CHAPTER 30

Anesthesia for Patients with Kidney Disease

KEY CONCEPTS

1. The utility of serum creatinine measurement as an indicator of glomerular filtration rate (GFR) is limited in critical illness: the rate of creatinine production, and its volume of distribution, may be abnormal in the critically ill patient, and the serum creatinine concentration often does not accurately reflect GFR in the physiological disequilibrium of acute kidney injury (AKI).
2. Creatinine clearance measurement is the most accurate method available for clinically assessing overall renal function.
3. The accumulation of morphine and meperidine metabolites has been reported to prolong respiratory depression in patients with kidney failure.
4. Succinylcholine can be safely used in patients with kidney failure in the absence of hyperkalemia at the time of induction.
5. Extracellular fluid overload from sodium retention, in association with increased cardiac demand imposed by anemia and hypertension, makes patients with end-stage renal disease particularly prone to congestive heart failure and pulmonary edema.
6. Delayed gastric emptying secondary to autonomic neuropathy may predispose patients to aspiration perioperatively.
7. Controlled ventilation should be considered for patients with kidney failure. Inadequate spontaneous or assisted ventilation with progressive hypercarbia under anesthesia can result in respiratory acidosis that may exacerbate preexisting acidemia, lead to potentially severe circulatory depression, and dangerously increase serum potassium concentration.
8. Correct anesthetic management of patients with renal insufficiency is as critical as management of those with frank kidney failure, especially during procedures associated with a relatively high incidence of postoperative kidney failure, such as cardiac and aortic reconstructive surgery.
9. Intravascular volume depletion, sepsis, obstructive jaundice, crush injuries, and renal toxins such as radiocontrast agents, certain antibiotics, angiotensin-converting enzyme inhibitors, and NSAIDs are major risk factors for acute deterioration in renal function.
10. Renal protection with adequate hydration and maintenance of renal blood flow is indicated for patients at high risk for AKI and kidney failure undergoing cardiac, major aortic reconstructive, and other surgical procedures associated with significant physiological trespass. The use of mannitol, low-dose dopamine infusion, loop diuretics, or fenoldopam for renal protection is controversial and without conclusive proof of efficacy.

Acute kidney injury (AKI) is a common problem, with an incidence of up to 5% in all hospitalized patients and up to 8% in critically ill patients. Postoperative AKI may occur in 1% or more of general surgery patients, and up to 30% of patients undergoing cardiothoracic and vascular procedures. Perioperative AKI greatly increases hospitalization costs, mortality rate, and perioperative morbidity, including fluid and electrolyte derangements, major cardiovascular events, infection and sepsis, and gastrointestinal hemorrhage. Preoperative risk factors for perioperative AKI include preexisting kidney disease, hypertension, diabetes mellitus, liver disease, sepsis, trauma, hypovolemia, multiple myeloma, and age greater than 55 years. The risk of perioperative AKI is also increased by exposure to nephrotoxic agents such as nonsteroidal antiinflammatory drugs (NSAIDs), radiocontrast agents, and antibiotics (see Table 29–4).When addressing abnormalities in renal function, the clinician must possess a thorough understanding of the differential diagnosis of AKI (**Figure 30–1**).

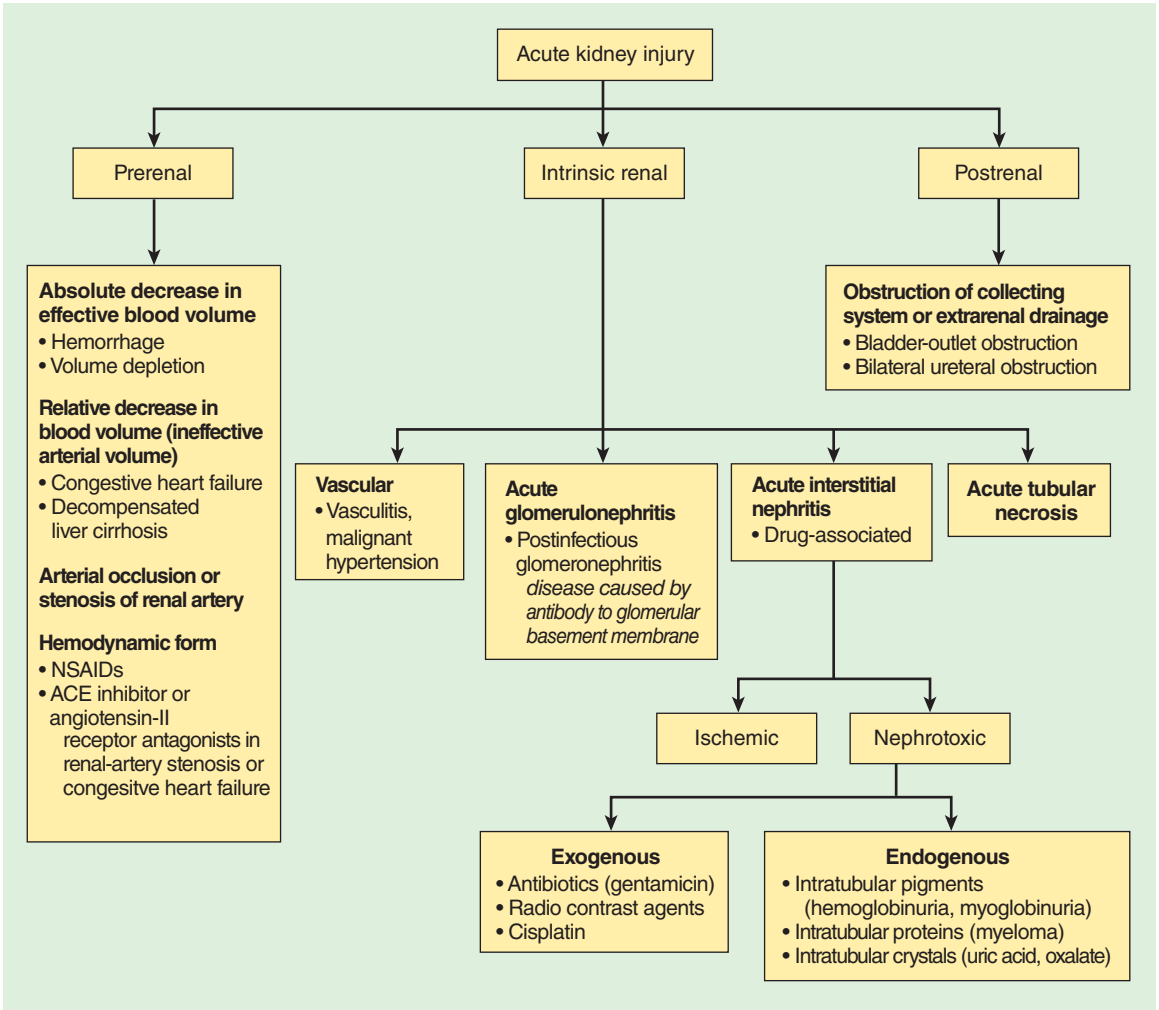

FIGURE 30–1 Differential diagnosis of acute kidney injury. ACE, angiotensin-converting enzyme; NSAID, nonsteroidal antiinflammatory drug. (Reproduced, with permission, from Lameire N, Van Biesen W, Vanholder R: Acute renal failure. Lancet 2005;29:417.)

Evaluating Renal Function

Renal impairment can be due to glomerular dysfunction, tubular dysfunction, or obstruction of the urinary tract. Because abnormalities of glomerular function cause the greatest derangements and are most readily detectable, the most useful laboratory tests utilized currently are those related to assessment of glomerular filtration rate (GFR). Accurate clinical assessment of renal function is often difficult and relies heavily on laboratory determinations such as the creatinine clearance (Table 30–1). Two systems for classification of AKI are helpful in defining and staging the degree of renal dysfunction; these are the Acute Dialysis Quality Initiative RIFLE criteria (Figure 30–2) and the Acute Kidney Injury Network (AKIN) staging system (Table 30–2). A great deal of research is currently evaluating plasma and urine biomarkers associated with AKI, such as cystatin C, neutrophil gelatinase–associated lipocalin, interleukin-18, and kidney injury molecule-1. It is likely that biomarkers will play a prominent role in the near future for diagnosis, staging, and prognostic assessment of AKI.

TABLE 30–1 Severity of kidney injury according to glomerular function.

	Creatinine Clearance (mL/min)
Normal	100–120
Decreased renal reserve	60–100
Mild renal impairment	40–60
Moderate renal insufficiency	25–40
Kidney failure	<25
End-stage renal disease[1]	<10

[1]This term applies to patients with chronic kidney failure.

BLOOD UREA NITROGEN

The primary source of urea in the body is the liver. During protein catabolism, ammonia is produced from the deamination of amino acids. Hepatic conversion of ammonia to urea prevents the buildup of toxic ammonia levels:

$$2NH_3 + CO_2 \rightarrow H_2N - CO - NH_2 + H_2O$$

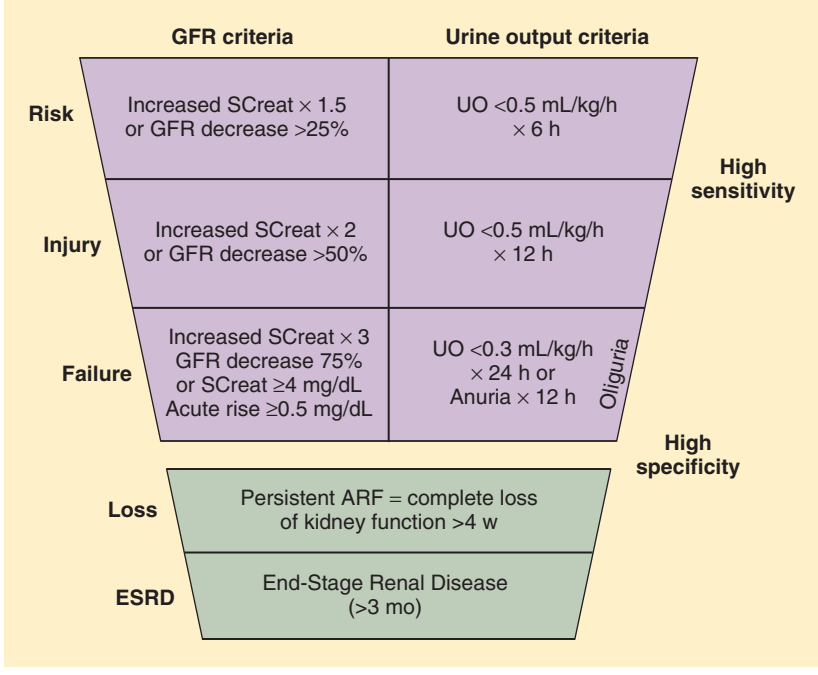

FIGURE 30–2 RIFLE criteria for acute kidney injury. ARF, acute renal failure; GFR, glomerular filtration rate; SCreat, serum creatinine concentration; UO, urine output. (Reproduced, with permission, from Bellomo R, Ronco C, Kellum JA, et al: Acute renal failure—definition, outcome measures, animal models, fluid therapy and information technology needs: The Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004;8:R204.)

TABLE 30–2 Acute kidney injury network (AKIN) staging system for acute kidney injury.[1]

Stage	Serum Creatinine Criteria	Urine Output Criteria
1	Increase in serum creatinine of ≥0.3 mg/dL (≥26.4 µmol/L) or increase to ≥150–200% (1.5- to 2-fold) from baseline	Less than 0.5 mL/kg/h for more than 6 h
2	Increase in serum creatinine ≥200–300% (>2- to 3-fold) from baseline	Less than 0.5 mL/kg/h for more than 12 h
3	Increase in serum creatinine to >300% (>3-fold) from baseline (or serum creatinine of ≥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

[1]Reproduced, with permission, 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:R31.

Blood urea nitrogen (BUN) is therefore directly related to protein catabolism and inversely related to glomerular filtration. As a result, BUN is not a reliable indicator of the GFR unless protein catabolism is normal and constant. Moreover, 40–50% of the urea filtrate is normally reabsorbed passively by the renal tubules; hypovolemia increases this fraction.

The normal BUN concentration is 10–20 mg/dL. Lower values can be seen with starvation or liver disease; elevations usually result from decreases in GFR or increases in protein catabolism. The latter may be due to a high catabolic state (trauma or sepsis), degradation of blood either in the gastrointestinal tract or in a large hematoma, or a high-protein diet. BUN concentrations greater than 50 mg/dL are generally associated with impairment of renal function.

SERUM CREATININE

Creatine is a product of muscle metabolism that is nonenzymatically converted to creatinine. Creatinine production in most people is relatively constant and related to muscle mass, averaging 20–25 mg/kg in men and 15–20 mg/kg in women. Creatinine is then filtered (and to a minor extent secreted) but not reabsorbed in the kidneys. Serum creatinine concentration is therefore directly related to body muscle mass but inversely related to glomerular filtration (Figure 30–3). Because body muscle mass is usually relatively constant, serum creatinine measurements are generally reliable indices of GFR in the healthy patient. However, the utility of a single serum creatinine measurement as an indicator of GFR is limited in critical illness: the rate of creatinine production, and its volume of distribution, may be abnormal in the critically ill patient, and a single serum creatinine measurement often will not accurately reflect GFR in the physiological disequilibrium of AKI.

The normal serum creatinine concentration is 0.8–1.3 mg/dL in men and 0.6–1 mg/dL in women. Note from Figure 30–3 that each doubling of the serum creatinine represents a 50% reduction in GFR. Large meat meals, cimetidine therapy, and increases in acetoacetate (as during ketoacidosis) can increase serum creatinine measurements without a change in GFR. Meat meals increase the creatinine load, and high acetoacetate concentrations interfere with the most common laboratory method for measuring creatinine. Cimetidine

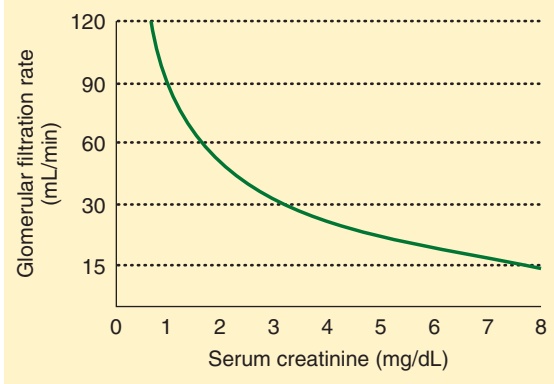

FIGURE 30–3 The relationship between the serum creatinine concentration and the glomerular filtration rate.

appears to inhibit creatinine secretion by the renal tubules.

GFR declines with increasing age in most individuals (5% per decade after age 20), but because muscle mass also declines, the serum creatinine remains relatively normal; creatinine production may decrease to 10 mg/kg. Thus, in elderly patients, small increases in serum creatinine may represent large changes in GFR. Using age and lean body weight (in kilograms), GFR can be estimated by the following formula for men:

$$\text{Creatinine clearance} = \frac{[(140 - \text{age}) \times \text{lean body weight}]}{(72 \times \text{plasma creatinine})}$$

For women, this equation must be multiplied by 0.85 to compensate for a smaller muscle mass.

The serum creatinine concentration requires 48–72 h to equilibrate at a new level following acute changes in GFR.

CREATININE CLEARANCE

2 Creatinine clearance measurement is the most accurate method available for clinically assessing overall renal function (actually, GFR). Although measurements are usually performed over 24 h, 2-h creatinine clearance determinations are reasonably accurate and easier to perform. Mild impairment of renal function generally results in creatinine clearances of 40–60 mL/min. Clearances between 25 and 40 mL/min produce moderate renal dysfunction and nearly always cause symptoms. Creatinine clearances less than 25 mL/min are indicative of overt kidney failure.

Progressive kidney disease enhances creatinine secretion in the proximal tubule. As a result, with declining renal function the creatinine clearance progressively overestimates the true GFR. Moreover, relative preservation of GFR may occur early in the course of progressive kidney disease due to compensatory hyperfiltration in the remaining nephrons and increases in glomerular filtration pressure. It is therefore important to look for other signs of deteriorating renal function such as hypertension, proteinuria, or other abnormalities in urine sediment.

BLOOD UREA NITROGEN: CREATININE RATIO

Low renal tubular flow rates enhance urea reabsorption but do not affect creatinine handling. As a result, the BUN to serum creatinine ratio increases above 10:1. Decreases in tubular flow can be caused by decreased renal perfusion or obstruction of the urinary tract. **BUN: creatinine ratios greater than 15:1 are therefore seen in volume depletion and in edematous disorders associated with decreased tubular flow (eg, congestive heart failure, cirrhosis, nephrotic syndrome) as well as in obstructive uropathies.** Increases in protein catabolism can also increase this ratio.

URINALYSIS

Urinalysis continues to be routinely performed for evaluating renal function. Although its utility for that purpose is justifiably questionable, urinalysis can be helpful in identifying some disorders of renal tubular dysfunction as well as some nonrenal disturbances. A routine urinalysis typically includes pH; specific gravity; detection and quantification of glucose, protein, and bilirubin content; and microscopic examination of the urinary sediment. Urinary pH is helpful only when arterial pH is also known. A urinary pH greater than 7.0 in the presence of systemic acidosis is suggestive of renal tubular acidosis (see Chapter 50). Specific gravity is related to urinary osmolality; 1.010 usually corresponds to 290 mOsm/kg. A specific gravity greater than 1.018 after an overnight fast is indicative of adequate renal concentrating ability. A lower specific gravity in the presence of hyperosmolality in plasma is consistent with diabetes insipidus.

Glycosuria is the result of either a low tubular threshold for glucose (normally 180 mg/dL) or hyperglycemia. Proteinuria detected by routine urinalysis should be evaluated by means of 24-h urine collection. Urinary protein excretions greater than 150 mg/d are significant. Elevated levels of bilirubin in the urine are seen with biliary obstruction.

Microscopic analysis of the urinary sediment detects the presence of red or white blood cells, bacteria, casts, and crystals. Red cells may be

indicative of bleeding due to tumor, stones, infection, coagulopathy, or trauma. White cells and bacteria are generally associated with infection. Disease processes at the level of the nephron produce tubular casts. Crystals may be indicative of abnormalities in oxalic acid, uric acid, or cystine metabolism.

Altered Renal Function & the Effects of Anesthetic Agents

Most drugs commonly employed during anesthesia (other than volatile anesthetics) are at least partly dependent on renal excretion for elimination. In the presence of renal impairment, dosage modifications may be required to prevent accumulation of the drug or its active metabolites. Moreover, the systemic effects of AKI can potentiate the pharmacological actions of many of these agents. This latter observation may be the result of decreased protein binding of the drug, greater brain penetration due to some breach of the blood–brain barrier, or a synergistic effect with the toxins retained in kidney failure.

INTRAVENOUS AGENTS

Propofol & Etomidate

The pharmacokinetics of both propofol and etomidate are minimally affected by impaired renal function. Decreased protein binding of etomidate in patients with hypoalbuminemia may enhance its pharmacological effects.

Barbiturates

Patients with kidney disease often exhibit increased sensitivity to barbiturates during induction, even though pharmacokinetic profiles appear to be unchanged. The mechanism appears to be an increase in free circulating barbiturate as a result of decreased protein binding. Acidosis may also favor a more rapid entry of these agents into the brain by increasing the nonionized fraction of the drug (see Chapter 26).

Ketamine

Ketamine pharmacokinetics are minimally altered by kidney disease. Some active hepatic metabolites are dependent on renal excretion and can potentially accumulate in kidney failure.

Benzodiazepines

Benzodiazepines undergo hepatic metabolism and conjugation prior to elimination in urine. Because most are highly protein bound, increased sensitivity may be seen in patients with hypoalbuminemia. Diazepam and midazolam should be administered cautiously in the presence of renal impairment because of a potential for the accumulation of active metabolites.

Opioids

Most opioids currently in use in anesthetic management (morphine, meperidine, fentanyl, sufentanil, and alfentanil) are inactivated by the liver; some of these metabolites are then excreted in urine. Remifentanil pharmacokinetics are unaffected by renal function due to rapid ester hydrolysis in blood. With the exception of morphine and meperidine, significant accumulation of active metabolites generally does not occur with these agents. The accumulation of morphine (morphine-6-glucuronide) and meperidine (normeperidine) metabolites has been reported to prolong respiratory depression in patients with kidney failure, and increased levels of normeperidine has been associated with seizures. The pharmacokinetics of the most commonly used opioid agonist–antagonists (butorphanol, nalbuphine, and buprenorphine) are unaffected by kidney failure.

Anticholinergic Agents

In doses used for premedication, atropine and glycopyrrolate can generally be used safely in patients with renal impairment. Because up to 50% of these drugs and their active metabolites are normally excreted in urine, however, the potential for accumulation exists following repeated doses. Scopolamine is less dependent on renal excretion, but its central nervous system effects can be enhanced by the physiological alterations of renal insufficiency.

Phenothiazines, H_2 Blockers, & Related Agents

Most phenothiazines, such as promethazine, are metabolized to inactive compounds by the liver. Droperidol may be partly dependent on the kidneys for excretion. Although their pharmacokinetic profiles are not appreciably altered by renal impairment, potentiation of the central depressant effects of phenothiazines by the physiological milieu of renal insufficiency can occur.

All H_2-receptor blockers are dependent on renal excretion, and their dose must be reduced for patients with renal insufficiency. Proton pump inhibitor dosage does not need to be reduced for patients with renal insufficiency. Metoclopramide is partly excreted unchanged in urine and will accumulate in kidney failure. Although up to 50% of dolasetron is excreted in urine, no dosage adjustments are recommended for any of the 5-HT_3 blockers in patients with renal insufficiency.

INHALATION AGENTS

Volatile Agents

Volatile anesthetic agents are ideal for patients with kidney disease because of lack of dependence on the kidneys for elimination, ability to control blood pressure, and minimal direct effects on renal blood flow. Although patients with mild to moderate renal impairment do not exhibit altered uptake or distribution, accelerated induction and emergence may be seen in severely anemic patients (hemoglobin <5 g/dL) with chronic kidney failure; this observation may be explained by a decrease in the blood:gas partition coefficient or by a decrease in minimum alveolar concentration. Some clinicians avoid sevoflurane (with <2 L/min gas flows) for patients with kidney disease who undergo lengthy procedures (see Chapters 8 and 29).

Nitrous Oxide

Some clinicians omit entirely or limit the use of nitrous oxide to 50% concentration in severely anemic patients with end-stage renal disease in an attempt to increase arterial oxygen content. This may be justified in patients with hemoglobin below 7 g/dL, in whom even a small increase in the dissolved oxygen content may represent a significant percentage of the arterial to venous oxygen difference (see Chapter 23).

MUSCLE RELAXANTS

Succinylcholine

4 Succinylcholine can be safely used in patients with kidney failure, in the absence of hyperkalemia at the time of induction. When the serum potassium is known to be increased or is in doubt, a nondepolarizing muscle relaxant should be substituted. Although decreased plasma cholinesterase levels have been reported in uremic patients following dialysis, significant prolongation of neuromuscular blockade is rarely seen.

Cisatracurium & Atracurium

Cisatracurium and atracurium are degraded by plasma ester hydrolysis and nonenzymatic Hofmann elimination. These agents are often the drugs of choice for muscle relaxation in patients with kidney failure, especially in clinical situations where neuromuscular function monitoring is difficult or impossible.

Vecuronium & Rocuronium

The elimination of vecuronium is primarily hepatic, but up to 20% of the drug is eliminated in urine. The effects of large doses of vecuronium (>0.1 mg/kg) are only modestly prolonged in patients with renal insufficiency. Rocuronium primarily undergoes hepatic elimination, but prolongation in patients with severe kidney disease has been reported. In general, with appropriate neuromuscular monitoring, these two agents can be used with few problems in patients with severe kidney disease.

Curare (d-Tubocurarine)

Elimination of d-tubocurarine is dependent on both renal and biliary excretion; 40–60% of a dose of curare is normally excreted in urine. Increasingly prolonged effects are observed following repeated doses in patients with renal insufficiency. Smaller

doses and longer dosing intervals are therefore required for maintenance of optimal muscle relaxation. In the days before intermediate acting neuromuscular blockers, curare was the nondepolarizing paralytic of choice for patients with kidney disease.

Pancuronium

Pancuronium is primarily dependent on renal excretion (60–90%). Although pancuronium is metabolized by the liver into less active intermediates, its elimination half-life is still primarily dependent on renal excretion (60–80%). Neuromuscular function should be closely monitored if these agents are used in patients with abnormal renal function.

Reversal Agents

Renal excretion is the principal route of elimination for edrophonium, neostigmine, and pyridostigmine. The half-lives of these agents in patients with renal impairment are therefore prolonged at least as much as any of the above relaxants, and problems with inadequate reversal of neuromuscular blockade are usually related to other factors (see Chapter 11). In other words, "recurarization" due to inadequate duration of reversal agents is unlikely.

Anesthesia for Patients with Kidney Failure

PREOPERATIVE CONSIDERATIONS

Acute Kidney Failure

This syndrome is a rapid deterioration in renal function that results in retention of nitrogenous waste products (azotemia). These substances, many of which behave as toxins, are byproducts of protein and amino acid metabolism. Impaired renal metabolism of circulating proteins and peptides may contribute to widespread organ dysfunction.

Kidney failure can be classified as prerenal, renal, and postrenal, depending on its cause(s), and the initial therapeutic approach varies accordingly (see Figure 30–1 and Table 30–3). Prerenal kidney failure results from an acute decrease in renal perfusion; intrinsic kidney failure is usually due to underlying renal disease, renal ischemia, or nephrotoxins; and postrenal failure is the result of urinary tract obstruction or disruption. Both prerenal and postrenal forms of kidney failure are readily reversible in their initial stages but with time progress to intrinsic kidney failure. Most adult patients with kidney failure first develop oliguria. Nonoliguric patients (those with urinary outputs >400 mL/d) continue to form urine that is qualitatively poor; these patients tend to have greater preservation of GFR. Although glomerular filtration and tubular function are impaired in both cases, abnormalities tend to be less severe in nonoliguric kidney failure.

TABLE 30–3 Management priorities in patients with acute kidney failure.[1]

- Search for and correct prerenal and postrenal causes
- Review medications and patient-administered substances and stop any potential nephrotoxins
- Administer medications in doses appropriate for their clearance
- Optimize cardiac output and renal blood flow
- Monitor fluid intake and output; measure body weight daily
- Search for and treat acute complications (hyperkalemia, hyponatremia, acidosis, hyperphosphatemia, pulmonary edema)
- Search for and aggressively treat infections and sepsis
- Provide early nutritional support
- Provide expert supportive care (management of catheter and skin care; pressure sore and deep venous thromboembolic prophylaxis; psychological support).

[1]Reproduced, with permission, from Lameire N, Van Biesen W, Vanholder R: Acute renal failure. Lancet 2005;365:417.

The course of intrinsic acute kidney failure varies widely, but the oliguria typically lasts for 2 weeks and is followed by a diuretic phase marked by a progressive increase in urinary output. This diuretic phase often results in very large urinary outputs and is usually absent in nonoliguric kidney failure. Urinary function improves over the course of several weeks, but may not return to normal for up to 1 year. The course of prerenal and postrenal kidney failure is dependent on correction of the causal condition.

End-Stage Renal Disease

The most common causes of end-stage renal disease (ESRD) are hypertensive nephrosclerosis, diabetic nephropathy, chronic glomerulonephritis, and

TABLE 30–4 Manifestations of uremia.

Neurological	**Metabolic**
Peripheral neuropathy	Metabolic acidosis
Autonomic neuropathy	Hyperkalemia
Muscle twitching	Hyponatremia
Encephalopathy	Hypermagnesemia
Asterixis	Hyperphosphatemia
Myoclonus	Hypocalcemia
Lethargy	Hyperuricemia
Confusion	Hypoalbuminemia
Seizures	**Hematological**
Coma	Anemia
Cardiovascular	Platelet dysfunction
Fluid overload	Leukocyte dysfunction
Congestive heart failure	**Endocrine**
Hypertension	Glucose intolerance
Pericarditis	Secondary hyperparathyroidism
Arrhythmia	Hypertriglyceridemia
Conduction blocks	**Skeletal**
Vascular calcification	Osteodystrophy
Accelerated atherosclerosis	Periarticular calcification
Pulmonary	**Skin**
Hyperventilation	Hyperpigmentation
Interstitial edema	Ecchymosis
Alveolar edema	Pruritus
Pleural effusion	
Gastrointestinal	
Anorexia	
Nausea and vomiting	
Delayed gastric emptying	
Hyperacidity	
Mucosal ulcerations	
Hemorrhage	
Adynamic ileus	

TABLE 30–5 Complications of hemodialysis.

Neurological
Disequilibrium syndrome
Dementia
Cardiovascular
Intravascular volume depletion
Hypotension
Arrhythmia
Pulmonary
Hypoxemia
Gastrointestinal
Ascites
Hematological
Anemia
Transient neutropenia
Residual anticoagulation
Hypocomplementemia
Metabolic
Hypokalemia
Large protein losses
Skeletal
Osteomalacia
Arthropathy
Myopathy
Infectious
Peritonitis
Transfusion-related hepatitis

polycystic kidney disease. The uncorrected manifestations of this syndrome (Table 30–4)—collectively referred to as **uremia**—are usually seen only after the GFR decreases below 25 mL/min. Patients with GFR below 10 mL/min are dependent on renal replacement therapy (RRT) for survival. RRT may take the form of hemodialysis, hemofiltration, peritoneal dialysis, or renal transplantation.

The generalized effects of uremia can usually be controlled by RRT. The majority of patients who do not undergo renal transplantation receive hemodialysis three times per week, and there are complications directly related to hemodialysis itself (Table 30–5). Hypotension, neutropenia, hypoxemia, and the disequilibrium syndrome are generally transient and resolve within hours after hemodialysis. Factors contributing to hypotension during dialysis include the vasodilating effects of acetate dialysate solutions, autonomic neuropathy, and rapid removal of fluid. The interaction of white cells with cellophane-derived dialysis membranes can result in neutropenia and leukocyte-mediated pulmonary dysfunction leading to hypoxemia. Disequilibrium syndrome is characterized by transient neurological symptoms that appear to be related to a more rapid lowering of extracellular osmolality than intracellular osmolality.

Manifestations of Kidney Failure

A. Metabolic

Multiple metabolic abnormalities, including hyperkalemia, hyperphosphatemia, hypocalcemia, hypermagnesemia, hyperuricemia, and hypoalbuminemia, typically develop in patients with kidney failure. Water and sodium retention can result in worsening hyponatremia and extracellular fluid overload, respectively. Failure to excrete nonvolatile acids produces a high anion gap metabolic acidosis (see

Chapter 50). Hypernatremia and hypokalemia are uncommon complications.

Hyperkalemia is a potentially lethal consequence of kidney failure (see Chapter 49). It usually occurs in patients with creatinine clearances of less than 5 mL/min, but it can also develop rapidly in patients with higher clearances in the setting of large potassium loads (eg, trauma, hemolysis, infections, or potassium administration).

The hypermagnesemia is generally mild unless magnesium intake is increased (commonly from magnesium-containing antacids). Hypocalcemia is secondary to resistance to parathyroid hormone, decreased intestinal calcium absorption secondary to decreased renal synthesis of 1,25-dihydroxycholecalciferol, and hyperphosphatemia-associated calcium deposition into bone. Symptoms of hypocalcemia rarely develop unless patients are also alkalotic.

Patients with kidney failure also rapidly lose tissue protein and readily develop hypoalbuminemia. Anorexia, protein restriction, and dialysis are contributory.

B. Hematological

Anemia is nearly always present when the creatinine clearance is below 30 mL/min. Hemoglobin concentrations are generally 6–8 g/dL due to decreased erythropoietin production, decreased red cell production, and decreased red cell survival. Additional factors may include gastrointestinal blood loss, hemodilution, and bone marrow suppression from recurrent infections. Even with transfusions, it is often difficult to maintain hemoglobin concentrations greater than 9 g/dL. Erythropoietin administration may partially correct the anemia. Increased levels of 2,3-diphosphoglycerate (2,3-DPG), which facilitates the unloading of oxygen from hemoglobin (see Chapter 23), develop in response to the decrease in blood oxygen-carrying capacity. The metabolic acidosis associated with ESRD also favors a rightward shift in the hemoglobin–oxygen dissociation curve. In the absence of symptomatic heart disease, most ESRD patients tolerate anemia well.

Both platelet and white cell function are impaired in patients with kidney failure. Clinically, this is manifested as a prolonged bleeding time and increased susceptibility to infections, respectively. Most patients have decreased platelet factor III activity as well as decreased platelet adhesiveness and aggregation. Patients who have recently undergone hemodialysis may also have residual anticoagulant effects from heparin.

C. Cardiovascular

Cardiac output increases in kidney failure to maintain oxygen delivery due to decreased blood oxygen-carrying capacity. Sodium retention and abnormalities in the renin–angiotensin system result in systemic arterial hypertension. Left ventricular hypertrophy is a common finding in ESRD.

5 Extracellular fluid overload from sodium retention, in association with increased cardiac demand imposed by anemia and hypertension, makes ESRD patients prone to congestive heart failure and pulmonary edema. Increased permeability of the alveolar–capillary membrane may also be a predisposing factor for pulmonary edema associated with ESRD (see below). Arrhythmias, including conduction blocks, are common, and may be related to metabolic abnormalities and to deposition of calcium in the conduction system. Uremic pericarditis may develop in some patients, who may be asymptomatic, may present with chest pain, or may present with cardiac tamponade. Patients with ESRD also characteristically develop accelerated peripheral vascular and coronary artery atherosclerotic disease.

Intravascular volume depletion may occur in high-output acute kidney failure if fluid replacement is inadequate. Hypovolemia may occur secondary to excessive fluid removal during dialysis.

D. Pulmonary

Without RRT or bicarbonate therapy, ESRD patients may be dependent on increased minute ventilation as compensation for metabolic acidosis (see Chapter 50). Pulmonary extravascular water is often increased in the form of interstitial edema, resulting in a widening of the alveolar to arterial oxygen gradient and predisposing to hypoxemia. Increased permeability of the alveolar–capillary membrane in some patients can result in pulmonary edema even with normal pulmonary capillary pressures.

E. Endocrine

Abnormal glucose tolerance is common in ESRD, usually resulting from peripheral insulin resistance

(indeed, type 2 diabetes mellitus is one of the most common causes of ESRD). Secondary hyperparathyroidism in patients with chronic kidney failure can produce metabolic bone disease, with osteopenia predisposing to fractures. Abnormalities in lipid metabolism frequently lead to hypertriglyceridemia and contribute to accelerated atherosclerosis. Increased circulating levels of proteins and polypeptides normally degraded by the kidneys are often present, including parathyroid hormone, insulin, glucagon, growth hormone, luteinizing hormone, and prolactin.

F. Gastrointestinal

Anorexia, nausea, vomiting, and adynamic ileus are commonly associated with uremia. Hypersecretion of gastric acid increases the incidence of peptic ulceration and gastrointestinal hemorrhage, which occurs in 10–30% of patients. Delayed gastric emptying secondary to autonomic neuropathy may predispose patients to perioperative aspiration. Patients with chronic kidney failure also have an increased incidence of hepatitis B and C, often with associated hepatic dysfunction.

G. Neurological

Asterixis, lethargy, confusion, seizures, and coma are manifestations of uremic encephalopathy, and symptoms usually correlate with the degree of azotemia. Autonomic and peripheral neuropathies are common in patients with ESRD. Peripheral neuropathies are typically sensory and involve the distal lower extremities.

Preoperative Evaluation

The systemic effects of kidney failure mandate a thorough evaluation of the patient. Most perioperative patients with acute kidney failure are critically ill, and their kidney failure is frequently associated with trauma or postoperative complications. Patients with acute kidney failure also tend to be in a catabolic metabolic state. Optimal perioperative management is dependent on dialysis. Hemodialysis is more effective than peritoneal dialysis and can be readily accomplished via a temporary internal jugular, subclavian, or femoral dialysis catheter. Continuous renal replacement therapy (CRRT) is often used when patients are too hemodynamically unstable to tolerate intermittent hemodialysis. Indications for dialysis are listed in Table 30–6.

TABLE 30–6 Indications for dialysis.

Fluid overload
Hyperkalemia
Severe acidosis
Metabolic encephalopathy
Pericarditis
Coagulopathy
Refractory gastrointestinal symptoms
Drug toxicity

Patients with chronic kidney failure commonly present to the operating room for creation or revision of an arteriovenous dialysis fistula under local or regional anesthesia. However, regardless of the intended procedure or the anesthetic employed, one must be certain that the patient is in optimal medical condition; potentially reversible manifestations of uremia (see Table 30–4) should be addressed. Preoperative dialysis on the day of surgery or on the previous day is typical.

The history and physical examination should address both cardiac and respiratory function. Signs of fluid overload or hypovolemia should be sought. Patients are often relatively hypovolemic immediately following dialysis. A comparison of the patient's current weight with previous predialysis and postdialysis weights may be helpful. Hemodynamic data and a chest radiograph, if available, are useful in confirming clinical impressions. Arterial blood gas analysis is useful in evaluating oxygenation, ventilation, hemoglobin level, and acid–base status in patients with dyspnea or tachypnea. The electrocardiogram should be examined for signs of hyperkalemia or hypocalcemia (see Chapter 49) as well as ischemia, conduction block, and ventricular hypertrophy. Echocardiography can assess cardiac function, ventricular hypertrophy, wall motion abnormalities, and pericardial fluid. A friction rub may not be audible on auscultation of patients with a pericardial effusion.

Preoperative red blood cell transfusions are usually administered only for severe anemia as guided by the patient's clinical needs. A bleeding time and coagulation studies may be advisable, particularly if neuraxial anesthesia is being considered. Serum

TABLE 30–7 Drugs with a potential for significant accumulation in patients with renal impairment.

- **Muscle relaxants**
  - Pancuronium
- **Anticholinergics**
  - Atropine
  - Glycopyrrolate
- **Metoclopramide**
- **H_2-receptor antagonists**
  - Cimetidine
  - Ranitidine
- **Digitalis**
- **Diuretics**
- **Calcium channel antagonists**
  - Diltiazem
  - Nifedipine
- **β-Adrenergic blockers**
  - Atenolol
  - Nadolol
  - Pindolol
  - Propranolol
- **Antihypertensives**
  - Captopril
  - Clonidine
  - Enalapril
  - Hydralazine
  - Lisinopril
  - Nitroprusside (thiocyanate)
- **Antiarrhythmics**
  - Bretylium
  - Disopyramide
  - Encainide (genetically determined)
  - Procainamide
  - Tocainide
- **Bronchodilators**
  - Terbutaline
- **Psychiatric**
  - Lithium
- **Antibiotics**
  - Aminoglycosides
  - Cephalosporins
  - Penicillins
  - Tetracycline
  - Vancomycin
- **Anticonvulsants**
  - Carbamazepine
  - Ethosuximide
  - Primidone

electrolyte, BUN, and creatinine measurements can assess the adequacy of dialysis. Glucose measurements guide the potential need for perioperative insulin therapy.

Drugs with significant renal elimination should be avoided if possible (Table 30–7). Dosage adjustments and measurements of blood levels (when available) are necessary to minimize the risk of drug toxicity.

Premedication

Alert patients who are stable can be given reduced doses of a benzodiazepine or an opioid, if needed. Aspiration prophylaxis with an H_2 blocker or proton pump inhibitor may be indicated in patients with nausea, vomiting, or gastrointestinal bleeding. Metoclopramide, 10 mg orally or slowly intravenously, may be useful in accelerating gastric emptying and decreasing the risk of aspiration. Preoperative medications—particularly antihypertensive agents—should be continued until the time of surgery (see Chapter 21). The management of diabetic patients is discussed in Chapter 34.

INTRAOPERATIVE CONSIDERATIONS

Monitoring

Patients with renal insufficiency and kidney failure are at increased risk of perioperative complications, and their general medical condition and the planned operative procedure dictate monitoring requirements. Because of the risk of thrombosis, blood pressure should not be measured by a cuff on an arm with an arteriovenous fistula. Continuous intraarterial blood pressure monitoring may also be indicated in patients with poorly controlled hypertension, regardless of the procedure.

Induction

Patients with nausea, vomiting, or gastrointestinal bleeding should undergo rapid-sequence induction. The dose of the induction agent should be reduced for debilitated or critically ill patients, or for patients who have recently undergone hemodialysis (because of relative hypovolemia immediately following hemodialysis). Propofol, 1–2 mg/kg, or etomidate, 0.2–0.4 mg/kg, is often used. An opioid, β blocker (esmolol), or lidocaine may be used to blunt the hypertensive response to airway instrumentation and intubation. Succinylcholine, 1.5 mg/kg, can be used to facilitate endotracheal intubation in the absence of hyperkalemia. Vecuronium (0.1 mg/kg) or cisatracurium (0.15 mg/kg), or propofol–lidocaine induction without a relaxant, may be considered for intubation in patients with hyperkalemia.

Anesthesia Maintenance

The ideal anesthetic maintenance technique should control hypertension with minimal deleterious effect on cardiac output, because increased cardiac output is the principal compensatory mechanism for tissue oxygen delivery in anemia. Volatile anesthetics, propofol, fentanyl, sufentanil, alfentanil, and remifentanil are satisfactory maintenance agents. Nitrous oxide should be used cautiously in patients with poor ventricular function and should probably not

be used for patients with very low hemoglobin concentrations (<7 g/dL) to allow the administration of 100% oxygen (see above). Meperidine is not an ideal choice because of the accumulation of its metabolite normeperidine. Morphine may be used, but some prolongation of its effects should be expected.

7 Controlled ventilation should be considered for patients with kidney failure. Inadequate spontaneous ventilation with progressive hypercarbia under anesthesia can result in respiratory acidosis that may exacerbate preexisting acidemia, lead to potentially severe circulatory depression, and dangerously increase serum potassium concentration (see Chapter 50). On the other hand, respiratory alkalosis may also be detrimental because it shifts the hemoglobin dissociation curve to the left, can exacerbate preexisting hypocalcemia, and may reduce cerebral blood flow.

Fluid Therapy

Superficial operations involving minimal tissue trauma require replacement of only insensible fluid losses. Procedures associated with major fluid losses require isotonic crystalloids, colloids, or both (see Chapter 51). Lactated Ringer's injection is best avoided in hyperkalemic patients when large volumes of fluid may be required, because it contains potassium (4 mEq/L); normal saline may be used instead. Glucose-free solutions should generally be used because of the glucose intolerance associated with uremia. Blood that is lost should generally be replaced with colloid or packed red blood cells as clinically indicated. Allogeneic blood transfusion may decrease the likelihood of rejection following renal transplantation because of associated immunosuppression.

Anesthesia for Patients with Mild to Moderate Renal Impairment

PREOPERATIVE CONSIDERATIONS

The kidney normally possesses large functional reserve. GFR, as determined by creatinine clearance, can decrease from 120 to 60 mL/min without any clinically perceptible change in renal function. Even patients with creatinine clearances of 40–60 mL/min usually are asymptomatic. These patients have only mild renal impairment but should still be thought of as having decreased renal reserve. The emphasis in the care of these patients is preservation of the remaining renal function, which is best accomplished by maintaining normovolemia and normal renal perfusion.

When creatinine clearance decreases to 25–40 mL/min, renal impairment is moderate, and patients are said to have renal insufficiency. Azotemia is always present, and hypertension and ane-

8 mia are common. Correct anesthetic management of this group of patients is as critical as management of those with frank kidney failure, especially during procedures associated with a relatively high incidence of postoperative kidney failure, such as cardiac and aortic recon-

9 structive surgery. Intravascular volume depletion, sepsis, obstructive jaundice, crush injuries, and renal toxins such as radiocontrast agents, certain antibiotics, angiotensin-converting enzyme inhibitors, and NSAIDs (see Table 29–4) are additional major risk factors for acute deterioration in renal function. Hypovolemia and decreased renal perfusion are particularly important causative factors in the development of acute postoperative kidney failure. The emphasis in management of these patients is on prevention, because the mortality rate of postoperative kidney failure may surpass 50%. The combination of diabetes and preexisting kidney disease markedly increases the perioperative risk of renal function deterioration and of kidney failure.

10 Renal protection with adequate hydration and maintenance of renal blood flow is indicated for patients at high risk for kidney injury and kidney failure undergoing cardiac, major aortic reconstructive, and other surgical procedures associated with significant physiological trespass. The use of mannitol, low-dose dopamine infusion, loop diuretics, or fenoldopam for renal protection is controversial and without conclusive proof of efficacy (see above). The value of renal protection with *N*-acetylcysteine prior to the administration of radiocontrast agents is reviewed in Chapter 29.

INTRAOPERATIVE CONSIDERATIONS

Monitoring

The American Society of Anesthesiologists' basic monitoring standards are used for procedures involving minimal fluid losses. For procedures associated with significant blood or fluid loss, close monitoring of hemodynamic performance and urinary output is useful (see Chapter 51). Although maintenance of urinary output does not ensure preservation of renal function, urinary outputs greater than 0.5 mL/kg/h are preferable. Continuous intraarterial blood pressure monitoring is also important if rapid changes in blood pressure are anticipated, such as in patients with poorly controlled hypertension and in those undergoing procedures associated with abrupt changes in sympathetic stimulation or in cardiac preload or afterload.

Induction

Selection of an induction agent is not as important as ensuring an adequate intravascular volume prior to induction; induction of anesthesia in hypovolemic patients with renal insufficiency frequently results in hypotension. Unless a vasopressor is administered, such hypotension typically resolves only following intubation or surgical stimulation. Renal perfusion, which may already be compromised by preexisting hypovolemia, may then deteriorate further, first as a result of hypotension, and subsequently from sympathetically or pharmacologically mediated renal vasoconstriction. If sustained, the decrease in renal perfusion may contribute to postoperative renal impairment or failure. Preoperative hydration usually prevents this sequence of events.

Maintenance of Anesthesia

All anesthetic maintenance agents are acceptable, with the possible exception of sevoflurane administered with low gas flows over a prolonged time period. Intraoperative deterioration in renal function may result from adverse effects of the operative procedure (hemorrhage, vascular occlusion, abdominal compartment syndrome, arterial emboli) or anesthetic (hypotension secondary to myocardial depression or vasodilation), from indirect hormonal effects (sympathoadrenal activation or antidiuretic hormone secretion), or from impeded venous return secondary to positive-pressure ventilation. Many of these effects are almost completely avoidable or reversible when adequate intravenous fluids are given to maintain a normal or slightly expanded intravascular volume. The administration of large doses of predominantly α-adrenergic vasopressors (phenylephrine and norepinephrine) may also be detrimental to preservation of renal function. Small, intermittent doses, or brief infusions, of vasoconstrictors may be useful in maintaining renal blood flow until other measures (eg, transfusion) are undertaken to correct hypotension.

Fluid Therapy

As reviewed above, appropriate fluid administration is important in managing patients with impaired renal function. Concern over fluid overload is justified, but problems are rarely encountered in such patients with normal urinary outputs if rational fluid administration guidelines and appropriate monitoring are employed (see Chapter 51). The adverse consequences of excessive fluid overload—namely, pulmonary congestion or edema—are far easier to treat than those of AKI and kidney failure.

CASE DISCUSSION

A Patient with Uncontrolled Hypertension

A 59-year-old man with a recent onset of hypertension is scheduled for reconstruction of a stenotic left renal artery. His preoperative blood pressure is 180/110 mm Hg.

What is the likely cause of this patient's hypertension?

Renovascular hypertension is one of the few surgically correctable forms of hypertension. Others include coarctation of the aorta, pheochromocytoma, Cushing's disease, and primary hyperaldosteronism.

Most studies suggest that renovascular hypertension accounts for 2–5% of all cases of hypertension. Characteristically it manifests as a relatively sudden onset of hypertension in persons younger than 35 years or older than 55 years of age. Renal artery stenosis can also be responsible for the development of accelerated or malignant hypertension in previously hypertensive persons of any age.

What is the pathophysiology of the hypertension?

Unilateral or bilateral stenosis of the renal artery decreases the perfusion pressure to the kidney(s) distal to the obstruction. Activation of the juxtaglomerular apparatus and release of renin increase circulating levels of angiotensin II and aldosterone, resulting in peripheral vascular constriction and sodium retention, respectively. The resulting systemic arterial hypertension is often severe.

In nearly two thirds of patients, the stenosis results from an atheromatous plaque in the proximal renal artery. These patients are typically men over the age of 55 years. In the remaining one third of patients, the stenosis is more distal and is due to malformations of the arterial wall, commonly referred to as *fibromuscular hyperplasia* (or, *dysplasia*). This latter lesion most commonly presents in women younger than 35 years. Bilateral renal artery stenosis is present in 30–50% of patients with renovascular hypertension. Less common causes of stenosis include dissecting aneurysms, emboli, polyarteritis nodosa, radiation, trauma, extrinsic compression from retroperitoneal fibrosis or tumors, and hypoplasia of the renal arteries.

What clinical manifestations other than hypertension may be present?

Signs of secondary hyperaldosteronism can be prominent. These include sodium retention in the form of edema, metabolic alkalosis, and hypokalemia. The latter can cause muscle weakness, polyuria, and even tetany.

How is the diagnosis made?

The diagnosis is suggested by the clinical presentation previously described. A midabdominal bruit may also be present, but the diagnosis requires laboratory and radiographic confirmation. A definitive diagnosis is made by renal arteriography, and percutaneous balloon angioplasty with stenting may be performed at the same time. The functional significance of the restrictive lesion(s) may be evaluated by selective catheterization of both renal veins and subsequent measurement of plasma renin activity in blood from each kidney. Restenosis rates following angioplasty are estimated to be <15% after 1 year. Patients who are not candidates for angioplasty and stenting are referred for surgery.

Should this patient undergo surgical correction given his present blood pressure?

Optimal medical therapy is important in preparing these patients for operation. Relative to patients with well-controlled hypertension, those with poorly controlled hypertension have a high incidence of intraoperative problems including marked hypertension, hypotension, myocardial ischemia, and arrhythmias. Ideally, arterial blood pressure should be well controlled prior to surgery. Patients should be evaluated for preexisting renal dysfunction, and metabolic disturbances such as hypokalemia should be corrected. Patients should also be evaluated as indicated for the presence and severity of coexisting atherosclerotic disease, according to current ACC/AHA guidelines (see Chapter 21).

What antihypertensive agents are most useful for controlling blood pressure perioperatively in these patients?

β-Adrenergic blocking drugs are frequently utilized for blood pressure control in the perioperative period. They are particularly effective because secretion of renin is partly mediated by β_1-adrenergic receptors. Although parenteral selective β_1-blocking agents such as metoprolol and esmolol would be expected to be most effective, nonselective agents such as propranolol appear equally effective. Esmolol may be the intraoperative β_1-blocking agent of choice because of its short half-life and titratability.

Direct vasodilators such as nitroprusside and nitroglycerin are also useful in controlling intraoperative hypertension.

ACE inhibitors and angiotensin converting enzyme receptor blockers are contraindicated in bilateral renal artery stenosis or in unilateral renal artery stenosis where there is only one functioning kidney because they can precipitate kidney failure.

What intraoperative considerations are important for the anesthesia provider?

Revascularization of a kidney is a major procedure, with the potential for major blood loss, fluid shifts, and hemodynamic changes. One of several procedures may be performed, including transaortic renal endarterectomy, aortorenal bypass (using a saphenous vein, synthetic graft, or segment of the hypogastric artery), a splenic to (left) renal artery bypass, a hepatic or gastroduodenal to (right) renal artery bypass, or excision of the stenotic segment with reanastomosis of the renal artery to the aorta. Rarely, nephrectomy may be performed. Regardless of the procedure, an extensive retroperitoneal dissection often necessitates relatively large volumes of intravenous fluid replacement. Large-bore intravenous access is mandatory because of the potential for extensive blood loss. Heparinization contributes to increased blood loss. Depending on the surgical technique, aortic cross-clamping, with its associated hemodynamic consequences, often complicates anesthetic management (see Chapter 22). Continuous intraarterial blood pressure monitoring is mandatory, and central venous pressure monitoring is often very helpful. Goal-directed hemodynamic and fluid therapy utilizing arterial pulse contour analysis, esophageal Doppler, or transesophageal echocardiography should be considered for patients with poor ventricular function, and may be advisable in most patients to guide fluid management (see Chapter 51). The choice of anesthetic technique is generally determined by the patient's cardiovascular function.

Urinary output should be followed carefully. Generous hydration and maintenance of adequate cardiac output and blood pressure are important to protect both the affected and the normal kidney against acute ischemic injury. Topical cooling of the affected kidney during the anastomosis may also be employed.

What postoperative considerations are important?

Although in most patients hypertension is ultimately cured or significantly improved, arterial blood pressure is often quite labile in the early postoperative period. Close hemodynamic monitoring should be continued well into the postoperative period. Reported operative mortality rates range from 1% to 6%, and most deaths are associated with myocardial infarction. The latter probably reflects the relatively high prevalence of coronary artery disease in older patients with renovascular hypertension.

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