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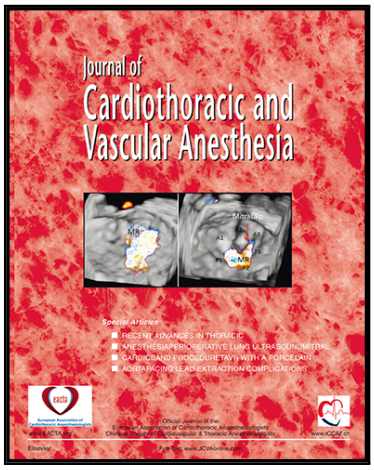

Adult Cardiac Surgery Associated Acute Kidney Injury: Joint Consensus Report of the PeriOperative Quality Initiative (POQI) and the Enhanced Recovery After Surgery (ERAS®) Cardiac Society

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SPECIAL ARTICLE

Adult Cardiac Surgery Associated Acute Kidney Injury: Joint Consensus Report of the PeriOperative Quality Initiative (POQI) and the Enhanced Recovery After Surgery (ERAS®) Cardiac Society*

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ABSTRACT

Objective: Acute kidney injury (AKI) is increasingly recognized as a source of poor patient outcomes after cardiac surgery. The purpose of the present report is to provide perioperative teams with expert recommendations specific to cardiac surgery associated AKI (CSA-AKI).

Methods: This report and consensus recommendations were developed during a joint, in-person, multi-disciplinary conference between POQI and the Enhanced Recovery After Surgery (ERAS®) Cardiac Society. Multinational practitioners with diverse expertise in all aspects of cardiac surgical perioperative care, including clinical backgrounds in anesthesiology, surgery, and nursing, met from October 20 - 22, 2021 in Sacramento, California and used a modified Delphi process and a comprehensive review of evidence to formulate recommendations. The quality of evidence and strength of each recommendation was established using the GRADE methodology. Recommendations were endorsed by majority vote.

Results: Based on available evidence and group consensus, a total of 13 recommendations were formulated (4 for the preoperative phase, 4 for the intraoperative phase, and 5 for the postoperative phase) and are reported here.

Conclusion: Because there are no reliable or effective treatment options for CSA-AKI, evidence-based practices that highlight the prevention and early detection are paramount. CSA-AKI incidence may be mitigated, and postsurgical outcomes improved, by focusing additional attention on pre-surgical kidney health status; implementing a specific cardiopulmonary bypass bundle; employing strategies to maintain intravascular euvolemia; leveraging advanced tools such as the electronic medical record, point-of-care ultrasound, and biomarker testing; and using patient-specific, goal-directed therapy to prioritize oxygen delivery and end-organ perfusion over static physiologic metrics.

KEY WORDS

Expert consensus; perioperative care; acute kidney injury; cardiac surgery; goal-directed therapy.

ABBREVIATIONS

ADQI – Acute Disease Quality Initiative

AI – artificial intelligence

AKI – acute kidney injury

CKD – chronic kidney disease

CPB – cardiopulmonary bypass

CSA-AKI – cardiac surgery associated acute kidney injury

DO_2 – global oxygen delivery

eGFR – estimated glomerular filtration rate

EMR – electronic medical record

ESRD – end-stage renal disease

GDT – goal-directed therapy

HHS – U.S. Department of Health and Human Services

HIS – U.S. Department of Health and Human Services, Indian Health Service

IGFBP7 – insulin growth factor binding protein 7

KDIGO - Kidney Disease: Improving Global Outcomes

KHA – kidney health assessment

POQI – Perioperative Quality Initiative

RRT- renal replacement therapy

TIMP-2 – tissue inhibitor of metalloproteinases

INTRODUCTION

Acute kidney injury (AKI) is among the most serious perioperative complications for patients undergoing cardiac surgery.[1–4] The complex nature of the cases, the hemodynamic perturbations encountered during cardiac surgery, and underlying patient comorbidities make these patients more susceptible to kidney injury than other surgical patients. Cardiac surgery associated AKI (CSA-AKI) is thought to complicate as many as a third of procedures, leading to numerous undesirable clinical sequelae and doubling total hospitalization costs.[5, 6] Its clinical consequences are multi-fold and encompass increased in-hospital mortality, poor long-term survival, development of chronic kidney disease (CKD), and permanent loss of renal function requiring ongoing renal replacement therapy.[3, 7–12]

CSA-AKI is one of the strongest risk factors for death after cardiac surgery. The majority of CSA-AKI cases, roughly 90%, are considered mild; however, even mild AKI is associated with worse outcomes compared to patients who do not develop AKI and is an independent predictor of 30-day postoperative mortality.[4, 11] Mortality rates rise with increasing severity of AKI and may be as high as 50% in the small portion (2-5%) of cardiac surgery patients who develop severe CSA-AKI that requires renal replacement therapy.[13, 14] Economically, CSA-AKI places a significant burden on healthcare resources and expenditures.[1, 3, 12, 15–19]

Treatment options are ineffective at circumventing kidney injury and have made prevention and early identification of AKI the primary focus.[20] Further, there is a growing body of clinical evidence that the incidence of CSA-AKI can be ameliorated by the application of bundled preoperative interventions and perioperative mitigation strategies.[21–23] In those patients who develop CSA-AKI, interventions promoting the early recovery of renal function have been associated with improved long-term survival.[24]

METHODS

The PeriOperative Quality Initiative (POQI) and the ERAS® Cardiac Society are both non-profit organizations that assemble panels of international experts to collaborate on the development of consensus-based recommendations covering various aspects of perioperative medicine.[25, 26] Details outlining the POQI consensus-building process have been previously published and are summarized in Supplemental Online Table 1.[26] The POQI methodology combines aspects of evidence appraisal with expert opinion and is therefore different from a systematic review or

Cochrane analysis; this combined approach helps clinicians make important decisions about patient care while waiting for the completion of large, prospective, randomized controlled trials.[26] The review process is a non-systematic, scoping review of the literature. The goals are several-fold: 1, to generate consensus statements that acknowledge the limitations of the literature; 2, to produce practical recommendations for patient care that are based on current evidence and are agreed on by the panel of experts attending the conference; and 3, to encourage future research where data are lacking.

The 8th meeting of POQI convened with the ERAS Cardiac Society between October 20 - 22, 2021 in Sacramento, California, with an in-person assembly of multinational practitioners with diverse expertise in all aspects of cardiac surgical perioperative care, including clinical backgrounds in anesthesiology, surgery, and nursing to address perioperative practices in cardiac surgery. This report is the result of a subgroup with expertise in AKI in the setting of cardiac surgery.

Prior to the conference, the POQI Board and conference directors assembled AKI workgroup members, led by 2 co-chairs. The group performed individual electronic literature searches for the purpose of stimulating discussion on the current knowledge gaps and areas of controversy or lack of consensus in the diagnosis, management and treatment of AKI after cardiac surgery. An electronic literature search was conducted by searching Pubmed, Medline, Embase, and Cochrane CENTRAL with terms “cardiac surgical procedures,” “cardiac surgery,” “acute kidney injury,” and “acute renal failure” and excluding case reports, editorials, and commentaries, as well as articles not published in the English language and those published before 2000. After an iterative review of titles and abstracts, the subgroup members identified manuscripts judged relevant for full text review and agreed upon reference applicability. Relevant articles were consolidated to a central repository. Topics chosen by the workgroup for focus included a concentrated investigation of biomarkers, goal-directed therapy (GDT)/ volume status, point-of-care ultrasound, and machine learning and artificial intelligence (AI).

[26]During the conference, a 3-day interactive meeting agenda was divided into plenary sessions, during which questions, statements and recommendations were presented, debated, and refined in a systematic progression of repeated rounds of voting, intertwined with smaller breakout sessions in which each workgroup addressed issues arising from the plenary sessions. Using this modified Delphi process, the group formulated a set of recommendations based on the current CSA-AKI diagnostic, management, and treatment evidence, then grouped them according to the perioperative phase of implementation. Content refinement continued until agreement was achieved, thereby resulting in a formal consensus document. The strength and level of evidence of each recommendation was established using Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework,[27–29] an approach widely adopted by more than 100 organizations including the World College of Physicians and the American College of Physicians, for example. Recommendations evaluated using the GRADE system receive two scores: one that rates the *quality of evidence* (graded A through D), and one indicating the *strength of the recommendation* ("strong" or "weak"). When evidence is lacking, recommendations may be designated as ungraded and therefore identify areas for further research. The strength of the recommendation is not always reflective of the quality of evidence, but rather is determined by the balance between two interventions, one with desirable effects and

the other with undesirable effects. "Strong" recommendations therefore represent interventions with desirable or undesirable effects that clearly outweigh the other. However, when evidence suggests that these effects are more closely balanced, the recommendation becomes "Weak." Therefore, in some instances the level of evidence and the strength of the recommendation may be discordant.

Voting was conducted openly and included the review of each working group's statements by all conference members. Bias, influence, and partiality could not be completely excluded; however, dissenting opinions were encouraged, recognized, and accounted for. All of the final recommendations from the present meeting were endorsed by unanimous vote.

RESULTS: RECOMMENDATIONS FOR THE PREVENTION AND MANAGEMENT OF AKI AFTER CARDIAC SURGERY

Preoperative Strategies (Table 1)

RECOMMENDATION I: We recommend health systems demonstrate a deliberate commitment to optimize kidney health and outcomes of patients at risk for, or who develop, CSA-AKI (Evidence ungraded; Weak recommendation).

The incidence of CSA-AKI is both alarming and a clear cause for action.[30, 31] It has been shown in non-surgical contexts that comprehensive programs such as those fostered by the Indian Health Service (IHS) can decrease the incidence of end-stage renal disease (ESRD) in specific populations by as much as 40%.[32] We encourage systems and individual hospitals to adopt goals paralleling those of IHS and the U.S. Department of Health and Human Services. These goals should be developed with the input of all stakeholders, including hospital system leadership, administrators, and individual providers across the continuum of care. Goal-setting should include provider education and awareness and the development of measurable targets for optimizing not just reactive response and treatment but also surveillance, early detection, prevention, follow-up, and long-term outcomes.[13, 33] An excellent framework for guiding such an initiative is provided in a 2021 review published by Kane-Gill.[34]

RECOMMENDATION II: We recommend that every patient should undergo a Kidney Health Assessment prior to cardiac surgery, which should include assessment of proteinuria and serum creatinine concentration (Evidence ungraded; Strong recommendation).

Any comprehensive, perioperative mitigation strategy requires preoperative recognition of risk factors that may contribute to the development of postoperative complications (Table 2).[20, 35] Appropriate preventive renal-support strategies should be planned in advance of surgery, tailored to the patient's unique risk profile, and instituted throughout the perioperative period.

The 3 most common preoperative risk scoring systems for renal complications after cardiac surgery, focusing primarily on renal replacement therapy (RRT), are those from Thakar and colleagues at the Cleveland Clinic,[36] the Mehta Score,[37] and the Toronto Simplified Renal Index.[38] The majority of cardiac surgery patients who develop AKI, however, develop mild to moderate disease not requiring RRT. Because even mild to moderate AKI contributes to an economic burden on the healthcare system and places emotional and financial strain on patients and their families, it is important to capture baseline risk factors in all patients by implementing a thorough preoperative assessment that focuses on key questions and laboratory tests.

We recommend that a formal kidney health assessment (KHA) be incorporated into the routine preoperative workup to aid in the detection of renal dysfunction and to help reduce the incidence of CSA-AKI. An algorithm for a risk-based KHA before and after non-cardiac surgery has been described by the Acute Disease Quality Initiative (ADQI) in conjunction with POQI,[39] and we recommend following this framework while accounting for risk factors unique to cardiac surgery.

The extent of the required assessments will naturally vary between low-risk and high-risk patients, and may be limited to a simple history focusing on previous history of AKI, cardiovascular health, and medications in conjunction with a physical examination.[39, 40] A simple screening tool, available from the National Kidney Foundation, consists of 8 simple questions that most patients can answer themselves.[41] This information can be combined with supplemental data from the patient's electronic medical record (EMR) to alert providers to an elevated risk and the need for further investigation.

Preoperative proteinuria has been associated with CSA-AKI independent of preoperative eGFR.[42, 43] It is a powerful predictor of ESRD, stroke, and long-term all-cause mortality after cardiac surgery.[43, 44] We recommend the inexpensive, simple, and useful dipstick assessment of proteinuria plus serum creatinine or, when a patient's risk is elevated, a more detailed measure of current kidney function, stress, and subclinical or overt damage.[45] A positive dipstick protein score of 1+ (30 mg/dl protein) combined with increasing serum creatinine could prompt providers to order a primary care evaluation or early nephrology consult for further workup, and to be on heightened alert for periprocedural hypotension, nephrotoxins, and perfusion deficits.[42–46]

RECOMMENDATION III: We recommend leveraging the electronic medical record to provide timely identification of patients who are at risk for CSA-AKI and to prompt further evaluation (Grade C evidence; Weak recommendation).

Despite increased use of care bundles and checklists, risk assessment and early recognition of developing CSA-AKI remain challenging for many clinicians. This is clear from studies showing a 70-80% discrepancy between the documentation or coding of AKI—a surrogate indicator of recognition—and evidence of AKI as confirmed by Kidney Disease: Improving Global Outcomes (KDIGO) criteria.[47, 48]

The EMR, coupled with the use of clinical-decision support tools,[49, 50] other health information technology applications, and rapid progress in the field of machine learning technology and AI, has the potential to dramatically increase CSA-AKI awareness, reduce under-recognition, improve documentation, and therefore attenuate the severity and consequences of AKI through prevention and continuity of care.[51, 52] Data within the EMR can and should be leveraged to improve recognition of CSA-AKI indicators as they develop, detect patterns and push alerts to providers to ensure timely assessment and appropriate intervention that may prevent or mitigate disease progression, and improve outcomes.[53]

Clinicians need robust assessment tools that interface with the data captured within the EMR regarding medical history, clinical signs and symptoms, laboratory tests results, and diagnostic biomarkers. Artificial intelligence can and should be further developed to note changes from baseline, predict risk, and offer protocols and checklists for addressing those indicators.[54, 55]

While it has been shown previously that formal documentation of AKI in the EMR is associated with reduced 30-day mortality, it has also been shown that electronic documentation of AKI may occur in less than 50% of cases.[56] Thus, the design of EMRs and AI tools must take into account human-factors engineering to ensure optimal datasets and performance of various electronic tools for AKI alerts.[57]

RECOMMENDATION IV: We recommend allowing the consumption of clear liquids up until 2 hours before general anesthesia to reduce the risk of dehydration (Grade A evidence; Strong recommendation).

Both dehydration and fluid overload are undesirable states in patients undergoing major surgery and are especially detrimental to kidney health. Further, suboptimal fluid management resulting in dehydration during one phase of an episode of care can undermine the benefits of euvolemia in another phase. This is especially important in cardiac surgery, where fluid shifts are common during and after cardiopulmonary bypass (CPB). Therefore, perioperative fluid management should be individualized, goal-directed, and considered in the context of a continuum from the preoperative phase through the intraoperative and postoperative phases of care.[58]

In particular, patients should be well-hydrated and euvolemic when they arrive in the operating room. Evidence supports the practice of allowing and even encouraging otherwise healthy patients to continue oral consumption of clear liquids until 2 hours before non-cardiac surgery.[59–61] This practice has been adopted by ERAS Cardiac programs with no reported evidence of increased risk of aspiration, though this topic warrants further, formal study.[25, 62, 63] It is important to note however, that in patients with underlying heart failure or delayed gastric emptying, preoperative fluid intake requires judicious attention.

Intraoperative Strategies (Table 3)

RECOMMENDATION V: We recommend the use of a *cardiopulmonary bypass bundle* in all patients to minimize CSA-AKI (Grade C evidence; Weak recommendation).

The consistent implementation of a standardized bundle of evidence-based practices designed around a given procedure or intervention can help to improve patient care and outcomes.[64, 65] In order to minimize the incidence of CSA-AKI, we have developed a *cardiopulmonary bypass bundle* (**Figure 1**).

This bundle is built on the foundation of the 2017 KDIGO recommendations for non-cardiac surgery patients,[23] modified to reflect subsequent evidence from the literature,[66] and the unique physiological stresses encountered during CPB. It considers the need for active management of factors at the cellular, hemodynamic, and systemic levels in order to decrease CSA-AKI and improve outcomes.

- Perform goal-directed perfusion by targeting global oxygen delivery (DO_2) greater than 280 ml/min/m^2.[67] Additional detail is provided in recommendations VI and VIII. [67]
- Actively manage blood pressure during CPB to avoid periods of hypotension.[8, 30, 39]
- Avoid severe anemia, maintaining hematocrit above a prescribed threshold.[20] Consider use of intraoperative blood salvage. If time permits, preoperative iron therapy or erythropoietin can be used.[68] Transfusion is also a potential risk factor for CSA-AKI and should be avoided if DO_2 is not critically low.
- Optimize glycemic control by maintaining blood glucose below 180 mg/dL.[8, 39]
- Avoid hyperthermia.[69]
- Avoid excessive ultrafiltration. Additional detail is provided in recommendation VII.
- Individualize the continuation or discontinuation of angiotensin converting enzyme inhibitors and angiotensin receptor blockers in the immediate perioperative period based on the risk-benefit profile for each patient, taking into account renal and other postoperative outcomes.[70] At the current time, common practice is to withhold these medications for at least 24 hours prior to surgery to avoid perioperative hypotension as the incidence of AKI is reduced when withholding these medications;[30, 71, 72] however, management strategies remain heavily debated.[70, 73, 74]
- Avoid use of nephrotoxins (nonsteroidal anti-inflammatory drugs, loop diuretics, and aminoglycoside antibiotics) whenever possible.[8, 39]

RECOMMENDATION VI: We recommend preservation of adequate intravascular volume in the setting of dynamic fluid shifts and cardiopulmonary compromise (Grade B evidence; Strong recommendation).

Dynamic fluid shifts are not uncommon during cardiac surgery and are the result of inflammatory and physiologic changes and blood and fluid losses that precipitate movement of fluid from the intravascular to the interstitial space.[75] Because renal perfusion is sensitive to changes in arterial blood flow and renal afterload, maintenance of adequate intravascular blood volume and hemodynamic stability are essential to protecting the kidneys from insult. To prevent CSA-AKI, intravascular blood volume, cardiac output, blood pressure, and oxygen flux (expressed as DO_2), must be carefully balanced to maintain complete oxygenation of organs and tissues.[76] Of these, the most difficult to measure and manage—consequent to the lack of a dependable indicator for euvolemia—is intravascular blood volume.[77]

Despite these challenges, clinicians can optimize intravascular blood volume using a multifaceted approach that considers the underlying cause of the fluid shift, the response to treatment, and the patient's clinical condition. Available intraoperative tools to assess volume status include transesophageal echocardiography, blood pressure, stroke volume variation, and pulse pressure variation. Preference varies across the US;[78] According to the POQI 5 Consensus group, assessing fluid responsiveness, conceptually defined as the state of recruitable stroke volume in response to fluid administration, is one of the most effective methods to guide fluid therapy.[76]

RECOMMENDATION VII: We recommend against the use of excessive ultrafiltration during cardiopulmonary bypass (Grade C evidence; Strong recommendation).

Because both anemia and red blood cell transfusion have been linked to AKI,[79]strategies including conventional ultrafiltration, aimed at counteracting the effects of hemodilution during CPB, have been utilized. Conventional ultrafiltration minimizes CPB-related hemodilution effects with the goal of maintaining hemoglobin levels above a prescribed threshold, through the removal of excess plasma water. However, excessive ultrafiltration during CPB leading to significant hemoconcentration at the conclusion of CPB may cause intravascular volume depletion, hypotension, and the need for vasopressors.[80, 81] Paugh and colleagues have found that increasing continuous ultrafiltration volumes were associated with an increased AKI risk in patients with glomerular filtration rate less than 99.6 mL/min, and therefore concluded that lower volumes of conventional ultrafiltration should be considered in these patients.[82] Manning and colleagues reached similar conclusions;[83] however, conflicting results by other studies finding no association between the volume of ultrafiltrate removed and AKI risk demonstrate the need for large randomized controlled trials to further guide recommendations.[84] As previously described, hypovolemia is deleterious to kidney function in the setting of cardiac surgery, and therefore these tools should be used only according to prespecified goals.[83, 85]

RECOMMENDATION VIII: We recommend the use of individualized, perioperative goal-directed therapy to reduce the incidence of CSA-AKI (Grade B evidence; Strong recommendation).

Goal-directed therapy is a highly patient-specific approach to maintaining oxygen delivery and end-organ perfusion that uses specialized techniques to continuously monitor and balance physiologic variables that serve as surrogate measures of patient health at the cellular, microcirculatory, and macrocirculatory levels. These include cardiac output, stroke volume, mean arterial pressure, central venous and mixed venous oxygen saturation, and urine output.[39, 58, 59, 76, 86–88] Instead of targeting specific individual metrics for each parameter, in GDT, careful attention is paid to dynamic shifts in these parameters to help normalize and stabilize the patient's fluid balance, hemodynamic parameters, cardiac output, and oxygen delivery to the tissues.

While many clinicians use an informal approach, GDT uses standardized algorithms designed to align improvement in patient outcomes.[25] Evidence supports the use of GDT to reduce the risk of AKI after non-cardiac surgery.[58, 59, 76, 86–88] We recommend its application in cardiac surgery as well, given evidence to suggest the use of GDT is beneficial in cardiac surgical patients,[89, 90] although we acknowledge this remains a matter of debate and may be most useful for patients with evidence of kidney stress or injury.[91]

Postoperative Strategies (Table 4)

RECOMMENDATION IX: We recommend use of point-of-care ultrasound to augment the evaluation of postoperative intravascular volume status (Grade C evidence; Weak recommendation).

Hemodynamic assessment and management is an important strategy for CSA-AKI prevention, as low cardiac output has been linked to adverse outcomes after cardiac surgery.[92] While ventricular performance should remain a target for optimization, venous congestion and volume overload after cardiac surgery must also be managed to mitigate their adverse effects on renal hemodynamics.[93] Furthermore, accurate assessment of fluid status is critical to the appropriate treatment of AKI.

Point-of-care ultrasound (POCUS) is a useful, simple, and validated adjunct for rapid assessment of the extent of venous congestion and adequacy of intravascular blood volume.[94, 95] Following cardiac surgery, a transhepatic view from the right chest is sufficient when chest tubes and dressings are in place in the subxiphoid location. The dynamic measures that may be derived from POCUS, including assessment of fluid responsiveness using arterial pulse contour analysis and the cardiac output response to intravenous fluid bolus administration, have been shown to be a more accurate gauge of patient volume than central venous pressure, skin turgor, or fluid balance charts.[95] More recent POCUS-based assessments that also yield practical information about the intravascular blood volume status include dynamic measurement of the diameter of the inferior vena cava and calculation of its collapsibility and distensibility indices,[96, 97] as well as indices of hepatic venous, portal venous, and intrarenal blood flow (the Venous Excess Ultrasound Score).[98, 99]

RECOMMENDATION X: We recommend the use of a urinary biomarker-driven care bundle to enhance the evaluation of kidney health and to reduce CSA-AKI in the postoperative period (Grade C evidence; Weak recommendation).

Once CSA-AKI has been recognized, it is imperative that protocols to prevent further progression are initiated as quickly as possible. It has been shown that patients with CSA-AKI who recover renal function early are at improved odds of long-term survival.[24]

Traditional measures of kidney function, such as serum creatinine levels and urinary output, are insufficient for a timely diagnosis of CSA-AKI. Fluid administration and the effect of CPB may dilute sCr, while decreased urine output may be a physiologic response to hypovolemia and therefore an unreliable indicator of CSA-AKI. To improve CSA-AKI risk prediction and early detection and to guide management decisions, we recommend including an evaluation of urinary biomarkers at appropriate intervals after cardiac surgical procedures.[100, 101]

To date, insulin growth factor binding protein 7 (IGFBP7), and tissue inhibitor of metalloproteinases (TIMP-2), which are clinical indicators of tubular renal cell damage, renal stress, and risk for AKI are the best-studied.[21–23, 100, 102–104] In a single-center, randomized trial of cardiac surgery patients identified as moderate to high risk (urinary TIMP-2/IGFBP7 biomarker panel result of >0.3 ng/dL), implementation of a KDIGO bundle in resulted in meaningful reductions in both the frequency and severity of AKI after cardiac surgery, compared to similar patients treated with standard of care.[22] A subsequent multicenter, multinational randomized trial with similar design showed that occurrence of both moderate and severe AKI was significantly lower in at-risk patients identified using the biomarker panel when a KDIGO-based intervention bundle was applied, compared to the control group.[23] A randomized trial in non-cardiac surgery patients has shown similar results.[21] A detailed example of a urinary TIMP-2/IGFBP7 biomarker- driven, staged algorithm for the prevention of postoperative CSA-AKI, which can be adapted for use into interested readers' clinical practices, can be found in Table 5. In an 847-patient evaluation of the algorithm, implementation of resulted in an 89% relative reduction in the incidence of stage 2 or 3 AKI.[100]

RECOMMENDATION XI: We recommend against prophylactic or otherwise routine use of diuretic therapy. (Grade A evidence; Strong recommendation).

Despite often being markedly fluid-positive immediately following cardiac surgery, patients may nevertheless be volume-depleted, intravascularly. Diuretics should be administered selectively and with specific fluid-management goals in mind because the liberal, indiscriminate use of diuretic therapy in the early postoperative timeframe may exacerbate hypovolemia and therefore AKI.[8] In patients with pre-existing renal dysfunction, an association exists between the use and dose of diuretics and the development of AKI. Diuretics should only be considered for managing fluid overload and not for preventing AKI.[39] The indiscriminate use of diuretics has not been consistently associated with improved renal function and cannot reverse the onset of oliguric renal failure unless it is caused by hypervolemic venous congestion.[8]

RECOMMENDATION XII: We recommend that the development of new KDIGO Stage 2 or 3 CSA-AKI should prompt referral for long-term follow-up (Grade A evidence; Strong recommendation).

It has been shown that patients who develop perioperative CSA-AKI—even if it is only transient KDIGO stage 1 or 2— have a significantly higher risk of death and are at increased risk of developing CKD and other complications.[105–108] In addition, recurrent AKI is not uncommon, affecting up to 25% of AKI survivors and is related to the severity of the initial AKI insult and the presence of underlying comorbidities such as diabetes and CKD.[109] It is estimated that 80% of patients with moderate to severe AKI are unaware of their diagnosis.[110] Disease recurrence and progression can be mitigated through proper education, disease awareness, and care.[111]

Evidence suggests that an AKI rehabilitation program can decrease the risk of rehospitalization or mortality at 30 days.[112]

Unfortunately, the current rate of follow-up care with a nephrologist is less than 50% in high-risk patients with severe AKI.[113] There are currently no standards to dictate who receives follow-up care;[114] patient risk factors and the degree of kidney injury and recovery should dictate the intensity of follow-up, though all patients, including those with KDIGO Stage 1 AKI, warrant some level of outpatient assessment and monitoring.[113] Given that this represents almost one-third of cardiac surgical cases, we recommend prioritizing the allocation of limited specialty healthcare resources to patients with Stage 2 and 3 AKI due to their higher risk, and to prevent overburdening the healthcare system. Increasing duration and severity of in-hospital CSA-AKI should prompt a nephrology specialty care provider follow-up within a timeframe of weeks rather than months after hospital discharge.[115, 116] Guidance on appropriate care should evolve as evidence-based guidelines emerge regarding which subsets of patients are most likely to benefit from follow-up care and at which intervals and duration.[116]

RECOMMENDATION XIII: We recommend that the development of new, persistent, dialysis-dependent CSA-AKI should prompt a multidisciplinary review similar to other serious adverse hospital-acquired conditions (Evidence ungraded; Strong recommendation).

With appropriate care, attention, and adherence to evidence-based best practices, the progression of new-onset CSA-AKI to persistent, dialysis-dependent CSA-AKI can, in many cases, be mitigated and should be an extremely rare event.[33] Given that a hospital's rate of postoperative

AKI requiring dialysis is a formal Quality Indicator within the Agency for Healthcare Research and Quality (AHRQ) framework, as well as a component of the Patient Safety and Adverse Events Composite (CMS PSI 90) that is included in the AHRQ's Hospital Acquired Condition Reduction Program, we recommend that cardiac surgery teams and institutions embrace the designation of CSA-AKI as a hospital-acquired condition that is identifiable, addressable, and deserving of multidisciplinary review and continuous improvement efforts.

DISCUSSION:

There is a concerted effort to standardize evidence-based best practice to improve outcomes and prevent the development of CSA-AKI. This is reflected in recent publications such as the Clinical Practice Guidelines for the prevention of CSA-AKI by The Society of Thoracic Surgeons (STS), Society of Cardiovascular Anesthesiologists (SCA), and the American Society of Extracorporeal Technology (AmSECT),[117] and the Clinical Practice Update for the management of CSA-AKI by the SCA's Continuing Practice Improvement Acute Kidney Injury Working Group.[66]

These manuscripts offer useful information and are a welcome and valuable addition to current efforts to prevent and manage CSA-AKI. While there is some overlap in the recommendations between these publications and the guidance offered in this manuscript, there are some differences as well. For example, the STS/SCA/AmSECT guidelines are highly focused on intraoperative strategies while the present document broadens the recommendations to include other perioperative phases. The STS/SCA/AmSECT guidelines also suggest fenoldopam may be reasonable to reduce the risk of CSA-AKI. While the authors acknowledge heterogeneity in available studies, clinicians should carefully consider and weigh the risks and benefits in this off-label use.

Another recent publication, the SCA's Clinical Practice Update for the management of CSA-AKI, is based on a survey of SCA members to select the 6 most reno-protective strategies.[66] The evidence-based review resulted in a limited number of high quality, randomized trials that were insufficient to support making specific recommendations but were in favor of only 3 strategies including the application of a KDIGO bundle of care, use of vasopressin in vasoplegic shock and goal-directed oxygen delivery during CPB.

It is encouraging to see a growing emphasis on the potential impact of interventions to prevent CSA-AKI and efforts being made to decrease its severity and improve patient outcomes. The value of the GRADE ranking system used here is that, in some instances in which high-quality evidence is scarce, clinical consensus among experts can be valuable and useful in guiding decision-making and informing best practices. It is important, however, to continue to evaluate and update consensus recommendations as new evidence becomes available. We are pleased to contribute our recommendations that highlight a comprehensive approach from the beginning to end of the perioperative journey, including a preoperative kidney health assessment, intraoperative and postoperative bundles of care, and long-term follow-up.

CONCLUSIONS

Given the evidence that there are no reliable or effective treatment options to cure or reverse CSA-AKI, we would like to emphasize that prevention and early detection must be the primary focus. Through evidence-based practices and guidance from experts in the field, the risk of postoperative CSA-AKI may be reduced. It follows that hospitals, hospital systems, and the multidisciplinary teams providing perioperative care for cardiac surgery patients need to take action to reduce the incidence and impact of this life-threatening complication (**Graphical Abstract**).

The implementation of a thorough assessment of kidney health prior to undergoing cardiac surgery, the use of electronic alerts and novel tools for the early identification of kidney injury, bundles of care for best-practice management, and early and appropriate follow-up can positively affect outcomes and provide a clear argument for aggressive mitigation strategies.

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FIGURE LEGENDS

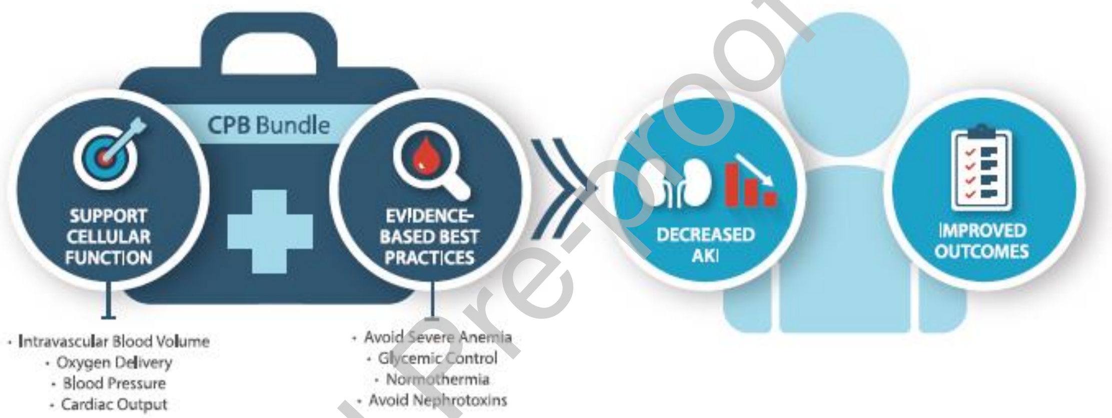
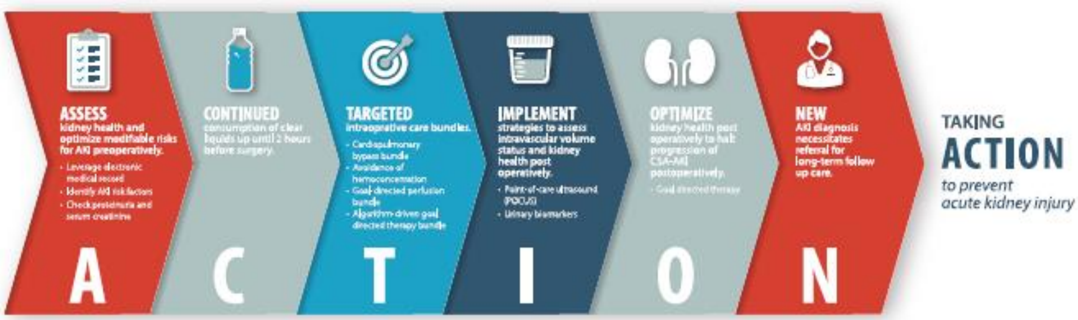


Figure 1: The cardiopulmonary bypass bundle should address multiple factors at the level of cellular function, circulation, and systemic physiology in order to decrease the risk of cardiac surgery-associated acute kidney injury.



Graphical Abstract: The ACTION plan for preventing cardiac surgery-associated acute kidney injury. This graphic and mnemonic serves to highlight the essential components of the consensus recommendations from the PeriOperative Quality Initiative (POQI) and the Enhanced Recovery After Surgery (ERAS®) Cardiac Society. Abbreviations: AKI, acute kidney injury; CSA-AKI, cardiac surgery associated acute kidney injury.

Table 1: Strategies for preoperative prevention of CSA-AKI

Consensus Statement		Strength of Recommendation	Evidence Grade
I	We recommend health systems demonstrate a deliberate commitment to optimize kidney health and outcomes of patients at risk for/or who develop CSA-AKI	Weak	U
II	We recommend that every patient should undergo a Kidney Health Assessment prior to cardiac surgery, which should include assessment of proteinuria and serum creatinine concentration	Strong	U
III	We recommend leveraging the electronic medical record to provide timely identification of patients who are at risk for CSA-AKI and	Weak	C

	prompt further evaluation		
IV	We recommend allowing the consumption of clear liquids up until 2 hours before general anesthesia to reduce the risk of dehydration	Strong	A

Grades of Evidence: A, strong; B, moderate; C, weak; U, ungraded.

Table 2: Risk factors for renal hypoperfusion and CSA-AKI[20, 35, 77]

Phase		
Preoperative	Advanced age	Previous cardiac surgery
	Female sex	Emergency Surgery
	Proteinuria	Diabetes mellitus
	Chronic kidney disease	Hypertension
	Chronic lung disease	Obesity
	Congestive heart failure	Anemia
Intraoperative	Duration of cardiopulmonary bypass	Hypothermia
		Intra-aortic balloon pump use
	Complex surgery	Hemodilution
	Aortic cross-clamp time	Blood transfusion
	Nephrotoxic products of hemolysis	
Postoperative	Low cardiac output	Hypovolemia
	Cardiogenic shock	Hypervolemia
	Atheroembolism	Hypotension
	Nephrotoxins	Sepsis
	Reoperation	

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Table 3: Strategies for intraoperative prevention of CSA-AKI

Consensus Statement		Strength of Recommendation	Evidence Grade
V	We recommend the use of a cardiopulmonary bypass bundle in all patients to minimize CSA-AKI	Weak	C
VI	We recommend preservation of adequate intravascular volume in the setting of dynamic fluid shifts and cardiopulmonary compromise	Strong	B
VII	We recommend against the use of excessive ultrafiltration during cardiopulmonary bypass bundle	Strong	C
VIII	We recommend the use of individualized, perioperative goal-directed therapy to reduce the incidence of CSA-AKI	Strong	B

Grades of Evidence: A, strong; B, moderate; C, weak; U, ungraded.

Table 4: Strategies for postoperative prevention of CSA-AKI

Consensus Statement		Strength of Recommendation	Evidence Grade
IX	We recommend use of point-of-care ultrasound to augment the evaluation of postoperative intravascular volume status	Weak	C
X	We recommend the use of a urinary biomarker-driven care bundle to enhance the evaluation of kidney health and to reduce CSA-AKI in the postoperative period	Weak	C
XI	We recommend against prophylactic or otherwise routine use of diuretic therapy.	Strong	A
XII	We recommend that the development of new KDIGO Stage 2 or 3 CSA-AKI should prompt referral for long-term follow up	Strong	A
XIII	We recommend that the development of new, persistent, dialysis-dependent CSA-AKI should prompt a multidisciplinary review similar to other serious adverse hospital-acquired conditions	Strong	U

Grades of Evidence: A, strong; B, moderate; C, weak; U, ungraded.

Table 5: A Urinary-Biomarker-Driven, Staged Algorithm for Postoperative Prevention of Cardiac Surgery Associated AKI

Nephrocheck test intended use:	Intended to aid in assessing the risk of moderate-to-severe acute kidney injury (AKI) in the following 12 hours
Who to test	All cardiac surgery patients on postoperative day 1 at 05:30
Who not to test	Pre-op creatinine > 2, on dialysis, or received methylene blue
AKI ACTION PLAN	
Urinary TIMP-2/IGFBP7 Negative (< 0.3) ng/dL **Low-risk for AKI** **FAST TRACK**	● Remove Foley, arterial line, central line. ● Transfer to telemetry if all other criteria met (cardiac index, heart rate, respiratory function). ● Liberal diuretics. ● May use: ARBs/ACE-I, ● Transfusion threshold Hgb < 7.0 ● Check sCr daily
Urinary TIMP-2/IGFBP7 Low positive (0.3 – 0.7) ng/dL **Mod-high risk for AKI** **TELEMETRY UNIT at 4PM**	● Keep Foley and monitor hourly urine output until afternoon rounds. ● Transfer to telemetry after 4 PM if all other transfer criteria are met (cardiac index, heart rate, respiratory function) and no oliguria treatment was required. ● Avoid nephrotoxins: NSAIDs, ARBs/ACE-I, Vancomycin, Gentamycin ● Transfusion threshold Hgb < 7.0 unless oliguric ● If patient becomes oliguric (urine output <0.5 cc/kg/h for 3 h) activate AKRT/nephrology consult ● Use lactated Ringer's boluses if CVP < 8; PAD<14; hold Lasix unless CVP > 20 or CHF. ● Repeat Nephrocheck in 24 h
Urinary TIMP-2/IGFBP7 High positive (> 0.7) ng/dL **ACTIVATE ACUTE KIDNEY RESPONSE TEAM (AKRT)**	● Keep Foley and monitor hourly urine output. ● Maintain hemodynamic monitoring ● Avoid nephrotoxins: NSAIDs, ARBs/ACE-I, Vancomycin, Gentamycin ● Renal dosing of medications ● Goal Directed Therapy (keep PAD > 14 with LR, no diuretics unless PAD > 20 or CHF) ● Reassess transfusion threshold. ● CI > 2.5. SBP > 130. Monitor SVO2; Echo if < 55% ● Nephrology consult ● Repeat Nephrocheck in 24 h

Adapted from Engelman DT, Crisafi C, Germain M et al. Using urinary biomarkers to reduce acute kidney injury following cardiac surgery. J Thorac Cardiovasc Surg. 2020;160:1235-1246.e2 and Engelman DT, Shaw AD. A turnkey order set for prevention of cardiac surgery-associated acute kidney injury. Ann Thorac Surg. In Press.

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