Perioperative Risk Assessment, Prevention, and Treatment of Acute Kidney Injury

Sean A. Josephs, MD
Charuhas V. Thakar, MD
University of Cincinnati College of Medicine
Cincinnati, Ohio

Introduction

In the perioperative period, physicians strive to provide optimal care for their patients by first performing a thorough evaluation of all organ systems. This is most important for elective and nonelective high-risk procedures and for procedures performed on critically ill or medically complex patients. The perioperative period is unique as it is a distinct event in a patient's health where certain hemodynamic derangements and insults are somewhat predictable based on the preoperative state of the patient and the type of surgery required. It is a time when preventive therapy can be instituted for certain patient populations if their risk is adequately determined. The field of perioperative medicine is advancing in many areas. For instance, many studies have focused on the risk and prevention of perioperative cardiac events.[1–5] The risk and prevention of acute kidney injury (AKI) is less well understood and shall be the topic of this chapter.

Definition and Incidence of Perioperative AKI

Until recently, the definition of AKI was not standardized. Authors have used terms such as renal insufficiency, renal dysfunction, acute renal failure (ARF), and renal failure requiring dialysis somewhat

Reprints: Sean A. Josephs, MD, Department of Anesthesiology, University of Cincinnati College of Medicine, Cincinnati, OH, E-mail: Josephs@ucmail.uc.edu

INTERNATIONAL ANESTHESIOLOGY CLINICS
Volume 47, Number 4, 89–105

interchangeably. Parameters used to define these terms include absolute creatinine values, absolute and percentage changes in creatinine values, absolute and percentage changes in estimated glomerular filtration rates (GFR), and reduction in urine output. The term "acute kidney injury" has been recently introduced in 2 different classification systems. As seen in Table 1, these definitions include creatinine change, GFR change, and measurements of urine output. The first system was the RIFLE criteria (with worsening function progressing from Risk to Injury to Failure to Loss to End-Stage Renal Failure) of the Acute Dialysis Quality Initiative.[6] More recently, the Acute Kidney Injury Network, a consensus panel involving national and international societies in nephrology and critical care, proposed standard definitions of AKI, and graded the severity of kidney injury into 3 stages.[7] These criteria define AKI as an increase in serum creatinine level by 0.3 mg/dL (or 1.5 times) relative to baseline. Subsequently, the severity is divided into 3 stages based on degree of creatinine elevation (stage I–1.5 to 2 times increase; II– >2 to 3 times increase; and III– >3 times increase, new requirement of dialysis, or an

Table 1. *Definitions of Acute Kidney Injury*

Acute Kidney Injury Network Criteria			RIFLE Criteria		
	Creatinine/ GFR	Urine Output		Creatinine/ GFR	Urine Output
Stage 1	Increased Cr 0.3mg/dL or Cr 150% baseline	UOP<0.5 mL/kg/h for>6h	Risk (R)	Increased Cr 1.5 × or GFR decreased <25%	UOP <0.5mL/ kg/h for >6h
Stage 2	Cr 200%- 300% baseline	UOP<0.5 mL/kg/h for >12h	Injury (I)	Increased Cr 2 × or GFR decreased <50%	UOP <0.5mL/ kg/h for >12h
Stage 3	Cr>300% of baseline or >4mg/dL with 0.5mg/ dL acute increase	UOP<0.3 mL/kg/h for 24 h or anuria for 12h	Failure (F)	Increased Cr 3 × or GFR decreased <75% or Cr >4mg/ dL with 0.5mg/dL acute increase	UOP <0.3mL/kg/ h for 24h or anuria for 12 h
			Loss (L)	Persistent ARF >4wk	
			ESKD (E)	Persistent loss >3mo	

For illustration and comparison, both AKIN (preferred descriptive criteria for AKI) and RIFLE criteria are provided.
Adapted from *Crit Care*. 2007;11:R31[7] and *Crit Care*. 2004;8:R204–R212.[6]
ARF indicates acute renal failure; Cr, chromium; ESKD, end-stage kidney disease; GFR, glomerular filtration rate; UOP, urine output.

absolute creatinine value of >4 mg/dL with at least a 0.5 mg/dL increment). There are caveats to these criteria, in that they await broader validation across all patient care settings. However, it allows a streamlined approach in recognition of the disease, clinical research, as well as future delivery of care. Given the wide range of definitions previously used in the literature, for the purposes of this article we will not be able to specifically group kidney injury by current definitions.

The rate of perioperative AKI is difficult to know precisely as it is dependent on definitions used and type of surgery studied. In cardiac surgery, rates of kidney injury range between 7.7% and 11.4%[8–10] when defined broadly, whereas frequency of AKI requiring dialysis is generally lower, ranging between <1% and 5%.[8,9,11,12] In gastric bypass surgery AKI reportedly occurs in 8.5% of patients.[13] Kheterpal et al[14] recently studied a noncardiac surgery population with preoperative normal renal function and noted an incidence of renal failure defined by GFR less than 50 mL/min as 0.8%. After aortic aneurysm repair, incidences of renal failure of various definitions have been reported at 15% to 46%.[15,16] The setting of solid organ transplant poses the risk of nephrotoxicity from immunosuppressive medications in addition to other perioperative insults. Expectedly, the incidence of AKI after cardiac transplant is generally higher than nontransplant cardiac surgery; in a single center study involving over 750 cardiac transplants the incidence of AKI requiring dialysis was 6%.[17] On the basis of historical comparisons, this observation was about 6-fold higher than nontransplant cardiac surgery performed during the same time period at that institution. Similarly, liver transplant is also associated with a high frequency of AKI. It is reported that 48% to 94% of patients suffer from acute worsening in renal function after liver transplantation.[18–24] Such patients require renal replacement therapy (RRT) 8% to 17% of the time.[19,22] To summarize, the reported incidence of AKI varies based on the definition used, however, there is sufficient information to indicate that clinical settings play an important role in this variability. It is plausible that the perioperative risk profile associated with each surgical setting is linked with the variation in the incidence and severity of AKI.

■ Impact of AKI on Mortality: A Case for Perioperative Assessment

Postoperative AKI is one of the most serious complications during hospitalization, increasing morbidity, mortality, length of stay, and costs of care. There is increasing evidence that AKI is associated with increased risk of both short-term and long-term risk of death, as well as risk of progressive renal failure. It is also recognized that there is an incremental risk of death with worsening severity of kidney injury; reported crude hospital mortality rates associated with AKI are as high

as 60%, with 7-fold to 10-fold increase in risk-adjusted odds of mortality than those without AKI.[25,26] Thus, the epidemiologic information strongly suggests that prevention or treatment of AKI and amelioration of its severity would result in improved patient outcomes. Therapeutic options in AKI are limited. Experimental studies suggest that to achieve beneficial effects, therapies to reduce severity of injury need to be applied either before or soon after ischemic or toxic tubular injury.[27] Applying this information to clinical settings is extremely difficult, as it is not always possible to anticipate renal insult. Postoperative kidney injury, thus, represents an exciting "clinical model" where a healthcare provider has an opportunity to assess perioperative risk of kidney injury, and provides an ideal platform to translate the success of experimental research to clinical settings.

When AKI occurs perioperatively, morbidity and mortality increase. In cardiac surgery many studies have reported increased mortality related to renal failure requiring dialysis. Zanardo et al[8] reported a mortality rate of 0.8% in patients without renal dysfunction, 9.5% mortality rate with renal dysfunction, and 44.4% in patients with renal failure. Some have reported mortality as high as 89% when renal failure occurs after cardiac procedures.[9]

In noncardiac surgery, AKI also substantially worsens outcomes. It is notable that in a retrospective study of more than 15,000 patients without preexisting renal dysfunction the 30-day, 60-day, and 1-year mortality increased from 2.7% to 15%, 5.1% to 17%, and 15% to 31%, respectively in patients who developed ARF.[14] After surgery for ruptured abdominal aortic aneurysm (AAA), patients that require RRT have mortality rates ranging from 53% to 75%.[16,28,29] Similar rates of mortality (66%) have been reported in elective repairs of AAAs.[29] Survivors to hospital discharge with renal failure have approximately 50% 5-year mortality rates.[16] Factors that have been found to adversely affect survival include the need for ionotropic support, ventilation for more than 3 days or failure to wean from mechanical ventilation, age greater than 65, vascular disease score, need for additional surgery, and the presence of systemic inflammatory response syndrome or multi-organ failure.[16,28,29]

A population of liver transplant recipients was recently studied showing that 6.4% required intraoperative continuous RRT (CRRT) for preexisting renal dysfunction.[30] Of these patients 1-month survival was 97.6% and 1-year survival was 75.6%. All of these patients were independent of RRT at 1 year although their mean GFR was only 54.7 mL/min/m^2. Significant renal dysfunction was noted in 62.1% of their patients with a GFR <60 mL/min/m^2. Another retrospective study reported a mortality rate of 16.7% in patients with ARF versus 3.8% in patients without ARF.[18] As might be expected, the need for RRT for liver recipients increases mortality with odds ratio of up to 4.4.[22] In a

study by Bilbao et al,[22] the need for dialysis was associated with a mortality of 50% versus 13.4% in nondialysis requiring AKI. Dialysis was also associated with poorer 1-year actuarial graft survival (40.9% vs. 73.4%). Other risk factors that increase mortality with AKI include peak serum creatinine greater than 3 mg/dL and multiple liver transplants.[21] However, the need for RRT in liver transplant patients is not associated with as poor survival when compared with cardiac and aortic surgery populations.

■ Preoperative Risk Factors

It can be hypothesized that AKI after a surgical procedure results from preoperative comorbid status, the type of surgical procedure, and immediate postoperative course. Regarding the preoperative risk factors of AKI, advanced age is consistently associated with increased risk of AKI, regardless of the clinical setting.[14,28,31–34] In cardiac surgery, baseline renal function is likely the most important determinant of postoperative AKI, particularly severe AKI requiring dialysis. Additionally, the cardiovascular status of the patient also influences the postoperative AKI risk. For example, functional status of congestive heart failure, presence of peripheral vascular disease, and preoperative use of intra-aortic balloon pump have all been associated with increased risk of AKI.[26] Other comorbid conditions such as diabetes, along with the extent of glycemic control are also independently associated with development of AKI after surgery.[9] Many of these factors may be modifiable, and need to be tested in a prospective way. On the basis of a single center study which included over 30,000 cardiac surgery patients, Thakar et al[11] developed a risk index based on preoperative risk factors to predict postoperative need for dialysis. Female sex, type of surgery (valve replacement with or without coronary-artery bypass grafting), preoperative cardiovascular status, and preoperative renal function were identified as significant predictors of postoperative AKI. This clinical score (Table 2) discriminates predicted probability of AKI between <1% and >20%, based on a simple bedside risk-assessment tool. Similar algorithms have since been developed and have been externally validated in separate cohorts.[35] Overall, the predictive accuracy of these epidemiologic studies vary with area under the receiver operating characteristic curve (ROC-AUC) values between 0.77 and 0.84 for cardiac surgical patients.

In noncardiac surgery, different risk factors for AKI have been identified. As previously cited, Kheterpal et al[14] studied patients with preoperative normal renal function for noncardiac surgery and developed a preoperative renal-risk index that identified the following independent risk factors for renal failure: age, emergent surgery, liver disease, body mass index, high-risk surgery, peripheral vascular

Table 2. *Preoperative Risk Score for AKI After Cardiac Surgery*

Risk Factor	Points
Female sex	1
Chronic obstructive pulmonary disease	1
Insulin dependent diabetes mellitus	1
Congestive heart failure	1
Left ventricular ejection fraction<35%	1
Prior surgery	1
Emergency surgery	2
Preoperative intra-aortic balloon pump	2
Preoperative creatinine value	
1.2 to<2.1 mg/dL	2
>2.1 mg/dL	5
Surgery type	
Valve replacement only	1
Coronary artery bypass graft + valve replacement	2
Other	2

Adapted from *J Am Soc Nephrol*. 2005;16:162–168.[11]
AKI indicates Acute Kidney Injury.

occlusive disease, and chronic obstructive pulmonary disease (requiring chronic bronchodilator therapy). On the basis of the incremental score, the frequency of renal failure increased ranging between 0.3% and 4.5%, respectively. The ROC-AUC was 0.77 and 0.73, respectively for weighted and unweighted models.

It is well known that ARF can be associated with vascular surgery, especially repair of AAAs.[31,32] Baseline renal function, ischemia time (aortic cross-clamp time), and intraoperative hypotension are key determinants of postoperative AKI in this setting. Observational studies also indicate that endovascular aneurysm repair may be associated with lower risk of AKI than open surgeries.[36] Patients undergoing gastric bypass surgery present a unique comorbidity profile which includes a high prevalence of diabetes, hypertension, hyperlipidemia, and osteoarthritis; thus these patients are commonly prescribed drug classes which include angiotensin converting enzyme inhibitors (ACE-I), diuretics, and nonsteroidal anti-inflammatory agents. In a single center study, risk of AKI was associated with body mass index greater than 30, hyperlipidemia, and preoperative use of the ACE-Is or angiotensin receptor blockers.[13]

In liver transplantation, Cabezuelo et al[18] recently retrospectively studied 184 consecutive orthotopic liver transplant procedures defining ARF as a persistent rise in creatinine of 50% or more. In multifactorial regression analysis, they showed serum albumin <3.2 g/dL and preoperative ARF to be associated with postoperative ARF. Another

group studied 172 consecutive liver transplants in 158 patients and found preoperative creatinine >1.5 g/dL as an independent risk factor.[22] In the setting of cardiac transplantation, Boyle et al[17] examined preoperative risk factors of dialysis requirement during immediate postoperative period. Serum creatinine, serum albumin, and history of diabetes mellitus were identified as independent predictors of AKI.

■ Intraoperative Risk Factors

Several intraoperative risk factors have been associated with AKI. These factors are difficult to quantify, unless they were meticulously recorded during the surgery, and may still represent as surrogate for unmeasured events during the surgical procedure. In cardiac surgery intraoperative risk factors for postoperative renal failure include use of intra-aortic balloon pump, the need for deep hypothermic circulatory arrest, low-output syndrome, low urine output during cardiopulmonary bypass (CPB), need for pressors before CPB, number of blood transfusions during surgery.[8,17,37] One risk factor, which has consistently been linked with AKI is the use of and duration of exposure to CPB circuit.[9,26] In those patients undergoing on-pump surgery, the risk of AKI seems to increase beyond a threshold of 100 to 120 minutes of bypass time.[9,25,33] Exposure to CPB circuit may promote a pro-inflammatory state which is deleterious to renal perfusion, given a certain set of preoperative risk factors.[38] Additionally, experimental evidence suggests that lack of pulsatile blood flow can impair renal perfusion, despite relative preservation of mean arterial pressure.[39] Thus, performing off-pump bypass surgery has gained recent interest as a potentially modifiable risk factor to reduce the risk of AKI. Several observational and randomized studies have compared renal outcomes in patients undergoing on-pump versus off-pump procedures. Nigwekar et al[40] recently performed a systematic review and meta-analysis of all studies that have reported renal outcomes and compared exposure with CPB. Overall, the performance of off-pump surgery had a favorable impact on renal function during the postoperative period. The caveats are that the definitions of AKI were variable and the randomized controlled studies included relatively smaller sample sizes. But it is reasonable to propose, that given a high-risk preoperative profile for AKI, if feasible, off-pump surgery should be considered as a potential option to reduce the AKI risk.

In noncardiac surgery, there are fewer studies describing intraoperative risk factors that are independently associated with AKI. Kheterpal et al[14] determined that the predictive value of their previously mentioned renal risk prediction index improved from ROC-AUC of 0.77 to 0.79 if the intraoperative risk factors of use of a vasopressor infusion, mean number of vasopressor bolus doses

administered, and the administration of furosemide or mannitol were added to the analysis. In liver transplantation, Rueggeberg et al[41] developed a risk stratification model for predicting AKI immediately at the end of the transplantation procedure. In it they included the intraoperative risk factors of units of packed red blood cells required, hypotension defined as mean arterial pressure less than 50 mm Hg, and maximum lactate concentration. Their model had a sensitivity of 0.78, a specificity of 0.92, and a negative predictive value of 0.96 for AKI at the end of transplantation.[41] Although the value of each of these individual risk factors is unknown, the absence of them is reassuring.

Less invasive procedures may provide a protective effect in AKI. In vascular surgery, the need for ionotropic support has been linked to AKI.[28] Significant hemodynamic derangements are likely in open aortic repairs where aortic clamping and significant hemorrhage are possible. In thoracic aortic repair, there are suggestions that endovascular techniques are associated with lower rates of AKI compared with open techniques, especially in high-risk patients.[42,43] Interestingly however, in some types of less invasive laparoscopic surgery, specifically for nephrectomy, AKI has been linked to rhabdomyolysis when associated with male patients, high body mass index, lateral decubitus positioning, and prolonged surgical times.[44,45] Thus increasing surgical time or requiring abnormal positioning to avoid open procedures may have deleterious effects with regard to preventing AKI.

■ Postoperative Assessment

Several events during the postoperative period can influence renal function. The literature in this regard is more difficult to interpret due to the lack of clear temporality between nonrenal events and AKI. In cardiac surgery, Slogoff et al[37] reported postoperative blood loss, excessive postoperative transfusion, postoperative myocardial infarction, and need for emergent reoperation as independent risk factors for new renal dysfunction. In the setting of cardiac transplantation, Boyle et al[17] examined the timing of dialysis initiation with respect to the timing of patients' meeting criteria for sepsis or systemic inflammatory response syndrome or other nonrenal complications such as cardiac failure. Majority of the cases (~60%) of AKI requiring dialysis were preceded by other nonrenal serious complications.

Postoperative serious events also lead to AKI in noncardiac surgery. In vascular surgery, the overall need for ionotropic support and the need for longer postoperative mechanical ventilation have been associated with AKI.[28,29] In liver transplantation, Cabezuelo et al[18] noted that treatment with dopamine longer than 6 days, liver graft dysfunction II-IV, surgical reoperation, and postoperative bacterial infection were all significantly associated with postoperative ARF after

liver transplantation. In this study, reoperations were primarily necessary for intra-abdominal bleeding, biliary fistulas, and intra-abdominal abscesses. The major sources of bacterial infections were bacteremia, intra-abdominal infection, and pulmonary infection. Most organisms were nosocomial suggesting the need for careful daily assessments of the need for and condition of indwelling catheters, tubes, and lines in these patients. Liver graft dysfunction grade III-IV was an independent risk factor in Bilbao et al's[22] study as well.

There is ample evidence that postoperative AKI is associated with other nonrenal complications, and together, the number of organ failures contributes to an increased mortality risk. In 1 study, Thakar et al[46] (Kidney International 2003) examined postoperative AKI and sepsis/infections. There was increased risk of postoperative infections with worsening degree of severity of AKI. Although temporality was not able to be determined, the data suggest that kidney injury uremia may impact other organ system function; a notion that has been well described and supported in experimental models of renal ischemia reperfusion injury.

■ Interventions

Although many factors have been shown to contribute to AKI in surgical patients (Table 3), there are very few interventions demonstrated to prevent AKI. Of these interventions, there is no obvious cure for perioperative renal injury. Although a complete review of such interventions is beyond the scope of this chapter, some of these approaches are discussed below. They can be divided into dialytic and nondialytic therapies.

Dialytic Therapies

Dialysis has not been shown to decrease perioperative AKI, however, it can treat the associated acidosis, hyperkalemia, and hypervolemia that may otherwise be associated with poor outcomes. For instance, after ruptured aortic aneurysm repair, renal support with dialysis may actually reduce operative 30-day mortality rates in patients that develop loss of renal function.[15] As many as 75% of these survivors may regain kidney function and become independent of dialysis.

RRT is considered for use intraoperatively during liver transplantation. Townsend et al[30] recently reported their experiences with intraoperative CRRT in orthotopic liver transplantation. CRRT was used in 6.4% of their liver transplants with the only noted complication of filter circuit clotting 40% of the time. In their patients, CRRT was initiated for standard reasons related to renal failure (hyperkalemia, acidosis, hypervolemia) but also considered issues specific to liver transplantation

Table 3. *Summary of Risk Factors for Acute Kidney Injury*

Surgical Setting	Risk Factors
Cardiac	Advanced age
	Baseline renal function
	Diabetes
	Poor glycemic control
	Female sex
	Congestive heart failure
	Low ejection fraction
	Peripheral vascular disease
	Preoperative intra-aortic balloon pump use
	Intraoperative intra-aortic balloon pump use
	Need for deep hypothermic circulatory arrest
	Low-output syndrome
	Pressor need prior to cardiopulmonary bypass
	Valve replacement surgery
	Cardiopulmonary bypass time >100-120λmin
	Postoperative blood loss
	Excessive postoperative transfusion requirement
	Myocardial infarction
	Emergent reoperation
Vascular	Advanced age
	Baseline renal function
	Aortic cross-clamp time
	Intraoperative hypotension
	Open procedure
	Need for vasopressor or ionotropic support
	Extended postoperative mechanical ventilation (>3 days)
Liver transplantation	Preoperative albumin <3.2
	Preoperative creatinine >1.5
	Diabetes mellitus
	Number of transfused packed red blood cells
	Hypotension
	Severity of lactic acidosis
	Prolonged dopamine use
	Liver graft dysfunction
	Reoperation
	Postoperative bacterial infection
Gastric Bypass	Preoperative angiotensin-converting enzyme use
	Preoperative angiotensin receptor blocker use
	Body mass index >30
	Hyperlipidemia

Table 3. *(Continued)*

Surgical Setting	Risk Factors
Laparoscopic (rhabdomyolysis)	Male sex
	High body mass index
	Lateral decubitus positioning
	Prolonged surgical times (>4 h)
Other	Advanced age
	Liver disease
	High body mass index
	Peripheral vascular disease
	Chronic obstructive pulmonary disease
	Emergency surgery
	Use of vasopressor infusion
	Mean number of vasopressor boluses
	Administration of furosemide
	Administration of mannitol

Known risk factors for acute kidney injury in various surgical settings are summarized. Within each surgical setting, risk factors are listed from top to bottom progressing from preoperative to intraoperative to postoperative risk factors.

such as need for significant transfusion, lactic acidosis, hypernatremia, and hyponatremia. Their patients generally had high preoperative risk with Model for End-Stage Liver Disease mean score of 38. The majority of their cases ran CRRT more than 50% of the operative time and allowed them to run even or negative fluid balance in 92.7% of their cases. Given the fluid, electrolyte, and acid/base abnormalities associated with liver transplantation this can be a very useful tool in managing these patients.

Nondialytic Therapies

Preoperative assessment and optimization of renal function should theoretically aid in the prevention of perioperative AKI. We have already discussed the fact that poor preoperative renal function is associated with increased risk of postoperative AKI in some settings.[11,22] Currently there is no good evidence to suggest that optimal therapy for renal dysfunction such as ACE-I therapy, diuretic therapy, or regular visits to a nephrologist prevents a decline in kidney function around the time of surgery. In fact, some studies have suggested that the use of some of these therapies perioperatively may be associated with AKI.[13,14] Thakar et al[13] as well as other studies suggest that avoidance of ACE-I or ARB therapies around the time of surgery may be advisable, especially when hypotension is anticipated.[47] To such an end thorough coordination of care might help modulate tapering of such therapies preoperatively and reinstituting them judiciously postoperatively.

Perioperative optimization of cardiac function does seem appropriate for prevention of AKI. In cardiac surgery, congestive heart failure and low ejection fraction are significant risk factors for AKI.[11] Nonoptimized volume states, tachycardia, or severe hypertension can lead to myocardial ischemia and perioperative myocardial infarction. Indiscriminant use of diuretics, β-blockers, or vasodilators on the day of surgery may complicate hemodynamic management and may lead to hypotension or low cardiac output states. Again careful preoperative coordination of care could assist with this.

It makes physiologic sense that maintaining somewhat normal hemodynamic parameters during the operative period could prevent AKI. Hypotension, diuretic use, and bleeding requiring transfusion are cited risk factors for perioperative AKI. Aside from holding antihypertensives or diuretics physicians should be aware of anesthetic techniques that may add to or prevent hemodynamic instability.[48,49] Avoidance of vasodilators and judicious use of vasoconstrictors to counteract the venous and arterial dilating properties of certain anesthetics may be useful. More aggressive use of invasive arterial monitoring in higher-risk patients to assist with rapid recognition of hypotension may also help.

Administration of several medications has been thought to prevent renal dysfunction. Scavengers of oxygen free radicals such as mannitol and *N*-acetylcysteine have been given to prevent ischemia reperfusion injury. *N*-acetylcysteine has been studied primarily in cardiac surgery. A recent meta-analysis failed to show benefit of perioperative *N*-acetylcysteine therapy in the reduction of ARF, ARF requiring dialysis, or mortality in cardiac surgery patients.[50] For years mannitol has been administered before aortic clamping, especially supra-renal clamping, during AAA surgery. Although commonly cited as useful, Hersey and Poullis[51] recently reviewed mannitol administration in open AAA repair and concluded that no clinical trials have sufficiently shown reductions in renal failure in this population of patients.

The use of furosemide to prevent renal ischemia, especially during aortic cross clamping, has been the topic of many studies and reviews.[52–55] Although it would seem that inhibition of oxygen consumption in the renal tubules by giving a loop diuretic would prevent ischemia during times of low oxygen delivery, studies have not shown significant clinical reductions in postoperative AKI. Furosemide does increase urine output and can convert oliguric patients to nonoliguric patients.[53] If the use of furosemide or other diuretics is allowed to cause hypovolemia, it may actually be harmful and has been associated with worse renal outcomes in some surgical populations.[54] Intraoperatively, the reliance on diuretics to augment urine output without regard to volume status should be discouraged.

Many interventions have been shown to decrease multiple organ dysfunction in critically ill surgical patients. Early hemodynamic

resuscitation was shown to decrease mortality and multiple organ dysfunction scores.[56] Rivers et al[56] showed that patients with septic shock randomized to early therapy with fluid and pressors to improve central venous oxygen saturation, lactate concentration, base deficit, and pH had lower organ dysfunction scores than patients resuscitated in a nonearly goal-directed fashion. Although renal function is not specifically reported by Rivers et al, its contribution to organ dysfunction scores is generally high and it is reasonable to consider early hydration as a therapy for preventing renal dysfunction in critically ill patients.

In a population of surgical intensive care unit patients, van den Berghe et al[57] showed that aggressive control of hyperglycemia with insulin reduced dysfunction of many different organs including kidneys. They showed a significant reduction of patients with peak creatinine greater than 2.5 mg/dL (9.0%-12.3%), blood urea nitrogen greater than 54 mg/dL (7.7%-11.2%), and those requiring dialysis (4.8%-8.2%) by controlling glucose aggressively (goals 80-110 mg/dL) with an insulin infusion protocol. More recent studies suggest higher glucose levels should be allowed maintaining reasonable glycemic control with values less than 180 mg/dL in perioperative critically ill patients.[58]

Patients with acute lung injury are often difficult to manage perioperatively. Their potential for hypoxia can often compete with their need for hydration. Optimal fluid management of these patients was recently assessed in a randomized dual intervention model. Both liberal (high volume) versus conservative (low volume) fluid management and central venous line versus pulmonary artery line monitoring were studied as interventions.[59,60] It was shown that liberal and conservative fluid management strategies resulted in no difference in the need for renal replacement or the number of days of renal replacement when it was required.[59] It was also shown that pulmonary artery catheter monitoring did not reduce the need for RRT over central venous pressure monitoring in patients with acute lung injury.[60] Although practice patterns vary with invasive monitoring of such patients, this study did not show a significant advantage to 1 type of monitoring protocol.

■ Summary

There appears to be no single therapy that will prevent perioperative AKI. Clinical risk factors are similar but not identical in different surgical populations. Although developing single therapies that prevent AKI may be possible, they will likely only work populations of patients with specific risk profiles. It is more likely that we will reduce perioperative AKI through better optimization and management of the many comorbidities and hemodynamic derangements that have been shown to impact renal function. As we develop more accurate risk

prediction indices for patients in the various surgical settings, we will have the challenge of deciding which patients will receive clinical benefit from our most aggressive and expensive efforts. As surgery is a somewhat predictable and isolated event, the perioperative period is an ideal time to prospectively study our preventive and therapeutic interventions for AKI.

■ References

1. Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation*. 1999;100:1043–1049.
2. Boersma E, Poldermans D, Bax JJ, et al, and Decrease Study Group (Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography). Predictors of cardiac events after major vascular surgery: role of clinical characteristics, dobutamine echocardiography, and beta-blocker therapy. *JAMA*. 2001;285: 1865–1873.
3. Poldermans D, Boersma E, Bax JJ, et al. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. *N Engl J Med*. 1999;341:1789-1794.
4. Grines CL, Bonow RO, Casey DE Jr, et al, American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, American Dental Association, and American College of Physicians. Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. *Circulation*. 2007;115: 813–818.
5. Rabbitts JA, Nuttall GA, Brown MJ, et al. Cardiac risk of noncardiac surgery after percutaneous coronary intervention with drug-eluting stents. *Anesthesiology*. 2008; 109:596–604.
6. Bellomo R, Ronco C, Kellum JA, et al, and Acute Dialysis Quality Initiative workgroup. Acute renal failure-definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care*. 2004;8: R204–R212.
7. Mehta RL, Kellum JA, Shah SV, et al, and Acute Kidney Injury Network. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care*. 2007;11:R31.
8. Zanardo G, Michielon P, Paccagnella A, et al. Acute renal failure in the patient undergoing cardiac operation. Prevalence, mortality rate, and main risk factors. *J Thorac Cardiovasc Surg*. 1994;107:1489–1495.
9. Mangano CM, Diamondstone LS, Ramsay JG, et al. Renal dysfunction after myocardial revascularization: risk factors, adverse outcomes, and hospital resource utilization. The Multicenter Study of Perioperative Ischemia Research Group. *Ann Intern Med*. 1998;128:194–203.
10. Yeboah ED, Petrie A, Pead JL. Acute renal failure and open heart surgery. *Br Med J*. 1972;1:415–418.
11. Thakar CV, Arrigain S, Worley S, et al. A clinical score to predict acute renal failure after cardiac surgery. *J Am Soc Nephrol*. 2005;16:162–168.

12. Chertow GM, Lazarus JM, Christiansen CL, et al. Preoperative renal risk stratification. *Circulation*. 1997;95:878–884.
13. Thakar CV, Kharat V, Blanck S, et al. Acute kidney injury after gastric bypass surgery. *Clin J Am Soc Nephrol*. 2007;2:426–430.
14. Kheterpal S, Tremper KK, Englesbe MJ, et al. Predictors of postoperative acute renal failure after noncardiac surgery in patients with previously normal renal function. *Anesthesiology*. 2007;107:892–902.
15. Gordon AC, Pryn S, Collin J, et al. Outcome in patients who require renal support after surgery for ruptured abdominal aortic aneurysm. *Br J Surg*. 1994;81:836–838.
16. Barratt J, Parajasingam R, Sayers RD, et al. Outcome of acute renal failure following surgical repair of ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg*. 2000;20:163–168.
17. Boyle JM, Moualla S, Arrigain S, et al. Risks and outcomes of acute kidney injury requiring dialysis after cardiac transplantation. *Am J Kidney Dis*. 2006;48:787–796.
18. Cabezuelo JB, Ramirez P, Rios A, et al. Risk factors of acute renal failure after liver transplantation. *Kidney Int*. 2006;69:1073–1080.
19. Yalavarthy R, Edelstein CL, Teitelbaum I. Acute renal failure and chronic kidney disease following liver transplantation. *Hemodial Int*. 2007;11(suppl 3):S7–S12.
20. Nuno J, Cuervas-Mons V, Vicente E, et al. Renal failure after liver transplantation: analysis of risk factors in 139 liver transplant recipients. *Transplant Proc*. 1995;27: 2319–2320.
21. McCauley J, Van Thiel DH, Starzl TE, et al. Acute and chronic renal failure in liver transplantation. *Nephron*. 1990;55:121–128.
22. Bilbao I, Charco R, Balsells J, et al. Risk factors for acute renal failure requiring dialysis after liver transplantation. *Clin Transplant*. 1998;12:123–129.
23. Ishitani M, Wilkowski M, Stevenson W, et al. Outcome of patients requiring hemodialysis after liver transplantation. *Transplant Proc*. 1993;25:1762–1763.
24. Rimola A, Gavaler JS, Schade RR, et al. Effects of renal impairment on liver transplantation. *Gastroenterology*. 1987;93:148–156.
25. Chertow GM, Levy EM, Hammermeister KE, et al. Independent association between acute renal failure and mortality following cardiac surgery. *Am J Med*. 1998;104: 343–348.
26. Thakar CV, Liangos O, Yared JP, et al. ARF after open-heart surgery: Influence of gender and race. *Am J Kidney Dis*. 2003;41:742–751.
27. Star RA. Treatment of acute renal failure. *Kidney Int*. 1998;54:1817–1831.
28. Berisa F, Beaman M, Adu D, et al. Prognostic factors in acute renal failure following aortic aneurysm surgery. *Q J Med*. 1990;76:689–698.
29. Braams R, Vossen V, Lisman BA, et al. Outcome in patients requiring renal replacement therapy after surgery for ruptured and non-ruptured aneurysm of the abdominal aorta. *Eur J Vasc Endovasc Surg*. 1999;18:323–327.
30. Townsend DR, Bagshaw SM, Jacka MJ, et al. Intraoperative renal support during liver transplantation. *Liver Transpl*. 2009;15:73–78.
31. Chawla SK, Najafi H, Ing TS, et al. Acute renal failure complicating ruptured abdominal aortic aneurysm. *Arch Surg*. 1975;110:521–526.
32. Olsen PS, Schroeder T, Perko M, et al. Renal failure after operation for abdominal aortic aneurysm. *Ann Vasc Surg*. 1990;4:580–583.
33. Conlon PJ, Stafford-Smith M, White WD, et al. Acute renal failure following cardiac surgery. *Nephrol Dial Transplant*. 1999;14:1158–1162.
34. Waikar SS, Liu KD, Chertow GM. Diagnosis, epidemiology and outcomes of acute kidney injury. *Clin J Am Soc Nephrol*. 2008;3:844–861.
35. Candela-Toha A, Elias-Martin E, Abraira V, et al. Predicting acute renal failure after cardiac surgery: external validation of two new clinical scores. *Clin J Am Soc Nephrol*. 2008;3:1260–1265.

36. Wald R, Waikar SS, Liangos O, et al. Acute renal failure after endovascular versus open repair of abdominal aortic aneurysm. *J Vasc Surg*. 2006;43:460, 466; discussion 466.
37. Slogoff S, Reul GJ, Keats AS, et al. Role of perfusion pressure and flow in major organ dysfunction after cardiopulmonary bypass. *Ann Thorac Surg*. 1990;50:911–918.
38. Orime Y, Shiono M, Hata H, et al. Cytokine and endothelial damage in pulsatile and nonpulsatile cardiopulmonary bypass. *Artif Organs*. 1999;23:508–512.
39. Sezai A, Shiono M, Orime Y, et al. Major organ function under mechanical support: comparative studies of pulsatile and nonpulsatile circulation. *Artif Organs*. 1999;23: 280–285.
40. Nigwekar SU, Kandula P, Hix JK, et al. Off-pump coronary artery bypass surgery and acute kidney injury: a meta-analysis of randomized and observational studies. *Am J Kidney Dis*. 2009. [Epub ahead of print]
41. Rueggeberg A, Boehm S, Napieralski F, et al. Development of a risk stratification model for predicting acute renal failure in orthotopic liver transplantation recipients. *Anaesthesia*. 2008;63:1174–1180.
42. Stouffer CW, Mansour MA, Ott MM, et al. Initial results of a thoracic aortic endovascular program: safer in high-risk patients. *Ann Vasc Surg*. 2009;23:478–484.
43. Bavaria JE, Appoo JJ, Makaroun MS, et al, and Gore TAG Investigators. Endovascular stent grafting versus open surgical repair of descending thoracic aortic aneurysms in low-risk patients: a multicenter comparative trial. *J Thorac Cardiovasc Surg*. 2007;133:369–377.
44. Glassman DT, Merriam WG, Trabulsi EJ, et al. Rhabdomyolysis after laparoscopic nephrectomy. *JSLS*. 2007;11:432–437.
45. Rehman J, Boglia J, Chughtai B, et al. High body mass index in muscular patients and flank position are risk factors for rhabdomyolysis: case report after laparoscopic live-donor nephrectomy. *J Endourol*. 2006;20:646–650.
46. Thakar CV, Yared JP, Worley S, et al. Renal dysfunction and serious infections after open-heart surgery. *Kidney Int*. 2003;64:239–246.
47. Kheterpal S, Khodaparast O, Shanks A, et al. Chronic angiotensin-converting enzyme inhibitor or angiotensin receptor blocker therapy combined with diuretic therapy is associated with increased episodes of hypotension in noncardiac surgery. *J Cardiothorac Vasc Anesth*. 2008;22:180–186.
48. Malinowska-Zaprzalka M, Wojewodzka M, Dryl D, et al. Hemodynamic effect of propofol in enalapril-treated hypertensive patients during induction of general anesthesia. *Pharmacol Rep*. 2005;57:675–678.
49. Reich DL, Hossain S, Krol M, et al. Predictors of hypotension after induction of general anesthesia. *Anesth Analg*. 2005;101:622–628.
50. Nigwekar SU, Kandula P. N-acetylcysteine in cardiovascular-surgery-associated renal failure: a meta-analysis. *Ann Thorac Surg*. 2009;87:139–147.
51. Hersey P, Poullis M. Does the administration of mannitol prevent renal failure in open abdominal aortic aneurysm surgery? *Interact Cardiovasc Thorac Surg*. 2008;7: 906–909.
52. Schoenwald PK. Intraoperative management of renal function in the surgical patient at risk. Focus on aortic surgery. *Anesthesiol Clin North America*. 2000;18:719–737.
53. Mahesh B, Yim B, Robson D, et al. Does furosemide prevent renal dysfunction in high-risk cardiac surgical patients? Results of a double-blinded prospective randomised trial. *Eur J Cardiothorac Surg*. 2008;33:370–376.
54. Lassnigg A, Donner E, Grubhofer G, et al. Lack of renoprotective effects of dopamine and furosemide during cardiac surgery. *J Am Soc Nephrol*. 2000;11:97–104.
55. Sirivella S, Gielchinsky I, Parsonnet V. Mannitol, furosemide, and dopamine infusion in postoperative renal failure complicating cardiac surgery. *Ann Thorac Surg*. 2000;69:501–506.

56. Rivers E, Nguyen B, Havstad S, et al, and Early Goal-Directed Therapy Collaborative Group. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med*. 2001;345:1368–1377.
57. van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in the critically ill patients. *N Engl J Med*. 2001;345:1359–1367.
58. Finfer S, Chittock DR, Su SY, et al, Nice-Sugar Study Investigators. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med*. 2009;360: 1283–1297.
59. Wiedemann HP, Wheeler AP, Bernard GR, et al, National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med*. 2006;354:2564–2575.
60. Wheeler AP, Bernard GR, Thompson BT, et al, National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Pulmonary-artery versus central venous catheter to guide treatment of acute lung injury. *N Engl J Med*. 2006;354:2213–2224.