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EDITORIALS

A Turnkey Order Set for Prevention of Cardiac Surgery–Associated Acute Kidney Injury

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With an annual incidence of up to 30%, cardiac surgery-associated acute kidney injury (CSA-AKI) may be one of the most underappreciated yet frequent complications after cardiac surgery. Underlying patient comorbidities, combined with perioperative hemodynamic fluctuations, increase cardiac surgery patients' vulnerability to acute kidney injury (AKI). As many as 80% of cardiac surgery patients may have stage 1 or greater CSA-AKI according to the strict, consensus-based guidelines published by the Kidney Disease Improving Global Outcomes (KDIGO) group.[1]

For related article, see page 34

Importantly, even KDIGO stage 1 AKI is deleterious, with a 2-fold risk of persistent kidney dysfunction, which can lead to chronic kidney disease (CKD).[1] The development of reversible stage 2 or 3 CSA-AKI is associated with increased length of stay, readmissions, and cost. Most importantly, CSA-AKI increases short- and long-term mortality risk. Unfortunately, the lack of standardized preoperative, intraoperative, and postoperative evidence-based protocols for patient management has hampered a meaningful reduction in its occurrence.

NEW CSA-AKI GUIDELINES

Given the scope and magnitude of the problem, we applaud the publication of new 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).[2] The STS/SCA/AmSECT guidelines formalize use of the KDIGO bundle of care for surgical patients at high risk for CSA-AKI, including discontinuation of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers up to 48 hours before surgery, use of alternatives to radiocontrast agents, avoidance of other nephrotoxic agents (eg, nonsteroidal anti-inflammatory drugs, loop diuretics, and aminoglycoside antibiotics) when possible, maintenance of normoglycemia for 72 hours, hemodynamic optimization, and monitoring of serum creatinine (sCr) and urine output.[2]

Specific to the cardiac surgery patient, the STS/SCA/AmSECT guidelines offer 4 recommendations classified as strong or moderate, consisting of avoidance of hyperthermic perfusion (>37 °C), use of goal-directed oxygen delivery for patients on cardiopulmonary bypass, selective use of fenoldopam, and adoption of minimally invasive extracorporeal circulation.[2]

COMPARISON WITH OTHER RECENT GUIDELINES

A multidisciplinary drive toward improving outcomes through standardization of care is evidenced by the recent publication of 3 other expert consensus manuscripts for CSA-AKI prevention: the Acute Disease Quality Initiative (ADQI) Consensus Statement,[3] the Enhanced Recovery After Surgery (ERAS) Cardiac Society Guidelines,[4] and a joint consensus statement from the PeriOperative Quality Initiative (POQI) and ERAS Cardiac Society (unpublished data, 2022).

We have compared the strong and moderate, low-risk recommendations from each of these publications in Table 1.

GREATER NEED FOR PREOPERATIVE CARE MEASURES. The STS/SCA/AmSECT guidelines place insufficient emphasis on preoperative-phase assessments. We suggest a formal kidney health assessment should be incorporated into the routine preoperative workup to determine a patient's susceptibility for CSA-AKI as well as modifiable risk factors that may be addressed before their procedure. For example, preoperative proteinuria can be detected from a simple urinalysis and has been associated with CSA-AKI, independent of the preoperative glomerular filtration rate. A positive dipstick protein score, combined with an increasing sCr

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Abbreviations and Acronyms

AKI = acute kidney injury
AmSECT = American Society of Extracorporeal Technology
CKD = chronic kidney disease
CSA-AKI = cardiac surgery–associated acute kidney injury
EMR = electronic medical record
KDIGO = Kidney Disease Improving Global Outcomes
SCA = Society of Cardiovascular Anesthesiologists
sCr = serum creatinine
STS = The Society of Thoracic Surgeons

and other information in the patient's electronic medical record (EMR), should prompt orders for further evaluation or an early nephrology consult.

POSTOPERATIVE USE OF BIOMARKER ASSESSMENT. The STS/SCA/AmSECT guidelines do not include a discussion of the utility of, or recommendations for, biomarker-based assessments to direct KDIGO strategies for prevention of CSA-AKI. While sCr concentration and urine output are mainstays of monitoring kidney function, these functional biomarkers are trailing indicators for CSA-AKI. In some cases, oliguria may be the only presentation of impending kidney dysfunction. However, decreased urine output does not always indicate CSA-AKI; it can also be a physiological response to hypovolemia. In addition, the effect of cardiopulmonary bypass and intraoperative fluid administration may dilute sCr concentration and delay recognition of CSA-AKI. The PrevAKI (Biomarker-guided Implementation of the Cardiovascular [CV] Surgery AKI Bundle to Reduce the Occurrence of AKI After Cardiac Surgery- Prevention of AKI) clinical trial and others assessed the combined urinary concentration of tissue inhibitor of metalloproteinase 2

TABLE 1 Comparison of Cardiac Surgery–Associated Acute Kidney Injury Consensus and Guideline Publications

Strong and Moderate Recommendations	STS/SCA/AmSECT Guidelines[2]	ADQI Consensus[3]	ERAS Cardiac Guidelines[4]	POQI/ERAS Consensus[a]
Preoperative				
Perform a kidney health assessment				✓
Consume clear liquids up until 2-4 hours before general anesthesia			✓	✓
Discontinue ACE inhibitors and ARBs	✓	✓		✓
Optimize preoperative glycemic control by maintaining blood glucose <180 mg/dL		✓	✓	
Intraoperative				
Preserve adequate intravascular volume in the setting of dynamic fluid shifts and cardiopulmonary compromise				✓
Restrict the use of excessive ultrafiltration and hemoconcentration during cardiopulmonary bypass		✓		✓
Use individualized, perioperative goal-directed therapy to reduce the incidence of CSA-AKI				✓
Avoid hyperthermic perfusion (>37 °C) on cardiopulmonary bypass	✓		✓	
Use a goal-directed oxygen delivery strategy on cardiopulmonary bypass.	✓			✓
Optimize intraoperative glycemic control by maintaining blood glucose 80-180 mg/dL	✓	✓	✓	✓
Use intraoperative blood salvage to maintain hematocrit above a prescribed threshold				✓
Postoperative				
Avoid prophylactic or otherwise routine use of diuretic therapy		✓		✓
Refer new KDIGO stage 2 or 3 CSA-AKI for long-term follow-up				✓
Perform a multidisciplinary review of all new, persistent, dialysis-dependent CSA-AKI				✓
Implement a KDIGO bundle of care[b] for patients at high risk for AKI	✓	✓	✓	✓
Optimize postoperative glycemic control by maintaining blood glucose 80-180 mg/dL	✓	✓	✓	✓
Use a low tidal volume ventilation strategy (<10 mL/kg)		✓	✓	

[a]Unpublished data, 2022; [b]KDIGO bundle of care: Goal-directed fluid therapy, avoidance of nephrotoxins and hyperglycemia, serum creatinine/urinary output monitoring, hemodynamic optimization. ACE, angiotensin-converting enzyme, ADQI, Acute Disease Quality Initiative; AKI, acute kidney injury; AmSECT, American Society of Extracorporeal Technology; ARB, angiotensin receptor blockers, CSA-AKI, cardiac surgery–associated acute kidney injury; ERAS, enhanced recovery after surgery; KDIGO, Kidney Disease Improving Global Outcomes; POQI, PeriOperative Quality Initiative; SCA, Society of Cardiovascular Anesthesiologists; STS, The Society of Thoracic Surgeons.

TABLE 2 Turnkey Order Set for Cardiac Surgery–Associated Acute Kidney Injury

Preoperative
Perform a kidney health assessment, including medical and medication history, baseline kidney function, previous episodes of AKI, nephrotoxin exposure, and assessment of anemia.
Perform a complete urinalysis. Consult nephrology for proteinuria.
Optimize glycemic control by maintaining blood glucose 80-180 mg/dL.
Hold ACE inhibitors and ARBs for up to 48 hours preoperatively.
Limit aminoglycoside antibiotics. Use vancomycin judiciously.
Give clear liquids until 2 hours before general anesthesia.
Intraoperative
Optimize glycemic control by maintaining blood glucose 80-180 mg/dL with an insulin infusion.
Limit aminoglycoside antibiotics.
Perform goal-directed perfusion targeting global oxygen delivery >270 mL/min/m^2.
Avoid patient temperature >37 °C on rewarming from cardiopulmonary bypass.
Postoperative (first 24-48 hours)
Optimize glycemic control by maintaining blood glucose at 80-180 mg/dL with an insulin infusion.
Hold ACE inhibitors and ARBs in oliguric/high-AKI-risk patients.
Limit aminoglycoside antibiotics.
Avoid nonsteroidal anti-inflammatory drugs.
Avoid intravenous radiocontrast agents.
Use lactated Ringers as the preferred fluid for a bolus intervention.
Monitor hourly single-lumen indwelling urinary catheter, call for oliguria (UO <0.5 mL/kg/h using lean body mass).
Optimize intravascular blood volume using continuous invasive or noninvasive functional hemodynamic hourly monitoring with:
Fluid challenges with lactated Ringers for responsiveness if oliguric, cardiac index <2.0 L/min/m^2 and CVP <5 mm Hg, PAD <14 mm Hg, or SVV >13% in a ventilated patient in normal sinus rhythm.
Diuretics if CVP >15 mm Hg or PAD >20 mm Hg. Consider ultrafiltration if diuretic unresponsive.
Implement goal-directed hemodynamic therapy in oliguric/high-AKI-risk/positive-biomarker patients (NephroCheck[a] >0.7). Use fluids, diuretics, and inotropes to maintain:
Systolic blood pressure 100-130 mm Hg or mean arterial pressure 65-90 mm Hg[b]
Cardiac index > 2.2 L/min/m^2
UO >0.5 mL/kg/h (using lean body mass)
Svo_2 >55%
Monitor sCr daily and UO hourly until there are no further indicators of CSA-AKI.
Limit transfusion of PRBC to a hemoglobin <7.0 g/dL or <8.0 g/dL in the presence of oliguria, lactic acidosis, low cardiac output, or positive urinary biomarkers.
For persistent oliguria (UO <0.5 mL/kg/h for 3 hours) or sCr rise >0.3 mg/dL, adjust medication dosing/interval for renal function per institutional policies or discontinue nephrotoxic medications.

[a]bioMérieux, Inc; [b]Individualized to the patient's baseline blood pressure. ACE, angiotensin-converting enzyme; AKI, acute kidney injury; ARB, angiotensin receptor blocker; CSA-AKI, cardiac surgery–associated acute kidney injury; CVP, central venous pressure; MAP, mean arterial pressure; PAD, pulmonary artery diastolic pressure; sCr, serum creatinine; Svo_2, mixed venous oxygen saturation, SVV, stoke volume variation, UO, urine output.

and insulin-like growth factor-binding protein 7 in biomarker-guided implementation of the KDIGO bundle.[5,6] Current evidence and consensus documents support the use of new biomarkers that can detect subclinical AKI in the presence of early tubular damage before the filtration dysfunction emerges.[7]

INTRAVASCULAR VOLUME AND PRESSURE ASSESSMENT AND TREATMENT WITH GOAL-DIRECTED FLUID THERAPY. Greater attention must be paid to maintenance of optimal intravascular volume and mean arterial pressure in the perioperative time frame. Prolonged episodes of hypotension decrease renal perfusion and may precipitate CSA-AKI in patients with impaired autoregulation. Prompt assessment and preservation of intravascular volume is a priority in the setting of dynamic fluid shifts and cardiopulmonary compromise. In addition, mean arterial pressure in the range of 60 to 75 mm Hg may improve renal oxygen saturation and the glomerular filtration rate.

Just as important, intravascular fluid overload can contribute to CSA-AKI. A high central venous pressure can increase renal venous pressure, which reduces renal perfusion pressure and increases renal venous congestion. This can increase AKI progression in critically ill patients.[8] Diuretic agents should be used aggressively for a central venous pressure >15 mm Hg, concurrent with measures such as inotropic agents to support right ventricular dysfunction, with the cumulative effect of decreasing CSA-AKI.

A CLOSER REVIEW OF FENOLDOPAM. We note one significant area of controversy. The STS/SCA/AmSECT guidelines state that fenoldopam, "may be reasonable to reduce

the risk of CSA-AKI, as long as hypotension is avoided (Class IIb)."[2] We do not agree. The literature does not show a consistent positive signal for fenoldopam. This selective agonist of dopamine D1 receptors has been studied in several randomized trials, but only 1 has shown a benefit. A separate multicenter randomized controlled trial was stopped for futility. Meta-analyses have suggested a decrease in renal replacement therapy in patients with CSA-AKI, but there was an increased frequency of hypotension. As the STS/SCA/AmSECT authors acknowledge, the available studies show considerable heterogeneity with respect to patient populations, administration variables, and comparators. Thus, we believe greater caution is warranted, because this recommendation encourages off-label use of a drug with uncertain risks and benefits.

PUTTING THE GUIDELINES TOGETHER: A TURNKEY ORDER SET

Clinical strategies for prevention and treatment of CSA-AKI are inadequate and mainly supportive; at present, no specific medications or devices are available for therapeutic intervention to reverse renal injury once it has been sustained. A standardized CSA-AKI order set may be the first step.

In aggregate, the recommendations offered by current consensus statements and guidelines provide a firm, if potentially unwieldy, foundation for such an order set. To improve their utility, we have combined their higher-graded, lower-risk recommendations into a modifiable turnkey order set (Table 2). This should be viewed as a template to guide clinicians in creating institution-specific, evidence-based protocols for patient care.

FUTURE DIRECTIONS

Few institutions have fully leveraged their EMR platforms for identifying and treating CSA-AKI. A robust EMR with algorithm-driven, automated alerts could hasten clinician response times to physiologic changes that could signal, or exacerbate, CSA-AKI onset and progression. Clinical workflows should include integration of continuous monitoring of urine output into the EMR with automatically generated alerts to clinicians when this falls below prescribed limits. EMR data can also be leveraged for machine learning and artificial intelligence. This may improve risk stratification of patients, early detection of CSA-AKI, and provide clinical decision support, including predicting further adverse events and long-term prognosis.

Finally, intra-abdominal hypertension $\geq$12 mm Hg is associated with organ dysfunction, particularly AKI, in critically ill patients. Elevations suggested via bladder pressure measurement have been found to predict CSA-AKI and may offer a future path for early detection and intervention.[9]

CONCLUSION

The guidelines that STS/SCA/AmSECT have published in this issue are a welcome and valuable addition to current efforts to prevent and mitigate CSA-AKI and improve outcomes after cardiac surgery. Given the complementary nature of available guidelines and consensus statements, clinicians must determine which of the recommendations to integrate into their standard order sets. The turnkey order set offered here is meant to relieve some of the burden of that endeavor.

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