# Minimizing perioperative complications in patients with renal insufficiency

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Development of acute renal failure perioperatively is associated with considerable mortality and often with incomplete recovery regardless of baseline renal function. A thorough evaluation of perioperative risk in patients with renal insufficiency should therefore include an additional assessment of the risk for renal injury that might require dialysis and add to the operative mortality.

This article will describe the risk for renal injury, elucidate the mechanisms of injury, review the impact of serum creatinine elevations and changes on operative outcomes, and suggest specific measures to reduce perioperative risk.

## KIDNEYS ARE SUSCEPTIBLE TO VASCULAR INSULT

Kidneys are highly vascular and therefore at risk for problems that affect the renal vascular bed. The older and sicker a patient is, the likelier that his or her body will be unable to autoregulate renal perfusion and preserve the glomerular filtration rate (GFR). The resultant kidney injury in turn increases susceptibility to complications in a variety of common surgical settings.

Acute renal injury causes tubular damage, resulting in backleak or tubular obstruction, which reduces glomerular filtration and the kidney's ability to concentrate the urine and reabsorb sodium. Any vascular insult may reduce renal blood flow and the filtration fraction, thereby reducing overall GFR.

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Disclosure: Dr. Schreiber reported that he receives grant support from the Amgen corporation, is a consultant to the Johnson & Johnson corporation, and is on the speakers' bureaus of the Baxter and Johnson & Johnson corporations.

## ACUTE RENAL FAILURE: A SERIOUS PERIOPERATIVE COMPLICATION

Acute renal failure is a serious complication: only about 15% of patients who develop acute renal failure perioperatively fully recover. About half of patients who develop acute renal failure postoperatively die, approximately 5% survive but remain in renal failure, and approximately 5% recover incompletely and have continually declining renal function. Another 15% recover incompletely and remain stable for a time but are at increased risk of developing chronic kidney disease. Patients who are older, are sicker, or sustain a more severe insult are especially at risk of a poor outcome.

### Monitoring acute changes in renal function

Of the approaches to monitor acute changes in renal function perioperatively, monitoring serum creatinine is currently the most commonly employed and clinically practical method. The serum creatinine measurement, while not as precise as iothalamate or inulin clearance techniques, can be used to estimate GFR accurately in a stable patient in the outpatient setting.

**Serum creatinine.** The serum creatinine varies inversely with GFR. An elevated serum creatinine level is a late indicator of renal injury: even a relatively minor increase is clinically significant, indicating that damage is already established and a patient has lost his or her renal reserve.

Thakar et al,[1] in a study of more than 31,000 patients who underwent cardiac surgery, found that a greater than 30% decline in postoperative GFR increases the risk of mortality, regardless of the baseline creatinine level. Even renal dysfunction not requiring dialysis is an independent risk factor for mortality after cardiac surgery. Lassnigg et al[2] studied more than 4,000 patients after cardiac or thoracic aortic surgery and found that compared with a mild fall in serum creatinine, an increase in serum creatinine of more than 0.5 mg/dL within 48 hours postoperatively is associated with more than an 18-fold greater risk of mortality over the next 30 days.

Estimating GFR based on the Modification of Diet in Renal Disease (MDRD) equation, while helpful in the outpatient setting for estimating residual renal function, is less accurate in the hospitalized patient with a "new" increase in serum creatinine. It correlates poorly with the more accurate method of measuring GFR using iodine 125-iothalamate.[3]

Biomarkers in the urine (eg, kidney injury molecule-1, cystatin C, neutrophil gelatinase-associated lipocalin) or in the blood (cystatin C) will likely be used increasingly in the future to screen patients for renal failure postoperatively, prior to an actual increase in serum creatinine. Markers are being sought to promptly identify "early" injury in a patient with apparent renal insult (whether due to nephrotoxic injury, a perioperative ischemic event, trauma, or radiocontrast agents).

## ASSESSING RISK OF RENAL FAILURE PREOPERATIVELY

### Case: A woman with diabetes and congestive heart failure facing cardiac surgery

A 60-year-old woman is scheduled to undergo mitral valve replacement and two-vessel coronary artery bypass graft (CABG) surgery. She has diabetes, peripheral vascular disease, a history of myocardial infarction, and congestive heart failure (ejection fraction, 40%). Her serum creatinine is 2.3 mg/dL.

What is her risk of postoperative acute renal failure?

Traditionally, a serum creatinine of less than 3.0 mg/dL has justified a "watchful waiting" approach, provided the patient has no protein in the urine and the GFR is greater than 30 mL/min. The projected risk of acute renal failure in this setting was more often based on anecdotal experience rather than well-designed databases.

More recently, Thakar et al[4] assessed the risk of acute renal failure in 22,589 patients who underwent open heart surgery at The Cleveland Clinic between 1993 and 2000. Acute renal failure was defined in three ways: (1) acute renal failure requiring dialysis during the postoperative period, (2) a 50% or greater decline in creatinine clearance but not requiring dialysis, and (3) a 50% or greater decline in GFR or requirement of dialysis. Important risk factors for developing acute renal failure after open heart surgery were identified, as detailed below.

Combined procedure. The frequency of acute renal failure requiring dialysis or a 50% or greater decline in GFR was 3.8% among patients undergoing CABG, 4.5% among those undergoing a valve procedure, and 7.9% among those who underwent both CABG and valve replacement.

Female gender. Nearly 29% of women with a baseline serum creatinine level of more than 4.0 mg/dL developed acute renal failure, and women had a higher risk of developing acute renal failure than men at every level of baseline serum creatinine, with increasing risk observed at higher levels.

Other risk factors. Other variables associated with an elevated risk of acute renal failure requiring dialysis included a greater cardiopulmonary bypass time, having emergency surgery, the presence of peripheral vascular disease, and having preoperative intra-aortic balloon pumping. Black race was found to be a risk factor for acute renal failure by univariate analysis, but not by multivariate logistic regression analysis.

### Consequences beyond kidney function

Consequences of postoperative acute renal failure extend beyond kidney function: acute renal failure requiring dialysis is associated with a 60% frequency of serious infection and a 26% risk of sepsis; patients with acute renal failure not requiring dialysis have nearly a 25% chance of serious infection and a 13% chance of sepsis.[5] Both infections and sepsis are important determinants of mortality. Other factors associated with acute renal failure and higher mortality rates include proinflammatory and anti-inflammatory cytokines, levels of the insulin-like growth factor binding proteins IGFBP-1 and IGFBP-3, and hyperglycemia.

### Predicting risk based on preoperative factors

Predicting the risk of acute renal failure after open heart surgery can be approached with an algorithm based on preoperative factors (Figure 1).[6] If we implement this algorithm for the patient in our case study (see bold arrows in Figure 1), her risk of acute renal failure requiring dialysis is 5.6%, and her risk for a 50% or greater decline in GFR is 8.7%.

An alternative approach to predicting risk is with a system that awards points based on risk factors (Table 1).[7] In this system, our patient would earn 1 point for being a woman, 2 points for use of an intra-aortic balloon pump preoperatively, 1 point for having congestive heart failure, 2 points for her scheduled CABG and valve procedure, and 5 points for having a preoperative serum creatinine level of 2.1 mg/dL or greater. With 11 points, her corresponding risk of acute renal failure is approximately 20% under the scoring model developed (21.5% of patients in the model with risk scores of 9 to 13 developed acute renal failure).

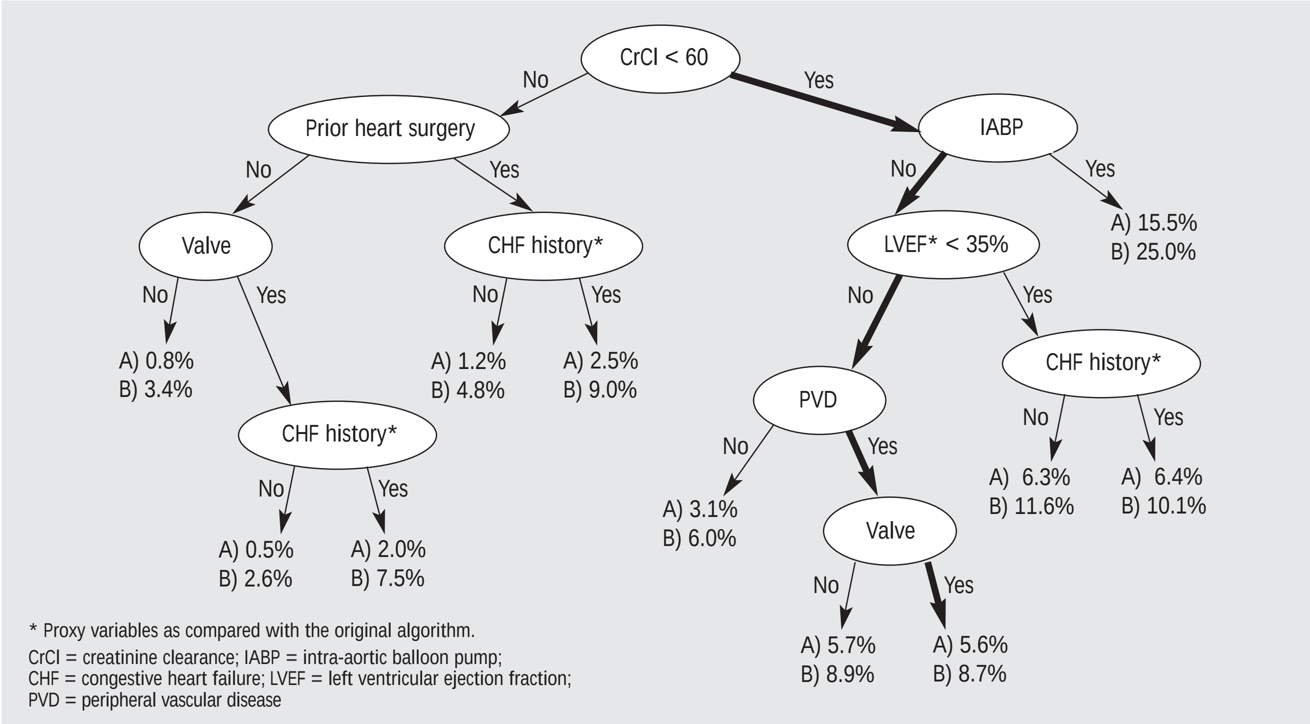


**FIGURE 1.** An algorithm that incorporates preoperative risk factors can be used to estimate the risk of acute renal failure after open heart surgery. Based on the clinical scenario, the algorithm estimates the risk of acute renal failure, defined as either requiring dialysis (values designated as "A") or a 50% or greater decline in glomerular filtration rate or requiring dialysis (values designated as "B"). The arrows in boldface indicate the risk factors present in the patient in the case study (see text). Adapted, with permission, from reference 6.

It is important that a patient at high risk be informed and that the medical team also is made aware of the risk, since prevention is a more powerful approach than attempted treatment after an established insult.

## PREOPERATIVE MEASURES TO PREVENT RENAL FAILURE

After assessing the degree of risk, based on a patient's individual risk and the characteristics of the procedure, several preoperative measures to prevent renal injury should be considered.

### Adjust medications

Calculate the estimated GFR preoperatively and determine which medications warrant adjustment based on residual renal function. Avoid medications such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and nonsteroidal anti-inflammatory drugs as well as overzealous diuresis, each of which may compromise maintenance of effective filtration pressure.

### Optimize volume and solute status

Volume status must be optimized perioperatively to decrease the risk of renal ischemia from renal hypoperfusion in the setting of either dehydration or congestive heart failure with hypotension. Patients with diabetes also present more of a challenge both preoperatively and postoperatively because the alveolar-arterial gradient for the same central venous pressure is broader compared with nondiabetic patients, highlighting an increased risk for respiratory failure with hypervolemia in diabetes.

### Ensure adequate urine flow, but avoid high-dose loop diuretics

Achieving an adequate urine flow rate (> 100 to 150 mL/hour) is critical to avoiding tubular obstruction with acute renal failure.

A danger in patients with high volume overload is overly aggressive use of loop diuretics in an attempt to remove fluids. High-dose loop diuretics may decrease GFR, activate neurohormones (sympathetic nervous system, renin-angiotensin-aldosterone system), cause sodium reaccumulation, and adversely affect clinical outcomes (eg, length of hospital stay, mortality).

Mehta et al[8] categorized 552 patients with acute renal failure in intensive care units by their use of diuretics immediately before nephrology consultation. Diuretic use was associated with a significant increase in the risk of death and nonrecovery of renal function. Even in light of the significant comorbidities in this population, these findings raise concerns regarding the link between high-dose diuretics and poor outcome.

A patient at risk of developing acute renal failure who does not respond to reasonable doses of diuretics

**TABLE 1**

**This table adapted from reference 7. Permission not granted to reprint this table online.**

Please see original source table (table 5) in: *Thakar CV, Arrigain S, Worley S, Yared J-P, Paganini EP. A clinical score to predict acute renal failure after cardiac surgery. J Am Soc Nephrol 2005; 16:162–168.*

**TABLE 2**
Regimens for continuous intravenous infusion of diuretics

For patients in stable chronic renal failure (creatinine clearance rate about 18 mL/min), use the following:

- Furosemide: 20 to 40 mg/hr
  or
- Bumetanide: 1 to 2 mg/hr
  or
- Torsemide: 10 to 20 mg/hr

If ineffective, add a thiazide diuretic or use hemofiltration

(Table 2) should undergo volume removal by an extracorporeal therapy to allow the kidney to reset itself. A number of therapies can be used perioperatively, including standard hemodialysis, hemofiltration and ultrafiltration.

## Consider options to enhance diuretic administration and effect

Clinical trials have failed to prove that perioperative administration of dopamine infusions with furosemide improves urine flow rate or is protective against renal dysfunction.[9,10]

Patients who are hypoalbuminemic are often resistant to diuresis, however, and it is theoretically possible that administering albumin may improve delivery of furosemide to the endothelium. Infusing furosemide and salt-poor albumin has not proven effective in clinical studies.[11,12]

Whether diuretics should be administered intravenously or as a bolus is another controversial issue. Diuresis is enhanced by continuous infusion rather than boluses in certain clinical settings with low colloid osmotic pressure and increased extracellular volume. A bolus results initially in high rates of diuretic excretion, but rates soon taper off. With high boluses, renal function may deteriorate because of vasoconstriction from neurohormonal activation. Furosemide delivered by bolus also has the disadvantage that it may cause ototoxicity, especially in elderly patients. Patients who do not respond to a bolus are less likely to respond to continuous infusion. Extracorporeal support should be considered earlier, especially in patients with relative hypotension, hypervolemia, congestive heart failure, and minor increases in serum creatinine on standard diuretic therapy.

## Optimize hematocrit levels

The true impact of hematocrit levels and erythropoietin on perioperative acute renal failure and outcomes is not well defined. Comparisons of risk factors for hospital mortality among dialysis patients have identified hematocrit in the intensive care unit as the most dominant risk factor in this population. Moreover, cardiopulmonary bypass hemodilution (< 24%) is associated with a systematically increased likelihood of renal injury. Experimental data suggest that erythropoietin has unexpected cytokine actions that may be important for recovery from acute renal failure. Further study of erythropoietin therapy in this setting is warranted.

## Limit use of intravenous contrast agents

Contrast agents increase vasoconstriction and cause tubular ischemia, sloughing of tubules, and obstruction.

Patients who already have renal insufficiency or develop it acutely are at risk for contrast-induced nephropathy after coronary angiography or other procedures requiring contrast. Patients with any elevation in serum creatinine should be viewed as high risk for acute renal failure.

If contrast is needed, a nonionic agent is preferable, delivered with intravenous fluids before and after procedures to increase urine flow to protect against obstruction. Sodium bicarbonate infusion may also reduce the risk of contrast-induced nephropathy and should be used, especially in high-risk patients. Measures to possibly ameliorate risk, including giving the antioxidant acetylcysteine or fenoldopam, a dopamine-1 receptor agonist, are currently under investigation, and conclusions are still uncertain.[13–15]

## SUMMARY

Patients with an elevated serum creatinine or whose serum creatinine levels increase postoperatively, regardless of baseline levels, are at increased risk for elevated mortality. Women have a higher risk from acute renal failure than men at every level of serum creatinine. Acute renal failure confers an increased risk of mortality, chronic renal insufficiency, and postoperative infection independent of other postoperative complications. Preoperative measures to reduce risk of acute renal failure include optimizing volume and solute status, ensuring adequate urine flow, avoiding high doses of diuretics, optimizing hematocrit levels, and avoiding contrast agents.

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