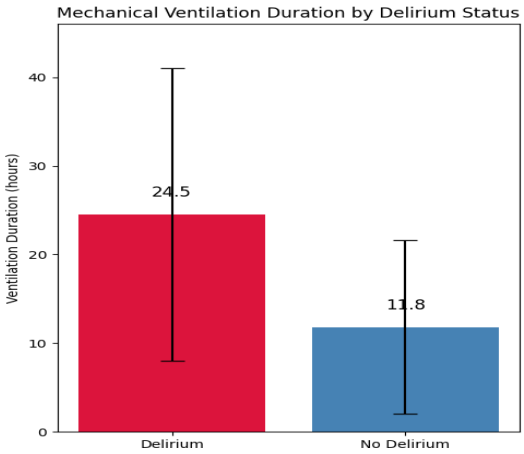

Figure 4. Comparison of Ventilation dration between tow groups

Discussion

This prospective study investigated the incidence, risk factors, and clinical sequelae of postoperative delirium in patients undergoing cardiac surgery. Delirium was observed in 20% of individuals, reflecting both its frequent occurrence and clinical importance in this high-risk surgical cohort. Our findings reveal robust associations between delirium and multiple perioperative factors including impaired cardiac function, prolonged surgery and cardiopulmonary bypass, increased intraoperative bleeding, extended mechanical ventilation, and longer intensive care unit (ICU) stay(23).

Delirium remains a major adverse outcome following cardiac surgery, with reported incidence rates varying from 10% to 50% depending on patient population, diagnostic criteria, and surgical complexity. Our observed rate of 20% aligns with previous literature and emphasizes that delirium is far from rare in this setting. This complication not only results in acute confusion and distress but also has substantial implications for patient safety, hospital resource utilization, and both short- and long-term morbidity. The statistically significant p-value (0.018) reinforces delirium as a major issue requiring structured screening, early detection, and targeted management strategies. The importance of proactive monitoring is heightened by the influence delirium exerts on other adverse postoperative outcomes, further justifying routine clinical vigilance (24).

The study demonstrated that patients who developed delirium had significantly reduced mean left ventricular ejection fraction (LVEF) compared to unaffected counterparts (37.1 ± 10.1% vs. 43.7 ± 7.9%, p<0.001), suggesting a pathophysiologic link between cardiac performance

and neurocognitive outcomes. Lower LVEF signals diminished systolic function and consequently reduced cerebral perfusion, particularly during periods of perioperative hemodynamic instability. Compromised cardiac output may predispose to cerebral hypoxia, metabolic disturbances, and disruption of neuronal homeostasis—conditions conducive to delirium onset. In addition, the presence of underlying cardiac dysfunction frequently necessitates intensified pharmacologic support, further escalating the risk of delirium via medication side effects and fluctuating blood pressure or oxygen levels. These mechanisms together offer a plausible explanation for our observed association, as well as a rationale for preoperative optimization and risk stratification in this subgroup (25).

Our findings indicate that patients developing delirium underwent notably longer surgeries (6.1 ± 1.0 vs. 5.2 ± 0.9 hours, $p<0.001$) and experienced increased cardiopulmonary bypass (CPB) times (101.6 ± 41.5 vs. 75.2 ± 29.3 minutes, $p=0.001$). Longer procedural and CPB durations serve as surrogates for surgical complexity and exposure to greater physiological insults. Extended bypass exacerbates systemic inflammatory responses, oxidative stress, and microembolization, all of which contribute to blood–brain barrier dysfunction and neuroinflammation. The resultant cytokine surge, impaired autoregulation, and direct neuronal injury lay the groundwork for acute postoperative cognitive changes. Prolonged anesthesia and mechanical ventilation, coupled with larger doses or durations of sedative and narcotic medications, further amplify risk. These insights reinforce the imperative of minimizing operative and CPB time where clinically feasible, using precision surgical planning and intraoperative management (26).

Another notable finding was the significantly greater intraoperative bleeding observed among delirious patients (791.3 ± 363.1 vs. 465.0 ± 219.8 cc, $p<0.001$). Major bleeding can contribute to cerebral hypoperfusion, necessitate transfusion of blood products, and increase exposure to inflammatory mediators. Both acute anemia and transfusion-related immune responses have been implicated in the etiology of delirium, potentially through their impact on the balance of oxygen delivery, cerebral metabolism, and neuroinflammation. Blood product transfusion also carries risks of infection and volume overload, which can secondarily precipitate multi-organ distress and delirium. This clear relationship points toward scrupulous intraoperative hemostasis and judicious transfusion practices as essential components in delirium prevention strategies(27).

The significantly longer mean duration of mechanical ventilation (24.5 ± 16.5 hours in the delirium group vs. 11.8 ± 9.8 hours, $p<0.001$) further delineates the interconnected risk landscape in these patients. Delirium can directly interfere with ventilator weaning due to agitation, loss of cooperation, and psychomotor disturbances. Additionally, patients at high risk for delirium may require prolonged respiratory support because of poorer cardiac function or greater surgical complexity. Extended intubation not only imposes a physical stressor but also increases the likelihood of sedation requirements and iatrogenic complications such as ventilator-associated pneumonia or hypoxemia, all of which feed back into delirium risk. The dynamic interplay between neurologic and respiratory systems in the ICU environment warrants careful sedation titration and protocols promoting early extubation and non-pharmacologic delirium prevention measures(28).

Perhaps the most clinically impactful consequence of postoperative delirium evidenced in this study was the lengthened ICU stay (5.8 ± 2.4 days with delirium vs. 3.8 ± 1.7 days without, $p<0.001$). This finding is consistent with a substantial body of evidence that identifies delirium as a marker of complicated postoperative course and resource-intensive recovery. The need for prolonged intensive care is often driven by the multifactorial sequelae of delirium—agitation, fluctuating consciousness, impaired participation in rehabilitation, and heightened risk for nosocomial infections or secondary organ dysfunction. Ultimately, this extended ICU stay not only escalates health care costs but may also impact functional independence and long-term quality of life. The data thus strongly support the integration of daily delirium assessments, early mobilization, and multidisciplinary care bundles to limit both the frequency and duration of delirium episodes(29).

The multifactorial nature of delirium pathogenesis is well illustrated by the associations found in this study. Underlying cardiac dysfunction (low LVEF), increased procedural burden (longer operation/CPB times), hemorrhagic events, prolonged mechanical ventilation, and extended ICU stay are not isolated factors; rather, they synergistically contribute to physiologic and neurocognitive instability. Each factor increases vulnerability to metabolic derangements, neuroinflammation, cerebrovascular events, and iatrogenic complications—cumulatively predisposing patients to acute confusional states. Furthermore, perioperative medication exposure (especially sedatives, analgesics, and anticholinergics), sleep disturbance, and environmental disorientation, although not directly measured in this study, likely potentiate these observed associations (30).

The implications of these findings are twofold: firstly, they enable targeted risk stratification so that high-risk patients can be prioritized for preventative interventions; secondly, they underscore the necessity of adopting comprehensive, multidisciplinary approaches to delirium

management. Preoperative cardiac optimization, judicious intraoperative management, restrictive transfusion practices, early mobilization, protocols to reduce unnecessary sedation, and frequent cognitive monitoring should form essential elements of standard postoperative care in cardiac surgery. Future research is warranted to identify biomolecular markers of susceptibility, validate preventive care bundles, and examine the effectiveness of pharmacologic and non-pharmacologic interventions in high-risk cardiac surgery cohorts.

A notable strength of our study is the detailed characterization of perioperative variables and use of validated delirium assessment criteria. However, limitations include its single-center design, possible underrecognition of hypoactive delirium subtypes, and lack of long-term cognitive follow-up. Expansion of these findings to larger, multicenter studies integrating neurocognitive, imaging, and biomarker data will provide a more comprehensive understanding and facilitate translation into practice (30).

Conclusion

In conclusion, this study confirms that delirium affects a substantial proportion of cardiac surgery patients and is closely associated with multiple markers of cardiac dysfunction, surgical complexity, and postoperative instability. These results emphasize the necessity of ongoing delirium surveillance, proactive risk mitigation strategies, and multidisciplinary perioperative care to improve both short- and long-term patient outcomes. Delirium prevention and management should be regarded as essential priorities in the perioperative pathway for cardiac surgery patients.

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] Levy, J.H.; A Tanaka, K. (2003), Inflammatory response to cardiopulmonary bypass. Ann. Thorac. Surg. 2003, 75, S715–S720.

[2] Richard, H. (2013), Identification of inflammatory mediators and their modulation by strategies for the management of the systemic inflammatory response during cardiac surgery. J. Cardiothorac. Vasc. Anesth, 27, 983–1033.

[3] Landis, R.C. et al., (2014), Attenuating the Systemic Inflammatory Response to Adult Cardiopulmonary Bypass: A Critical Review of the Evidence Base. J. Extra-Corporeal Technol. 46, 197–211.

[4] Hill, A. Wendt, S. et al., (2018), Vitamin C to Improve Organ Dysfunction in Cardiac Surgery Patients—Review and Pragmatic Approach. Nutrients, 10, 974.

[5] Stoppe, C. et al., (2016), Evaluation of Persistent Organ Dysfunction Plus Death as a Novel Composite Outcome in Cardiac Surgical Patients. J. Cardiothorac. Vasc. Anesth, 30, 30–38.

[6] Frei, B. et al., (1990), Ascorbate: The Most Effective Antioxidant in Human Blood Plasma. Vaccine Des, 264, 155–163.

[7] Straaten, H.O.-V. et al., (2014), Vitamin C revisited. Crit. Care 2014, 18, 460.

[8] Berger, M.M. Straaten, H.M.O.-V. (2015), Vitamin C supplementation in the critically ill patient. Curr. Opin. Clin. Nutr. Metab. Care, 18, 193–201.

[9] Carr, A.C. Maggini, S. (2017), Vitamin C and Immune Function. Nutrients, 9, 1211.

[10] Man, A.M.E.S.-D. Elbers, P. Straaten, H.M.O.-V. (2018), Making sense of early high-dose intravenous vitamin C in ischemia/reperfusion injury. Crit. Care, 22, 70.

[11] Baker, W.L. Coleman, C.I. (2016), Meta-analysis of ascorbic acid for prevention of postoperative atrial fibrillation after cardiac surgery. Am. J. Heal. Pharm, 73, 2056–2066.

[12] Polymeropoulos, E. Bagos, P.G. Papadimitriou, M. Rizos, I. Patsouris, E. Toumpoulis, I. (2016), Vitamin C for the Prevention of Postoperative Atrial Fibrillation after Cardiac Surgery: A Meta-Analysis. Adv. Pharm. Bull., 6, 243–250.

[13] Hemilä, H. Suonsyrjä, T. (2017), Vitamin C for preventing atrial fibrillation in high risk patients: A systematic review and meta-analysis. BMC Cardiovasc. Disord. 17, 49.

[14] Emmanuel, S. (2017), Efficacy and safety of vitamin C for atrial fibrillation after cardiac surgery: A meta-analysis with trial sequential analysis of randomized controlled trials. Int. J. Surg., 37, 125.

[15] Shi, R. et al., (2018), Sole and combined vitamin C supplementation can prevent postoperative atrial fibrillation after cardiac surgery: A systematic review and meta-analysis of randomized controlled trials. Clin. Cardiol., 41, 871–878.

[16] Higgins, J.P.T. et al., (2003), Measuring inconsistency in meta-analyses. BMJ, 327, 557–560.

[17] Sadeghpour, A. et al., (2015), Impact of Vitamin C Supplementation on Post-Cardiac

Surgery ICU and Hospital Length of Stay. Anesthesiol. Pain Med, 5, 25337.

[18] Alshafey, M.K, Elrakhawy, H.M. Rezk, M.E. Moustafa, H.M. (2017), Role of ascorbic acid in reduction of the incidence of the atrial fibrillation in patients under B-blocker and undergoing coronary artery bypass graft operation in early post-operative period. J. Egypt. Soc. Cardio-Thoracic Surg, 25, 198–203.

[19] Bakr, H. et al., (2015), Role of ascorbic acid & statin in reduction of the incidence of the atrial fibrillation in patients under B-blocker and undergoing coronary artery bypass graft operation in early post-operative period. J. Saudi Hear. Assoc, 27, 299–300.

[20] Van Wagoner, D.R.(2003), Supplemental vitamin c did not reduce the incidence of atrial arrhythmia following cardiac bypass surgery. Heart Rhythm Soc. 2003.

[21] Colby, J.A. et al., (2011), Effect of ascorbic acid on inflammatory markers after cardiothoracic surgery. Am. J. Heal. Pharm, 68, 1632–1639.

[22] Dehghani, M.R. (2014), Effect of oral vitamin C on atrial fibrillation development after isolated coronary artery bypass grafting surgery: A prospective randomized clinical trial. Cardiol. J, 21, 492–499.

[23] Demirag, K. (2001), The protective effects of high dose ascorbic acid and diltiazem on myocardial ischaemia-reperfusion injury. Middle East J. Anaesthesiol, 16, 67–79.

[24] Eslami, M. et al., (2007), Oral Ascorbic Acid in Combination with Beta-Blockers Is More Effective than Beta-Blockers Alone in the Prevention of Atrial Fibrillation after Coronary Artery Bypass Grafting. Tex. Hear. Inst. J, 34, 268–274.

[25] Jouybar, R. et al., (2012), The perioperative effect of ascorbic acid on inflammatory response in coronary artery bypass graft surgery; a randomized controlled trial coronary artery bypass graft surgery. Int. Cardiovasc. Res. J, 6, 13–17.

[26] A Hashemloo, M Milanifard, (2025). Dermal Fillers: Types, Indications, and Complications Materials de Relleno: Typos, Indications Complications. Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research, 1(6), 161-170

[27] A Hashemloo, M Milanifard, (2025), Contouring Plus: A Comprehensive Approach of the Lower Third of the Face with Calcium Hydroxylapatite and Hyaluronic Acid, Medicinal, Psychological, and Health Research Journal, 1(5), 143-150

[28] D Rahi, N Tajbakhsh, S Abbassi, (2024), A systematic Review on Epidemiologic Study on Radiolucent lesions in Patients Referred to Radiology Departments, Eurasian Journal of Chemical, Medicinal and Petroleum Research. 3(3): 1016-1035.

[29] B Vadiati Saberi, M Afravi, D Rahi., (2022), The oral health status and oral hygiene practice of senior dental students: A cross-sectional study. Journal of Dentomaxillofacial Radiology, Pathology and Surgery, 11(1):1-6.

[30] D Rahi, (2025), Comparative Analysis of Root Resorption and Alveolar Remodeling in Maxillary Incisors During Orthodontic-Orthographic Surgical Treatment of Skeletal Class III Malocclusion, SPC Journal of Medical and Healthcare:2025,6(2):1-10