Surgery in the Patient with Renal Dysfunction

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KEYWORDS

• Chronic kidney disease • Acute kidney injury • Renal failure
• Renal protection • Preoperative evaluation

Millions of patients with renal dysfunction have surgery each year. The social and financial impact on the health care system is enormous.[1] Preoperative evaluation should attempt to reduce morbidity and mortality and improve quality in this complex patient population.

Renal dysfunction represents a spectrum of disease with potentially far-ranging consequences on surgical and anesthetic management due to not only the underlying disease processes but also from the intervening medical and surgical therapies. Furthermore, optimization of the patient with renal dysfunction needs to not only consider the preexisting renal function but also the potential risk of acute kidney injury (AKI) in the perioperative setting.

In this context, the goal of this review is to focus on perioperative evaluation and optimization of care in surgical patients who have renal dysfunction. Two different sections are presented. The first section focuses on definitions and the epidemiology of chronic kidney disease (CKD), end-stage renal disease (ESRD), and AKI. The surgical risk factors for AKI are also reviewed. The second section focuses on an approach to preoperative evaluation, with particular emphasis on potential areas of conflict between the primary care physician or nephrologist, surgeon, and anesthesiologist. Recent research findings on perioperative renal protection strategies are also reviewed.

RENAL DYSFUNCTION

Chronic Kidney Disease

CKD as defined in 2002 by the Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation is either kidney damage or decreased kidney function

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for 3 or more months.[2] Proteinuria or abnormalities in imaging tests are markers for kidney damage and a reduction in glomerular filtration rate (GFR) is a marker for decreased kidney function.[3] ESRD is a government-derived administrative term that only indicates chronic treatment by dialysis or transplantation. It does not refer to a specific degree of kidney function.[3]

The National Kidney Foundation classifies CKD based on pathology:

- Diabetic glomerulosclerosis
- Glomerular diseases (primary or secondary)
- Vascular diseases (including hypertension and microangiopathy)
- Tubulointerstitial diseases (including obstructive or reflux nephropathy)
- Cystic diseases
- Diseases in renal transplant recipients (rejection, drug toxicity, recurrence of disease)

A GFR of less than 60 mL/min/1.73 m^2 is considered the threshold for CKD.[4] GFR varies with sex, age, and body size, and is typically estimated with calculations based on serum creatinine (SCr) level.[4] Stevens and colleagues[4] review the limitations of the SCr-based Cockcroft-Gault formula and the Modification of Diet in Renal Disease (MDRD) equation. Proximal tubular cells in the kidney secrete creatinine and therefore creatinine clearance surpasses GFR. However, in the steady state SCr is related to the reciprocal of GFR.[4]

As shown in **Table 1**, there are 5 different stages of CKD.[2] Kidney failure is defined as either GFR less than 15 mL/min/1.73 m^2 or a need for dialysis or renal transplantation.

Acute Kidney Injury

There are many different definitions for an acute change in renal function. The term acute renal failure (ARF) has been supplanted by the term AKI.[5] AKI encompasses the entire range of ARF from small changes in SCr to loss of function requiring dialysis. In an effort to standardize the classification of AKI, in 2004 the Acute Dialysis Quality Initiative (ADQI) Group proposed the RIFLE criteria.[6] As shown in **Fig. 1**, RIFLE stands for Risk of renal dysfunction; Injury to the kidney; Failure of kidney function; Loss of kidney function; and End-stage kidney disease. It relies on measurement of GFR or SCr and urine output (UO) to classify the severity of ARF. Since their initial publication, the RIFLE criteria have been validated in numerous studies of intensive care unit (ICU), postsurgical, and hospital patients as independent predictors of mortality.[7–9] In 2007 the Acute Kidney Injury Network (AKIN) proposed a modification to the RIFLE criteria.[5] As shown in **Table 2**, the AKIN definition considers 3 different stages of AKI, adds a 48-hour time frame for the diagnosis of AKI, and changes the criteria for "Risk,"

Table 1
Stages of chronic kidney disease

Stage	Description	GFR (mL/min/1.73 m^2)
1	Kidney damage with normal or increased GFR	$\geq$90
2	Kidney damage with mild decrease in GFR	60–89
3	Moderate decrease in GFR	30–59
4	Severe decrease in GFR	15–29
5	Kidney failure	<15 (or dialysis)

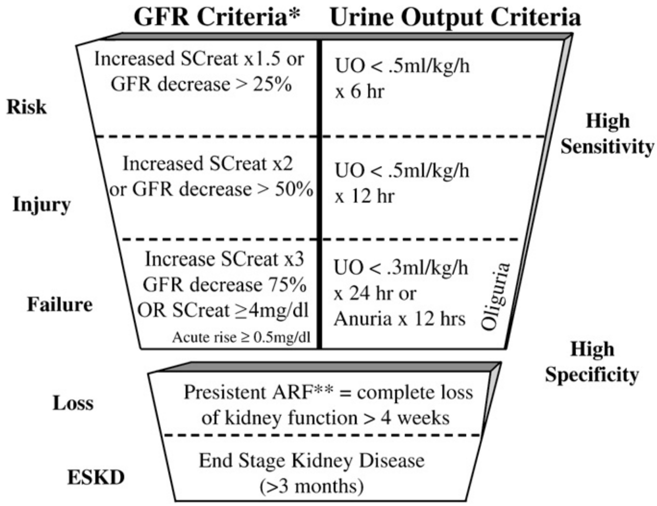

Fig. 1. Proposed classification scheme for acute renal failure (ARF). The classification system includes separate criteria for creatinine and output (UO). A patient can fulfill the criteria through changes in serum creatinine (SCreat) or changes in UO, or both. ARF, acute renal failure; GFR, glomerular filtration rate. (*From* Bellomo R, Ronco C, Kellum JA, et al. 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(4):R204–12; with permission.)

or Stage 1 AKI, to include patients with increases in SCr level of greater than or equal to 0.3 mg/dL ($\geq$26.4 μmol/L). In a 5-year analysis of more than 120,000 ICU admissions in Australia, investigators found no significant differences in the predictive ability of the RIFLE criteria compared with the AKIN definition.[10]

Despite their use in current definitions of AKI, SCr and UO are not the ideal markers for AKI and significant research efforts are underway to identify biomarkers of AKI.[11] Potential biomarkers of AKI include neutrophil gelatinase-associated lipocalin (NGAL), cystatin C, and interleukin-18.[11]

AKI can be classified according to prerenal, renal, and postrenal causes.[12] Perioperatively the most common cause of AKI is secondary to acute tubular necrosis (ATN).[12] A study in ICU patients found the most common causes of AKI were septic shock, major surgery, cardiogenic shock, hypovolemia, and drug-induced AKI.[13]

Surgical Risk Factors for AKI

Patients with kidney disease may present for a wide variety of surgical procedures. Access for dialysis is the most common procedure followed by procedures for peripheral vascular disease, coronary artery disease, and kidney transplantation.[14]

Overall, the risk of AKI in surgical patients has been estimated to be approximately 1%.[15] However, certain patient populations are at much higher risk. Factors identified as increasing the risk of AKI include age, past history of kidney disease, left ventricular ejection fraction less than 35%, cardiac index less than 1.7 L/min/m^2, hypertension, peripheral vascular disease, diabetes mellitus, emergency surgery, and type of surgery.[15] The highest risk surgeries include coronary artery surgery, cardiac valve surgery, aortic aneurysm surgery, and liver transplant surgery.[16–18] The literature is difficult to evaluate given the many different definitions of AKI, but rates of AKI or

Table 2
Classification/staging system for AKI[a]

Stage	Serum Creatinine Criteria	Urine Output Criteria
1	Increase in serum creatinine of more than or equal to 0.3 mg/dL (≥ 26.4 μmol/l) or increase to more than or equal to 150% to 200% (1.5- to 2-fold) from baseline	Less than 0.5 mL/kg/h for more than 6 h
2[b]	Increase in serum creatinine to more than 200% to 300% (>2- to 3-fold) from baseline	Less than 0.5 mL/kg/h for more than 12 h
3[c]	Increase in serum creatinine to more than 300% (>3-fold) from baseline (or serum creatinine of more than or equal to 4.0 mg/dL [≥ 354 μmol/l] with an acute increase of at least 0.5 mg/dL [44 μmol/l])	Less than 0.3 mL/kg/h for 24 h or anuria for 12 h

[a] Modified from the RIFLE (Risk, Injury, Failure, Loss, and End-stage kidney disease) criteria. The staging system proposed is a highly sensitive, interim, staging system and is based on recent data indicating that a small change in serum creatinine level influences outcome. Only 1 criterion (creatinine level or urine output) has to be fulfilled to qualify for a stage.
[b] 200% to 300% increase = 2- to 3-fold increase.
[c] Given wide variation in indication and timing of initiation of renal replacement therapy (RRT). Individuals who receive RRT are considered to have met the criteria for stage 3 irrespective of the stage they are in at the time of RRT.

Adapted from Mehta RL, Kellum JA, Shah SV, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11(2):R31; with permission.

need for dialysis range from 3% to 5% for cardiac surgery with cardiopulmonary bypass to more than 50% for emergency abdominal aortic aneurysm repair.[15]

Perioperative Morbidity of Kidney Disease

The United Stated Renal Data System (USRDS) collects data on the ESRD population in the United States.[1] The 2007 USRDS report estimates that approximately 15% of the general population has CKD.[1] They also estimate that all-cause hospitalization rates are 3 times higher for patients with CKD and that rates of hospitalization due to AKI are approximately 6 times higher for patients with CKD.

The presence of CKD increases the rates of morbidity and mortality for several different surgical procedures. Investigators found estimated GFR (eGFR) calculated by the MDRD equation to be an independent predictor of mortality after coronary artery bypass graft surgery (CABG).[19] The mean eGFR was 64.7 mL/min/1.73 m^2 for survivors compared with 57.9 mL/min/1.73 m^2 in the patients who died.[19] Similar findings correlating eGFR with increased morbidity and mortality have also been published for elective major vascular surgery, hip fracture and repair, and endovascular aortic aneurysm surgery.[20–23]

A review found the overall mortality rate from AKI between 1956 and 2003 was comparatively unchanged at approximately 50%.[24] AKI during the perioperative period had an even poorer prognosis with mortality rates of 64% to 83% depending on the surgical population.[24,25] Even small changes in SCr correlate with a significant increase in the risk of death. In 1 study, patients with SCr increases of 0.3 to 0.4 mg/dL had a 70% increase in the risk for death compared with patients with little or no change in SCr.[25]

An important point is that surgery presents significant risks to patients with CKD or to those with, or at risk of, AKI. These risks need to be effectively communicated to patient and family so they can make informed decisions about their medical therapy. Furthermore, when evaluating the health care systems for patients with CKD, systems need to be in place to manage a potential deterioration in renal function in the perioperative period.

PREOPERATIVE EVALUATION AND PERIOPERATIVE RENAL PROTECTION

Given the array of diseases that can affect kidney function, a patient with kidney dysfunction who presents for surgery requires a comprehensive evaluation. The National Kidney Foundation recommends the following assessments for patients with CKD:[2]

- Diagnosis (type of kidney disease)
- Comorbid conditions
- Severity, assessed by level of kidney function
- Complications, related to level of kidney function
- Risk for loss of kidney function
- Risk for cardiovascular disease

These assessments hold true for the preoperative evaluation but they must be put into context of the requirement for the underlying surgery and the inherent surgical risk. As should be apparent, patients with CKD may have complex and overlapping medical problems: diabetes, cardiovascular disease, hypertension, anemia, dyslipidemia, poor nutritional status, bone disease, neuropathy, and an overall decreased quality of life.[2] Optimization of modifiable risk factors is the main goal of the preoperative assessment. Depending on the patient's status and the surgical procedure, the preoperative evaluation may require close communication between the primary care physician, nephrologist, surgeon, and anesthesiologist to determine if a patient is optimized for surgery. It cannot be stressed enough that a patient with kidney dysfunction is not cleared for surgery. The dictum "avoid hypoxia, avoid hypotension, avoid succinylcholine" is similarly ineffective. Areas that require close coordination to avoid conflict include the following:

- Preoperative goals: blood pressure, timing of dialysis
- Medications in the perioperative period
- Preoperative laboratory studies
- Preoperative tests

Preoperative Goals

Intraoperative hypotension and decreased renal perfusion is often considered a risk factor for the development of perioperative AKI.[11] Patients with hypertension and diabetes undergoing noncardiac surgery with a mean arterial pressure greater than 110 mmHg are at increased risk of intraoperative hypotension, and hypotension and hypertension are associated with higher rates of cardiovascular and renal complications.[26] Hence, adequate control of blood pressure before a patient undergoes surgery is paramount. The seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC VII) recommends patients with CKD or diabetes have a blood pressure less than 130/80 mmHg.[27] To minimize the risks of volume overload, electrolyte imbalances, and uremic bleeding, arrangements should be made for patients requiring dialysis to receive it within 24 hours of surgery.[28]

Medications in Perioperative Period

Angiotensin-converting enzyme inhibitors (ACEI) and angiotensin II antagonists (ARA) are commonly used to treat hypertension in patients with CKD, and they are also commonly associated with intraoperative hypotension, particularly with induction of general anesthesia.[29,30] Discontinuation of ACEI or ARA therapy for at least 10 hours before general anesthesia is recommended to reduce the risk of postinduction hypotension.[30] Given the risk of cardiovascular disease, ischemic stroke, and peripheral arterial disease, clopidogrel bisulfate (Plavix) is another medication commonly used in the CKD patient population. The decision to continue or hold clopidogrel in the perioperative period relates to the risk of the underlying condition indicated for its use, particularly in the setting of coronary stents, versus the risk of bleeding during surgery. For example, studies in the cardiac surgery literature recommend stopping clopidogrel for 5 to 7 days before cardiac surgery.[31] Anesthesiologists will not generally perform neuraxial techniques (epidural or spinal anesthesia) on patients who have taken clopidogrel within 7 days of surgery.[32] Ultimately the decision to continue or hold clopidogrel will depend on a risk assessment of the underlying condition, the bleeding risk during surgery, and the choice of anesthetic technique.

Preoperative Laboratory Studies

Several preoperative laboratory studies are recommended for patients with CKD but the more important question is what to do with the results. An eGFR should be calculated to not only ensure that correct dosage adjustments are made for renally excreted medications but also to help quantify perioperative risk. AKI in the setting of CKD should prompt an evaluation to identify precipitating factors and elective procedures should be postponed until resolution. Urgent surgical procedures, such as those related to underlying cancer or certain orthopedic injuries, in patients with AKI require an evaluation to determine if the precipitating cause(s) of AKI can be managed before the surgical issue deteriorates further.

Anemia may necessitate preoperative transfusion or supplementation with iron or erythropoietin. Typing and screening for blood should be done before operations with potential for significant blood loss. Patients with CKD may have received multiple transfusions and they can develop antibodies that can significantly delay processing for packed red blood cells. Electrolyte disturbances are common and hyperkalemia is a frequent concern. It is typically recommended that potassium levels be no more than 5 to 5.5 mmol/L. However, there are studies that show hyperkalemia is not associated with increased morbidity in vascular access surgery patients or when succinylcholine is used as a muscle relaxant.[33,34] These studies underscore that the management of patients with CKD needs to be individualized, as mild to moderate hyperkalemia is common in patients with CKD. Some studies suggest that more than 50% of patients with CKD have hyperkalemia and that acute intervention should be reserved for potassium levels greater than 6.5 mmol/L.[35] Overall, the preoperative potassium level needs to be evaluated in the context of its rate of change from previous levels, the potential blood transfusion requirements during surgery, and the potential for alterations in acid/base status perioperatively.

Preoperative Tests

The extent of preoperative testing is dependent on a patient's comorbid diseases and often includes an electrocardiogram and chest radiograph. Cardiovascular disease is the number 1 cause of mortality in patients with kidney failure.[2] To stratify cardiovascular risk the American College of Cardiology/American Heart Association 2007 guidelines on perioperative cardiovascular evaluation for noncardiac surgery are recommended.[36]

Surgical Risk

Surgical risk as related to CKD can be divided into the following areas: need for surgery, specific surgical techniques, fluid shifts and blood loss, analgesic requirements, intravenous access, anesthetic techniques, and expected disposition.

The need for surgery can be stratified as elective, urgent, or emergent. As discussed previously, emergent surgery is associated with increased morbidity and mortality for patients with CKD. Urgent and elective surgery can be deferred until the patient's status is optimized, particularly if they have concomitant AKI. Surgery can help to expedite the resolution of AKI if it is treating the underlying precipitating event. Again, communication between primary care and perioperative physicians is crucial to make this determination and to plan an appropriate course of action.

Surgical techniques include the use of nonionic contrast agents or the use of intra-abdominal laparoscopy and they may need to be modified for patients with CKD or AKI. Earlier studies on endovascular patients with CKD suggested that nonionic contrast agents might increase the risk of death in patients with CKD.[37] Other studies show clinically insignificant changes, particularly when preoperative prevention strategies are employed.[38] The ideal strategy to prevent contrast-induced nephropathy (CIN) is unknown but current recommendations include hydration, avoidance of other nephrotoxic medications, prevention of hypotension, and possibly use of adjuvants such as sodium bicarbonate or *N*-acetylcysteine.[39,40] Laparoscopic surgery with abdominal pneumoperitoneum is a common technique favored for its noninvasive nature, faster wound healing, and reduction in postoperative pain. However, laparoscopy is also associated with a reduction in renal perfusion.[41] To preserve renal blood flow, abdominal insufflation pressures more than 15 mmHg are not recommended. Laparoscopy can also cause hypotension, which will further aggravate reductions in renal perfusion. To mitigate these changes, adequate fluid replacement is recommended.[41,42]

Maintenance of euvolemia and renal perfusion seem like obvious goals for patients with CKD or AKI. However, assessing their adequacy in the perioperative period is not a simple task. Features of hypovolemia can be masked by anesthesia and surgery. Invasive monitoring may improve assessment but disease states, such as sepsis, can cause maldistribution of intravascular volume due to vasodilatation and altered capillary permeability.[11] Intraoperative blood loss and fluid shifts during surgery can compound these problems. Typically the anesthesia team will aim for a mean arterial pressure greater than 65 to 70 mmHg, or higher for the uncontrolled hypertensive patient, UO >0.5 ml/kg/h as applicable, central venous pressure 10 to 15 mmHg, and pulmonary artery wedge pressure of 10 to 15 mmHg. Intraoperative transesophageal echocardiography and newer monitors of stroke volume may also be used to assess adequacy of cardiac preload.[11,42] Fluid resuscitation is typically with either crystalloids or colloids or blood products as indicated. The ideal crystalloid is debatable and many texts continue to recommend normal saline as the choice of intravenous fluid for patients with kidney dysfunction.[43] Normal saline is hypertonic and hyperchloremic compared with plasma and volumes of greater than 30 ml/kg can lead to hyperchloremic metabolic acidosis and exacerbation of hyperkalemia. A study of kidney transplant recipients found that normal saline for fluid management was associated with a higher incidence of hyperkalemia and acidosis than patients managed with lactated Ringer solution.[43] Over hydration and goal-directed therapy to supranormal values can have a negative effect on patient outcome such as ileus, pulmonary edema, and prolonged hospital admission.[42]

Analgesic requirement in the perioperative period is an important area to consider given that opioids may accumulate in patients with CKD, placing them at higher risk of respiratory depression.[44] Nonsteroidal antiinflammatory drugs are not recommended for patients with CKD or AKI. Other options for moderate to severe postoperative pain include indwelling peripheral nerve catheters, long-lasting peripheral nerve blocks, or epidural catheters, as applicable. Managing postoperative pain in patients with CKD may require inpatient admission or coordination of outpatient nursing services.

Intravenous access is not a trivial matter for patients with CKD. Hemodialysis fistulas, previous blood draws, and previous surgeries all contribute to making intravenous access more difficult in this patient population. Central line placement may be required or a peripherally inserted central catheter (PICC) can be placed preoperatively for cases not associated with significant fluid losses or for cases requiring ongoing postoperative intravenous medical therapies.

Anesthetic techniques for surgery can be grouped into general anesthesia, neuraxial anesthesia, peripheral nerve blockade, or sedation. The ideal anesthetic technique for a patient with CKD or AKI having a particular procedure is unknown. Studies comparing general anesthesia versus regional anesthesia often look at outcomes such as functional recovery, bleeding risks, coagulation risks, or neurologic outcome. Ultimately the selected anesthetic technique will be determined by the patient's coexisting disease, surgical approach, and desired anesthetic goals.

After surgery, patients will generally be discharged from the postanesthesia care unit to home (outpatient surgery), hospital admission, or the ICU. Patients with CKD are at higher risk of complications and prolonged hospital or ICU stay.[14]

Perioperative Renal Protection

Beyond the standard goals of maintaining euvolemia, maintaining renal perfusion, and avoiding nephrotoxins, there is a great deal of research underway to identify methods of perioperative renal protection. Unfortunately, often promising results in animal models of AKI have not translated into successful clinical trials in humans.[45] Recent research suggests that fenoldopam may hold promise in this area.

Fenoldopam mesylate is a dopamine-1 receptor agonist that was initially approved for treatment of hypertensive emergencies. It has been studied in a variety of surgical and intensive care populations and been shown to reduce the risk of AKI.[46,47] A meta-analysis of 16 randomized studies found that fenoldopam reduced the risk of AKI and in-hospital death.[48] Doses of fenoldopam vary, but many of the positive trials used approximately 0.1 μg/kg/min and initiated treatment with the induction of surgery. These findings if replicated in a multicentered randomized controlled trial would represent a breakthrough in the treatment of AKI.

SUMMARY

Patients with CKD or AKI who present for surgery often have complex medical problems. Preoperative evaluation should strive to identify and correct any modifiable risks. Communication between the primary care team, nephrologist, surgeon, and anesthesiologist should ensure timely and appropriate investigation. Despite optimization, patients with CKD or AKI are at significantly higher risk of morbidity and mortality during the perioperative period. These risks need to be communicated to the patient or caregivers so that informed medical decisions can be made. Perioperative goals for euvolemia, maintenance of renal perfusion, and avoidance of nephrotoxins may require modifications in the usual surgical or anesthetic care. Despite intense research into perioperative renal protection, many successful therapies in animal models have not achieved success in human populations. Fenoldopam, as a prophylactic therapy in patients with CKD undergoing high risk surgery or for those patients at high risk of AKI, may be beneficial. Ultimately more research is required for a definitive answer to this elusive goal.

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