Evaluation of acute kidney injury among hospitalized adult patients

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INTRODUCTION — Patients with kidney disease have a variety of different clinical presentations. Some have symptoms or signs that are directly related to the kidney (such as gross hematuria) or to reduced renal function (edema, hypertension, signs of uremia). Many patients are asymptomatic and are incidentally found to have an elevated serum creatinine concentration, abnormal urine studies (such as proteinuria or microscopic hematuria), or abnormal radiologic imaging of the kidneys.

Specific disorders generally cause acute, subacute, or chronic kidney injury. Acute kidney injury (AKI) develops over hours to days and is usually diagnosed in the emergency department, in hospitalized patients, or following a procedure. Occasionally, AKI is incidentally noted on outpatient laboratory evaluation.

This topic reviews the evaluation of hospitalized patients who present with AKI. Patients who present to the emergency department with a creatinine above the recent baseline value may be acute or subacute. If recent baseline is not known, the kidney disease may be chronic in nature.

The evaluation of patients who present with subacute kidney injury is discussed elsewhere. (See "Diagnostic approach to adult patients with subacute kidney injury in an outpatient setting".)

The evaluation of patients with newly identified chronic kidney disease (CKD) is discussed elsewhere. (See "Diagnostic approach to the patient with newly identified chronic kidney disease".)

DEFINITION — AKI is defined by a rise in the serum creatinine concentration or a decline in urine output that has developed within hours to days. The proposed criteria for AKI include an increase in serum creatinine by ≥0.3 mg/dL (27 micromol/L) within 48 hours or an increase to ≥1.5 times the presumed baseline value that is known or presumed to have occurred within the prior seven days, or a decrease in urine volume to <3 mL/kg over six hours (Kidney Disease: Improving Global Outcomes [KDIGO]-AKI) (table 1) [1]. (See "Definition and staging criteria of acute kidney injury in adults".)

CLINICAL MANIFESTATIONS — Patients with AKI may present with symptoms and signs resulting directly from diminished kidney function. These typically include edema, hypertension, and/or decreased urine output or, in severe AKI, anuria. However, many patients have no clinical symptoms, and an increase in creatinine is detected by laboratory tests that are routinely obtained among hospitalized patients.

Laboratory tests may also reveal increased urea (blood urea nitrogen [BUN]) and hyperkalemia. Some patients, particularly those who are fluid overloaded, are hyponatremic.

A urinalysis may show albuminuria and/or an abnormal urine sediment. (See "Diagnostic approach to adult patients with subacute kidney injury in an outpatient setting", section on 'Urinalysis'.)

DIAGNOSIS — As noted above, AKI is occasionally accompanied by the onset of symptoms or signs related to reduced kidney function, all which suggest the diagnosis. (See 'Clinical manifestations' above.)

Among hospitalized patients who generally have frequent monitoring of the serum creatinine, the diagnosis of AKI is easily established by demonstrating an increase in the serum creatinine and/or decrease in urine output. A number of other biomarkers for changes in kidney function are being investigated, but serum creatinine currently remains the only lab value used in formal definitions AKI and the biomarker most commonly used in clinical practice (see 'Estimation of glomerular filtration rate' below). All subsequent evaluation is directed at determining the underlying cause of AKI in order to allow for prompt treatment. (See 'Evaluation' below.)

Early diagnosis of AKI may allow for intervention to improve outcomes, and some studies have suggested that early nephrologist involvement in hospital-acquired AKI confers benefits [2]. However, a randomized, controlled trial of an electronic alert system to promote early recognition of AKI did not result in reduced severity of injury nor improve clinical outcomes [3]. Thus, the addition of alerts for AKI to hospital information systems is not indicated at this time.

EVALUATION — It is important to quickly establish the cause of AKI. In many cases, AKI is reversible if the underlying cause is quickly identified and addressed. Our approach to evaluation of AKI is based on our understanding of the major causes.

Major causes and classification of AKI — The causes of AKI are traditionally classified by the portion of the renal anatomy that is most affected [4]. The traditional approach to AKI has thus been to categorize the clinical etiology as prerenal (decreased renal perfusion pressure), intrinsic renal (pathology of the vessels, glomeruli, or tubules-interstitium), or postrenal (obstruction of urinary flow). However, diseases often cross these nosological boundaries. As examples, prolonged prerenal azotemia can lead to intrinsic acute tubular necrosis (ATN), and untreated urinary tract obstruction eventually causes fibrosis and atrophy of the obstructed kidney(s).

- **Prerenal disease -** Acute prerenal injury occurs with ineffective perfusion commonly seen in hypovolemic states, such as in acute hemorrhage, diarrhea, or unreplenished insensible losses. Renal perfusion pressure may also be low in hypervolemic states with low effective circulating (arterial) volume, such as severe systolic heart failure with reduced ejection fraction (see "Cardiorenal syndrome: Definition, prevalence, diagnosis, and pathophysiology", section on 'Pathophysiology') or acutely decompensated liver disease with portal hypertension (see "Hepatorenal syndrome"). Alterations in renal vascular autoregulation, such as afferent arteriole vasoconstriction caused by nonsteroidal anti-inflammatory drugs (NSAIDs) or iodinated radiocontrast media, may cause acute prerenal kidney injury (see "NSAIDs: Acute kidney injury (acute renal failure)" and "Pathogenesis, clinical features, and diagnosis of contrast-induced nephropathy"). Angiotensin blockade (angiotensin-converting enzyme inhibitor [ACEi] or angiotensin receptor blocker [ARB] medications) also alter the kidney's ability to autoregulate blood flow during states of decreased renal blood flow; these medications thus commonly exacerbate prerenal AKI. (See "Major side effects of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers".)

  Low perfusion pressure to the renal parenchyma may result from low arterial pressure, as in the etiologies mentioned above, but, since perfusion pressure to any capillary bed is the difference between arterial and venous pressures, markedly elevated renal venous pressures, as seen in severe diastolic heart failure or in abdominal compartment syndrome, may also cause low perfusion pressure and AKI. (See "Cardiorenal syndrome: Definition, prevalence, diagnosis, and pathophysiology", section on 'Increased renal venous pressure' and "Abdominal compartment syndrome in adults".)

- **Intrinsic renal vascular disease -** Intrinsic renal vascular diseases directly affect both small-and large-sized blood vessels within the kidneys. Acute intrinsic diseases that primarily involve small blood vessels include small vessel vasculitides and diseases that cause microangiopathy and hemolytic anemia (MAHA), including thrombotic thrombocytopenic purpura-hemolytic uremic syndrome (TTP/HUS), scleroderma, atheroembolic disease, and malignant hypertension. (See "Clinical presentation, evaluation, and treatment of renal atheroemboli" and "Moderate to severe hypertensive retinopathy and hypertensive encephalopathy in adults", section on 'Clinical manifestations and diagnosis' and "Renal disease in

systemic sclerosis (scleroderma), including scleroderma renal crisis" and "Glomerular disease: Evaluation and differential diagnosis in adults".)

Diseases that affect larger vessels and cause AKI include renal infarction from aortic dissection, systemic thromboembolism, or renal artery abnormality (such as aneurysm) and acute renal vein thrombosis. Severe AKI from renal vascular catastrophe suggests bilateral involvement or involvement of a solitary functioning kidney.

- **Intrinsic glomerular disease -** Disorders that produce glomerular disease can be classified as being primary (idiopathic, not associated with systemic disease) or secondary (such as paraneoplastic, drug induced, or part of a systemic rheumatologic disease). Two general patterns are observed (with considerable overlap in some diseases):

  - A nephritic pattern (proliferative glomerulonephritis) produces an active urine sediment with dysmorphic red cells and white cells; granular, red cell, and other cellular casts; and a variable degree of proteinuria [5,6]. Rapidly progressive glomerulonephritis (RPGN), which causes AKI, always presents with a nephritic pattern. (See "Glomerular disease: Evaluation and differential diagnosis in adults".)

  - A nephrotic pattern (nonproliferative glomerulopathy) is an exceedingly rare cause of AKI in the hospitalized patient. (See "Acute kidney injury (AKI) in minimal change disease and other forms of nephrotic syndrome" and "Glomerular disease: Evaluation and differential diagnosis in adults".)

    The quantification of protein excretion is discussed elsewhere. (See "Assessment of urinary protein excretion and evaluation of isolated non-nephrotic proteinuria in adults".)

- **Intrinsic tubular and interstitial disease -** Tubular and interstitial (tubulointerstitial) diseases commonly cause AKI. The most common acute tubulointerstitial disease is ATN, which typically occurs following concurrent ACEi/ARB medications with NSAIDs, radiocontrast media or other nephrotoxin administration, following cardiac surgery, or in the setting of sepsis, shock, or a prerenal state.

  Other tubulointerstitial diseases that cause AKI include acute interstitial nephritis (AIN; which is often drug induced) and cast nephropathy in multiple myeloma.

  Less common causes of tubulointerstitial AKI that should be considered in the appropriate setting are tumor lysis syndrome (acute urate nephropathy), which occurs among patients with high tumor burden lymphoma or following chemotherapy; crystalline nephropathy associated with intravenous acyclovir and other medications; and acute phosphate nephropathy following a phosphate-containing bowel preparation [7]. (See "Etiology and diagnosis of prerenal disease and acute tubular necrosis in acute kidney injury in adults" and "Clinical manifestations and diagnosis of acute interstitial nephritis" and "Epidemiology, pathogenesis, and etiology of kidney disease in multiple myeloma and other monoclonal gammopathies" and "Clinical manifestations of hypercalcemia", section on 'Renal insufficiency' and "Tumor lysis syndrome: Definition, pathogenesis, clinical manifestations, etiology and risk factors" and "Acute phosphate nephropathy".)

- **Postrenal disease (obstructive nephropathy) -** Obstruction may occur anywhere in the urinary tract. Among patients who do not have underlying chronic kidney disease (CKD), a substantial reduction in the glomerular filtration rate (GFR) suggests bilateral obstruction (or unilateral obstruction of a single functioning kidney). This is most commonly due to prostatic disease (hyperplasia or cancer) or metastatic cancer. Retroperitoneal fibrosis is a rare cause of progressive ureteral obstruction (see "Clinical manifestations and diagnosis of retroperitoneal fibrosis"). If untreated, obstructive nephropathy leads to irreversible tubulointerstitial fibrosis (ie, intrinsic disease).

Relative frequency of AKI etiologies — The most detailed epidemiologic data on AKI are in hospitalized patients in developed countries. Most of the relevant studies were published prior to the relatively recently proposed definitions of AKI (see "Definition and staging criteria of acute kidney injury in adults"). Nonetheless,

those studies provide important information about the causes of AKI. Among hospitalized patients, ATN and prerenal disease are the most common causes. A report from Madrid evaluated all 748 cases of AKI at 13 tertiary hospital centers [8] and suggests the common etiologies involved. The most frequent causes were:

- ATN – 45 percent
- Prerenal disease – 21 percent
- Acute superimposed on CKD – 13 percent (mostly due to ATN and prerenal disease)
- Urinary tract obstruction – 10 percent (most often older men with prostatic disease)
- Glomerulonephritis or vasculitis – 4 percent
- AIN – 2 percent
- Atheroemboli – 1 percent

A study from the Program to Improve Care in Acute Renal Disease (PICARD) examined the etiology of AKI in a more acutely ill population of 618 patients in five intensive care units (ICUs) in the United States [9]. Many patients had more than one possible cause. Over 70 percent of cases were thought to be due to ATN related to sepsis and hypotension. Other causes included prerenal disease (eg, hypovolemia, heart failure, and hepatorenal syndrome), contrast-induced nephropathy, and rhabdomyolysis. Some patients had two or more causes of AKI.

Our approach to evaluation

Overview — For all patients, we carefully review the history and particularly the timing of onset of AKI. The timing of onset often suggests the underlying etiology. The date of onset can very often be precisely timed if the serum creatinine concentration has been measured frequently as part of routine blood testing or if there is accurate documentation of urine output. As an example, suppose that a patient has had a stable serum creatinine concentration, which then begins to rise progressively on hospital day 5. Careful study of the patient's chart may identify the precipitating event on day 3 or 4 (eg, hypotension or radiocontrast exposure) or identify cumulative insults prior to the increase in creatinine. An important caveat here is that patients who receive aggressive volume resuscitation may have the increase in serum creatinine blunted due to dilution in a larger volume of distribution [10]. (See "Pathogenesis, clinical features, and diagnosis of contrast-induced nephropathy" and "Crystal-induced acute kidney injury (acute renal failure)", section on 'Acyclovir'.)

A careful review of medications is imperative. Often, nephrotoxic medications have been started prior to the onset of AKI, which suggests an etiology. In addition, even longstanding medications (particularly ACEi or ARBs) render patients vulnerable to AKI from prerenal factors or ATN.

A physical examination may reveal the etiology. Common examples include:

- Signs of volume contraction suggest a prerenal etiology of AKI. (See "Etiology and diagnosis of prerenal disease and acute tubular necrosis in acute kidney injury in adults", section on 'History and physical examination'.)
- A typical "drug rash" suggests AIN. (See "Clinical manifestations and diagnosis of acute interstitial nephritis", section on 'Clinical manifestations'.)
- Blue toes suggest cholesterol emboli. (See "Clinical presentation, evaluation, and treatment of renal atheroemboli", section on 'History and physical examination'.)
- Significant volume overload and signs of heart failure suggest cardiorenal syndrome. (See "Cardiorenal syndrome: Definition, prevalence, diagnosis, and pathophysiology".)

- Ascites and jaundice suggest liver disease with portal hypertension and hepatorenal syndrome. (See "Hepatorenal syndrome".)

Initial testing should include reagent strip urinalysis (dipstick) with automated urine microscopy and the quantification of urine protein or albumin (by random or "spot" protein-to-creatinine ratio or albumin-to-creatinine ratio) (see "Assessment of urinary protein excretion and evaluation of isolated non-nephrotic proteinuria in adults"). Manual urine microscopy for the assessment of urine sediment is best performed by an experienced operator (algorithm 1).

Among patients who are considered at higher risk for multiple myeloma based on key clinical features, we obtain a serum protein electrophoresis (SPEP), urine protein electrophoresis (UPEP) with immunofixation, and a serum light chain assay at the time of the initial evaluation. Patients who are considered at higher risk for myeloma include all patients who are >40 years of age who have no other obvious cause for increased creatinine, such as NSAID use, contrast exposure, or sepsis. Other features, such as hypercalcemia, unexplained anemia, and increased globulin gap (the difference between total protein and albumin in the serum), may increase suspicion of monoclonal gammopathy. Another important clue to the presence of abnormal immunoglobulins in kidney disease is a discrepancy between undetectable urinary protein by dipstick reagent and concurrently high random urine protein-to-creatinine ratio. (See "Clinical features, evaluation, and diagnosis of kidney disease in multiple myeloma and other monoclonal gammopathies", section on 'Patients presenting with acute or subacute kidney injury'.)

Patients who have hematuria without recent urinary tract instrumentation and/or an abnormally increased albumin-to-creatinine ratio should be evaluated for glomerular disease or vasculitis. (See "Glomerular disease: Evaluation and differential diagnosis in adults".)

Patients who have sterile pyuria should be evaluated for interstitial nephritis. (See "Clinical manifestations and diagnosis of acute interstitial nephritis".)

Radiographic imaging is generally performed in patients with AKI when the underlying cause is not immediately apparent. The major reason for performing imaging is to assess for urinary tract obstruction.

Patients who have an obvious cause of AKI do not require imaging, at least initially. As an example, we do not initially perform imaging when the history and physical examination reveal an obvious cause of ATN (such septic shock) and/or urine microscopy is consistent with ATN. Some clinicians will perform an ultrasound if renal function does not improve after a few days, but the diagnostic yield is low.

The most commonly used radiographic technique in patients with AKI is renal ultrasound. Ultrasound is safe, easy to perform, and sensitive for obstruction. Helical computed tomography (CT) scan without contrast is generally preferred among patients with possible urolithiasis. Such patients usually, though not always, present with flank pain and hematuria. (See "Radiologic assessment of renal disease" and "Diagnosis and acute management of suspected nephrolithiasis in adults", section on 'Diagnostic imaging'.)

Magnetic resonance imaging (MRI) with gadolinium should be avoided, if possible, among patients with AKI. Among patients with moderate to advanced kidney disease with estimated glomerular filtration rate (eGFR) <30 mL/min, the administration of gadolinium has been associated with the potentially severe syndrome of nephrogenic systemic fibrosis (NSF). (See "Nephrogenic systemic fibrosis/nephrogenic fibrosing dermopathy in advanced renal failure".)

Bladder outlet obstruction can be assessed by checking post-void bladder volume by ultrasound or by placement of a bladder catheter, which may, in some situations, be both diagnostic and therapeutic. (See "Clinical manifestations and diagnosis of urinary tract obstruction and hydronephrosis".)

The results of the urinalysis and ultrasound generally direct the remainder of the diagnostic evaluation. Patients who have newly developed hydronephrosis or hydroureter usually require prompt intervention to relieve or bypass the obstruction and further urologic investigation to determine the cause. (See "Clinical manifestations and diagnosis of urinary tract obstruction and hydronephrosis".)

For patients who have normal renal imaging, minimal proteinuria, benign urine sediment on urinalysis/microscopy (no red cells or cellular casts), and no clear explanation for AKI, further evaluation is determined by the severity of disease and rate of further decline.

- If the creatinine is markedly elevated or if an initially mild increase in the creatinine worsens over the course of days, then a kidney biopsy should be performed. A biopsy usually provides a more definitive tissue diagnosis and may allow a therapeutic intervention to prevent end-stage renal disease (ESRD).

  In some cases, even without kidney biopsy, the etiology of kidney disease can be ascertained with reasonable certainty with tissue diagnosis from other sites. As an example, a bone marrow biopsy among patients with multiple myeloma or a fat pad biopsy among patients with amyloidosis may avert the need for a kidney biopsy. The indications for renal biopsy are discussed in more detail elsewhere. (See "Indications for and complications of renal biopsy".)

- Among patients who have signs and symptoms of rapidly progressive or unexplained systemic disease, a renal biopsy is warranted, even if the eGFR remains stable after initial increase.

- Among patients who have mild decrements in eGFR (eg, to 45 to 60 mL/min/1.73 m^2) that subsequently remain stable, we often just follow the serum creatinine. If the creatinine remains stable, we generally continue to follow creatinine, urine studies (urinalysis/microscopic studies, urine protein/creatinine), and blood pressure until a clear temporal pattern is established.

Estimation of glomerular filtration rate — The most common methods utilized to estimate the GFR in adults are the serum creatinine concentration, the creatinine clearance, and equations based upon the serum creatinine concentration and variables such as age, sex, and race. (See "Assessment of kidney function", section on 'Estimation of GFR'.)

The equations that use serum creatinine concentration to estimate GFR were derived in nonhospitalized patients with stable kidney function. Although more complex formulas have been proposed to estimate GFR from the change in creatinine values among patients with AKI [11,12], any equation that uses creatinine may lead to errors among patients who are not in steady state. As an example, early in the course of AKI, the serum creatinine could be low because there has not yet been adequate time for it to accumulate; in such cases, equations that use creatinine will overestimate kidney function.

Urinalysis — The urinalysis involves both use of a urine dipstick and microscopic examination of the urine sediment. The dipstick can test for protein (albumin), pH, glucose, hemoglobin (or myoglobin), leukocyte esterase (reflecting pyuria), and specific gravity. Microscopic examination of the urine sediment by an experienced operator is an important component of the diagnostic evaluation since characteristic findings strongly suggest certain diagnoses (table 2). (See "Urinalysis in the diagnosis of kidney disease", section on 'Urine dipstick'.)

Urine sodium excretion — The urine sodium may be measured with calculation of fractional urine excretion (FENa) in patients with AKI. In an oliguric patient whose effective circulating volume is difficult to assess, the FENa may help to distinguish prerenal AKI from ATN. However, there are many instances where the FENa is not helpful, and we believe that the evaluation of AKI is better guided by history, physical, and other lab findings. The fractional excretion of urea may also provide information in some patients. (See "Fractional excretion of sodium, urea, and other molecules in acute kidney injury (acute renal failure)" and "Etiology and diagnosis of prerenal disease and acute tubular necrosis in acute kidney injury in adults", section on 'Fractional excretion of sodium and urine sodium concentration'.)

Urine volume — Trending and comparing volume of fluid going in and coming out of a patient (including urine output) are helpful physiologic parameters in patients with AKI.

Oliguria (typically defined as <0.3 mL/kg per hour or <500 mL/day of urine output) may or may not occur in AKI with rising creatinine. Normal urine output can be maintained even with an abnormally low GFR in patients

with nonoliguric ATN. The prognosis of nonoliguric AKI is generally better than oliguric or anuric disease [13-16].

Anuria (<50 mL/day) reflects severe AKI, which will likely require dialytic therapy. Anuria generally occurs as a result of severe prolonged shock, bilateral urinary tract obstruction, pregnancy-related cortical necrosis, or bilateral renal artery obstruction.

Although the administration of diuretics in AKI has not been shown to improve renal function or creatinine trajectory, the increase of urine output (ie, the conversion of anuric or oliguric AKI to nonoliguric AKI) spontaneously or with the use of diuretics often reflects renal recovery or less severe injury [17]. Furthermore, increasing urine output will mitigate the risk of volume overload and pulmonary edema, thus potentially allowing the patient to be managed without dialysis. (See "Urine output and residual kidney function in kidney failure" and "Nonoliguric versus oliguric acute kidney injury".)

Abrupt decline in urine volume may suggest new obstruction (such as plugged bladder catheter) as a cause of AKI.

Serologic testing and role of renal biopsy — Depending on the history, physical, radiographic, and urine findings, particularly those that suggest nephritic glomerular disease, serologic testing is ordered to further characterize the etiology of kidney disease. (See "Glomerular disease: Evaluation and differential diagnosis in adults".)

A native (nontransplanted) kidney biopsy is most commonly obtained when noninvasive evaluation has been unable to establish the correct diagnosis [18,19].

Biopsy may be deferred if other findings and serologic testing strongly support diagnostic and therapeutic decision making or if the risk of biopsy outweighs the expected benefit. Issues related to renal biopsy, including indications, when biopsy may not be necessary, prebiopsy evaluation, technique, and complications, are discussed separately. (See "Indications for and complications of renal biopsy".)

SOCIETY GUIDELINE LINKS — Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Acute kidney injury in adults".)

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Chronic kidney disease (The Basics)" and "Patient education: Acute kidney injury (The Basics)")
- Beyond the Basics topics (see "Patient education: Chronic kidney disease (Beyond the Basics)" and "Patient education: Dialysis or kidney transplantation — which is right for me? (Beyond the Basics)" and "Patient education: Hemodialysis (Beyond the Basics)" and "Patient education: Peritoneal dialysis (Beyond the Basics)" and "Patient education: Protein in the urine (proteinuria) (Beyond the Basics)" and "Patient education: Split urine collection for orthostatic proteinuria (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- Acute kidney injury (AKI) is defined by a rise in the serum creatinine concentration or a decline in urine output that has developed within hours to days. The proposed criteria for AKI include an increase in serum creatinine by ≥0.3 mg/dL (27 micromol/L) within 48 hours or an increase to ≥1.5 times the presumed baseline value that is known or presumed to have occurred within the prior seven days or a decrease in urine volume to <3 mL/kg over six hours. (See 'Definition' above.)

- Patients with AKI may present with symptoms and signs resulting directly from diminished kidney function. These include edema, hypertension, and/or decreased urine output. However, many patients have no clinical symptoms, and an increase in serum creatinine is detected by routine laboratory tests. (See 'Clinical manifestations' above.)

- Among hospitalized patients who generally have frequent monitoring of the serum creatinine and/or urine output, the diagnosis of AKI is easily established based on increases in serum creatinine or the development of oliguria. All subsequent evaluation is directed at determining the underlying cause of AKI in order to allow for prompt treatment. (See 'Diagnosis' above.)

- The major components to the evaluation of patients with an elevated creatinine include a careful history and physical examination, examination of the urine by both qualitative chemical tests and microscopic examination, radiographic imaging of the kidneys, serologic testing in the setting of possible glomerulonephritis, and tissue diagnosis with renal biopsy if noninvasive evaluation is not sufficient for diagnosis (algorithm 1). (See 'Evaluation' above.)

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GRAPHICS

Criteria for acute kidney injury

	RIFLE[1]	AKIN[2]	KDIGO[3]
Diagnostic criteria*			
		Increase in serum creatinine of ≥0.3 mg/dL or ≥50% within 48 hours OR Urine output of <0.5 mL/kg/hour for >6 hours	Increase in serum creatinine of ≥0.3 mg/dL within 48 hours or ≥50% within 7 days OR Urine output of <0.5 mL/kg/hour for >6 hours
Staging criteria			
Risk (RIFLE) or stage 1 (AKIN/KDIGO)	Increase in serum creatinine of 50 to 99% OR Urine output of <0.5 mL/kg/hour for 6 to 12 hours	Increase in serum creatinine of ≥0.3 mg/dL or 50 to 100% OR Urine output of <0.5 mL/kg/hour for 6 to 12 hours	Increase in serum creatinine of ≥0.3 mg/dL or 50 to 99% OR Urine output of <0.5 mL/kg/hour for 6 to 12 hours
Injury (RIFLE) or stage 2 (AKIN/KDIGO)	Increase in serum creatinine of 100 to 199% OR Urine output of <0.5 mL/kg/hour for 12 to 24 hours	Increase in serum creatinine of >100 to 200% OR Urine output of <0.5 mL/kg/hour for 12 to 24 hours	Increase in serum creatinine of 100 to 199% OR Urine output of <0.5 mL/kg/hour for 12 to 24 hours
Failure (RIFLE) or stage 3 (AKIN/KDIGO)	Increase in serum creatinine of ≥200% OR Increase in serum creatinine by >0.5 mg/dL to >4.0 mg/dL OR Urine output of <0.3 mL/kg/hour for >24 hours or anuria for >12 hours OR Initiation of renal replacement therapy	Increase in serum creatinine of >200% OR Increase in serum creatinine by >0.5 mg/dL to ≥4.0 mg/dL OR Urine output of <0.3 mL/kg/hour for >24 hours or anuria for >12 hours OR Initiation of renal replacement therapy	Increase in serum creatinine of ≥200% OR Increase in serum creatinine of ≥0.3 mg/dL to ≥4.0 mg/dL¶ OR Urine output of <0.3 mL/kg/hour for ≥24 hours or anuria for ≥12 hours OR Initiation of renal replacement therapy
Loss (RIFLE)	Need for renal replacement therapy for >4 weeks		
End stage (RIFLE)	Need for renal replacement therapy for >3 months		

RIFLE: risk, injury, failure, loss, ESRD; AKIN: Acute Kidney Injury Network; KDIGO: Kidney Disease: Improving Global Outcomes; ESRD: end-stage renal disease.

* AKIN and KDIGO provided both diagnostic and staging criteria. RIFLE provided a graded definition of AKI that is implicit in the staging criteria.

¶ In patients <18 years, stage 3 AKI is also defined by KDIGO as a decrease in estimated glomerular filtration rate (eGFR) to <35 mL/min/1.73 m^2.

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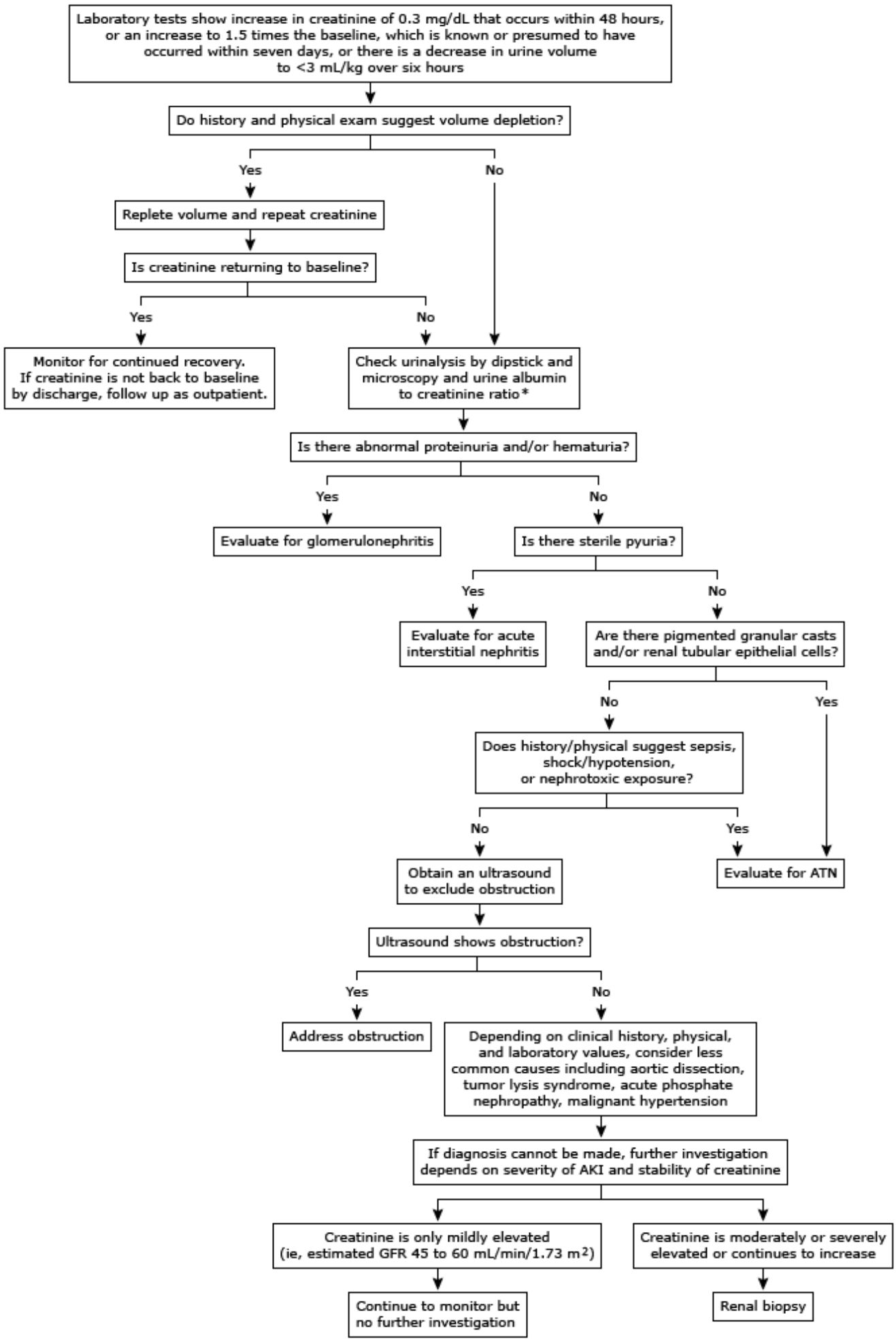
Graphic 83168 Version 11.0

Evaluation of acute kidney injury among hospitalized patients



ATN: acute tubular necrosis; AKI: acute kidney injury; GFR: glomerular filtration rate; SPEP: serum protein electrophoresis; UPEP: urine protein electrophoresis.
* For patients who are at higher risk for multiple myeloma, we also check SPEP, UPEP with immunofixation, and a serum free light chain assay. Higher-risk patients include all patients >40 years who have no other obvious cause for increased creatinine.

Graphic 105743 Version 3.0

Urinary patterns associated with different kidney diseases

Urinary pattern	Kidney disease suggested by pattern
Hematuria with dysmorphic red blood cells, red blood cell casts, varying degrees of albuminuria	Proliferative glomerulonephritis (eg, IgA nephropathy, ANCA-associated vasculitis, lupus nephritis)
Heavy albuminuria with minimal or absent hematuria	Nonproliferative glomerulopathy (eg, diabetes, amyloidosis, membranous nephropathy, focal segmental glomerulosclerosis, minimal change)
Multiple granular and epithelial cell casts with free epithelial cells	Acute tubular necrosis in a patient with underlying acute kidney injury
Isolated pyuria	Infection (bacterial, mycobacterial) or tubulointerstitial disease
Normal urinalysis with few cells, no casts, and no or minimal proteinuria	In presence of acute kidney injury: prerenal disease, urinary tract obstruction, hypercalcemia, acute phosphate nephropathy, myeloma cast nephropathy
	In presence of chronic kidney disease: ischemic nephropathy, hypertensive nephrosclerosis, urinary tract obstruction, hepato renal disease, cardiorenal disease

IgA: immunoglobulin A; ANCA: antineutrophil cytoplasmic antibody.

Graphic 56160 Version 10.0

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