Chapter 29
Acute Kidney Injury

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Introduction

Acute kidney injury (AKI) is defined as a deterioration in kidney function, detected by an increase in serum creatinine and decrease in glomerular filtration rate (GFR). Urine output during AKI can be variable, ranging from non-oliguria (> 400 mL/day), oliguria (< 400 mL/day), to anuria (< 100 mL/day). Many classification systems have been used for the diagnosis of AKI, including the RIFLE (Risk, Injury, Failure, Loss of Kidney Function and End-Stage Renal Disease) criteria, the Acute Kidney Injury Network (AKIN) staging, and the Kidney Disease Improving Global Outcomes (KDIGO) criteria [1–4] (Tables 29.1 and 29.2). In general, AKI is defined as an absolute change in serum creatinine by ≥ 0.3 mg/dL within 48 h, or an increase in serum creatinine ≥ 1.5 times from baseline within the prior 7 days, or a urine volume < 0.5 mL/kg/h for 6 h [5]. KDIGO criteria combine RIFLE and AKIN criteria [3] (Table 29.2). Although serum

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Table 29.1 RIFLE criteria

	Serum creatinine	GFR	Urine output
Risk	Increased ×1.5	Decreased > 25%	< 0.5 mL/kg/h × 6 h
Injury	Increased ×2	Decreased > 50%	< 0.5 mL/kg/h × 12 h
Failure	Increased ×3 or SCr ≥ 4 mg/dL (with acute rise ≥ 0.5 mg/dL)	Decreased > 75%	< 0.3 mL/kg/h × 24 h or anuria × 12 h
Loss	Complete loss of renal function for > 4 weeks requiring dialysis		
ESRD	End-stage renal disease (> 3 months)		

GFR glomerular filtration rate, *SCr* serum creatinine
Adapted from references [1, 4]

creatinine is a commonly used marker for kidney function, it has several limitations. Gender and muscle mass can influence the serum creatinine value; lower levels are observed in females, malnourished patients, and in those with low muscle mass and liver disease. Some medications (trimethoprim) can affect the tubular secretion of creatinine, resulting in higher creatinine levels despite no change in GFR.

AKI is very common in the hospital setting and is associated with a high risk of mortality and increased risk of chronic kidney disease (CKD) [6]. Community-acquired AKI is similarly associated with increased risk of CKD and risk of death [7]. Sometimes it is difficult to distinguish whether the elevated serum creatinine is the result of an acute process or represents progression of CKD, especially when a baseline

TABLE 29.2 AKIN and KDIGO staging (Adapted from references [2–4])

AKIN staging			KDIGO staging		
Stage	**Serum creatinine**	**Urine output**	**Stage**	**Serum creatinine**	**Urine output**
1	Increased ×1.5 or ≥ 0.3 mg/dL from baseline	< 0.5 mL/kg/h × 6 h	1	1.5–1.9× baseline or ≥ 0.3 mg/dL	< 0.5 mL/kg/h × 6–12 h
2	Increased ×2 from baseline	< 0.5 mL/kg/h × 12 h	2	2.0–2.9× baseline	< 0.5 mL/kg/h × ≥ 12 h
3	Increased ×3 from baseline or Cr ≥ 4 mg/dL (with acute rise ≥ 0.5 mg/dL) or all those patients who receive RRT	< 0.3 mL/kg/h × 24 h or anuria ×12 h	3	3.0× baseline or increase to ≥ 4.0 mg/dL or initiation of RRT or in patients < 18 years, decrease in eGFR to < 35 mL/min per 1.73 m^2	< 0.3 mL/kg/h × ≥ 24 h or anuria × ≥ 12 h

eGFR estimated glomerular filtration rate, *RRT* renal replacement therapy

serum creatinine is not available. Sonographic findings of small echogenic kidneys and laboratory evidence of anemia and secondary hyperparathyroidism are suggestive of CKD.

Differential Diagnosis

AKI is classified into prerenal, intrinsic, and postrenal depending on the etiology (Algorithm 1, Fig. 29.1) [8, 9]. Prerenal AKI results from compromised renal perfusion due to decreased volume (from gastrointestinal or renal losses), effective volume depletion (seen in patients with congestive

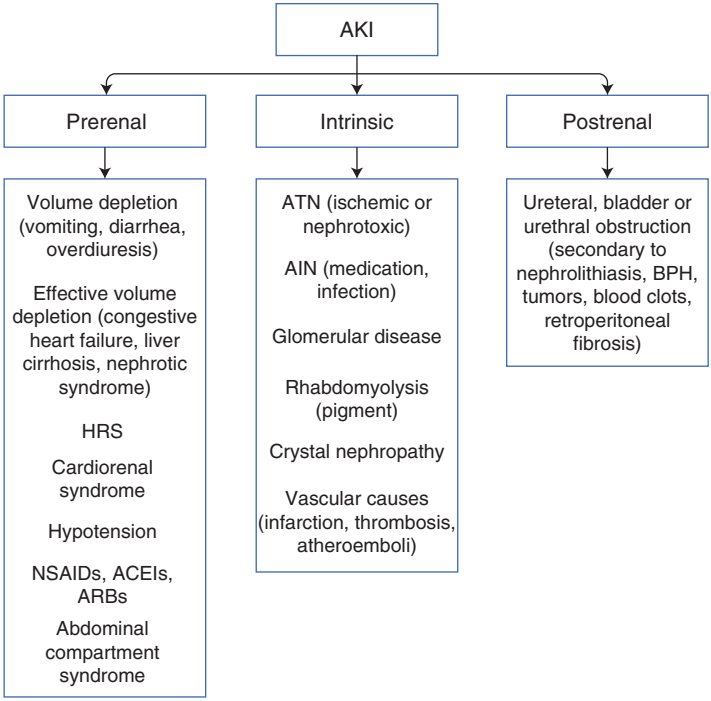

Fig. 29.1 Classification of AKI into prerenal, intrinsic, and postrenal

heart failure, liver disease, or nephrotic syndrome), or hypotension related to sepsis. In those with advanced liver disease, hepatorenal syndrome (HRS) is a form of prerenal AKI and is a diagnosis of exclusion. Nonsteroidal anti-inflammatory drugs (NSAIDs) can compromise renal perfusion due to impaired prostaglandin-mediated afferent arteriolar vasodilatation. GFR can also decline in patients taking angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) due to impaired compensatory vasoconstriction of the efferent arteriole in the setting of impaired renal perfusion.

Intrinsic AKI can be categorized according to the compartment involved: tubular, interstitial, glomerular, or vascular. Acute tubular necrosis results from either prolonged ischemic injury or nephrotoxic injury [10]. Other forms of tubular injury include myoglobinuria from rhabdomyolysis and hemoglobinuria from hemolysis, which can lead to pigment nephropathy. Crystal deposition can be seen with numerous drugs (acyclovir) and tumor lysis syndrome. The involvement of the interstitial compartment in acute interstitial nephritis (AIN) can be secondary to medication, infections, and other systemic diseases. The triad of rash, eosinophilia, and fever is not commonly seen (occurs in 5–10% of cases), and eosinophiluria has a low specificity and sensitivity for the diagnosis of AIN [11]. Glomerulonephritis is characterized by proteinuria, hematuria, and presence of dysmorphic red blood cells (RBCs) and RBC casts in the urinary sediment. Vascular events such as acute renal infarction, renal vein thrombosis and atheroemboli are other causes of intrinsic AKI.

Postrenal AKI results from obstruction of both kidneys or ureters (unless the patient has a single functioning kidney) or the bladder outlet. Benign prostate hypertrophy (BPH), nephrolithiasis, or masses are potential culprits. Renal ultrasound (US) is often helpful, but in retroperitoneal fibrosis and acute obstruction (< 48 h), hydronephrosis can be absent. (Fig. 29.1)

Key History and Physical Exam

A detailed history focused on certain symptoms is essential (Fig. 29.2) [8]. The clinician should inquire about symptoms suggestive of volume loss (vomiting, diarrhea, and excessive diuresis), weight loss, and decreased oral intake. Urinary symptoms such as difficulty with urination, decreased urine output, hematuria, and foamy urine should be reviewed. A review of systems with other associated symptoms, including flank pain, fever, or chills should be completed. A thorough review of the medication list, documenting use of over-the-counter medications, supplements, NSAIDs, proton pump inhibitors (PPIs), and recent medications taken (antibiotics), is of great importance. In the hospital setting, review of recent events (hypotension, recent cardiac catheterization, or contrast administration) could be revealing and point to the etiology of AKI.

Physical examination (Fig. 29.3) should include assessment of vital signs and weight. The physician should evaluate for the presence of exam findings suggestive of volume overload (neck vein distention, S3, crackles, and peripheral edema) or volume depletion (orthostasis, dry mucous membranes, and

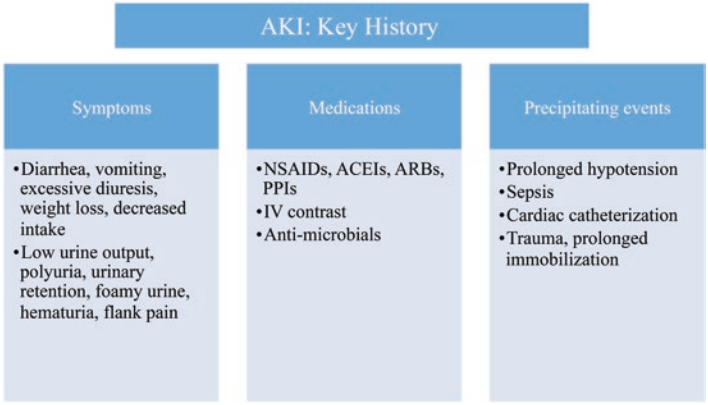

FIG. 29.2 Key elements in the history taking of a patient with AKI

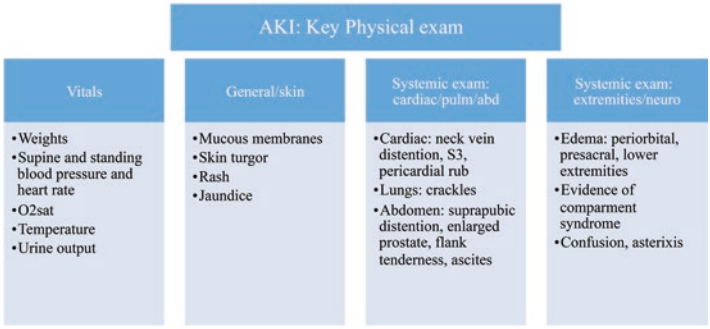

FIG. 29.3 Key elements in the physical examination of a patient with AKI

decreased skin turgor). A thorough exam should evaluate for flank tenderness and for the presence of suprapubic distention. Signs of uremia (pericardial rub, confusion, asterixis) should be evaluated carefully. The clinician should also conduct a thorough skin examination, looking for rash, petechiae, purpura, or skin color changes. In those with history of trauma or recent surgery, the clinician should assess for presence of compartment syndrome on physical exam.

Decision-Making/Treatment

The initial work-up of AKI involves the evaluation of a urinalysis (UA) to assess the urine specific gravity, pH, and for the presence of proteinuria, hematuria, and pyuria (Algorithm 2, Fig. 29.4) [8]. Evaluation of the urine sediment is crucial [12]. The presence of casts and cells can point toward the etiology of kidney injury: granular/muddy brown casts and renal tubular epithelial cell casts are seen in ATN and pigmented casts in rhabdomyolysis and hemolysis, and white blood cell (WBC) casts are suggestive of AIN or pyelonephritis. Hyaline casts are nonspecific and can be seen in patients with prerenal AKI or those with a concentrated urine. The presence of dysmorphic RBCs and RBC

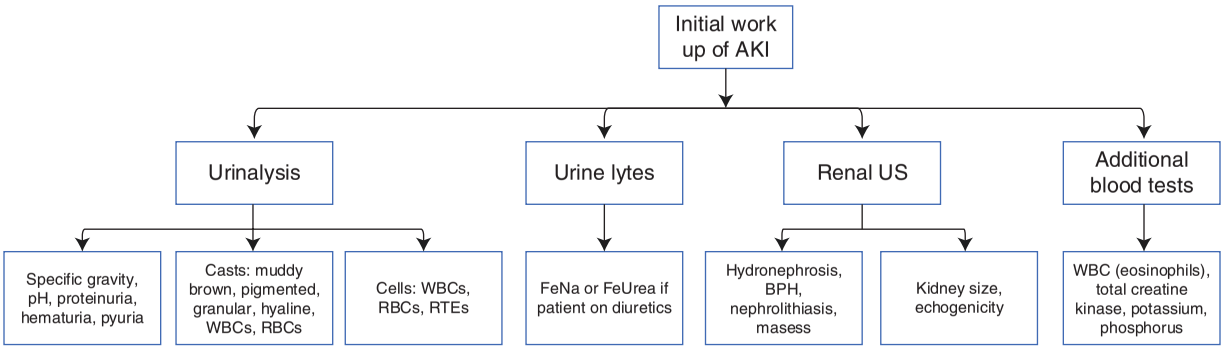

FIG. 29.4 Initial laboratory and radiologic testing in a patient with AKI

casts is suggestive of a glomerulonephritis, while isomorphic RBCs are typically seen in patients with nephrolithiasis and tumors.

The fractional excretion of sodium (FENa), calculated as FENa = (urinary sodium/plasma sodium) × (plasma creatinine/urinary creatinine) × 100, is typically low (< 1%) in AKI from prerenal etiologies and high (> 2%) in the setting of other etiologies of AKI [13]. The fractional excretion of urea (FeUrea), calculated as FeUrea = (urinary urea/plasma urea) × (plasma creatinine/urinary creatinine) × 100, is more useful in those patients that have been taking diuretics. A value < 35% is suggestive of prerenal azotemia, while > 50% suggests ATN. However these urine chemistries suffer from low sensitivity and specificity [14].

A renal US is valuable when obstruction is suspected, especially if the patient has a large postvoid residual (defined as > 100 mL of urine) or cancers that involve the retroperitoneum. Lastly, kidney biopsy may be necessary if the cause of AKI remains unclear (Fig. 29.4).

The treatment of AKI is directed toward correcting the underlying etiology and providing supportive measures. Other important steps include as follows:

- Prompt relief of obstruction and monitoring for post obstructive diuresis.
- Avoiding further nephrotoxins is essential.
- Medications should be dosed for the patient's renal function (based on either creatinine clearance or estimated GFR).
- Hydration with intravenous isotonic fluids (IVFs) can be used if the clinical scenario is suggestive of volume depletion, but care should be undertaken if the patient is oliguric or anuric, as volume overload is a common complication.
- Diuretics can be used if the patient has evidence of volume overload [15].
- The clinician should monitor carefully for indications that would prompt dialysis, such as refractory hyperkalemia, acidosis, volume overload, uremic encephalopathy, and uremic pericarditis.

Clinical Pearls

- A thorough history and physical examination are essential in patients with AKI.
- ACEIs and ARBs can cause an increase in serum creatinine level. A change of 20–30% is acceptable. In patients with a higher increase in serum creatinine, hypotension, or significant hyperkalemia (serum potassium > 5.5 mEq/L), the ACEI or ARB should be discontinued.
- Use phosphate-containing bowel preparations with caution in patients with CKD, as acute phosphate nephropathy can occur.
- For prevention of contrast-induced AKI, minimize contrast volume and provide isotonic fluid when possible. Dialysis has no role in prevention of contrast-induced AKI. In those with end-stage renal disease (ESRD) already on dialysis, removal of contrast on the next scheduled dialysis session is appropriate.
- Contrast studies with gadolinium should be employed cautiously in patients with GFR < 30 mL/min due to increased risk of nephrogenic systemic fibrosis (NSF).
- Referral to a nephrologist is advisable for patients with established stage 3 CKD (GFR < 60 mL/min per 1.73 m^2) and recommended for those with stage 4 CKD (GFR < 30 mL/min per 1.73 m^2).
- In patients with CKD, the use of peripherally inserted central catheters (PICC) and subclavian catheters should be avoided, as the resulting central vein stenosis makes access difficult for those requiring dialysis in the future.

Don't Miss This!

- Watch for indications for dialysis: refractory hyperkalemia/severe acidosis, uremic encephalopathy/pericarditis, refractory volume overload.
- Review the medications the patient has been taking, and don't forget to check for over-the-counter medications. Adjust all medications for the patient's renal function.

- Evaluate for urinary obstruction. It is a highly reversible cause of AKI when detected and treated early.
- Trimethoprim is associated with a spurious increase in serum creatinine without change in GFR due to blockage of tubular secretion of creatinine. True hyperkalemia can occur due to blockage of the epithelial sodium channel in the distal nephron.
- History of recent trauma, use of statins, and dark urine are suggestive of rhabdomyolysis: check a total creatine kinase level.

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