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Review

The Seven Pillars of Cardiac Surgery-Associated Acute Kidney Injury Management

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Abstract

Cardiac surgery-associated acute kidney injury (CSA-AKI) remains one of the most common and clinically important complications following cardiac surgery, affecting approximately 20–30% of patients and contributing to increased morbidity, mortality, healthcare utilization, and progression to chronic kidney disease. Although the pathophysiology of CSA-AKI is multifactorial, delayed recognition based on conventional creatinine criteria continues to hinder timely intervention. Recent advances in biomarker research and multi-marker approaches have improved early detection and risk stratification, enabling identification of patients at highest risk before overt kidney dysfunction develops. Current preventive strategies emphasize meticulous perioperative management, optimization of hemodynamics and fluid balance, avoidance of nephrotoxic exposures, and implementation of Kidney Disease: Improving Global Outcomes (KDIGO)-based care bundles; meanwhile, treatment of established CSA-AKI remains largely supportive. This review summarizes contemporary evidence using a practical framework based on seven key pillars: define, predict, detect, prevent, treat, progress, and follow-up, and discusses emerging concepts, including biomarker-guided care, precision medicine, and individualized postoperative surveillance. Nonetheless, continued integration of novel diagnostic tools with evidence-based preventive strategies will be essential to improve outcomes in this high-risk patient population.

Keywords: cardiac surgery-associated acute kidney injury; biomarkers; risk stratification; perioperative management; renal protection

1. Introduction

Cardiac surgery–associated acute kidney injury (CSA-AKI) remains one of the most frequent and clinically significant complications following cardiac surgery. Its incidence varies depending on the patient population, surgical complexity, and diagnostic criteria, but it is consistently reported as a common postoperative event, ranging from 20 to 30%, with substantial clinical impact [1,2,3,4,5]. Despite advances in perioperative care, CSA-AKI continues to contribute to prolonged hospitalization, increased resource utilization, and adverse patient outcomes [2,6].

The pathophysiology of CSA-AKI is complex and multifactorial, involving an interplay of hemodynamic, inflammatory, and biochemical mechanisms. Intraoperative factors such as cardiopulmonary bypass (CPB) contribute to renal hypoperfusion, ischemia–reperfusion injury, and haemolysis, leading to oxidative stress and tubular damage [2,4,6]. Oxidative stress has been identified as a key mediator of renal injury, particularly in patients with pre-existing renal dysfunction, where impaired antioxidant defences may exacerbate susceptibility to injury [7]. In addition to these mechanisms, systemic inflammatory responses triggered by surgical trauma and extracorporeal circulation further amplify renal injury through cytokine release and endothelial dysfunction [8].

Emerging evidence highlights the role of thromboinflammatory processes in the development of CSA-AKI [9]. Platelet activation has been associated with postoperative kidney injury, suggesting that microvascular dysfunction and platelet-mediated inflammation may contribute to impaired renal perfusion and tissue damage [10]. Furthermore, perioperative hemodynamic instability and fluid overload have been shown to worsen renal outcomes, em-

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phasizing the importance of maintaining optimal perfusion and fluid balance during and after the surgery [4,11].

The clinical consequences of CSA-AKI extend beyond the immediate postoperative period. Even mild forms of AKI are associated with increased short-term morbidity and mortality, as well as prolonged intensive care unit and hospital stays [6,11]. Importantly, CSA-AKI has been linked to long-term adverse outcomes, including progression to chronic kidney disease and reduced long-term survival [11,12,13]. Evidence suggests that AKI following cardiac surgery may serve as a critical trigger in the transition from acute kidney injury to chronic kidney disease and dialysis, underscoring the need for early recognition and preventive strategies [14,15].

Given its high incidence, complex pathophysiology, and significant short- and long-term consequences, CSA-AKI remains a major challenge in cardiac surgery. A comprehensive understanding of its underlying mechanisms and clinical implications is essential to guide risk stratification, early detection, and targeted preventive approaches. Thus, the aim of this narrative review is to provide a structured overview of contemporary evidence regarding CSA-AKI throughout its clinical course. The review is organized around seven key pillars—define, predict, detect, prevent, treat, progress, and follow-up—to summarize current knowledge, identify existing gaps, and discuss emerging approaches for improving outcomes in patients undergoing cardiac surgery.

2. Define

An accurate and standardized definition of CSA-AKI is essential for clinical decision-making, research comparability, and implementation of preventive strategies. The most widely accepted framework is provided by the Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines, which define acute kidney injury based on changes in serum creatinine and urine output [16]. KDIGO criteria integrate and refine earlier classification systems such as Acute Kidney Injury Network (AKIN) or RIFLE, offering improved sensitivity for early detection and facilitating consistent reporting across studies and clinical settings [2,17].

The adoption of KDIGO has enabled earlier recognition of CSA-AKI and improved risk stratification, particularly when combined with perioperative clinical variables and emerging biomarkers [18]. Even small increases in serum creatinine, previously considered clinically insignificant, have been shown to correlate with worse outcomes following cardiac surgery, underscoring the clinical relevance of sensitive diagnostic thresholds [19]. Beyond facilitating consistent diagnosis and reporting, KDIGO criteria provide the framework for targeted preventive strategies. In the randomized PrevAKI trial, application of a KDIGO-based care bundle in biomarker-identified high-risk patients resulted in a significant reduction in postoperative CSA-AKI, particularly moderate-to-severe AKI, demonstrating that early identification can translate into improved clinical outcomes [20].

Nevertheless, reliance on serum creatinine remains a major limitation of current diagnostic criteria. Creatinine is an indirect and delayed marker of kidney injury, often rising only after substantial loss of renal function has already occurred [21]. Furthermore, its levels are influenced by multiple nonrenal factors, including muscle mass, hemodilution, and perioperative fluid shifts, all of which are highly relevant in cardiac surgery patients [22]. As a result, creatinine-based definitions may underestimate the true incidence and affect the timing of CSA-AKI, delaying diagnosis and potential intervention. Recent evidence suggests that the optimal serum creatinine threshold for defining stage 1 CSA-AKI may differ from that used in the general AKI population. In a large cohort of patients undergoing coronary artery bypass grafting, a cardiac surgery-specific 48-hour serum creatinine increase of approximately 0.55 mg/dL demonstrated greater prognostic value for 30-day mortality than the current KDIGO threshold of 0.3 mg/dL, highlighting the potential need for procedure-specific diagnostic criteria [23].

Urine output criteria, while included in KDIGO definitions, are also subject to limitations in the perioperative setting, where diuretic use, fluid management strategies, and hemodynamic variability can confound interpretation [2].

To address these shortcomings, increasing attention has been directed toward the integration of novel biomarkers and multimodal diagnostic strategies that complement KDIGO criteria [22,24]. These approaches aim to detect kidney injury at an earlier stage, before overt changes in creatinine occur.

3. Predict

Accurate prediction of CSA-AKI is essential for identifying patients at increased risk before kidney injury becomes clinically evident. Accordingly, risk prediction should rely on preoperative and perioperative variables collected prior to fulfilment of AKI diagnostic criteria. In contrast, postoperative changes in laboratory parameters or biomarkers may be useful for early detection of evolving CSA-AKI but represent a distinct concept from true risk prediction [25,26]. Established clinical risk factors include advanced age, pre-existing chronic kidney disease, diabetes mellitus, and reduced baseline renal function, all of which have consistently been associated with increased susceptibility to postoperative kidney injury. In particular, preoperative renal dysfunction remains one of the strongest predictors of CSA-AKI and is associated with worse perioperative outcomes [27].

Several clinical risk scores, including the Cleveland Clinic Score [28], Mehta score [29], and Acute Kidney Injury Following Cardiac Surgery (AKICS) score [30], have

been developed to identify patients at increased risk of CSA-AKI. Recent external validation studies suggest that although the Cleveland Clinic Score remains useful for identifying patients at high risk of severe AKI and renal replacement therapy, its discrimination for mild AKI is only moderate, indicating that recalibration or incorporation of additional perioperative variables may improve predictive performance [28,31]. These models provide practical tools for identifying high-risk patients; however, their predictive ability is largely based on demographic and clinical epidemiological variables and therefore does not fully capture the dynamic perioperative pathophysiological processes that contribute to kidney injury. More recently, machine learning-based models integrating preoperative characteristics, intraoperative physiological data, conventional laboratory parameters, and novel kidney injury biomarkers have demonstrated improved predictive performance compared with conventional risk scores. Recent studies have successfully combined high-frequency hemodynamic data with biomarkers such as B-type natriuretic peptide (BNP) and [TIMP-2] × [IGFBP7] to predict CSA-AKI, highlighting the potential of multimodal artificial intelligence models for individualized perioperative risk stratification [32,33,34,35,36].

Intraoperative variables further contribute to risk stratification. Prolonged CPB time, hemodynamic instability, and perioperative fluid imbalance have been shown to significantly increase the likelihood and severity of CSA-AKI [4,11]. These factors reflect the impact of renal hypoperfusion, ischemia–reperfusion injury, and systemic inflammatory activation during cardiac surgery. Early postoperative changes, including even modest rises in serum creatinine, may also serve as important indicators of evolving kidney injury and adverse outcomes [19].

To improve predictive accuracy and better characterize the (patho)physiologic conditions that contribute to kidney injury during surgery, several clinical risk models have been developed that incorporate combinations of perioperative variables [33]. While these models provide useful stratification, their performance is often limited by heterogeneity in patient populations and variability in clinical practice [25]. More recent approaches have focused on enhancing prediction through the addition of biomarkers. The integration of urinary and plasma biomarkers with clinical risk scores has demonstrated improved discrimination for CSA-AKI compared with clinical models alone, supporting a multimodal approach to risk assessment [18,37].

Although machine learning-based prediction models frequently outperform conventional clinical risk scores, their clinical applicability remains constrained by significant development and validation challenges [32,34,35]. Many have undergone only limited external validation, require extensive perioperative datasets or specialized computational infrastructure, and often incorporate biomarkers that are not routinely available or cost-effective. In contrast to simpler and widely accessible tools such as the Thakar score, these advanced models have yet to demonstrate sufficient practicality and generalizability for universal adoption in routine cardiac surgical care.

4. Detect

Early detection aims to identify kidney injury after the perioperative insult has occurred but before conventional diagnostic criteria are fulfilled. This concept is referred to as subclinical AKI, in which structural kidney injury is detected by biomarkers despite normal serum creatinine concentrations and preserved urine output.

The central challenge of CSA-AKI detection is not merely identifying patients at risk, but recognizing evolving kidney injury at a stage when intervention may still alter its course. This has driven increasing interest in biomarkers and dynamic monitoring strategies capable of detecting structural or functional renal injury before overt fulfilment of conventional AKI criteria.

Serum creatinine, the cornerstone of KDIGO-defined AKI, is a delayed and indirect marker of renal injury, often rising only after significant loss of glomerular filtration has already occurred [21]. In cardiac surgery patients, this delay is further compounded by perioperative factors such as hemodilution, fluid shifts, and reduced muscle mass, which may mask early changes in renal function [22]. As a result, reliance on creatinine can lead to underestimation of the true incidence and delayed recognition of CSA-AKI. Although urine output criteria may provide additional information, their interpretation is often confounded by diuretic use and perioperative fluid management strategies [2]. Nevertheless, Karkouti et al. [19] and Vogt et al. [21] have shown that dynamic evaluation of creatinine could, despite these limitations, improve the predictive or early detection accuracy of sequential creatinine evaluation very early after surgery.

To overcome these limitations, substantial research has focused on the development of novel biomarkers capable of detecting kidney injury at an earlier stage (Table 1). Given the rapidly expanding number of candidate biomarkers for CSA-AKI, this review focuses primarily on those supported by the strongest clinical evidence, validation in cardiac surgery populations, and the greatest potential for clinical implementation. Biomarkers reflecting tubular damage, inflammation, and oxidative stress—such as neutrophil gelatinase-associated lipocalin (NGAL), cystatin C, kidney injury molecule-1 (KIM-1), tissue inhibitor of metalloproteinase-2 (TIMP-2), insulin like growth factor binding protein 7 (IGFBP7), and other emerging markers such as cysteine-rich protein 61 and Klotho—have demonstrated improved sensitivity for early detection of CSA-AKI compared with creatinine alone [8,22,24,38,39,40,41]. These markers may rise within hours of renal insult, providing a valuable window for early diagnosis and intervention. Because these biomarkers reflect different aspects of renal

Table 1. Biomarkers for early detection and risk stratification of cardiac surgery–associated acute kidney injury (CSA-AKI).

Biomarker	Basic advantages	Limitations	Potential clinical use	AUC
Cystatin C	• Reflects glomerular filtration more directly than creatinine. • Rises earlier than creatinine in some studies. • Less affected by muscle mass, age, and sex than creatinine.	• Conflicting results in cardiac surgery populations. • Lower sensitivity than NGAL. • Some studies found it no better than creatinine, and occasionally it rises later than creatinine. • Utility in CSA-AKI remains controversial.	• Preoperative risk stratification. • Adjunct marker within multimarker panels rather than a standalone diagnostic test. • Potential usefulness in other AKI settings (critical illness, burns, myocardial infarction).	0.65–0.83
NGAL	• Most extensively studied AKI biomarker. • Rapid rise within 2–6 hours after injury. • Excellent early predictive performance in several cardiac surgery studies. • Detects structural injury before creatinine rises.	• Influenced by inflammation, sepsis, cancer, anaemia, age, CKD, and major surgery. • Produced by extra-renal tissues, reducing specificity. • Lack of standardized cut-offs and assay variability.	• Early postoperative detection of CSA-AKI. • Risk stratification for AKI progression, dialysis requirement, mortality, and prolonged hospitalization. • Candidate biomarker for routine clinical implementation once standardization improves.	0.70–0.90
KIM-1	• Highly specific marker of proximal tubular injury. • Strong biological rationale; markedly upregulated after ischemic injury. • Performs better than creatinine and BUN in animal models.	• Human studies show only moderate diagnostic accuracy. • Influenced by age, sepsis, diabetes, hypertension, atherosclerosis, and contrast exposure. • Small and heterogeneous clinical studies.	• Detection of ischemic tubular injury. • Better suited as part of multimarker panels (e.g., with IL-18 or L-FABP) than as a standalone marker. • Potential prognostic biomarker in AKI progression.	0.61–0.68
TIMP-2 × IGFBP7	• Reflects cell-cycle arrest, one of the earliest responses to tubular stress. • Strong mechanistic link to AKI development. • Combination outperforms either marker alone. • Associated with renal recovery after AKI.	• Results vary according to patient risk profile. • Elevated in non-renal conditions such as diabetes. • Performance differs across AKI aetiologies.	• Early identification of patients at high risk for CSA-AKI. • Risk stratification and prediction of renal recovery. • One of the most clinically mature biomarker combinations discussed in the review.	0.80–0.87
CYR61	• Very early upregulation after ischemic injury (within ~1 hour in animal models). • Directly associated with inflammation and tissue injury pathways.	• Evidence limited to animal studies. • No human clinical data available. • No validated diagnostic thresholds.	• Potential ultra-early biomarker of ischemic AKI. • Possible therapeutic target due to involvement in inflammatory injury pathways. • Currently a research-only marker.	0.51
Klotho	• One of the earliest biomarkers identified in experimental AKI. • Downregulated within hours after ischemic injury. • Biologically linked to renal protection and anti-aging pathways.	• Evidence almost entirely from animal models. • No human validation studies in AKI at the time of the review. • Clinical thresholds and assay standardization are lacking.	• Early detection of AKI. • Potential biomarker and therapeutic agent simultaneously. • Promising translational target but not yet clinically applicable.	0.84

Table 1. Continued.

Biomarker	Basic advantages	Limitations	Potential clinical use	AUC
IL-18	• Early urinary marker of ischemic proximal tubular injury. • Reflects inflammatory response. • Rises before serum creatinine.	• Limited specificity due to elevation in sepsis, systemic inflammation, and other inflammatory conditions. • Limited routine availability.	• Early detection and risk stratification of CSA-AKI, particularly ischemic AKI.	0.73–0.82
L-FABP	• Sensitive marker of oxidative stress and proximal tubular injury. • Increases early after renal ischemia	• Influenced by chronic kidney disease and liver disease. • Limited availability and standardization.	• Early diagnosis of CSA-AKI and prediction of AKI severity.	0.70–0.80
NAG	• Established urinary marker of proximal tubular damage. • Non-invasive and detectable before creatinine elevation.	• Low specificity. • Elevated in CKD, diabetes, hypertension, and other renal disorders.	• Detection of tubular injury and adjunctive assessment of CSA-AKI risk.	0.68–0.76

CSA-AKI, cardiac surgery-associated acute kidney injury; IGFBP7, insulin-like growth factor-binding protein 7; KIM-1, kidney injury molecule-1; NGAL, neutrophil gelatinase-associated lipocalin; TIMP-2, tissue inhibitor of metalloproteinase-2; CYR61, cysteine-rich protein 61; CKD, chronic kidney disease; AUC, area under the receiver operating characteristic curve; BUN, blood urea nitrogen; IL-18, interleukin-18; L-FABP, liver-type fatty acid-binding protein; NAG; N-acetyl-β-D-glucosaminidase.

pathophysiology, their combined assessment may provide more comprehensive information than any single marker alone. Indeed, multimarker approaches integrating novel biomarkers with early postoperative changes in serum creatinine have demonstrated improved risk stratification for serious adverse outcomes following cardiac surgery [37]. Other biomarkers, including interleukin-18 (IL-18), liver-type fatty acid-binding protein (L-FABP), and N-acetyl-β-D-glucosaminidase (NAG), have also demonstrated potential for the early detection of tubular injury after cardiac surgery [22,42]. However, compared with NGAL, cystatin C, KIM-1, and [TIMP-2] × [IGFBP7], these biomarkers have been evaluated in fewer studies, show greater inter-study variability, and currently have more limited clinical applicability.

Importantly, recent evidence suggests that a multimarker panel may further enhance diagnostic accuracy [43]. The combination of multiple biomarkers with clinical variables has been shown to improve the detection of subclinical AKI and more accurately identify patients at risk of progression and adverse outcomes. Importantly, biomarkers reflecting different pathophysiological domains—including tubular injury (NGAL, KIM-1), impaired filtration (cystatin C) or cellular stress (TIMP-2 × IGFBP7)—provide complementary information that may not be captured by individual markers alone. In addition to kidney-specific biomarkers, markers of myocardial injury and cardiorenal stress may provide important prognostic information in patients undergoing cardiac surgery. Elevated concentrations of cardiac troponins, creatine kinase, and particularly BNP or N-terminal pro-B-type natriuretic peptide (NT-proBNP) have been associated with an increased risk of CSA-AKI, likely reflecting perioperative myocardial injury, ventricular dysfunction, venous congestion, systemic inflammation, and impaired renal clearance. Recent studies have demonstrated that perioperative NT-proBNP levels are independently associated with both the occurrence and severity of CSA-AKI, supporting the concept that cardiac and renal injury frequently evolve in parallel as manifestations of a shared cardiorenal pathophysiological process [44,45,46]. More recently, interpretable machine learning models have identified preoperative NT-proBNP as one of the strongest predictors of CSA-AKI, alongside serum creatinine, demonstrating that integration of these biomarkers with perioperative clinical variables can substantially improve predictive performance while preserving model interpretability through SHapley Additive exPlanations (SHAP)-based analyses [47].

Accordingly, multimarker strategies have emerged as a promising approach for enhancing risk stratification after cardiac surgery [33,43]. This integrated strategy aligns with the evolving understanding of CSA-AKI as a complex, multifactorial process involving hemodynamic, inflammatory, and oxidative pathways. In a contemporary cardiac surgery cohort, several biomarkers associated with haemolysis, inflammation, and tissue injury—including tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-10 (IL-10), NGAL, myoglobin, haptoglobin, and interleukin-1 receptor antagonist (IL-1RA)—showed significant associations with CSA-AKI. A predictive model incorporating 4-hour postoperative myoglobin, haptoglobin, and IL-1RA together with clinical variables

achieved excellent discrimination (area under the curve (AUC) 0.90), highlighting the value of integrating complementary biological pathways for early AKI detection [48].

Beyond individual biomarkers, advances in data integration and artificial intelligence have introduced new opportunities for early detection. Machine learning-based prediction models that integrate continuous perioperative physiological data, laboratory measurements, and biomarker profiles have shown promising performance for early identification of CSA-AKI, with reported AUC values approaching 0.90 [32,33,34,36]. By leveraging advanced analytical techniques, including tree-based algorithms and neural networks, these models can capture complex pathophysiological relationships that may not be adequately represented in traditional statistical risk models [32,34,35]. While artificial intelligence is associated with some limitations (algorithm interpretability, institutional variability, lack of validation), once successfully validated and embedded into hospital infrastructure, artificial intelligence (AI) models offer notable operational advantages. Their greatest long-term utility lies in their cost-effective scalability and relative simplicity of integration into existing electronic health record (EHR) alert systems. These approaches may enable real-time monitoring and dynamic risk assessment in the perioperative setting.

5. Prevent

Prevention of CSA-AKI remains a central objective in perioperative care, given the limited therapeutic options once kidney injury is established. Building on risk stratification and early detection, preventive strategies focus on optimizing modifiable perioperative factors and implementing structured care pathways to minimize renal insult.

Hemodynamic optimization is a cornerstone of prevention. Maintenance of adequate renal perfusion through careful management of blood pressure, cardiac output, and intravascular volume is essential to reduce the risk of ischemic injury. Perioperative hemodynamic instability and fluid overload have been consistently associated with increased severity of CSA-AKI and worse outcomes. These observations highlight the importance of individualized goal-directed fluid therapy, with the objective of preserving renal perfusion and oxygen delivery while avoiding fluid overload. Both hypovolemia-associated renal hypoperfusion and excessive fluid administration resulting in venous congestion and tissue oedema have been linked to an increased risk of CSA-AKI [4,11]. Strategies aimed at improving renal perfusion, including balanced forced diuresis, have demonstrated potential benefit in reducing the incidence of CSA-AKI in selected patient populations [49].

In addition to hemodynamic management, mitigation of oxidative stress and inflammation represents an important preventive target. CPB and surgical trauma induce significant oxidative and inflammatory responses, which contribute to renal injury [7,50]. Pharmacologic interventions such as ascorbic acid have been investigated for their potential renoprotective effects, although results remain inconsistent and largely limited to small or pilot studies [51,52]. Recent randomized trials highlight the complexity of pharmacologic prevention in CSA-AKI. While perioperative nitric oxide reduced AKI incidence in high-risk patients with chronic kidney disease, hyperoncotic albumin administration was associated with increased AKI risk, underscoring the importance of patient selection and targeted therapy [53,54]. Similarly, other pharmacologic strategies, including vasoactive agents and diuretics, have shown variable efficacy, and no single agent has demonstrated consistent benefit across diverse patient populations [55,56].

Structured, protocol-driven approaches have emerged as an effective means of prevention. Implementation of KDIGO-based care bundles in high-risk patients has been associated with a significant reduction in CSA-AKI incidence, particularly when guided by early risk identification [20]. These bundles typically include optimization of haemodynamics, avoidance of nephrotoxic agents, and close monitoring of renal function. The Enhanced Recovery After Surgery (ERAS) Cardiac guidelines also endorse use of the KDIGO bundle of care: avoid use of nephrotoxic agents, discontinue angiotensin-converting enzyme inhibitors and angiotensin receptor blockers for the first 48 hours after surgery, monitor serum creatinine levels and urine output, avoid hyperglycaemia in the first 72 hours after surgery, use alternatives to radiocontrast agents, utilize goal-directed perfusion with oxygen delivery index and closely monitor haemodynamics using a prespecified algorithm [57,58].

Cardioplegia strategy may also influence the risk of CSA-AKI, although current evidence remains limited. While most studies have demonstrated comparable postoperative renal function between conventional blood cardioplegia and del Nido cardioplegia, recent observational data suggest a lower incidence of AKI with blood cardioplegia [59]. However, these findings may be confounded by differences in operative complexity and aortic cross-clamp duration rather than the cardioplegia solution itself. Consequently, there is currently insufficient evidence to recommend one cardioplegia strategy over another specifically for renal protection, and further adequately powered randomized studies are warranted. Several additional perioperative strategies have been investigated to reduce the risk of CSA-AKI. These include pulsatile cardiopulmonary bypass, optimization of hemodilution during cardiopulmonary bypass, remote ischemic preconditioning, and optimization of perioperative volume status through preoperative hydration. Although individual studies have reported potential renoprotective effects, randomized trials and meta-analyses have produced inconsistent results, and current evidence remains insufficient to recommend routine implementation of most of these strategies solely for AKI prevention [60,61].

Despite these advances, prevention of CSA-AKI remains challenging due to the heterogeneity of patient populations and the multifactorial nature of renal injury. Current evidence supports a comprehensive approach that combines individualized risk assessment, meticulous perioperative management, and protocolized care pathways. Future preventive efforts should focus on translating risk prediction and biomarker assessment into actionable clinical interventions. In particular, early identification of high-risk patients may facilitate timely implementation of KDIGO-based care bundles, optimization of hemodynamic and fluid management, avoidance of nephrotoxic agents, and refinement of cardiopulmonary bypass strategies, thereby reducing the incidence and severity of postoperative CSA-AKI.

6. Treat

Management of CSA-AKI remains largely supportive, as no specific pharmacologic therapy has been shown to reverse established kidney injury. Consequently, treatment strategies focus on limiting further renal damage, optimizing organ perfusion, and managing complications associated with impaired kidney function.

Hemodynamic stabilization is the primary objective in patients with established CSA-AKI. Preservation of renal perfusion remains a cornerstone of CSA-AKI prevention and management. Current evidence supports individualized hemodynamic optimization aimed at maintaining adequate intravascular volume, cardiac output, and organ perfusion while avoiding both renal hypoperfusion and venous congestion [2,62]. Hypotension, low cardiac output states, and persistent volume depletion have consistently been associated with an increased risk of kidney injury, whereas excessive fluid administration may promote venous congestion, tissue oedema, and worsening renal function [1,20]. Accordingly, goal-directed fluid and hemodynamic management strategies are preferred over fixed-volume approaches. In patients with fluid overload, diuretic therapy may be required to achieve euvolemia; however, diuretics should not be used as a primary strategy for AKI prevention and should instead be reserved for the management of volume excess. Optimization of cardiac rhythm, contractility, and systemic perfusion pressure further contributes to maintaining renal blood flow and reducing the risk of ongoing kidney injury [4,11]. After correction of hypovolemia and optimization of cardiac output, vasopressor therapy should be used to maintain adequate mean arterial pressure and end-organ perfusion. Norepinephrine remains the preferred first-line agent, whereas vasopressin and other vasoactive therapies may be reserved for vasoplegia or refractory hypotension [2,62]. Close monitoring of urine output and fluid balance remains critical in guiding therapy.

Avoidance of nephrotoxic exposures is another key component of management. Adjustment of medication dosing according to renal function and minimization of potentially harmful agents (NSAIDs, aminoglycosides, vancomycin, contrast media, angiotensin-converting enzyme (ACE) inhibitors/angiotensin II receptor blockers (ARBs)) [62,63] are essential to prevent further kidney injury. In addition, the use of diuretics may be considered for volume management; however, their role is primarily supportive, and responsiveness to agents such as furosemide may provide prognostic information regarding AKI progression rather than direct therapeutic benefit [56].

Renal replacement therapy (RRT) remains a supportive rather than curative treatment for severe CSA-AKI and should be considered in the presence of refractory fluid overload, severe metabolic acidosis, persistent hyperkalaemia, overt uremic complications, or progressive kidney dysfunction accompanied by clinically significant organ congestion [2,3,5,9,57,62]. While several studies have evaluated accelerated or early initiation strategies, current evidence does not support routine initiation of RRT solely on the basis of biochemical criteria in the absence of clinical indications [64]. Instead, careful patient selection is essential. In the cardiac surgical population, particular attention should be given to fluid balance, as persistent volume overload and venous congestion are strongly associated with adverse renal and cardiovascular outcomes [65]. Accordingly, extracorporeal fluid removal, including ultrafiltration or continuous RRT modalities, may be beneficial in selected patients with refractory congestion, right ventricular dysfunction, or cardiorenal syndrome, even before classical indications for dialysis are fully established [1,2]. The choice of modality should be individualized according to hemodynamic stability, fluid management requirements, and the extent of metabolic derangement [64,66].

7. Progress

CSA-AKI is increasingly recognized not only as an acute perioperative complication but also as a condition with significant long-term consequences. The trajectory of renal recovery following CSA-AKI is highly variable, ranging from complete resolution to persistent dysfunction and progression to chronic kidney disease (CKD). Importantly, the clinical significance of CSA-AKI extends well beyond the immediate postoperative period. Approximately one-third of patients who develop CSA-AKI subsequently progress to acute kidney disease (AKD), a subacute phase characterized by persistent renal dysfunction lasting beyond seven days. AKD has emerged as an important intermediary step linking CSA-AKI to chronic kidney disease, with the likelihood of progression increasing according to the severity, duration, and completeness of recovery from the initial perioperative kidney injury. Even patients who appear to recover renal function early remain at increased risk of future CKD and adverse cardiovascular outcomes [11,12,15].

Beyond its impact on renal function, CSA-AKI is associated with substantial long-term morbidity and mortality. Multiple studies have demonstrated that patients who

develop postoperative AKI experience a two- to five-fold increase in long-term mortality compared with those without AKI, with risk increasing according to AKI severity [6]. CSA-AKI is also associated with a significantly higher incidence of CKD, heart failure, major adverse cardiovascular events, and recurrent hospitalizations, underscoring the close interaction between renal injury and cardiovascular dysfunction [10,11]. The bidirectional relationship between cardiac and renal dysfunction further contributes to disease progression, particularly in patients with pre-existing cardiovascular comorbidities. CSA-AKI has also been associated with an increased susceptibility to postoperative infectious complications, including pneumonia, urinary tract infection, bloodstream infection, and sepsis, potentially reflecting immune dysregulation, prolonged intensive care exposure, and the need for invasive support. In a propensity-matched cardiac surgery cohort, even stage 1 AKI was independently associated with more than a two-fold increase in postoperative infections. Furthermore, infectious complications such as deep sternal wound infection frequently coexist with postoperative renal dysfunction and contribute substantially to morbidity and mortality [9,67,68,69].

Given these long-term implications, CSA-AKI should be considered a marker of increased patient vulnerability rather than an isolated postoperative complication. Early identification of patients at risk for incomplete recovery or progression is essential for guiding follow-up and management strategies. Not all patients who experience CSA-AKI face the same long-term risk. Progression to acute kidney disease, incomplete recovery of renal function, higher AKI severity, pre-existing chronic kidney disease, diabetes, and prolonged cardiopulmonary bypass duration have consistently been associated with an increased likelihood of chronic kidney disease, cardiovascular events, and death during follow-up. Recognition of these high-risk phenotypes has enabled the development of prediction models with good discriminatory performance, supporting more individualized follow-up and renal protection strategies after cardiac surgery [11,26].

8. Follow-up

Despite growing recognition of the long-term consequences of CSA-AKI, there is currently no universally accepted follow-up strategy for affected patients. This represents an important gap in contemporary perioperative care. Based on available evidence, a structured follow-up pathway may be particularly justified in patients with stage 2–3 AKI, AKD, incomplete renal recovery at discharge, pre-existing CKD, diabetes, or the need for renal replacement therapy. Such follow-up could include reassessment of serum creatinine, estimated glomerular filtration rate, and albuminuria within 30–90 days after discharge, evaluation of cardiovascular risk factors, review of potentially nephrotoxic medications, and consideration of nephrology referral in patients with persistent renal dysfunction [57,58]. Although prospective studies are needed to define the optimal surveillance strategy, early identification of patients progressing along the AKI–AKD–CKD continuum may provide an opportunity for targeted interventions aimed at preserving long-term renal and cardiovascular health.

Renal recovery following CSA-AKI is highly variable. Some patients experience transient creatinine elevations with complete recovery within days, whereas others progress to AKD, characterized by persistent renal dysfunction beyond seven days, and subsequently to CKD. Emerging evidence suggests that the likelihood of progression is closely related to the severity and persistence of the initial injury, with incomplete renal recovery at discharge representing one of the strongest predictors of adverse long-term renal outcomes [13,14]. Notably, even patients with apparent early recovery may have subclinical injury that predisposes them to subsequent decline in renal function. The concept of AKD, representing the intermediate phase between acute injury and chronic dysfunction, underscores the importance of continued monitoring beyond the immediate postoperative period [15]. Among patients who require postoperative RRT, renal recovery remains possible despite the severity of the initial injury. A recent study demonstrated that more than two-thirds of patients surviving the perioperative period recovered renal function within one year, with a median recovery time of 56 days. Increasing age and greater perioperative blood transfusion requirements were associated with a lower likelihood of renal recovery, underscoring the importance of structured nephrology follow-up after hospital discharge [70].

Early post-discharge assessment should include evaluation of renal function using serum creatinine and estimated glomerular filtration rate, as well as review of fluid status and medication use. Assessment of fluid status is an essential component of post-CSA-AKI management and should be performed using a multimodal approach. Clinical evaluation includes monitoring of body weight, cumulative fluid balance, urine output, peripheral oedema, and signs of pulmonary congestion. Hemodynamic assessment may incorporate blood pressure, heart rate, central venous pressure trends, and, where available, advanced cardiac output monitoring. Increasingly, point-of-care ultrasound has emerged as a valuable bedside tool, allowing evaluation of inferior vena cava dimensions and collapsibility, ventricular filling, pulmonary congestion through lung ultrasound, and venous congestion using Doppler-based techniques such as the venous excess ultrasound (VExUS) score. Laboratory markers, including serum creatinine, lactate, haemoglobin concentration, and natriuretic peptides, may provide complementary information regarding volume status and end-organ perfusion. Integration of these findings facilitates individualized fluid management aimed at avoiding both renal hypoperfusion and fluid overload [26,46,71,72].

Longitudinal follow-up provides an opportunity to identify progressive renal decline and to initiate timely interventions aimed at slowing CKD progression. Strategies aimed at slowing CKD progression after CSA-AKI include optimization of blood pressure and glycaemic control, implementation of guideline-directed renoprotective therapies such as renin–angiotensin system inhibitors and sodium-glucose cotransporter-2 (SGLT2) inhibitors when appropriate, avoidance of nephrotoxic exposures and recurrent AKI episodes, management of cardiovascular risk factors and volume status, and structured nephrology follow-up for patients with persistent renal dysfunction or progression to acute kidney disease [2,16,62].

In addition to standard clinical assessment, emerging tools such as biomarkers and predictive models may enhance risk stratification during follow-up, although their routine use in this setting remains to be established [18,39]. Integration of perioperative data with outpatient monitoring strategies may further improve continuity of care and enable personalized management.

9. Conclusions and Perspectives

Cardiac surgery–associated acute kidney injury remains a frequent and clinically significant complication with far-reaching consequences extending beyond the perioperative period. Despite advances in surgical and anaesthetic techniques, its incidence and impact on morbidity, mortality, and long-term renal outcomes remain substantial. The multifactorial pathophysiology of CSA-AKI—encompassing hemodynamic disturbances, inflammation, oxidative stress, and thromboinflammatory mechanisms—underscores the complexity of this condition and the challenges associated with its prevention and management.

The integration of standardized definitions, particularly KDIGO criteria, has improved the recognition and comparability of CSA-AKI across clinical settings. However, reliance on serum creatinine continues to limit early diagnosis, highlighting the need for more sensitive detection strategies. Subclinical AKI occupies the important transition zone between risk and clinically overt injury. It is characterized by evidence of tubular damage or cellular stress detected by biomarkers despite the absence of a creatinine rise or oliguria sufficient to fulfil KDIGO criteria. Importantly, these patients are not merely “at risk” but may already have established renal injury that remains undetected by conventional diagnostic methods. Numerous studies have demonstrated that biomarker-positive/creatinine-negative patients have significantly worse short- and long-term outcomes than patients without evidence of injury, supporting the concept that subclinical AKI represents an early but clinically meaningful stage within the AKI–AKD–CKD continuum. Advances in biomarker research and multimodal risk prediction models offer promising avenues for earlier identification of kidney injury and improved risk stratification. These developments, combined with structured preventive approaches such as KDIGO-guided care bundles, represent important steps toward reducing the burden of CSA-AKI.

Effective treatment options for established CSA-AKI remain limited, and current management is largely supportive. This reality reinforces the importance of prevention, early detection, and comprehensive perioperative care. Nevertheless, the clinical value of earlier detection remains dependent on the availability of effective interventions. Biomarkers alone do not improve outcomes; rather, their utility lies in identifying patients who may benefit from intensified application of evidence-based preventive strategies. Future studies should therefore focus not only on improving diagnostic accuracy but also on determining which biomarker-guided interventions meaningfully alter the trajectory from subclinical injury to overt CSA-AKI, AKD, and CKD. Increasing recognition of the long-term consequences of CSA-AKI, including progression to chronic kidney disease, further emphasizes the need for structured follow-up and continuity of care beyond hospital discharge.

Future directions should also focus on the integration of precision medicine approaches, combining clinical risk factors, biomarkers, and real-time data analytics to enable individualized patient management. The application of artificial intelligence and machine learning holds particular promise in enhancing prediction, early detection, and clinical decision-making in this complex patient population. In parallel, further high-quality clinical trials are needed to identify targeted therapies and refine preventive strategies. While considerable attention has been focused on novel biomarkers, an alternative and potentially complementary approach is the use of dynamic changes in routinely available clinical, laboratory, and hemodynamic parameters. Serial assessment of serum creatinine, urine output trajectories, fluid balance, haemoglobin concentration, lactate clearance, vasoactive support requirements, and measures of cardiac output or venous congestion may provide valuable insight into evolving renal injury without the additional costs and logistical challenges associated with specialized biomarker testing. Increasingly, machine learning and predictive analytics are being applied to these continuously acquired perioperative data streams, enabling earlier recognition of patients at risk for CSA-AKI while leveraging information already available in routine clinical practice. Future research should determine whether such dynamic physiology-based approaches can provide comparable or additive value to biomarker-guided strategies.

In conclusion, CSA-AKI represents a continuum of injury that requires a comprehensive, multidisciplinary approach, preoperative risk assessment, intraoperative management, early detection, and long-term follow-up. Bridging the gap between emerging scientific insights and clinical implementation will be essential to improving outcomes for patients undergoing cardiac surgery.

Author Contributions

AD: Conceptualization; Investigation; Literature review; Methodology; Writing—original draft; Writing—review & editing. JMK, GS, MA: Conceptualization; Methodology; Supervision; Validation; Writing—review & editing. TS, MH, UI, HA, IK: Validation; Writing—review & editing. All authors critically revised the manuscript, approved the final version, meet all four ICMJE criteria for authorship, and agree to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflicts of Interest

The authors declare no conflicts of interest. Giuseppe Santarpino serves as the Editor-in-Chief, while Jurij Matija Kalisnik is a member of the journal's Editorial Board. We declare that Giuseppe Santarpino and Jurij Matija Kalisnik had no involvement in the peer review of this article and have no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Guowei Tu.

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