

Timing of Renal Replacement Therapy for Cardiac Surgery Associated Acute Kidney Injury (CSA-AKI)

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ABSTRACT

Cardiac surgery-associated acute kidney injury (CSA-AKI) occurs in 5–30% of patients and is linked to increased morbidity, mortality, and healthcare costs. Severe CSA-AKI often necessitates renal replacement therapy (RRT), yet the optimal timing of initiation remains controversial. This literature review synthesizes current evidence on the pathophysiology of CSA-AKI, definitions and rationales for early versus late RRT, comparative outcomes, and existing guideline recommendations. CSA-AKI arises from ischemia–reperfusion injury, systemic inflammation, oxidative stress, and microcirculatory dysfunction, compounded by perioperative hemodynamic instability and nephrotoxic exposures. Early RRT—commonly initiated within hours of KDIGO stage 2 AKI—may mitigate fluid overload, metabolic derangements, and inflammatory injury, with potential benefits in selected patients. Late RRT—delayed until persistent AKI or urgent indications—can avoid unnecessary intervention, reduce procedural risks, and preserve residual renal function. Comparative studies, including ELAIN, STARRT-AKI, and Crescenzi et al., reveal no universal survival advantage for either approach, with patient selection and clinical context being decisive factors. Current guidelines, such as KDIGO and ADQI, recommend individualized timing based on clinical urgency, hemodynamic status, and multidisciplinary input, with a preference for continuous modalities in unstable patients. Evidence supports a tailored strategy that balances the benefits of early intervention against the risks of overtreatment, while highlighting the need for standardized definitions and CSA-AKI-specific randomized trials to guide future protocols

KEYWORDS: Cardiac surgery-associated acute kidney injury, renal replacement therapy, early initiation, delayed initiation

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INTRODUCTION

Cardiac surgery is a critical intervention for managing advanced cardiovascular diseases, yet it carries significant postoperative risks, including acute kidney injury (AKI), a complication affecting 5–30% of patients^{1,2}. AKI severity ranges from mild dysfunction to complete renal failure, profoundly impacting clinical outcomes. Post-cardiac surgery AKI (CSA-AKI) is associated with prolonged hospitalization, increased mortality, and heightened healthcare costs, underscoring its clinical and economic burden^{3,4}.

Renal replacement therapy (RRT) remains a cornerstone for managing severe AKI, particularly in patients unresponsive to conservative treatments. However, the optimal timing of RRT initiation—early versus late—sparks considerable debate^{5,6}. Proponents of early RRT argue it may mitigate fluid overload, electrolyte imbalances, and inflammatory cascades, potentially improving survival. Conversely, critics caution against unnecessary interventions, citing risks such as hemodynamic instability and overutilization of resources.

Existing studies report conflicting results, compounded by heterogeneous definitions of "early" and "late" RRT and variability in patient populations^{7,8}. Recent meta-analyses and clinical guidelines highlight persistent uncertainty, with limited consensus on standardized protocols^{9–10}. This inconsistency underscores the need for a rigorous synthesis of current evidence tailored to post-cardiac surgery patients—a population uniquely vulnerable due to factors like cardiopulmonary bypass exposure and hemodynamic fluctuations^{11,12}. While recent trials like ELAIN (2016) and STARRT-AKI (2020) informed critical care guidelines, their applicability to post-cardiac surgery patients is limited by divergent pathophysiology and recovery trajectories⁵. Consequently, major guidelines (e.g., KDIGO) offer no procedure-specific recommendations, reflecting a critical evidence gap⁷. This literature review synthesizes current evidence on RRT timing in post-cardiac surgery AKI, evaluating impacts on survival, renal recovery, and complications. By contextualizing findings within the unique physiology of cardiac surgery, it aims to clarify

the risk-benefit balance of early vs. delayed RRT initiation, Identify population-specific predictors of RRT success, Guide future research toward standardized, evidence-based protocols. By addressing gaps in previous reviews, such as population specificity and methodological disparities, our findings seek to inform evidence-based clinical decisions and guide future research priorities. Ultimately, clarifying RRT timing could enhance patient outcomes, reduce healthcare burdens, and refine therapeutic guidelines in this high-risk population.

Pathophysiology of CSA-AKI

The pathophysiological mechanisms underlying CSA-AKI involve a complex interplay of hemodynamic, inflammatory, and nephrotoxic insults. During cardiopulmonary bypass (CPB), renal perfusion may be impaired due to systemic hypotension, non-pulsatile flow, and aortic cross-clamping, which lead to renal ischemia and subsequent tubular injury, particularly in the renal medulla where oxygen tension is lowest^{13,14}. Reperfusion following ischemia further exacerbates renal injury through oxidative stress and the generation of reactive oxygen species (ROS), contributing to endothelial dysfunction and cellular apoptosis¹⁵. Moreover, systemic inflammatory response syndrome (SIRS), triggered by surgical trauma and blood exposure to the extracorporeal circuit, leads to cytokine release (e.g., IL-6, TNF- α) and leukocyte activation, which damage renal microcirculation¹⁶. Hemolysis during CPB may release free hemoglobin, promoting oxidative nephrotoxicity, while complement activation and microembolization further impair renal perfusion¹⁷. Additionally, perioperative exposure to nephrotoxic agents (e.g., contrast media, antibiotics) and use of vasopressors compounds renal vulnerability. Importantly, pre-existing factors such as chronic kidney disease, diabetes, or advanced age potentiate the risk and severity of CSA-AKI by reducing renal functional reserve¹⁸. Thus, CSA-AKI results from both patient-specific vulnerabilities and intraoperative stressors that converge to cause acute tubular necrosis and impaired renal autoregulation.

The Early RRT VS Late RRT Definition

The optimal timing for initiating renal replacement therapy (RRT) in patients with cardiac surgery-associated acute kidney injury (CSA-AKI) remains an area of clinical debate. The distinction between “early” and “late” RRT is often study-dependent, lacking universal consensus, and varies based on clinical criteria such as urine output, serum creatinine levels, and timing from AKI onset. In many clinical trials, early RRT is defined as initiation within a fixed time window following AKI diagnosis—commonly within 8 to 24 hours after reaching KDIGO stage 2 criteria—before life-threatening complications develop^{19,20}. For example, in the ELAIN trial, early RRT was initiated within 8 hours of stage 2 AKI with neutrophil gelatinase-associated lipocalin (NGAL) >150 ng/mL, while delayed RRT was started after stage 3 AKI or when urgent indications arose⁶. Conversely, delayed or late RRT is typically initiated after a watchful waiting period, often exceeding 24–48 hours, or once classical urgent indications manifest, such as refractory fluid overload, hyperkalemia, severe acidosis, or uremic symptoms^{21,22}. In the study by Crescenzi et al., early RRT was defined as treatment begun after 6 hours of oliguria (<0.5 mL/kg/h), whereas the late approach initiated therapy only after 12 hours of persistent oliguria²³. These variations highlight the lack of standardized thresholds, often influenced by institutional protocols and patient-specific factors. This heterogeneity in definitions complicates direct comparisons across studies and underscores the need for harmonized criteria to guide clinical decision-making in CSA-AKI management.

Rationale in Early RRT

The rationale for early initiation of renal replacement therapy (RRT) in cardiac surgery-associated acute kidney injury (CSA-AKI) is grounded in the pathophysiology of AKI and the potential to prevent progression to irreversible renal damage and multi-organ dysfunction. Early RRT offers the advantage of promptly correcting metabolic derangements such as hyperkalemia, severe acidosis, and azotemia before they reach critical levels, thereby minimizing the systemic consequences of uremia^{22,24}. In the context of CSA-AKI, rapid fluid removal through continuous modalities can also prevent or reverse fluid overload, which is strongly associated with impaired cardiac performance, prolonged mechanical ventilation, and increased mortality^{25,26}. Early clearance of inflammatory mediators, which accumulate during cardiopulmonary bypass and ischemia–reperfusion injury, has been proposed as an additional mechanism by which early RRT may mitigate ongoing renal and systemic injury¹⁷. Furthermore, studies such as the ELAIN trial have demonstrated that initiating RRT within hours of reaching KDIGO stage 2 AKI was associated with shorter ICU stays, reduced RRT duration, and improved 90-day survival compared to delayed initiation⁶. Observational data in CSA-AKI suggest that early therapy may improve hemodynamic stability by avoiding abrupt shifts in fluid balance and enabling gradual solute control, particularly in patients with reduced cardiac reserve²⁷. While definitive mortality benefits remain debated, the theoretical and mechanistic rationale for early RRT lies in its potential to interrupt the cascade of AKI progression, reduce complications, and optimize recovery of renal function.

Rationale in Late RRT

The rationale for a delayed, or late, initiation of renal replacement therapy (RRT) in cardiac surgery-associated acute kidney injury (CSA-AKI) is based on the principle of avoiding unnecessary exposure to extracorporeal therapy in patients who may recover renal function spontaneously. Many patients with CSA-AKI, particularly those with transient oliguria or hemodynamic instability, improve with conservative measures such as optimization of cardiac output, careful fluid management, and avoidance of nephrotoxins, without ever requiring RRT^{20,28}. Early initiation may expose these patients to procedural risks—including vascular access complications, anticoagulation-related bleeding, infection, and hemodynamic perturbations—without clear survival benefit in all populations^{29,30}. Large multicenter trials in mixed ICU cohorts, such as the STARRT-AKI study, have shown that a delayed strategy can reduce the proportion of patients receiving RRT while achieving similar mortality outcomes compared to early initiation⁷. In the cardiac surgery setting, Crescenzi et al. reported that patients managed with a more conservative approach, initiating RRT only after persistent oliguria (>12 h) or classic urgent indications, demonstrated similar overall survival to early-treated patients, and in certain subgroups (e.g., pre-existing renal dysfunction), even showed improved outcomes²³. This approach may also preserve residual renal function, shorten RRT dependence, and reduce healthcare costs by minimizing device utilization³¹. Therefore, the late RRT strategy emphasizes individualized patient selection and careful

monitoring, reserving intervention for those with persistent or worsening AKI, thereby balancing the benefits of RRT with its potential harms.

Current Guidelines in RRT for CSA-AKI

Current recommendations for the management of cardiac surgery-associated acute kidney injury (CSA-AKI) are largely extrapolated from broader acute kidney injury (AKI) guidelines, such as those from the Kidney Disease: Improving Global Outcomes (KDIGO) initiative and critical care societies, due to the limited number of high-quality randomized controlled trials specifically in the CSA-AKI population^{4,8}. Preventive strategies form the cornerstone of guideline-based care, focusing on preoperative risk assessment, avoidance of nephrotoxins, optimization of hemodynamic status, and judicious fluid management³². KDIGO guidelines recommend close perioperative monitoring of renal function and urine output, with prompt identification and staging of AKI using KDIGO criteria to guide escalation of care⁸.

With regard to renal replacement therapy (RRT) timing, KDIGO does not prescribe a fixed early or delayed initiation strategy but advises starting RRT emergently in the presence of life-threatening fluid, electrolyte, and acid–base disturbances (e.g., refractory hyperkalemia, severe acidosis, pulmonary edema unresponsive to diuretics^{4,33}). In patients without urgent indications, guidelines suggest an individualized approach based on overall clinical context, hemodynamic stability, and likelihood of renal recovery^{8,33}. Continuous modalities (CRRT) are generally preferred in hemodynamically unstable postoperative patients, while intermittent modalities may be considered in stable patients or as part of a transition strategy^{34,35}.

Specific to cardiac surgery, expert consensus statements, such as those from the Acute Disease Quality Initiative (ADQI) and European Society of Intensive Care Medicine (ESICM), emphasize proactive hemodynamic optimization, early recognition of oliguria, and the use of risk prediction models (e.g., Cleveland Clinic score) to identify high-risk patients who may benefit from closer monitoring or pre-emptive nephrology involvement^{36,37}. They also highlight the importance of integrated multidisciplinary care, involving cardiac surgeons, intensivists, and nephrologists, to tailor therapy to patient-specific risk and perioperative course.

DISCUSSION

The debate between early and late initiation of renal replacement therapy (RRT) in cardiac surgery-associated acute kidney injury (CSA-AKI) reflects a fundamental trade-off between timely intervention to prevent organ damage and the risk of unnecessary treatment. Proponents of early RRT argue that rapid initiation—often within hours of reaching KDIGO stage 2 AKI—can promptly correct electrolyte disturbances, control fluid balance, and remove inflammatory mediators, potentially mitigating renal and systemic injury and improving survival^{6,24,27}. Trials such as ELAIN have shown reductions in ICU stay, RRT duration, and 90-day mortality with early initiation, particularly in high-risk surgical cohorts⁶. Conversely, advocates for a late or expectant approach emphasize the avoidance of treatment in patients likely to recover with conservative management, thereby reducing complications related to vascular access, anticoagulation, and hemodynamic instability^{7,28}. Large multicenter studies, including STARRT-AKI, suggest that delayed initiation can decrease the proportion of patients exposed to RRT without adversely affecting mortality⁷. In CSA-AKI-specific research, Crescenzi et al. reported comparable overall survival between early and late groups, with certain subgroups—such as those with pre-existing renal dysfunction—deriving greater benefit from a delayed strategy²³. Additionally, economic analyses indicate that early initiation may shorten hospital stay and lower costs, but these benefits must be weighed against the potential for overtreatment and resource utilization³¹. Taken together, the current evidence supports a tailored approach, integrating patient-specific risk factors, hemodynamic status, and evolving clinical trajectory, rather than a universal fixed-timing protocol for RRT initiation in CSA-AKI.

CONCLUSIONS

Cardiac surgery-associated acute kidney injury (CSA-AKI) represents a complex postoperative complication with multifactorial pathophysiology, involving ischemia–reperfusion injury, systemic inflammation, microcirculatory dysfunction, and patient-specific vulnerabilities. Its development significantly increases morbidity, mortality, and healthcare costs, making timely diagnosis and effective management essential. The optimal timing of renal replacement therapy (RRT) in CSA-AKI remains a subject of ongoing debate. Early initiation aims to prevent progression of renal injury and systemic complications by promptly correcting metabolic derangements, controlling fluid overload, and potentially removing inflammatory mediators. Evidence from trials such as ELAIN suggests benefits in certain patient subsets, including reduced ICU stay and improved short-term survival. Conversely, a delayed approach seeks to avoid unnecessary intervention in patients likely to recover renal function spontaneously, reducing exposure to RRT-related complications and preserving residual renal function, as supported by findings from studies like STARRT-AKI and Crescenzi et al.

Comparative analysis indicates that neither strategy universally outperforms the other; instead, outcomes are influenced by patient selection, severity of illness, and perioperative context. Current guidelines, including KDIGO and ADQI consensus statements, recommend individualized timing based on clinical status, urgent indications, and likelihood of recovery, with a preference for continuous modalities in hemodynamically unstable patients. In summary, the decision to initiate RRT in CSA-AKI should be guided by a nuanced balance between the potential benefits of early intervention and the risks of overtreatment. Future large-scale, CSA-AKI-specific randomized controlled trials are needed to establish standardized timing criteria that can be integrated into evidence-based clinical guidelines. Until such data are available, a multidisciplinary, patient-centered approach remains the most prudent strategy.

CONFLICT OF INTEREST

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AUTHORS' CONTRIBUTION

Zanella Yolanda Lie role are Conception and Design and drafting of the article, Yan Efrata Sembiring role are Critical revision of the article for important intellectual content and Final approval of the article.

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