Perioperative Acute Kidney Injury

Risk Factors and Predictive Strategies

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KEYWORDS

- Acute kidney injury • AKI • Prediction scores • CEUS • BOLD MRI • DWI MRI
- Biomarkers

KEY POINTS

- Acute kidney injury is common and is associated with many adverse perioperative outcomes.
- Clinical risk factors for AKI vary in different surgical populations, and preventable risk factors are often underappreciated before surgery.
- Surgical patients should have a systematic preoperative assessment of kidney health, with an emphasis on the patient's renal reserve and susceptibility to new injury.
- The exposure to any intraoperative risk, and the extent of any renal damage, needs to be evaluated using a combination of clinical parameters, biomarkers and imaging techniques.

INTRODUCTION

Acute kidney injury (AKI) is a common and morbid complication in surgical patients and is associated with significant increases in mortality, an increased risk for chronic kidney disease (CKD) and hemodialysis after discharge, and increased cost and resource utilization.^{1–11} It is characterized by inappropriate oliguria and/or an increase in serum creatinine levels beyond normal. Perioperative AKI complicates the hospital course for up to 50% of surgical patients.^{1,2,12–16} Despite this impact

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AKI remains among the most underdiagnosed and undertreated postoperative complications. Better understanding of the risk factors that contribute to perioperative AKI has led to recent advances in AKI prediction and will eventually lead to improved prevention of AKI, mitigation of injury when AKI occurs, and enhanced recovery in patients who sustain AKI. The development of advanced clinical prediction scores for AKI, new imaging techniques that enable more accurate detection of renal injury, and urinary and serum biomarkers of injury for early detection of AKI provides new tools toward these ends. Surgery provides a unique environment for the study of AKI, as the physiologic stress on the kidney at the time of surgery provides a well-defined opportunity for both risk stratification and the initiation of protective and preventive strategies.

DEFINITIONS AND EPIDEMIOLOGY

Before the development of consensus definitions of AKI, the reported incidence of AKI in the surgical population varied from 1% to 31%. The tendency was to focus on severe, and relatively rare, AKI as defined by large increases in serum creatinine and/or the need for dialysis.^{17,18} In 2004 the original Risk, Injury, Failure, Loss, and End-stage Kidney (RIFLE) consensus definition for AKI was released by the Acute Dialysis Quality Initiative. The RIFLE criteria graded less severe AKI stages and provided taxonomies for both severity and recovery.¹⁹ The current guidelines from Kidney Disease: Improving Global Outcomes (KDIGO) modified the RIFLE criteria to include changes in creatinine as small as 0.3 mg/dL²⁰ (Table 1). The KDIGO guidelines also provide an updated staging system from CKD (Table 2). The epidemiology of perioperative kidney disease has been almost completely redefined since the publication of these consensus definitions.

The consensus definition of AKI has not been uniformly incorporated into the clinical registries and databases used in the surgical community. The American College of Surgeons' (ACS) Committee on Trauma defines AKI as a serum creatinine increase greater or equal to 3.5 mg/dL, and the Society of Thoracic Surgeons Quality Performance Measures defines postoperative renal failure as an increase of serum creatinine to 4.0 mg/dL or greater or 3 times the most recent preoperative creatinine level. The ACS National Surgical Quality Improvement Project (NSQIP) defines AKI as an increase in serum creatinine greater than 2 mg/dL from patients' baseline or as the acute need for renal replacement therapy (RRT).²¹ Studies using the ACS NSQIP database typically have high mortality associated with a low incidence of reported AKI, giving the perception that AKI in surgical patients is rare and often fatal.²² It has been shown that the ACS NSQIP definition for AKI severely underestimates the incidence of AKI, as defined by consensus criteria, in postoperative patients.¹² The incidence of AKI in recent studies using current consensus criteria ranges from 25% in trauma patients² to as high as 75% for patients undergoing ruptured abdominal aortic aneurysm repair.²³

OUTCOMES

Postoperative AKI has been demonstrated to be common and associated with increased incidence of CKD, increased incidence of other postoperative complications, increased risk for short- and long-term mortality, and much higher cost and resource utilization compared with patients with no postoperative AKI.^{2,3,5,12,24-32} Two recent studies have demonstrated a continuous risk-adjusted association between postoperative increase in serum creatinine and worse clinical outcomes, and this association persisted at lower cutoffs than in the original RIFLE definition.^{12,24} The adverse effects of AKI persist for years even for those patients who demonstrate partial or even full recovery in renal function by the time of hospital discharge.^{3,4}

Table 1
Consensus definitions for acute kidney injury

Stage		Serum Creatinine or Glomerular Filtration Rate Criteria		Urine Output Criteria	
RIFLE	KDIGO	RIFLE	KDIGO	RIFLE	KDIGO
Risk	1	Increased sCr ≥ 1.5 times baseline or GFR decreased $>25\%$	Increased sCr 1.5–1.9 times baseline or ≥ 0.3 mg/dL increase	Urine output <0.5 mL/kg/h for ≥ 6 h	Urine output <0.5 mL/kg/h for 6–12 h
Injury	2	Increased sCr ≥ 2 times baseline or GFR decreased $>50\%$	Increased sCr 2.0–2.9 times baseline	Urine output <0.5 mL/kg/h for ≥ 12 h	Urine output <0.5 mL/kg/h for ≥ 12 h
Failure	3	Increased sCr ≥ 3 times baseline or GFR decreased $>75\%$ or sCr ≥ 4 mg/dL (acute increase ≥ 0.5 mg/dL)	Increased sCr 3.0 times baseline; or increase in sCr to ≥ 4.0 mg/dL; or initiation of RRT; or in patients <18 y of age, decrease in eGFR to <35 mL/min/1.73 m ²	Urine output <0.3 mL/kg/h for ≥ 24 h or anuria for ≥ 12 h	Urine output <0.3 mL/kg/h for ≥ 24 h or anuria for ≥ 12 h

Abbreviations: eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; RRT, renal replacement therapy; sCr, serum creatinine.

Table 2 Chronic kidney disease staging according to National Kidney Foundation kidney disease outcomes quality initiative guidelines		
Stage	Description	Estimated GFR, ^a mL/min/1.73 m ²
	At increased risk	≥90 (if CKD risk factors present)
1	Kidney damage with normal or increased GFR	≥90
2	Kidney damage with mildly decreased GFR	60–89
3	Moderately decreased GFR	30–59
4	Severely decreased GFR	15–29
5	Kidney failure	<15 (or dialysis)

Abbreviation: GFR, glomerular filtration rate.
^a Estimated glomerular filtration rate (GFR) is an estimate of kidney function and is calculated using an equation that includes serum creatinine, age, race, and sex. Most of clinical laboratories will report a corresponding estimated GFR when reporting serum creatinine.
Data from Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. *Kidney Inter Suppl* 2012;2:1–138.

Perioperative AKI is independently associated with a high risk for cardiovascular-specific mortality in diverse patient populations, a risk that is comparable with that observed with CKD.^{33,34} In surgical patients who sustain AKI, the risk-adjusted average cost for an episode of care was \$42,600 compared with \$26,700 for patients with no kidney injury.¹ Recognition of the prevalence and importance of AKI in surgical patients is the first step in improving perioperative care and in developing quality measures that could translate into improved care for surgical patients.

RISK FACTORS

Many perioperative factors have been shown to be predictors of AKI after surgery. Scoring systems used to attempt to predict the risk of AKI after cardiac surgery have relied primarily on preoperative clinical and demographic variables.³⁵ Systems using genetic polymorphisms for selected inflammatory and vasoconstrictor genes have shown a 2- to 4-fold improvement over clinical factors alone in explaining post-cardiac surgery AKI.³⁶ Preoperative factors, including total lymphocyte count less than 1500 cells per microliter and elevated C-reactive protein, have been shown to be associated with postcardiac surgery AKI.^{37,38} Preoperative factors related to the procedure itself increase the predictive power for patients undergoing noncardiac surgery.³⁹ The Norton scale score of risk for developing a pressure ulcer and preoperative use of diuretics and nonsteroidal antiinflammatory drugs (NSAIDs) have been associated with AKI following total hip arthroplasty.^{40,41} The use of fenestrated grafts and high doses of intravenous contrast are associated with a higher risk for AKI among patients undergoing endovascular abdominal aortic aneurysm repair.⁴² In patients sustaining severe trauma, an increase in serum creatinine, an increase in lactic acid, low body temperature, and any transfusion of blood products in the first day after admission were associated with the development of AKI² (see [Table 1](#)). The Model for End-Stage Liver Disease score, but not pretransplantation creatinine values, was predictive of AKI among patients undergoing liver transplantation.⁴³ Creating a risk score for AKI applicable to all patients has proven to be challenging.

Many important risk factors for AKI are preventable yet often ignored in surgical patients. Preoperative assessment of kidney function, combining estimated glomerular filtration rate (eGFR) using serum creatinine with albuminuria, is one of the most

valuable yet often underutilized clinical resources for clinicians. It is important both to evaluate for the risk for AKI and to quantitate the risk for all postoperative morbidity and mortality. CKD, affecting 5% of the US population,⁴⁴ is an independent predictor of cardiovascular morbidity and mortality.⁴⁵ An association between CKD severity and postoperative death comparable with that seen with diabetes, stroke, and coronary disease was seen in a review of 31 studies of patients undergoing elective surgery.⁴⁶ The adjusted hazard ratio for 30-day mortality in a study using the ACS NSQIP database for patients with CKD ranged from 2.30 (stage 3 CKD) to 3.05 (stage 5 CKD) compared with patients with no CKD.⁴⁷ Preoperative proteinuria without CKD was associated with a risk for AKI and was a powerful independent predictor of all-cause mortality and end-stage renal disease after cardiac surgery.^{48,49} Some perioperative risk indicator scores consider CKD an important prognostic factor in postoperative risk assessment,^{50–52} whereas others do not.^{53,54} One issue is that there is a complicated and poorly understood relationship between serum creatinine and the eGFR, which is calculated in many electronic health records.⁵⁵ Serum creatinine alone often does not give an accurate picture of the presence of CKD, as creatinine values within normal limits may correspond to a low eGFR, particularly in women and the elderly. Use of the eGFR, if available, can help to assure that CKD is evaluated as a risk factor for both AKI and for overall postoperative mortality.

Many potentially modifiable risk factors for AKI, in both cardiac and noncardiac surgery, include hemodilution, hemoglobin level, intraoperative transfusion, any hypotension, inadequate oxygen delivery, the use of diuretics, the use of vasopressors and inotropes, and the use of cardiopulmonary bypass.^{56–59} Interventions to optimize blood flow and pressure during surgery, including the use of invasive hemodynamic monitoring, showed no difference in short-term mortality; but the rates of kidney injury were significantly reduced.⁶⁰ Goal-directed intraoperative management to reduce the risk of postoperative AKI through optimizing renal perfusion is both feasible and underutilized. Preoperative medications have also been extensively evaluated as both risk and protective factors for a variety of postoperative complications. Several retrospective studies exploring any association between the preoperative use of statins and postoperative AKI have given conflicting results.^{61–63} In a recent retrospective study of 98,939 patients undergoing major surgery, the preoperative use of statins was associated with a 20% to 26% reduction in the incidence of AKI as defined by consensus criteria.⁶⁴ These results, and the wide-ranging pleiotropic actions of statins, have prompted several pending prospective trials evaluating the effect of statins on perioperative complications, including AKI.

PREDICTIVE STRATEGIES

The risk for postoperative complications, including AKI, arises from the interactions between patients' preoperative health that determines the physiologic capacity to withstand surgery-related stress, modulated by the type and quality of surgery and anesthesia that patients experience. Assessment of surgical risk requires accurate and dynamic synthesis of the large amount of collected clinical information to determine both susceptibility to acute stress and the magnitude of its effect on physiologic homeostasis. During surgery, intraoperative monitors capture complex physiologic time series data reflecting ongoing response to anesthesia and surgery. Given time constraints and the increasing information load on physicians, most of the gathered data can only be screened for overt abnormalities and then discarded. With widespread adoption of electronic health records and advancements in computational power and techniques, use of real-time predictive analytics of clinical data will emerge as

the most efficient initial approach for identification of patients at high risk for AKI. Once identified, the high-risk patients can be subjected to incrementally more complex and expensive evaluations with emerging biological biomarkers and imaging techniques depending on the response to initial low-cost and low-risk preventive therapies. This section outlines key clinical risk score, imaging, and biological marker techniques that can be applied in current clinical practice. The authors also provide an example of a pragmatic single-institution approach to standardized clinical assessment and management plans for AKI.

CLINICAL RISK SCORES

The utility of existing AKI scores is limited by several factors, including the use of severe AKI as an end point, restrictions in type of surgery, and lack of dynamic adjustment for preoperative and intraoperative risk factors. Huen and Parikh³⁵ performed a systematic review of studies among cardiac surgery patients³⁵ and reported 4 clinical risk scores for AKI requiring dialysis,^{65–68} all of which were limited to preoperative variables, and 3 scores to predict a broader definition of AKI.^{69–71} Two of the smaller studies included intraoperative data to calculate postoperative scores. The receiver operating characteristic–area under the curve (AUC) varied between 0.77 and 0.84 in both internal and validation cohorts, and most of the studies reported an array of common predictors using mainly logistic regression analysis as a computational tool. Two more recent studies in the United Kingdom and Australia used larger data registries for development and validation of predictive scores that included several intraoperative variables, although model performance remained less than 0.82.^{72,73} For patients undergoing noncardiac surgery, few preoperative predictive models were developed, using either only severe AKI as an end point or limiting inclusion to a specific type of surgery.^{22,32} Thottakkara and colleagues⁷⁴ recently reported a machine-learning computational approach for the development of a KDIGO AKI preoperative forecasting model, using the electronic health records of patients undergoing any type of major surgery. They used 59 variables and reported an AUC of 0.86 in the internal validation cohort.⁷⁴ Only a few studies have used intraoperative data in developing a predictive model for noncardiac surgery, and they showed only modest predictive power.^{75–77}

Lack of sophistication in data access and analysis in real-time has limited the use of the large volume of complex physiologic time series data generated during surgery for the development of prediction models. To date published postoperative risk scores have used only a snapshot value for hemodynamic monitoring data, such as a mean or lowest value for blood pressure, rather than using time series data applied in their continuity and complexity. An ability to rapidly apply machine learning computational approaches to intraoperative clinical data and physiologic time series data raises the prospect of real-time risk prediction for perioperative AKI as studies using these approaches are emerging.^{24,78,79}

IMAGING TECHNIQUES

Imaging techniques, including standard and Doppler ultrasound, have been used for years to help determine the cause of CKD in patients with a transplanted kidney and in patients at risk for renal artery stenosis. Three techniques have recently been developed to help assess AKI: the renal resistive index (RRI) measured using Doppler ultrasound, contrast-enhanced ultrasound (CEUS), and blood oxygenation level-dependent (BOLD) MRI.

RENAL RESISTIVE INDEX

Doppler ultrasound imaging can detect gross vascular abnormalities in the kidney as well as microvascular disorders. RRI, as determined by Doppler ultrasonography, is a measure of pulsatile blood flow that reflects the resistance to flow in the microvasculature. It quantifies changes in both renal vascular resistance and compliance, and an elevated RRI is associated with an increased risk for AKI.⁸⁰ An increased RRI has been shown to be associated with AKI associated with sepsis.^{81–84} In the immediate postoperative period after cardiac surgery with cardiopulmonary bypass, the RRI predicts both the development of AKI and its severity.^{85,86} The prediction of AKI by RRI as measured with intraoperative transesophageal echocardiography, for patients undergoing cardiac surgery, is comparable with that obtained by RRI through translumbar ultrasound.⁸⁷ Elevated RRI is associated with AKI in orthopedic surgery and in critically ill patients in the medical intensive care unit (ICU).^{88–90} RRI has also been shown to be useful in predicting the progression of postoperative AKI.⁹¹ Although RRI depends on renal vascular resistance and compliance, there are other factors that affect RRI, especially in unstable patients; the indications for the test are evolving.^{92,93}

CONTRAST-ENHANCED ULTRASOUND

CEUS has been used for years to help assess solid and cystic lesions in the kidney.^{94,95} It has more recently been used to assess renal perfusion.⁹⁶ In patients undergoing elective cardiac surgery who were considered to be at risk of AKI, renal perfusion as measured using CEUS decreased significantly within 24 hours after surgery.⁹⁷ CEUS shows early promise in assessing both the risk and prognosis of AKI in surgical patients.^{98–100}

MRI

MRI is evolving as a technique to aid in diagnosis of AKI. Newer contrast agents, including ultrasmall particles of iron oxide, are less toxic and are being used to study renal blood flow and volume.¹⁰¹ BOLD MRI uses deoxyhemoglobin as a nontoxic and endogenous contrast agent for the study of intrarenal oxygenation.¹⁰² The technique of BOLD MRI has been used to demonstrate changes in renal blood flow related to the use of nephrotoxins, including NSAIDs, intravenous contrast agents, and calcineurin inhibitors.¹⁰³ It has also been used to study changes in renal blood flow associated with CKD and hypertension.^{104–106} Despite the utility of BOLD MRI in studying renal oxygenation and function in animal models of AKI,^{107,108} one recent study evaluating BOLD MRI in the evaluation of AKI in humans found no correlation between MRI findings and glomerular filtration rate (GFR).¹⁰⁹ Another recently developed MRI technique known as diffusion-weighted imaging (DWI) detects the motion of water molecules within tissue and has been used to assess renal fibrosis in both AKI and CKD.⁷⁹ As with RRI, the indications and utility of BOLD MRI and DWI MRI for predicting AKI in surgical patients are not yet characterized.

USE OF URINE AND PLASMA BIOMARKERS

A new approach for assessing kidney injury is the analysis of serum and/or urine biomarkers. Early recognition of kidney injury using serum creatinine is problematic as creatinine is a measure of renal function not injury. The ideal biomarker will reveal early evidence of cellular stress before permanent damage even occurs. Serum troponins are useful as biomarkers for cardiac injury because they rapidly reflect myocardial stress and injury. Several urine and serum biomarkers have been studied for their ability to predict kidney stress and injury.^{110–115} Many biomarkers fail because of a lack of

sensitivity to early cellular stress, a lack of specificity to renal injury, because they cannot differentiate AKI from CKD, and because they are also elevated by the disease process that has caused the AKI. The variety of stressors faced by surgical patients also makes the search for an effective biomarker difficult. The disease process and/or surgical procedure often results in cellular stress and injuries in several organs, complicated by hemodynamic instability requiring fluid and vasopressor support, blood transfusion, and exposure to nephrotoxic drugs.

Biomarkers to detect kidney injury have been most widely studied in cardiac surgery. Early studies identified plasma and urine neutrophil gelatinase-associated lipocalin (NGAL) as a potential biomarker.^{116,117} Inflammation induces NGAL synthesis and its release from neutrophils throughout the body. A recent summary of NGAL in cardiac surgery patients demonstrated only moderate ability to discriminate AKI from other organ injury.¹¹⁴ Studies of critically ill patients in both medical and surgical ICUs showed similar moderate discriminative performance.^{83,118} The inability to discriminate between systemic and kidney-specific effects has limited the clinical use of NGAL.

A more kidney-specific functional biomarker that has undergone extensive evaluation, especially in pediatric patients, is cystatin C (CyC).^{119,120} CyC is a protease inhibitor produced by all nucleated cells of the body, released at a constant rate, filtered by the glomeruli, and then completely reabsorbed in the renal tubules. CyC is not normally found in urine; thus, the presence of urinary CyC may reflect early kidney injury. Because of the constant rate of its production, plasma CyC concentrations may be a better marker than serum creatinine of GFR; it has recently been proposed as a replacement for serum creatinine in the routine evaluation of GFR rather than as a biomarker of AKI.^{120,121} The role of CyC in risk stratification for postoperative AKI among surgical patients remains to be defined.¹¹²

A combination of 2 novel urinary biomarkers has recently been validated as a marker for AKI and has been approved by the US Food and Drug Administration to assess the risk of developing AKI in critically ill patients. Tissue inhibitor of metalloproteinases-2 (TIMP-2) and insulinlike growth factor binding protein 7 (IGFBP7) are cell-cycle arrest proteins, expressed by renal tubular cells and released into the urine during periods of stress due to toxin exposure, hypoxia, and inflammation, among others. Thus, these urinary biomarkers may indicate risk for injury before any actual AKI takes place.¹²²

Several multicenter studies have shown that the combination of urinary TIMP-2 and IGFBP7 (TIMP-2•IGFBP7) was predictive of moderate to severe AKI in critically ill patients within 12 hours.^{123–125} The power of the TIMP-2•IGFBP7 test to predict the risk of AKI in these studies was superior to serum creatinine and to other measured biomarkers. Patients with a TIMP-2•IGFBP7 higher than 0.3 (ng/mL)²/1000 had 7 times the risk for AKI (95% confidence interval 4–22) compared with patients with lower values. A validation study confirmed the high sensitivity and high negative predictive values of 89% and 97%, respectively, for the cutoff of 0.3.¹²⁶ The development and validation of this biomarker combination is an important advance in early and accurate diagnosis of AKI.

A PRAGMATIC APPROACH

The use of standardized clinical assessment and management plans that synthesize current medical knowledge with best clinical judgment decreases practice variability and improves patient care better than clinical guidelines.¹²⁷ Considering the high prevalence of AKI, and the adverse outcomes when it occurs, efforts at the authors' institution have focused on prevention of AKI, mitigation of further injury when AKI has already occurred, treatment of negative effects on other organs, and facilitation of renal recovery in patients with established AKI.

Using KDIGO clinical guidelines as a framework, and using the authors' institutional perioperative registry outcome data,²⁻⁴ the authors have developed a multistage approach for the determination of kidney health and risk stratification for AKI in the perioperative period and among critically ill surgical patients. This process requires assessment of patients' renal resilience and susceptibility to new injury, the extent of exposure to insult, and the resulting distress or damage sustained by that insult. The determination and management of potential causes of AKI, initiation of interventions, and reassessment of kidney distress in response to that therapy follows promptly afterward. This clinical pathway requires a medical team of experts that not only defines the standardization pathway for the institutions but also provides backup for the bedside care providers.

PREOPERATIVE PATHWAY

In the preoperative period an accurate assessment of kidney health is important because the extent of previous kidney disease significantly increases susceptibility to the acute stress of surgery. Assessment of renal resilience to acute insult requires a search for any evidence of previous functional or structural kidney damage. Review of the medical history should include diagnosis and staging of known CKD, evidence of previous AKI episodes, and presence of risk factors for CKD. The determination of functional renal reserve with a kidney stress test¹²⁸ may be indicated for more precise risk stratification among patients without apparent CKD who may be considered as high risk because of age or other comorbidities, such as hypertension, chronic obstructive pulmonary disease, vascular disease, diabetes, or liver disease.

POSTOPERATIVE PATHWAY

For those surgical patients admitted to an ICU, an assessment of kidney health is considered part of a detailed ICU admission assessment. All steps of this process, including the clinical risk stratification, the assessment of tubular distress, and the initiation of treatment, should occur within the first 12 to 24 hours of the ICU admission. Every patient admitted to the authors' ICU undergoes a simple, yet systematic assessment of kidney health. Assessment of renal resilience requires a review of the medical history for diagnosis and staging of known CKD, evidence of previous AKI episodes, and the presence of any risk factors for AKI and CKD. For each patient, the authors perform a calculation of eGFR using reference serum creatinine and, when available, a measurement of albuminuria with urine dipstick or random microalbumin/creatinine ratio tests as an inexpensive snapshot of baseline kidney function. The exposure to insult is quantified by a search of the preceding 24 hours for any evidence of hypotension, use of vasopressors or nephrotoxic medications, sepsis, severe trauma, or any other conditions associated with a high risk for AKI.

Based on this process, the authors have developed an automated algorithm built into the electronic health record note to quantify a clinical risk score for AKI (range 0–16). Patients with a low clinical risk for AKI can undergo usual ICU care. Only patients with a high score (≥ 3) are further tested for kidney stress using the urinary biomarker TIMP-2•IGFBP7. In the authors' experience, approximately 40% of new admissions to the surgical ICU have a high clinical risk score. Only patients with both a high clinical risk score and a high urinary biomarker test result are considered to be at high risk for AKI and are subjected to the authors' *AKI bundle* of diagnostic tests and preventive measures during the subsequent 48 hours in an attempt to prevent or ameliorate kidney injury (Fig. 1).

Fig. 1. A clinical pathway for evaluating and managing AKI. (From Bihorac A. Critical controversies: Guiding AKI prevention using biomarkers. Available at: <http://www.sccm.org/Communications/Critical-Connections/Archives/Pages/Guiding-AKI-Prevention-Using-Biomarkers.aspx>. Accessed August 10, 2016.)

This set of parallel clinical action pathways (risk, prevention, and reassessment) is focused on the identification of the cause of AKI, initiation of preventive therapies, and daily reassessment of the kidney response to initiated therapies. This set is more comprehensive than the KDIGO AKI management options (Fig. 2). This process

Fig. 2. AKI management options. pts, patients. (Data from Kellum JA. Acute kidney injury and AKI biomarkers in the ICU. Southeastern Critical Care Summit. 2016; Adapted from Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney Inter Suppl 2012;2:1-138.)

may involve specialized clinical, laboratory, and imaging tools and represents a coordinated effort between the ICU and nephrology teams. Preventive therapies include monitoring and optimizing hemodynamic status by goal-directed fluid management and blood pressure control, strict avoidance of nephrotoxic medications, monitoring of drug levels, and avoiding side effects by adjusting drug dosing in accordance with the GFR. The goal of this phase is to prevent the progression of tubular distress toward functional decline whenever possible and to avoid the negative consequences of fluid overload and drug toxicity in patients with established tubular distress and, thus, it is hoped, to prevent any decline in renal function. The consideration for early RRT may be appropriate for patients with large levels of tubular distress and rapid functional decline, whereby impaired handling of fluids may endanger other organs.

The authors' preliminary experience with protocol implementation and compliance was excellent. One obstacle to implementation was the high cost of the TIMP-2•IGFBP7 urinary biomarker test, which the authors overcame by limiting use of the test to those indications standardized within this protocol. Whether this implementation translates into better outcomes will require further evaluation and analysis.

SUMMARY

AKI is common and is associated with many adverse perioperative outcomes. Mild to moderate AKI is much more common than severe AKI and has become much more appreciated with the introduction of consensus definitions for AKI. All stages of AKI severity are associated with increased morbidity and mortality. Clinical risk factors for AKI vary in different surgical populations, and preventable risk factors are often underappreciated before surgery. Efforts must focus on better identification of risk factors, better risk stratification and, thus, prediction of AKI in susceptible patients, and ultimately the prevention of AKI if possible or the facilitation of renal recovery in those patients who sustain AKI. Every surgical patient should have a systematic preoperative assessment of kidney health, with an emphasis on patients' renal reserve and susceptibility to new injury. In the postoperative period the exposure to any intraoperative risk, and the extent of any renal damage, needs to be evaluated using a combination of clinical parameters, novel biomarkers, and evolving imaging techniques. The prompt initiation of treatment and measures to prevent further renal injury, and to promote renal recovery, can then be instituted.

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