BMJ Best Practice

Acute kidney injury

Straight to the point of care

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Summary

Acute kidney injury (AKI) is commonly associated with sepsis, cardiovascular collapse, congestive heart failure, major surgery, nephrotoxins (such as antibiotics, intravenous contrast, or other drugs), or urinary outflow obstruction.

May present with flank pain, hematuria, hypertension or hypotension, edema, lethargy, uremia, or decreased urine output; however, often asymptomatic and only diagnosed by laboratory tests.

An acute increase in serum creatinine is essential for diagnosis. Fluid overload, hyperkalemia, hyperphosphatemia, metabolic acidosis, and elevated urea nitrogen are common.

The mainstay of treatment is supportive care, with management of the underlying illness; correction of acid/base, electrolyte, and volume complications; removal or minimization of nephrotoxins; and relief of any associated obstruction being key.

Renal replacement therapy with dialysis may be required and is usually well tolerated.

Failure to treat may be associated with clinical deterioration and death. Outcome is dependent upon the severity of the kidney injury and the underlying disease.

Definition

AKI, previously known as acute renal failure (ARF), is an acute decline in renal function, leading to a rise in serum creatinine and/or a fall in urine output.[1] The change in terminology emphasizes that kidney injury presents as a disease spectrum from mild renal impairment to severe renal failure.[1] [2] [3] A standardized definition is important to facilitate clinical care and research.[4] AKI may be due to various insults such as impaired renal perfusion, exposure to nephrotoxins, outflow obstruction, or intrinsic renal disease. The resulting effects include impaired clearance and regulation of metabolic homeostasis, altered acid/base and electrolyte regulation, and impaired volume regulation.

THEORY

Epidemiology

The reported incidences of AKI vary, and are confounded by differences in diagnosis, definition criteria, or hospital discharge coding.[6] [7] The rate of hospitalizations for AKI in US Medicare patients increased by approximately 35% between 2010 and 2019.[8] Patients with diabetes were hospitalized with AKI at a greater than 2-fold higher rate compared with those without diabetes, and patients with chronic kidney disease (CKD) and diabetes were hospitalized with AKI at a more than 7.5-fold higher rate compared with patients with neither preexisting condition.[8] Overall incidence of AKI among hospitalized patients ranges from 13% to 22%.[3] [9] In the intensive care unit (ICU), the incidence of AKI is higher.[10] Prediction scores have been developed for outcomes of AKI, but have had variable success in terms of reproducibility or utility.[11] [12]

Acute tubular necrosis (ATN) accounts for 45% of cases of AKI. ATN is caused by sepsis in approximately 20% of ICU patients. Prerenal azotemia, obstruction, glomerulonephritis, vasculitis, acute interstitial nephritis, acute on chronic kidney disease, and atheroembolic injury account for most of the remainder.[13] [14]

The incidence of contrast nephropathy varies, and is reported to be the third most common cause of AKI in hospitalized patients. One large systematic review and meta-analysis reported a 9% incidence of contrast-induced nephropathy in patients undergoing angiography for any reason, including percutaneous intervention for coronary artery disease, with 0.5% of patients requiring dialysis.[15]

Up to 7% of patients hospitalized with AKI require renal replacement therapy.[16] In the ICU, the mortality rate exceeds 50% in patients with multiorgan failure who require dialysis.[13] [14] [16] Minor rises in creatinine (≥0.3 mg/dL) are associated with an increased risk of hospital mortality, increased risk of chronic kidney disease, and higher odds of progressing to end-stage renal failure.

Risk factors

Strong

advanced age

Advanced age is associated with chronic kidney disease, underlying renal vascular disease, and other comorbid medical conditions that predispose to AKI. Older patients with frailty appear to be at particular risk for AKI.[43]

underlying renal disease

Associated with increased susceptibility to AKI, particularly contrast-related AKI. Risks increase with increasing severity of chronic kidney disease.[5]

malignant hypertension

Malignant hypertension may cause AKI.[5]

diabetes mellitus

AKI incidence rates of 9% to 38% have been reported in patients with diabetes and chronic kidney disease undergoing contrast exposure.[44] There is evidence to suggest that diabetes mellitus is an independent risk factor for contrast-induced AKI.[45]

myeloproliferative disorders, such as multiple myeloma

Intratubular precipitation of light chains in times of volume contraction is associated with renal injury, especially in cases of contrast exposure with volume contraction in myeloma patients. Hypercalcemia predisposes to prerenal azotemia.[5] [46]

connective tissue disease

May present with AKI (e.g., systemic lupus erythematosus, scleroderma, antineutrophil cytoplasmic antibody-associated glomerulonephritis, antiglomerular basement membrane disease).[5]

sodium-retaining states (e.g., congestive heart failure, cirrhosis, nephrotic syndrome)

Associated with chronic kidney disease, but may present with AKI.[5]

radiocontrast

Exposure may cause AKI.[5] However, the association is controversial because population studies do not replicate risk.[33] [34] [35]

exposure to nephrotoxins (e.g., aminoglycosides, vancomycin + piperacillin-tazobactam, cancer therapies, nonsteroidal anti-inflammatory drugs, or ACE inhibitors)

May precede and lead to AKI.[5] [47] [48] [49]

trauma

There may be impaired renal perfusion causing prerenal azotemia, rhabdomyolysis predisposing to pigment-induced injury, or ischemia causing acute tubular necrosis.[50]

hemorrhage

The resulting impaired renal perfusion supports prerenal azotemia as cause of AKI or ischemia resulting in acute tubular necrosis.

sepsis

May result in acute tubular necrosis, infectious glomerulonephritis, prerenal azotemia from hypotension, or drug-induced injury from drugs used in treatment. Highest risk with bacteremia.[50] Coronavirus disease 2019 (COVID-19), which is caused by infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, is strongly associated with AKI via several proposed pathophysiologic mechanisms, some being similar to those of non-COVID sepsis.[51]

pancreatitis

There may be severe third spacing of fluid leading to intravascular volume depletion resulting in prerenal failure.

drug overdose

May precede AKI due to direct toxicity, rhabdomyolysis, and volume depletion.

surgery

May precede AKI from prerenal, intrinsic, or postrenal causes.[52] Cardiothoracic surgery is particularly high risk, although off-pump approaches may limit this risk.[53]

cardiac arrest

May precede prerenal azotemia or acute tubular necrosis, especially if there is severe and prolonged renal ischemia.

recent vascular intervention

May be associated with atheroembolic injury, perioperative ischemia, or contrast-induced AKI.

excessive fluid loss

From hemorrhage, vomiting, diarrhea, or sweating; hospitalized patients may have insufficient replacement fluids.

nephrolithiasis

May lead to AKI if significant obstruction occurs, especially with one functioning kidney.

Weak

drug abuse

AKI from nephrotoxicity, ischemia.

alcohol abuse

Suspect pigment-induced AKI if rhabdomyolysis is present (e.g., after prolonged loss of consciousness).

excessive exercise

Suspect pigment-induced AKI due to rhabdomyolysis.[54]

recent blood transfusion

AKI may be present from intravascular hemolytic transfusion reaction, deposition of immune complexes.

malignancy

May lead to postrenal AKI if mass effect is causing outflow obstruction, or AKI may result in association with myeloproliferative disorders or chemotherapy-related toxicities (i.e., tumor lysis). Immune complex glomerulonephritis may result from the malignancy.

genetic susceptibility

There is preliminary evidence that a genetic predisposition for AKI may exist, especially with apolipoprotein E (APO-E) genes.[41] Genome-wide searches have found other protective candidates, but much more work is needed to validate these findings.[42]

use of renin-angiotensin system inhibitors

Found to be a predictor of risk of postoperative AKI, but may be a marker rather than a mediator of risk. It is unclear whether there is any benefit to stopping agents prior to surgery in high-risk patients.[55] Patients previously taking renin-angiotensin system inhibitors should restart them following an episode of AKI, as there is evidence that they lower risk of death in this group.[56]

proton pump inhibitors

Proton pump inhibitors likely increase risk of AKI; however, more studies are needed to clarify this association.[57] [58]

herbal therapy

Case reports suggest that herbs and dietary supplements could potentially contribute to kidney injuries.[59]

Etiology

Etiology of AKI may be multifactorial, generally classified into prerenal, intrinsic, and postrenal causes.[17]

- Prerenal azotemia can be due to various causes of reduced renal perfusion, such as hypovolemia, hemorrhage, sepsis, third spacing of fluid (such as in severe pancreatitis), overdiuresis, or other causes of reduced renal perfusion such as heart failure. Hepatorenal syndrome, a form of prerenal azotemia not responsive to fluid administration, is seen in cases of severe liver disease. Renovascular disease, especially with the recent addition of an ACE inhibitor to a patient with bilateral renal artery stenosis, is also a consideration, and this sometimes leads to acute tubular necrosis (ATN).
- Intrinsic renal failure may be multifactorial. ATN, rapidly progressive glomerulonephritis, and interstitial nephritis are the most common etiologies. Vascular diseases, including hemolytic uremic syndrome, thrombotic thrombocytopenic purpura, scleroderma renal crisis, atheromatous embolization, and thrombosis, are also potential (rare) causes. Severe ischemic injury may result in cortical necrosis.
- Postrenal injury results from mechanical obstruction of the urinary outflow tract. Retroperitoneal fibrosis, lymphoma, tumor, prostate hyperplasia, strictures, renal calculi, ascending urinary infection (including pyelonephritis), and urinary retention are common causes.

Pathophysiology

Prerenal azotemia results from impaired renal perfusion and the changes seen are appropriate physiologic responses. The renal response to a lower perfusion pressure is to enhance sodium and water reabsorption. Baroreceptors in the carotid artery and aortic arch respond to lower blood pressure with sympathetic stimulation. This, along with vasoconstriction of the glomerular efferent arteriole and dilation of the afferent arteriole, is intended to maintain glomerular filtration within a relatively narrow range. Decreasing perfusion promotes activation of the renin/angiotensin/aldosterone system. Angiotensin II, a potent vasoconstrictor, stimulates aldosterone release, promoting sodium and water resorption at the collecting duct. Low blood volume is also a stimulus to the hypothalamus promoting antidiuretic hormone release and increased tubular water reabsorption, concentrating the urine.

Acute tubular necrosis (ATN) due to prolonged or severe ischemia, the most common form of AKI, is preceded by impaired renal perfusion and tissue hypoxemia, yielding direct microvascular endothelial injury and tubular ischemia typically most severe in the early proximal tubule and the outer medullary segments.[18] [19] Hypoxemia results in increased reactive oxygen species, reduction in available adenosine triphosphate, and cellular dysfunction and death.[20] Additionally, complement system activation, direct neutrophil activation, membrane attack complex activation, cytokines, chemokines, and vasoactive hormones have been studied and may be contributory.[21] [22] [23] [24] [25] [26] [27] [28] [29] ATN may also result from exposure to drugs, endotoxins, or radiocontrast media. Animal models suggest direct cytotoxic effects of the contrast as well as renal vasoconstriction resulting in impaired medullary blood flow, increased viscosity, and

hypoxemia.[30][31] [32] However, the association with radiocontrast exposure is controversial, as population studies do not replicate risk.[33] [34] [35] [36]

Renal injury associated with obstruction results from increased intratubular pressure yielding reductions in filtration pressure and potential tubular ischemia and atrophy. Evidence also suggests injury results from an influx of monocytes and macrophages. Cytokines, free radicals, proteases, and tumor necrosis factor-beta are released, causing irreversible tubular injury and fibrosis when obstruction becomes chronic.[37] [38] [39] [40]

There is preliminary evidence that a genetic predisposition for AKI may exist, especially with apolipoprotein E (APO-E) genes.[41] Genome-wide searches have found other protective candidates, but much more work is still needed to validate these findings.[42]

Classification

Kidney Disease: Improving Global Outcomes (KDIGO) definition of AKI[1]

Any of the following:

- Increase in serum creatinine by ≥0.3 mg/dL within 48 hours; or
- Increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume <0.5 mL/kg/hour for 6 hours.

Classification based on pathophysiology[5]

- Prerenal: failure due to impaired renal perfusion, with an appropriate renal response.
- Intrinsic: failure due to direct injury to renal parenchyma.
- Postrenal: failure due to obstruction of urinary outflow.

Case history

Case history #1

A 65-year-old male smoker with hypertension, dyslipidemia, and diabetes mellitus presents with chest pain. ECG changes suggest an acute myocardial infarction. He is taken for an emergent coronary angiogram. Three days later, he is noticed to have developed an elevated serum creatinine, oliguria, and hyperkalemia.

Case history #2

A 35-year-old man with a history of congenital valvular heart disease undergoes a dental procedure without appropriate antibiotic prophylaxis. Several weeks later, he presents with fever and respiratory distress. He is intubated, and *Streptococcus viridans* is isolated in all blood cultures drawn at the time

of admission. Echocardiography demonstrates a mitral valve vegetation. Laboratory tests reveal a rising serum creatinine and urine output decline. Urine analysis reveals more than 20 white blood cells per high power field, more than 20 red blood cells per high power field, and red cell casts. Urine culture is negative. Renal ultrasound is unremarkable. Serum erythrocyte sedimentation rate is elevated.

Other presentations

AKI may develop in the setting of normal urine output and an otherwise asymptomatic patient. Associated laboratory abnormalities including elevated serum creatinine (or cystatin C) and blood urea nitrogen, hyperkalemia, and anion gap or non-gap metabolic acidosis may be all that are seen. Symptoms such as arthralgias, myalgias, or rash may be seen in patients with vasculitis or glomerulonephritis.

AKI following vascular catheterization or systemic anticoagulation may result from atheroembolic injury. Abdominal masses or an enlarged bladder, found on exam or by imaging, may be found in otherwise asymptomatic individuals with obstructive nephropathy and renal failure. AKI with allergy symptoms (fever, rash, arthralgia), hematuria, and sterile pyuria may suggest interstitial nephritis.

Recommendations

Key Recommendations

AKI is diagnosed by an acutely rising blood urea nitrogen (BUN) and creatinine, or sustained oliguria, in line with validated criteria such as the Kidney Disease: Improving Global Outcomes (KDIGO) definition.[1] [3] The KDIGO criteria merge features of the RIFLE (Risk, Injury, Failure, Loss of kidney function, and Endstage kidney disease) and Acute Kidney Injury Network (AKIN) criteria into a single standardized definition.[4] [88] [89]

AKI is diagnosed if any of the following criteria are met:[1]

- Increase in serum creatinine by ≥0.3 mg/dL within 48 hours, or
- Increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days, or
- Urine volume <0.5 mL/kg/hour for 6 hours.

AKI should then be staged according to severity criteria using KDIGO, RIFLE, or AKIN classifications.[1] [88] [89]

The condition is often asymptomatic and only diagnosed by laboratory tests.[90] General symptoms may include nausea and vomiting. Uremia, including altered mental status, may occur but this is more commonly seen in advanced AKI or in advanced chronic kidney disease.

A history of trauma or predisposing disease (e.g., congestive heart failure, chronic kidney disease, diabetes, peripheral vascular disease, and connective tissue diseases such as systemic lupus erythematosus, scleroderma, and vasculitis) may be present. Several groups have published risk scores for AKI and these have been variably validated by follow-up studies.[50] [55] [91] [92]

History in prerenal failure

Patients may have a history of excessive fluid loss from hemorrhage, the gastrointestinal (GI) tract (vomiting, diarrhea), or sweating. Hospitalized patients may have insufficient replacement fluids to cover ongoing and insensible losses, especially if there is restriction of enteral input.

There may be a history of sepsis, burns, major surgery, or pancreatitis.[90][93]

Patients may present with symptoms of hypovolemia: thirst, dizziness, tachycardia, oliguria, or anuria. Orthopnea and paroxysmal nocturnal dyspnea may occur if advanced cardiac failure is present.

History in intrinsic renal disease

Typically, patients present with acute tubular necrosis (ATN) subsequent to severe infection, nephrotoxic drug exposure, or major surgery. The patient may have a history of rash, hematuria, or edema with hypertension suggesting nephritic syndrome and an acute glomerulonephritis or renal vasculitis. There might have been a recent vascular intervention preceding the AKI, leading to cholesterol emboli or contrast-induced injury. A history of myeloproliferative disorder such as multiple myeloma may predispose to AKI, particularly in volume-depleted patients.

A history of all current drugs and any recent radiologic examinations should be taken to establish any exposure to potential nephrotoxins. Acyclovir, methotrexate, triamterene, indinavir, or sulfonamides can cause tubular obstruction by forming crystals. Over-the-counter drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs) and sympathomimetics are often overlooked, and patients should be specifically queried about their use.[94] Allergic interstitial nephritis may be suspected in patients with

a history of NSAID use or recent administration of new drugs such as beta-lactam antibiotics. Other substances to consider include hallucinogens and "bath salts".[95]

Pigment-induced AKI, due to rhabdomyolysis, should be suspected in patients presenting with muscle tenderness, seizures, drug abuse or alcohol abuse, excessive exercise, or limb ischemia (e.g., from crush injury).

History in postrenal failure

Postrenal failure is more common in older men with prostatic obstruction. There is often a history of urgency, frequency, or hesitancy.

A history of malignancy, prostatism, nephrolithiasis, or previous surgery may coincide with the diagnosis of obstruction. Obstruction caused by renal calculi or papillary necrosis typically presents with flank pain and visible hematuria.

Physical exam

Hypotension, hypertension, pulmonary edema, or peripheral edema may be present. There may be asterixis or altered mental status when uremia is present.

Patients with fluid loss, sepsis, or pancreatitis may have hypotension along with other signs of circulatory collapse.[96]

Patients with glomerular disease typically present with hypertension and edema, proteinuria, and microscopic hematuria (nephritic syndrome). Severe nephrotic syndrome, with peripheral edema and relative hypotension, can also lead to AKI.[97]

The presence of rash, petechiae, or ecchymoses may suggest an underlying systemic condition such as vasculitis, thrombotic microangiopathy, or glomerulonephritis.[71]

Patients with ATN may present after hemorrhage, sepsis, drug overdose, surgery, cardiac arrest, or other conditions associated with hypotension and prolonged renal ischemia.

An underlying abdominal bruit may support renovascular disease.

The patient with prostatic obstruction may present with abdominal distension from a full bladder.

Initial tests

Initial workup should include basic metabolic profile (including BUN and creatinine), venous blood gases, complete blood count, urinalysis and culture, urine chemistries (for fractional excretion of sodium and urea), renal ultrasound (when appropriate by history or exam), chest x-ray, and ECG. Urine osmolality is rarely ordered but, if high, suggests prerenal azotemia (in the absence of contrast dyes). Urinary eosinophil counts have low sensitivity and specificity for acute interstitial nephritis, but may be elevated in patients with pyuria.[98]

Chest x-ray may reveal pulmonary edema or cardiomegaly.

ECG may demonstrate arrhythmias if hyperkalemia is present.

Bladder catheterization is recommended in all cases of AKI, if bladder outlet obstruction is suspected and cannot be quickly ruled out by ultrasound. It is diagnostic and therapeutic for bladder neck obstruction in addition to providing an assessment of residual urine and a sample for analysis.

A serum BUN to creatinine ratio ≥20:1 supports a diagnosis of prerenal azotemia, but other causes of elevated BUN must be ruled out (such as drug-induced elevations or GI bleeding).

A fractional excretion of sodium (FENa) of <1% supports prerenal azotemia but may also be seen in glomerulonephritis, hepatorenal syndrome (typically <0.2%), and some cases of obstruction and even ATN, as long as tubular function remains intact.[99] [100] The FENa is calculated as follows: (urine sodium x serum creatinine)/(serum sodium x urine creatinine) x 100%.

A fractional excretion of urea of <35% supports a diagnosis of prerenal azotemia and is helpful if the patient has had diuretic exposure. The fractional excretion of urea is calculated as follows: (urine urea x serum creatinine)/(serum urea x urine creatinine) x 100%.[99]

A fluid challenge may be administered with crystalloid or colloid (but not hydroxyethyl starch solutions), and is both diagnostic and therapeutic for suspected prerenal azotemia if renal function improves rapidly.

High urine osmolality (or an elevated urine specific gravity), seen in prerenal azotemia, suggests maintenance of normal tubular function and response to antidiuretic hormone in cases of hypovolemia. Urine sodium concentration of <20 mEq/L suggests avid sodium retention and is typical of renal hypoperfusion/prerenal azotemia.[99] High urinary sodium is often seen in ATN, but is not exclusive to the diagnosis. Urine osmolality may be very high as the result of radiocontrast dyes and mannitol.

Urinary eosinophils >5% to 7% weakly supports the presence of interstitial nephritis, but is not diagnostic.[98] Some guidelines (e.g., the American Association for Clinical Chemistry) advise against routine use of urinary eosinophils in the evaluation of AKI.[99]

If there is no identified cause of AKI, a renal ultrasound is ordered at onset of workup to assist in evaluation of obstructive causes as well as in the evaluation of renal architecture and size. It is also useful for diagnosis of underlying chronic kidney disease.

Subsequent tests

A computed tomography or magnetic resonance imaging scan may be required to further evaluate cases of obstruction suggested on ultrasound (e.g., possible masses or stones).

Nuclear renal flow scans can evaluate renal perfusion and function, and may be modified using captopril to evaluate for renal artery stenosis, or with furosemide to evaluate for obstruction in cases of mild hydronephrosis, when obvious mechanical obstruction is uncertain.

Further diagnostic tests may be determined by the suspected cause of AKI, such as cystoscopy for cases of suspected ureteral stenosis or serologic evaluation (e.g., antistreptolysin O, erythrocyte sedimentation rate, antinuclear antibodies, anti-DNA, complement, anti-glomerular basement membrane antibodies, antineutrophil cytoplasmic antibodies, acute hepatitis profile, HIV test, and cryoglobulins) if the history suggests autoimmune, vasculitis, infectious, or immune complex disease, as in cases of suspected glomerulonephritis. Novel serum and urinary biomarkers have potential as useful indicators for the diagnosis of AKI and as predictors of mortality after AKI; however, further studies are needed to determine their clinical utility.[101] [102] [103] [104] [105] [106] [107]

A renal biopsy may be performed for further evaluation of AKI when the history, physical exam, and other studies suggest systemic disease as etiology or when the diagnosis is unclear.

Biopsies may confirm acute tubular necrosis, but are rarely done for this condition.

History and exam

Key diagnostic factors

reduced urine production (common)

Oliguria and anuria are common in AKI. They are not suggestive of a particular etiology.

vomiting (common)

May precede AKI and suggest prerenal azotemia, or be a later manifestation resulting from uremia.

dizziness (common)

Orthostatic symptoms support prerenal azotemia.

orthopnea (common)

Symptoms of volume overload may result from impaired salt and volume regulation and decreased urine production.

paroxysmal nocturnal dyspnea (common)

Symptoms of volume overload may result from impaired salt and volume regulation and decreased urine production. Congestive heart failure increases risk for prerenal azotemia.

pulmonary edema (common)

Evidence of pulmonary edema (e.g., rales on exam) suggest volume overload resulting from impaired salt and volume regulation.

hypotension (common)

Supports prerenal azotemia that may progress to acute tubular necrosis.

tachycardia (common)

Supports prerenal azotemia.

orthostatic hypotension (common)

Orthostatic symptoms support prerenal azotemia.

hypertension (common)

Suggests intravascular volume expansion.

peripheral edema (common)

May result from impaired renal salt excretion.

muscle tenderness (uncommon)

Suspect rhabdomyolysis and pigment-induced AKI.

limb ischemia (uncommon)

Suspect rhabdomyolysis and pigment-induced AKI.

seizures (uncommon)

Suspect rhabdomyolysis and pigment-induced AKI.

prostatic obstructive symptoms (uncommon)

Postrenal failure can occur in older men with prostatic obstruction and symptoms of urgency, frequency, or hesitancy.

hematuria (uncommon)

May indicate obstruction caused by renal calculi, papillary necrosis, infection, tumor, or acute glomerulonephritis.

fever (uncommon)

If present, suspect interstitial nephritis, systemic disease, infectious complication, or vasculitis.

rash (uncommon)

If present, suspect interstitial nephritis, systemic disease, infectious complication, or vasculitis.

arthralgia/arthritis (uncommon)

If present, suspect interstitial nephritis, systemic disease, infectious complication, or vasculitis.

altered mental status (uncommon)

May be due to underlying illness; will also be seen in AKI when uremia ensues.

signs of uremia (uncommon)

Although more often seen in chronic renal failure, symptoms and signs may be seen in AKI prior to dialysis initiation (e.g., asterixis, pericardial rub).

Other diagnostic factors

nausea (common)

May precede AKI and suggest prerenal azotemia, or be a later manifestation resulting from uremia.

thirst (uncommon)

Suggests prerenal azotemia if normal physiologic responses and drives are present in a conscious patient.

flank pain (uncommon)

May indicate infection, obstruction caused by renal calculi, or papillary necrosis.

abdominal distention (uncommon)

Bladder outlet obstruction may manifest as distention and pain. Severe intra-abdominal pressure can lead to abdominal compartment syndrome.

abdominal bruit (uncommon)

Presence of renal bruits suggests renovascular disease.

livedo reticularis (uncommon)

The presence of classic findings for systemic diseases may suggest renal manifestations.

petechiae (uncommon)

The presence of classic findings for systemic diseases may suggest renal manifestations.

ecchymoses (uncommon)

The presence of classic findings for systemic diseases may suggest renal manifestations.

Tests

1st test to order

Test	Result
basic metabolic profile (including blood urea nitrogen [BUN] and creatinine) Often an acutely elevated serum creatinine may be the initial or only sign of decline in renal function.	acutely elevated serum creatinine, high serum potassium, metabolic acidosis
ratio of serum BUN to creatinine Consider other causes of elevated BUN (such as drug-induced elevations or gastrointestinal bleeding) when interpreting results.	serum BUN to creatinine ratio ≥20:1 supports prerenal azotemia
urinalysis Collected as clean-catch specimen. Patients with glomerular disease typically present with proteinuria and microscopic hematuria with hypertension and edema.	red blood cells, WBCs, cellular casts, proteinuria, bacteria, positive nitrite and leukocyte esterase (in cases of infection)
urine culture Collected if there is suspicion of infection on initial urinalysis.	bacterial or fungal growth may occur
complete blood count Anemia is suggestive of possible chronic kidney disease, blood loss, or acute inflammation. Leukocytosis may support infection. Thrombocytopenia can be seen in rare disorders such as cryoglobulinemia, hemolytic uremic syndrome, or thrombotic microangiopathy.	anemia, leukocytosis, thrombocytopenia
fractional excretion of sodium May also be seen in glomerulonephritis, hepatorenal syndrome, and some cases of obstruction, as long as tubular function remains intact.[99] [100] Increased levels are also caused by diuretics. The FENa is calculated as follows: (urine sodium x serum creatinine)/(serum sodium x urine creatinine) x 100%.	<1% supports prerenal azotemia; typically <0.2% in hepatorenal syndrome
fractional excretion of urea Test used if patient has been exposed to diuretics. The fractional excretion of urea is calculated as follows: (urine urea x serum creatinine)/(serum urea x urine creatinine) x 100%. [Fractional excretion of urea: calculator]	<35% supports prerenal azotemia
urinary eosinophil count Urinary eosinophil counts have low sensitivity and specificity for acute interstitial nephritis, but may be elevated in patients with pyuria.[98]	>5% to 7% weakly supports a diagnosis of interstitial nephritis but is not diagnostic

Test	Result
Some guidelines (e.g., the American Association for Clinical Chemistry) advise against routine use in the evaluation of AKI.[99] Eosinophiluria may also be seen with atheroembolic disease.	
venous blood gases Anion gap acidosis seen in acute and chronic renal failure due to impaired excretion of nonvolatile acids. Assists in further evaluation of acidosis, which is often suggested by the low bicarbonate on the basic metabolic profile.	diagnostic for metabolic acidosis and certain intoxications
fluid challenge May be administered with crystalloid or colloid (but not hydroxyethyl starch solutions), and is both diagnostic and therapeutic in suspected prerenal azotemia.	renal function may improve rapidly in prerenal azotemia
bladder catheterization Diagnostic and therapeutic for bladder neck obstruction in addition to providing an assessment of residual urine and a sample for analysis.	significant urine volume released after catheter placement (in cases of bladder outlet obstruction); minimal residual urine after catheter placement (in cases of impaired urine production or higher level obstruction)
urine osmolality Evaluates maintenance of normal tubular function and response to antidiuretic hormone in cases of hypovolemia.	high in prerenal azotemia (the effect of dyes and mannitol must be excluded); close to serum osmolality in acute tubular necrosis
urine sodium concentration High levels in acute tubular necrosis not exclusive to the diagnosis.	<20 mEq/L (suggests avid sodium retention in renal hypoperfusion and prerenal azotemia); high level (often with acute tubular necrosis)
renal ultrasound Assists in evaluation of postobstructive causes as well as in the evaluation of renal architecture and size (underlying chronic kidney disease).	dilated renal calyces (suggesting obstruction), reduced corticomedullary differentiation, or small and sclerotic-appearing kidneys (suggesting chronic kidney disease)

Test	Result
chest x-ray If renal failure is associated with heart failure.	may show signs of pulmonary edema and cardiomegaly
ECG Changes may occur with severe hyperkalemia.	peaked T waves, increased PR interval, widened QRS, atrial arrest, and deterioration to a sine wave pattern (if severe hyperkalemia)

Other tests to consider

Test	Result
antinuclear antibodies Elevated titer is supportive of a diagnosis of systemic lupus erythematosus, which often has renal manifestations.	normal or elevated
anti-DNA Elevated titer supports the diagnosis of systemic lupus erythematosus, which often has renal manifestations.	normal or elevated
complement (C3, C4, CH50) Low complement levels support an active disease process, such as systemic lupus erythematosus.	normal or depressed
anti-glomerular basement membrane antibodies Elevated antibody titers to the glomerular basement membrane, which may present in diseases of the kidney (e.g., Goodpasture syndrome and antiglomerular basement membrane syndrome).	normal or elevated
antineutrophil cytoplasmic antibodies Elevated titers are seen in vasculitic syndromes such as granulomatosis with polyangiitis (formerly known as Wegener granulomatosis), eosinophilic polyangiitis, and microscopic polyangiitis.	normal or elevated titers
acute hepatitis profile The presence of positive serology in active hepatitis C is associated with renal conditions such as membranoproliferative glomerulonephritis and cryoglobulinemia.	positive or negative serology
HIV serology HIV-associated nephropathy and certain drugs used in the management of HIV have renal complications.	positive or negative
cryoglobulins The presence of cryoglobulins support cryoglobulin-associated renal disease, if AKI is present.	positive or negative serology
erythrocyte sedimentation rate A normal erythrocyte sedimentation rate argues against the presence of inflammatory renal disease or embolic injury.	normal or elevated
antistreptolysin-O antibody An elevated titer supports but does not make a diagnosis of an infectious glomerulonephritis.	normal or elevated
abdominal computed tomography or magnetic resonance imaging scan Sometimes required to further evaluate cases of obstruction suggested on ultrasound.	image of mass or stone may be present

Test	Result
nuclear renal flow scan May be modified using captopril to evaluate for renal artery stenosis, or furosemide to evaluate for obstruction in cases of hydronephrosis where obvious mechanical obstruction is uncertain.	normal scan reveals appropriate renal perfusion, tracer uptake, and excretion; impaired tracer excretion (supportive of acute tubular necrosis); poor blood flow (supportive of obstruction of blood supply); normal blood flow and tracer excretion with tracer accumulation in the collecting system (supportive of obstruction of the urine outflow tract)
cystoscopy May be used if obstruction due to stenosis of the ureter is suspected.	direct visualization and treatment of ureteral stenosis if present
renal biopsy Biopsy is frequently required to further investigate positive serologic studies for suspected glomerulonephritis. Biopsies are also done when the cause of kidney injury is unclear. May confirm acute tubular necrosis, but not often performed for this diagnosis.	changes associated with acute tubular necrosis, glomerulonephritis, vasculitis, or other intrinsic renal disease may be present

Emerging tests

Test	Result
novel serum and urinary biomarkers Various novel serum and urinary biomarkers are showing potential as useful indicators for the diagnosis and classification of AKI and as predictors of mortality after AKI; however, further studies are needed to determine their clinical utility.[101] [102] [103] [104] [106] [107]	results indicative of renal damage

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Chronic kidney disease	• Reduced renal function with elevation of creatinine is chronic (>3 months), although there may be acute on chronic renal disease.	• An acutely elevated serum creatinine is diagnostic of AKI and indicative of reduced clearance. • There are no causes of chronically elevated serum creatinine other than reduced glomerular filtration (except for minor elevations in subjects with increased muscle mass and from certain drugs). • Creatinine elevation over time provides a chronological perspective and assists in differentiating acute from chronic kidney disease. • Twenty-four-hour urine study for creatinine clearance demonstrates the level of renal function; the use of inulin clearance or 131-I iothalamate disappearance is the definitive test for this purpose.
Increased muscle mass	• Any elevation of creatinine is minor and typically nonacute.	• Acutely elevated serum creatinine is diagnostic of AKI. • Minor elevations in creatinine from increased muscle mass may rarely be seen. • Twenty-four-hour urine study for creatinine clearance demonstrates normal renal function.
Drug side effect	• Certain drugs such as cimetidine or trimethoprim may lead to an elevation of creatinine that is minor and nonacute.	• Discontinuing the drug should result in normalizing of the serum creatinine. • 24-hour urine study for creatinine clearance should demonstrate normal function.

Criteria

Kidney Disease: Improving Global Outcomes (KDIGO) - definition criteria[1]

Any of the following:

- Increase in serum creatinine by ≥0.3 mg/dL within 48 hours; or
- Increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume <0.5 mL/kg/hour for 6 hours.

Kidney Disease: Improving Global Outcomes (KDIGO) - severity criteria[1]

- Stage 1
  - Serum creatinine 1.5 to 1.9 times baseline; or
  - ≥0.3 mg/dL increase in serum creatinine; or
  - Urine output <0.5 mL/kg/hour body weight for 6 to 12 hours
- Stage 2
  - Creatinine increased 2.0 to 2.9 times; or
  - Urine output <0.5 mL/kg/hour for 12 hours
- Stage 3
  - Creatinine increased 3.0 times; or
  - Increase in creatinine to ≥4.0 mg/dL; or
  - Initiation of renal replacement therapy; or
  - Urine output <0.3 mL/kg/hour for 24 hours OR anuria for 12 hours.

RIFLE (Risk, Injury, Failure, Loss of kidney function, and Endstage kidney disease) consensus criteria[88]

Laboratory test indicates reduced renal clearance.

Severity groups are as follows.

- Indicates risk:
  - Serum creatinine increased 1.5 times; or
  - Urine production of <0.5 mL/kg body weight for 6 hours.
- Indicates injury:
  - Creatinine increased 2.0 times; or
  - Urine production of <0.5 mL/kg for 12 hours.
- Indicates failure:
  - Creatinine increased 3.0 times; or

- Urine output <0.3 mL/kg for 24 hours or anuria for 12 hours.

- Indicates loss:
  - Persistent AKI for more than 4 weeks; complete loss of kidney function.

- Indicates ESRD:
  - ESRD (loss >3 months).

Recommendations

Key Recommendations

Treatment approaches for AKI vary according to the type of insult. The underlying illness requires treatment.

General therapy includes intervention in electrolyte and acid/base abnormalities and optimization of volume status, either by replacing volume in the volume-contracted patient or by fluid removal (either diuresis or renal replacement therapy) in patients with volume overload.

Review and adjustment of drugs is required in all cases to reduce exposure to nephrotoxic agents (e.g., aminoglycosides and other nephrotoxic antibiotics, many cancer therapies, nonsteroidal anti-inflammatory drugs).[110] Consult your local drug information source for more information on nephrotoxic drugs. Patients with AKI should not be given potentially nephrotoxic drugs unless there is no alternative. Electrolyte and acid-base balance should be monitored and optimized. For management of hyperkalemia, see Hyperkalemia in adults .

Early involvement by a nephrologist may be valuable; however, automated electronic alerts to identify AKI have not improved outcomes.[111] [112]

Prerenal renal failure

Prerenal azotemia is managed with techniques to improve the hemodynamic status of the patient.

The volume-contracted patient requires volume expansion with crystalloid or colloid to restore euvolemia.

Crystalloid (normal saline or balanced solutions, such as Ringer lactate [Hartmann solution]) or colloid (considered in cases of significant hypoalbuminemia) fluids are infused, along with packed red blood cells if there is significant anemia.[5] [113]

In the US, the Food and Drug Administration (FDA) issued safety labeling changes in July 2021 for solutions containing hydroxyethyl starch (HES) stating that HES products should not be used unless adequate alternative treatment is unavailable.[114] Solutions containing HES are associated with adverse outcomes including kidney injury and death, particularly in critically ill patients and those with sepsis.[115] [116] In view of the serious risks posed to these patient populations, the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency in February 2022 recommended suspending HES solutions for infusion in Europe.[117]

The US National Kidney Foundation states that crystalloids are preferred over colloids for most patients with AKI, and recommends that hydroxyethyl starches are avoided.[110]

All fluid resuscitation should be performed by a clinician with expertise in this area, with close patient monitoring.

Vasopressors are recommended if hypotension is severe, to augment blood pressure while optimizing the patient's volume status.[5] A common goal of vasopressors in this setting is to keep the mean arterial pressure (MAP) >65 mmHg.[1] (MAP is the diastolic pressure plus one third of the pulse pressure, where the pulse pressure is the systolic pressure minus the diastolic pressure.) Vasopressors and inotropic agents should be used only with appropriate hemodynamic monitoring in place.[1]

Management is often difficult if prerenal azotemia results from impaired cardiac function due to poor left or right ventricular systolic function when volume overload/venous congestion may occur concurrently with renal hypoperfusion.[118] It requires optimization of cardiac output and volume status by use of inotropes, diuretics, or renal replacement therapy as indicated by the clinical scenario, along with close monitoring of renal function and urine production during therapy.[5] [113]

Renal replacement therapy may be needed if severe acid/base, electrolyte, or uremic complications are present while the underlying cardiac or volume issues are treated. The use of diuretics may be helpful to manage volume in patients with ineffective circulating volume and prerenal AKI. Diuretic-unresponsive volume overload, increased potassium, severe metabolic acidosis, or uremic symptoms are indications to proceed to renal replacement therapy by means of dialysis or filtration.[5]

Intrinsic renal failure

Management of intrinsic renal failure varies according to etiology.

Volume expansion is required when coexisting prerenal azotemia exists. It is unclear whether a chloride-sparing intravenous fluid strategy improves outcomes in critically ill patients.[85] [86] Larger randomized studies remain necessary to alter practice.[86]

Generally, patients with volume overload require sodium restriction. The amount of sodium restriction depends on the clinical setting.[119] Volume overload may be managed with diuretics when responsive.

In cases of drug-induced AKI or interstitial nephritis, offending drugs should be stopped when possible, followed by consideration for corticosteroids.

Management of acute glomerulonephritis, vasculitis, and thrombotic microangiopathies may require corticosteroids, cytotoxic agents, or other immune-modifying drugs depending on the specific diagnosis, often determined by renal biopsy and serology studies.[120]

The management of acute glomerulonephritis requires a nephrologist consultation, particularly regarding the use of cytotoxic and immune-modifying agents. Doses and protocols for many of the drugs used vary by center. The Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guideline for glomerulonephritis can be consulted. [KDIGO clinical practice guideline for glomerulonephritis]

There is no specific therapy for acute tubular necrosis aside from maintaining volume status and controlling electrolyte and acid/base abnormalities. Nephrotoxins should be removed or minimized. Renal replacement therapy is generally required if there is severe acidosis, volume expansion refractory to diuretics, hyperkalemia, or uremia.

Obstructive renal failure

Bladder catheter placement should be done in all cases of AKI if bladder outlet obstruction cannot be quickly ruled out by ultrasound.

Urologic, radiologic, or surgical assistance for ureteral stenting, urinary diversion, debulking procedures, or other case-specific requirements may become necessary.

Ureteral stenting is indicated if there is a ureteral stricture, stone, or extrinsically obstructing mass. If obstruction is caused by stones at the ureteropelvic junction, lithotripsy or surgical removal may be needed.[121]

Percutaneous nephrostomy (placement of a catheter into the renal pelvis percutaneously for drainage of urine from a distal obstruction) may be undertaken by a urologist, surgeon, or interventional radiologist.[121]

Surgical consultation may be needed if the cause is tumor with mass effect. Exploratory laparotomy may be indicated with a view to surgical removal of a compressing tumor; this may be done following ureteral stenting.

Renal replacement therapy is generally required if there is severe acidosis, volume overload unresponsive to diuretics, or electrolyte or uremic complications while the underlying obstructive issue is being addressed.

Renal replacement therapy

Renal replacement therapy is indicated for refractory severe hyperkalemia, acidosis, volume overload, or uremia.

Conventional hemodialysis is often used when the indications for dialysis arise. Other modes of renal replacement include sustained low-efficiency dialysis (SLED), extended daily dialysis (EDD), rapid-start peritoneal dialysis, or continuous renal replacement therapy (CRRT).[122] [123] Arteriovenous and venovenous techniques may be used, although the most frequent approach is continuous venovenous treatment through a large double lumen catheter placed into the central venous system, such as the internal jugular or femoral vein. Major commonly used modalities include continuous venovenous hemofiltration (CVVH), continuous venovenous hemodialysis (CVVHD), and continuous venovenous hemodiafiltration (CVVHDF).[124] [125] [126] [127]

CRRT is mostly used in hemodynamically unstable patients or those in whom aggressive ultrafiltration within the conventional 4- to 6-hour treatment of hemodialysis would not be tolerated. Such patients include septic patients requiring vasopressors, or patients with severe heart failure with volume overload and a blood pressure that would not support conventional hemodialysis. Despite improved hemodynamic stability, studies have shown that CRRT or more intensive/frequent dialysis in critically ill patients with AKI confers no increased benefit with respect to other complications or mortality.[125] [126] [127]

Early dialysis appeared to reduce mortality compared with a delayed strategy in one small single-center randomized trial of critically ill patients with AKI, but subsequent meta-analyses found no clear mortality benefit associated with early initiation of renal replacement therapy.[71] [128] [129] [130] [131]

Peritoneal dialysis has generally been thought ineffective in AKI and hypercatabolic states, although some studies suggest comparable effectiveness in appropriate subjects. In developing countries, high-volume peritoneal dialysis (HVPD) provides an alternative form of therapy in selected cases.[132] [133] [134] [135]

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Acute (summary)

prerenal azotemia

1st		treatment of underlying condition
plus		review drugs and stop nephrotoxins
plus	with hypovolemia	volume expansion
consider		vasopressor
consider	with volume overload	diuretic
consider	with uremia, severe metabolic acidosis, hyperkalemia refractory to medical management, or volume overload unresponsive to diuretics	renal replacement therapy

intrinsic renal failure

1st		treatment of underlying condition
plus		review drugs and stop nephrotoxins
consider	with volume overload	diuretic
consider	with preexisting prerenal azotemia	volume expansion
consider	with uremia, severe metabolic acidosis, hyperkalemia refractory to medical management, or volume overload unresponsive to diuretics	renal replacement therapy

obstructive renal failure

1st		bladder catheterization
plus		review drugs and stop nephrotoxins
2nd		relief of obstruction above bladder neck
consider	with hypovolemia	volume expansion
consider	with volume overload	diuretic
consider	with uremia, severe metabolic acidosis, or hyperkalemia refractory	renal replacement therapy

Acute	(summary)
to medical management, or volume overload unresponsive to diuretics	

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Acute

prerenal azotemia

1st **treatment of underlying condition**

» Prerenal azotemia is managed with techniques to improve the hemodynamic status of the patient. The underlying cause must be identified and treated, along with restoring euvolemia and hemodynamic stability.

» Patients may have a history of excessive fluid loss from hemorrhage, the gastrointestinal (GI) tract, or sweating. There may be a history of sepsis, burns, major surgery, pancreatitis, or congestive heart failure.[90] [93]

» In practice, a fluid challenge can be both diagnostic and therapeutic in suspected hypovolemic prerenal azotemia. The US National Kidney Foundation states that crystalloids are preferred over colloids for most patients with AKI, and recommends that hydroxyethyl starches are avoided.[110]

» Electrolyte and acid-base balance should be monitored and optimized. For management of hyperkalemia, see Hyperkalemia in adults .

» Management is often difficult if prerenal azotemia results from impaired cardiac function due to poor left or right ventricular systolic function, when volume overload/venous congestion may occur concurrently with renal hypoperfusion.[118]

» It requires optimization of cardiac output and volume status as indicated by the clinical scenario, along with close monitoring of renal function and urine production during therapy.[5] [113]

plus **review drugs and stop nephrotoxins**

Treatment recommended for ALL patients in selected patient group

» Review and adjustment of drugs is required in all cases to reduce exposure to nephrotoxic agents (e.g., aminoglycosides and other nephrotoxic antibiotics, many cancer therapies, nonsteroidal anti-inflammatory drugs [NSAIDS]).[110]

Acute

» Consult your local drug information source for more information on nephrotoxic drugs.

with hypovolemia **plus** **volume expansion**

Treatment recommended for ALL patients in selected patient group

» Crystalloid (normal saline or balanced solutions, such as Ringer lactate [Hartmann solution]) is sufficient in most cases for volume expansion.[5] [113] Colloid might be used if there is significant hypoalbuminemia.

» In the US, the Food and Drug Administration (FDA) issued safety labeling changes in July 2021 for solutions containing hydroxyethyl starch (HES) stating that HES products should not be used unless adequate alternative treatment is unavailable.[114] Solutions containing HES are associated with adverse outcomes including kidney injury and death, particularly in critically ill patients and those with sepsis.[115] [116] In view of the serious risks posed to these patient populations, the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency in February 2022 recommended suspending HES solutions for infusion in Europe.[117]

» The US National Kidney Foundation states that crystalloids are preferred over colloids for most patients with AKI, and recommends that hydroxyethyl starches are avoided.[110]

» Hemorrhage requires blood product replacement.

consider **vasopressor**

Treatment recommended for SOME patients in selected patient group

» Vasopressors are recommended for severe hypotension, often with the goal of keeping mean arterial pressure (MAP) >65 mmHg. (MAP is the diastolic pressure plus one third of the pulse pressure, where the pulse pressure is the systolic pressure minus the diastolic pressure.) All vasopressors should be used only with appropriate hemodynamic monitoring in place.[1]

» The septic patient requires hemodynamic support with vasopressors as needed to support MAP and organ perfusion.

» Consult a specialist for guidance on suitable vasopressor regimen.

with volume overload **consider** **diuretic**

Acute

Treatment recommended for SOME patients in selected patient group

Primary options

» furosemide: 40-80 mg intravenously initially, increase by 20 mg/dose increments every 2 hours as necessary until clinical response

Secondary options

» torsemide: 20 mg intravenously once daily initially, increase gradually according to response, maximum 200 mg/day

OR

» bumetanide: 1-2 mg intravenously initially, may repeat in 2-3 hours for up to 2 doses if necessary, maximum 10 mg/day

OR

» metolazone: 5-20 mg orally once daily

» The use of diuretics may be helpful to manage volume in patients with ineffective circulating volume and prerenal AKI. Diuretic-unresponsive volume overload is an indication to proceed to renal replacement therapy by means of dialysis or filtration.

» Impaired urine production and volume expansion are commonly seen in cases of AKI.

» Loop diuretics (e.g., furosemide) and metolazone may be effective in promoting diuresis, although diuretic resistance is often seen.[118]

» Patients may also require sodium restriction.[119]

with uremia, severe metabolic acidosis, hyperkalemia refractory to medical management, or volume overload unresponsive to diuretics — **consider** — **renal replacement therapy**

Treatment recommended for SOME patients in selected patient group

» Nephrologist consultation is required.

» Conventional hemodialysis for 4 to 6 hours is used in hemodynamically stable patients.

» Other modes of renal replacement include sustained low-efficiency dialysis (SLED), extended daily dialysis (EDD), or continuous renal replacement therapy (CRRT).[124] Major commonly used modalities include continuous venovenous hemofiltration (CVVH), continuous

Acute

venovenous hemodialysis (CVVHD), and continuous venovenous hemodiafiltration (CVVHDF).

» CRRT is mostly used in hemodynamically unstable patients (e.g., patients with sepsis, or with severe congestive heart failure) or those in whom aggressive ultrafiltration within the conventional 4- to 6-hour treatment of hemodialysis would not be tolerated.

» Studies have shown that intensive dialysis in critically ill patients with AKI confers no increased benefit.[124] [125] [126] [127] [139]

» Early dialysis appeared to reduce mortality compared with a delayed strategy in one small single-center randomized trial of critically ill patients with AKI.[128] However, a larger study and meta-analysis found no benefit associated with early initiation of renal replacement therapy.[129] [140]

intrinsic renal failure

1st **treatment of underlying condition**

» Management of intrinsic renal failure varies according to etiology. The patient should be referred to a nephrologist if specific treatment is required. This might include dialysis or consideration for corticosteroids, immunosuppressants, or other immune-modifying drugs.[1]

» Electrolyte, fluid, and acid-base balance should be monitored and optimized. For management of hyperkalemia, see Hyperkalemia in adults .

plus **review drugs and stop nephrotoxins**

Treatment recommended for ALL patients in selected patient group

» Review and adjustment of drugs is required in all cases to reduce exposure to nephrotoxic agents (e.g., aminoglycosides and other nephrotoxic antibiotics, many cancer therapies, nonsteroidal anti-inflammatory drugs [NSAIDS]).[110]

» Consult your local drug information source for more information on nephrotoxic drugs.

with volume overload **consider** **diuretic**

Treatment recommended for SOME patients in selected patient group

MANAGEMENT

Acute

Primary options

» furosemide: 40-80 mg intravenously initially, increase by 20 mg/dose increments every 2 hours as necessary until clinical response

Secondary options

» torsemide: 20 mg intravenously once daily initially, increase gradually according to response, maximum 200 mg/day

OR

» bumetanide: 1-2 mg intravenously initially, may repeat in 2-3 hours for up to 2 doses if necessary, maximum 10 mg/day

OR

» metolazone: 5-20 mg orally once daily

» The use of diuretics in the management of AKI is primarily for volume control.[1] Diuretic-unresponsive volume overload is an indication to proceed to renal replacement therapy by means of dialysis or filtration.

» Impaired urine production and volume expansion are commonly seen in cases of AKI.

» Loop diuretics (e.g., furosemide) and metolazone may be effective in promoting diuresis, although diuretic resistance is often seen.

» Patients may also require sodium restriction.[119]

with preexisting prerenal azotemia — **consider** — **volume expansion**

Treatment recommended for SOME patients in selected patient group

» Crystalloid (normal saline or balanced solutions, such as Ringer lactate [Hartmann solution]) is sufficient in most cases for volume expansion.[5] [113] Colloid might be used if there is significant hypoalbuminemia.

» In the US, the Food and Drug Administration (FDA) issued safety labeling changes in July 2021 for solutions containing hydroxyethyl starch (HES) stating that HES products should not be used unless adequate alternative treatment is unavailable.[114] Solutions containing HES are associated with adverse outcomes including kidney injury and death,

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particularly in critically ill patients and those with sepsis.[115] [116] In view of the serious risks posed to these patient populations, the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency in February 2022 recommended suspending HES solutions for infusion in Europe.[117]

» The US National Kidney Foundation states that crystalloids are preferred over colloids for most patients with AKI, and recommends that hydroxyethyl starches are avoided.[110]

with uremia, severe metabolic acidosis, hyperkalemia refractory to medical management, or volume overload unresponsive to diuretics

consider

renal replacement therapy

Treatment recommended for SOME patients in selected patient group

» Nephrologist consultation recommended.

» Conventional hemodialysis is used in hemodynamically stable patients.

» Other modes of renal replacement include sustained low-efficiency dialysis (SLED), extended daily dialysis (EDD), rapid-start peritoneal dialysis, or continuous renal replacement therapy (CRRT).[122] [123] Major commonly used modalities include continuous venovenous hemofiltration (CVVH), continuous venovenous hemodialysis (CVVHD), and continuous venovenous hemodiafiltration (CVVHDF).

» CRRT is mostly used in hemodynamically unstable patients (e.g., patients with sepsis or severe congestive heart failure) or those in whom aggressive ultrafiltration within the conventional 4-to 6-hour treatment of hemodialysis would not be tolerated.

» Studies have shown that intensive dialysis in critically ill patients with AKI confers no increased benefit.[124] [125] [126] [127] [139]

» Early dialysis appeared to reduce mortality compared with a delayed strategy in one small single-center randomized trial of critically ill patients with AKI, but subsequent meta-analyses found no clear benefit associated with early initiation of renal replacement therapy.[71] [128] [129] [130] [131]

obstructive renal failure

1st

bladder catheterization

» Treatment of obstructive renal failure requires mechanical decompression at the level of obstruction.

MANAGEMENT

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» Bladder catheter placement should be done in all cases of AKI if bladder outlet obstruction cannot be quickly ruled out by ultrasound.

» Electrolyte, fluid, and acid-base balance should be monitored and optimized. For management of hyperkalemia, see Hyperkalemia in adults .

plus **review drugs and stop nephrotoxins**

Treatment recommended for ALL patients in selected patient group

» Review and adjustment of drugs is required in all cases to reduce exposure to nephrotoxic agents (e.g., aminoglycosides and other nephrotoxic antibiotics, many cancer therapies, nonsteroidal anti-inflammatory drugs [NSAIDS]).[110]

» Consult your local drug information source for more information on nephrotoxic drugs.

2nd **relief of obstruction above bladder neck**

» Further decompression more proximal in the genitourinary tract may be required if bladder neck obstruction is not the cause of the obstruction.

» Urologic, radiologic, or surgical assistance for ureteral stenting, urinary diversion, debulking procedures, or other case-specific requirements may become necessary.

» Ureteral stenting is indicated if there is a ureteral stricture, stone, or extrinsically obstructing mass. If obstruction is caused by stones at the ureteropelvic junction, lithotripsy or surgical removal may be needed.[121]

» Percutaneous nephrostomy (placement of a catheter into the renal pelvis percutaneously for drainage of urine from a distal obstruction) may be undertaken by a surgeon (usually a urologist) or interventional radiologist.[121]

» Surgical consultation may be needed if the cause is tumor with mass effect. Exploratory laparotomy may be indicated with a view to surgical removal of a compressing tumor; this may be done following ureteral stenting.

with hypovolemia **consider** **volume expansion**

Treatment recommended for SOME patients in selected patient group

Acute

» Crystalloid (normal saline or balanced solutions, such as Ringer lactate [Hartmann solution]) is sufficient in most cases for volume expansion.[5] [113] Colloid might be used if there is significant hypoalbuminemia.

» In the US, the Food and Drug Administration (FDA) issued safety labeling changes in July 2021 for solutions containing hydroxyethyl starch (HES) stating that HES products should not be used unless adequate alternative treatment is unavailable.[114] Solutions containing HES are associated with adverse outcomes including kidney injury and death, particularly in critically ill patients and those with sepsis.[115] [116] In view of the serious risks posed to these patient populations, the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency in February 2022 recommended suspending HES solutions for infusion in Europe.[117]

» The US National Kidney Foundation states that crystalloids are preferred over colloids for most patients with AKI, and recommends that hydroxyethyl starches are avoided.[110]

with volume overload **consider** **diuretic**

Treatment recommended for SOME patients in selected patient group

Primary options

» furosemide: 40-80 mg intravenously initially, increase by 20 mg/dose increments every 2 hours as necessary until clinical response

Secondary options

» torsemide: 20 mg intravenously once daily initially, increase gradually according to response, maximum 200 mg/day

OR

» bumetanide: 1-2 mg intravenously initially, may repeat in 2-3 hours for up to 2 doses if necessary, maximum 10 mg/day

OR

» metolazone: 5-20 mg orally once daily

» Diuretics should not be used in suspected complete obstruction.

» The use of diuretics in the management of AKI is primarily for volume control.

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» Diuretic-unresponsive volume overload is an indication to proceed to renal replacement therapy by means of dialysis or filtration.

» Impaired urine production and volume expansion are commonly seen in cases of AKI.

» Loop diuretics (e.g., furosemide) and metolazone may be effective in promoting diuresis, although diuretic resistance is often seen.

» Patients also require sodium restriction.

with uremia, severe metabolic acidosis, or hyperkalemia refractory to medical management, or volume overload unresponsive to diuretics — **consider** — **renal replacement therapy**

Treatment recommended for SOME patients in selected patient group

» Nephrologist consultation is recommended.

» Conventional hemodialysis is used in hemodynamically stable patients. Other modes of renal replacement include sustained low-efficiency dialysis (SLED), extended daily dialysis (EDD), or rapid-start peritoneal dialysis; continuous renal replacement therapy (CRRT) is used if the patient is hemodynamically unstable despite full support.[122] [123]

» Renal replacement therapy may be required to manage complications of obstruction while surgical interventions are planned and implemented.

Emerging

Novel therapeutic agents

The use of novel therapeutic agents, including atrial natriuretic peptide, theophylline, insulin-like growth factor, epidermal growth factor, free radical oxygen scavengers, antibodies to adhesion molecules, and prostaglandins, has been reviewed.[17] None have shown clear benefit in human AKI.[17] [141] The protective effect of statins (administered either pre-intervention or chronically) remains debated.[70] [142] [143] [144] [145] Controlled hypothermia and recombinant alkaline phosphatase infusion may be of benefit but need more experience.[146] [147] Erythropoietin does not appear to exert nephroprotective effects, and treatment with thyroid hormone has been associated with worse outcomes than other possible treatments for patients with established AKI; its role in preventing AKI was not adequately investigated.[148] [149] Remote ischemic preconditioning appeared to hold promise to prevent AKI, but two systematic reviews (including more than 28 randomized controlled trials) cast doubt on the value of this treatment.[110] [150] [151]

Primary prevention

Exposure to radiocontrast may cause AKI.[5] However, the association is controversial because population studies do not replicate risk.[33] [34] [35] [36] Evidence regarding the prevention of contrast-induced AKI is weak, and often conflicting.

- Administration of normal saline at a dose of 1 mL/kg/hour for several hours before and after the contrast is believed to be beneficial in the prevention of contrast nephropathy.[60] The American College of Radiology and the National Kidney Foundation recommend prophylaxis with normal saline for patients receiving iodinated contrast and AKI or estimated GFR less than 30 mL/minute/1.73 m^2.[61] The UK National Institute for Health and Care Excellence (NICE) recommends use of intravenous volume expansion only for inpatients considered at particularly high risk: for example, if they have preexisting renal impairment.[3][Evidence C] However, a large study did not show benefit from preventative intravenous hydration in patients at risk of contrast-induced nephropathy according to current guidelines.[62]
- Probucol, allopurinol, alprostadil, and atrial natriuretic peptide reduced the risk of contrast-induced AKI in small studies, but remain experimental.[63] [64] [65][66] [67] [68]
- High-dose statins appear to reduce risk of contrast-induced AKI in some patient groups.[69] [70] [71]

Sodium bicarbonate is unlikely to be superior to saline for the prevention of contrast-induced injury.[72] [73] Studies assessing the efficacy of acetylcysteine administration before contrast exposure have produced conflicting results, but larger trials show no significant benefit.[73] [74] [75] [76]

Treatment during cardiac surgery

- Sodium nitroprusside has been shown to be associated with improved renal function when given during the rewarming period of nonpulsatile coronary pulmonary bypass in the course of coronary artery bypass grafting surgery.[77]
- One large meta-analysis of 4605 adult patients undergoing cardiac surgery with cardiopulmonary bypass and receiving different forms of therapy, concluded that fenoldopam, atrial natriuretic peptide, and brain natriuretic peptide showed evidence of nephroprotection, although none reduced all-cause mortality.[78] These interventions remain hard to justify based on overall evidence.
- One study analyzing the effect of high-dose perioperative atorvastatin in patients undergoing elective coronary artery bypass grafting, valvular heart surgery, or ascending aortic surgery suggested no benefit.[79] In a similar patient population, AKI was more common among those randomized to perioperative rosuvastatin than to placebo.[80]
- Levosimendan, a calcium sensitizer used to improve cardiac output, appears to prevent AKI in patients undergoing cardiac surgery.[81] [82]
- Results from one meta-analysis suggest that preoperative intra-aortic balloon pump support for high-risk patients undergoing coronary artery bypass grafting surgery lessens the risk of postoperative AKI.[83]
- Compared with on-pump coronary artery bypass grafting, off-pump surgery appears to reduce the risk of postoperative AKI.[53]

- One meta-analysis of 1308 adult patients undergoing cardiac surgery concluded that perioperative administration of dexmedetomidine reduced the risk of AKI; however, there was no significant reduction in in-hospital mortality.[84]

Critically ill patients in intensive care unit setting

- It is unclear whether a chloride-sparing intravenous fluid strategy reduces the incidence of AKI in critically ill patients.[85] [86] Larger randomized studies remain necessary to alter practice.[86]

Severe metabolic acidosis

- One trial reported improved outcome and reduced mortality among a subset of critically ill patients with AKI who received sodium bicarbonate infusion for correction of metabolic acidemia.[87] However, sodium bicarbonate was not associated with clinical benefit in unselected critically ill patients with severe acidemia.

Patient discussions

Patients who have had an episode of AKI should be seen by a nephrologist before undergoing any diagnostic or therapeutic intervention that carries an increased risk of acute renal injury. Nonsteroidal anti-inflammatory drugs should be avoided.

FOLLOW UP

Monitoring

Monitoring

If recovery of function is complete and a normal glomerular filtration rate is re-established with no evidence of residual renal injury, no renal follow-up is required.

If the patient is left with residual chronic kidney disease (CKD) after AKI, nephrologist follow-up is recommended with interventions based on stage of CKD.[166]

The National Kidney Foundation KDOQI guidelines include recommendations regarding the management of patients who have developed CKD subsequent to AKI.[167] Management of chronic intrinsic renal diseases (e.g., glomerulonephritis and vasculitis) requires nephrologist intervention to manage therapies including corticosteroids, cytotoxic drugs, and immune-modifying drugs. Adverse effects and toxicities require close observation.

Complications

Complications	Timeframe	Likelihood
hyperphosphatemia	**long term**	**high**
A late complication usually arising several days after glomerular filtration falls. Treatment includes dietary restriction and the administration of phosphate binders, such as calcium acetate, calcium carbonate, sevelamer, or lanthanum carbonate. Hemodialysis is effective in phosphorus reduction. In patients in whom intense renal replacement is undertaken, such as those on continuous renal replacement therapies or daily dialysis regimens, phosphorus replacement may be required.		
uremia	**long term**	**medium**
Uremic toxins accumulate with severe and untreated renal failure, resulting in lethargy, confusion, and obtundation. Dialysis is required for management of uremia.		
volume overload (pulmonary edema, peripheral edema)	**variable**	**high**
Impaired volume regulation is common in AKI not occurring from prerenal azotemia.[162] Volume intake is limited and diuresis maximized with agents such as furosemide. Response to diuretics is variable. Ultrafiltration (volume removal by renal replacement therapy) may be required.		
hyperkalemia	**variable**	**high**
Results from impaired excretion of potassium, cell lysis, or tissue breakdown. Severe hyperkalemia may result in classic ECG findings of peaked T waves, increased PR interval, widened QRS, atrial arrest, and deterioration to a sine wave pattern. Restrictions on dietary potassium intake should be imposed on all patients and may be sufficient for mild hyperkalemia. Sodium polystyrene sulfonate may be used for moderate to severe cases of hyperkalemia. However, its effects are not immediate and serum potassium must be rapidly lowered. If these initial steps are not sufficient or if hyperkalemia is severe, medical intervention is mandated and includes cardiac evaluation by ECG. If classic changes are present, treatment with intravenous calcium is required immediately in addition to rapid lowering of serum potassium with insulin, glucose, and beta-agonists. Care should be taken to prevent extravasation when giving calcium salts intravenously, because they are highly toxic to tissues.		

Complications	Timeframe	Likelihood
If hyperkalemia is refractory to medical treatment or if cardiac manifestations are present, hemodialysis is indicated for rapid potassium normalization.		
metabolic acidosis	**variable**	**high**
Results from accumulation of nonvolatile acids. Oral or intravenous bicarbonate preparations such as sodium bicarbonate or sodium citrate/citric acid may be used to manage metabolic acidosis. Management often requires dialysis if severe and if respiratory compensation is unable to maintain pH.		
chronic progressive kidney disease	**variable**	**medium**
AKI may leave the patient with prolonged renal damage, and functional recovery may not return to the baseline. Recovery is dependent on the mechanism and severity of the injury and the underlying comorbid medical conditions. AKI in children may be associated with chronic renal disease that may progress to end-stage renal disease.[163] [164] Patients with partial or no recovery from AKI are at increased risk for congestive heart failure and acute myocardial infarction.[162][165]		
end-stage renal disease	**variable**	**medium**
Some patients may not recover from severe kidney injury, especially those with underlying kidney disease or other comorbid medical conditions. Chronic renal replacement therapy may be required.[157]		

Prognosis

Recovery for AKI is variable and depends on cause of injury and the severity and duration of AKI.[152] [153]

There is an independent association of AKI with a higher risk of death.[9] [152] [154] In-hospital mortality rates associated with AKI vary from 6% to 80%, and there is increased long-term mortality in those with AKI surviving hospitalization.[154]

Up to 6% of patients admitted to the intensive care unit have AKI requiring renal replacement therapy.[16] [152] [155] In hospital, when AKI requires dialysis, mortality exceeds 50%; those with multiorgan failure are at greatest risk.[13] [16] [155] Mortality rates are high due to death from underlying disease and complications, not just the AKI.

Five-year survival rates in patients with AKI requiring renal replacement therapy range from 15% to 35% (less than 10% of those patients are dialysis-dependent).[156]

AKI is irreversible in approximately 5% to 7% of adults and as many as 16% of older adult patients.[157] There is controversy as to whether prior AKI is a major risk factor leading to future chronic kidney disease, but evidence increasingly favors a strong association.[158] [159] [160] [161]

Diagnostic guidelines

International

AACC guidance document on laboratory investigation of acute kidney injury [99]

Published by: American Association for Clinical Chemistry **Last published:** 2021

ACR appropriateness criteria: renal failure [109]

Published by: American College of Radiology **Last published:** 2020

Management of acute kidney injury: core curriculum 2018 [110]

Published by: American Journal of Kidney Diseases **Last published:** 2018

Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guideline for acute kidney injury [1]

Published by: Kidney Disease: Improving Global Outcomes **Last published:** 2012

Treatment guidelines

International

Management of acute kidney injury: core curriculum 2018 [110]

Published by: American Journal of Kidney Diseases **Last published:** 2018

KDOQI US commentary on the 2012 KDIGO clinical practice guideline for acute kidney injury [2]

Published by: National Kidney Foundation **Last published:** 2013

Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guideline for acute kidney injury [1]

Published by: Kidney Disease: Improving Global Outcomes **Last published:** 2012

Online resources

1. Fractional excretion of urea: calculator *(external link)*

2. KDIGO clinical practice guideline for glomerulonephritis *(external link)*

Evidence tables

What are the effects of sodium chloride 0.9% (normal saline) in preventing contrast-induced acute kidney injury (CI-AKI) in at-risk adults?[3]#

This table is a summary of the analysis reported in a guideline (underpinned by a systematic review) that focuses on the above important clinical question.

View the full source guideline

Evidence C * Confidence in the evidence is very low or low where GRADE has been performed and there may be no difference in effectiveness between the intervention and comparison for key outcomes. However, this is uncertain and new evidence could change this in the future.

Population: Adults who are at risk of CI-AKI

Intervention: Sodium chloride 0.9%

Comparison: No intravenous hydration, oral fluids, sodium chloride 0.45%, sodium bicarbonate, oral sodium bicarbonate plus oral fluids

Outcome	Effectiveness (BMJ rating)†	Confidence in evidence (GRADE)‡
Sodium chloride 0.9% versus no intravenous hydration		
CI-AKI	No statistically significant difference	Low
In-hospital mortality	No statistically significant difference	Very Low
All-cause mortality	No statistically significant difference	Low
Need for renal replacement therapy: dialysis	No statistically significant difference	Low
Adverse events	No statistically significant difference	Very Low
Sodium chloride 0.9% versus oral fluids		
CI-AKI	No statistically significant difference	Very Low
All-cause mortality	No statistically significant difference	Very Low

Outcome	Effectiveness (BMJ rating)†	Confidence in evidence (GRADE)‡
Need for renal replacement therapy: dialysis	No statistically significant difference	Very Low
Sodium chloride 0.9% versus sodium chloride 0.45%		
CI-AKI	No statistically significant difference	Very Low
Mortality	No statistically significant difference	Very Low
Need for renal replacement therapy: dialysis	No statistically significant difference	Very Low
Adverse events	No statistically significant difference	Very Low
Sodium chloride 0.9% versus sodium bicarbonate		
CI-AKI	No statistically significant difference	Moderate
All-cause mortality (30 days)	No statistically significant difference	Very Low
All-cause mortality (>30 days)	No statistically significant difference	Very Low
In-hospital mortality	No statistically significant difference	Very Low
Need for renal replacement therapy	No statistically significant difference	Low
Adverse events	No statistically significant difference	Low
Adverse events: heart failure	No statistically significant difference	Very Low
Sodium chloride 0.9% versus oral sodium bicarbonate plus oral fluids		
CI-AKI	No statistically significant difference	Very Low

Recommendations as stated in the source guideline

For inpatients having iodine-based contrast media, consider intravenous volume expansion with either isotonic sodium bicarbonate or 0.9% sodium chloride if they are at particularly high risk; for example, if:

- They have an eGFR less than 30 ml/min/1.73 m2
- They have had a renal transplant
- A large volume of contrast medium is being used (for example, higher than the standard diagnostic dose or repeat administration within 24 hours)
- Intra-arterial administration of contrast medium with first-pass renal exposure is being used.

Note
The guideline committee undertook both network and pairwise meta-analyses. The results in this table are for the pairwise meta-analysis.

The guideline committee noted that evidence from the network meta-analysis showed that sodium chloride 0.9% and sodium bicarbonate appear to be equivalent for preventing CI-AKI. They also noted there was limited evidence on subgroup analyses and that none of those identified showed evidence of an effect from any of the interventions on the incidence of CI-AKI.

The guideline committee stated that the primary outcomes for the pairwise analysis were: CI-AKI, CKD progression at 3 months following CI-AKI diagnosis, mortality up to 12 months, need for renal replacement therapy, and adverse events. Other outcomes of interest were: length of hospital stay, readmission for AKI, and health-related quality of life. See the full guideline for details of these additional outcomes.

* Evidence levels

The Evidence level is an internal rating applied by BMJ Best Practice. See the EBM Toolkit for details.

Confidence in evidence

A - High or moderate to high

B - Moderate or low to moderate

C - Very low or low

† Effectiveness (BMJ rating)

Based on statistical significance, which demonstrates that the results are unlikely to be due to chance, but which does not necessarily translate to a clinical significance.

‡ Grade certainty ratings

High	The authors are very confident that the true effect is similar to the estimated effect.
Moderate	The authors are moderately confident that the true effect is likely to be close to the estimated effect.
Low	The authors have limited confidence in the effect estimate and the true effect may be substantially different.
Very Low	The authors have very little confidence in the effect estimate and the true effect is likely to be substantially different.

BMJ Best Practice EBM Toolkit: What is GRADE?

Key articles

- Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl. 2012 Mar;2(1):1-138. Full text
- Palevsky PM, Liu KD, Brophy PD, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for acute kidney injury. Am J Kidney Dis. 2013 May;61(5):649-72. Full text Abstract
- Moore PK, Hsu RK, Liu KD. Management of acute kidney injury: core curriculum 2018. Am J Kidney Dis. 2018 Jul;72(1):136-48. Full text Abstract

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