Acute kidney injury

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Summary

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

Acute kidney injury (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.
Epidemiology

The reported incidences of AKI vary, and are confounded by differences in diagnosis, definition criteria, or hospital discharge coding.[6][7] In the US, the total number of hospitalizations for AKI increased from 953,926 in 2000 to 3,959,560 in 2014.[8] Among people hospitalized in 2014 with AKI, 40% also had diabetes.[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.[11][12]

Acute tubular necrosis (ATN) accounts for 45% of cases of AKI. ATN is caused by sepsis in 19% 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. In a study of 7500 patients undergoing percutaneous intervention for coronary artery disease, 3.3% of all patients experienced AKI, defined as a rise in serum creatinine of 0.5 mg/dL or more, and 25% of patients with a baseline creatinine of at least 2.0 mg/dL experienced AKI.[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.

Aetiology

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, as 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 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] [33] [34] [35] However, the association with radiocontrast exposure is controversial, as population studies do not replicate risk.[36] [37] [38]

Renal injury associated with obstruction results from increased intratubular pressure yielding 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.[39] [40] [41] [42]

There is preliminary evidence that a genetic predisposition for AKI may exist, especially with apolipoprotein E (APO-E) genes.[43] Genome-wide searches have found other protective candidates, but much more work is needed to validate these findings.[44]

**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.
Acute kidney injury

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, more than 20 red blood cells, 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 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 suggests interstitial nephritis.
Approach

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] [72] [73]

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] [72] [73]

The condition is often asymptomatic and only diagnosed by laboratory tests. General symptoms may include nausea and vomiting. Uremia and an altered mental status may occur, but these are 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] [74] [75]

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, GI surgery, or pancreatitis.

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 medications 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 medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) and sympathomimetics are often overlooked,[76] and patients should be specifically queried about their use. Allergic interstitial nephritis may be suspected in patients with a
Acute kidney injury

**Diagnosis**

History of NSAID use or recent administration of new medications such as beta-lactam antibiotics. Other substances to consider include hallucinogens and “bath salts.”[77]

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 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.

Patients with glomerular disease typically present with hypertension and edema, proteinuria, and microscopic hematuria (nephritic syndrome).

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

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 of some use in patients with pyuria.[78]

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 $\geq$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, and some cases of obstruction and even ATN, as long as tubular function remains intact. The FENa is calculated as follows: $(\text{urine sodium } \times \text{serum creatinine})/(\text{serum sodium } \times \text{urine creatinine}) \times 100\%$.

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: $(\text{urine urea } \times \text{serum creatinine})/(\text{serum urea } \times \text{urine creatinine}) \times 100\%$. [Fractional excretion of urea: calculator](https://www.mdcalc.com/fractional-excretion-urea-feurea)

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 would be seen in renal hypoperfusion/prerenal azotemia. 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 of more than 5% to 7% supports, but is not diagnostic for, interstitial nephritis.

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 cytoplasmatic 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[79] [80] [81] however, further studies are needed to determine their clinical utility.[82] [83] [84] [85] [86] [87]

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 kidney injury, but are not diagnostic. 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 more common 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).

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.

echymoses (uncommon)
- The presence of classic findings for systemic diseases may suggest renal manifestations.

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.

**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.[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.[36] [37] [38]

**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]
Acute kidney injury

Diagnosis

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

**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 medications used in treatment. Highest risk with bacteremia.

**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. Cardiothoracic surgery is particularly high risk, although off-pump approaches may limit this risk.[49]

**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 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 is present.

**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.
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.[43] Genome-wide searches have found other protective candidates, but much more work is needed to validate these findings.[44]

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.[50]

proton pump inhibitors

- Proton pump inhibitors may increase risk of AKI; however, more studies are needed to clarify this association.[51]

herbal therapy

- Case reports suggest that herbs and dietary supplements could potentially contribute to kidney injuries.[52]
# Investigations

## 1st test to order

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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<tr>
<td><strong>basic metabolic profile (including blood urea nitrogen [BUN] and creatinine)</strong></td>
<td>acutely elevated serum creatinine, high serum potassium, metabolic acidosis</td>
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<td>• Often an acutely elevated serum creatinine may be the initial or only sign of decline in renal function.</td>
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<tr>
<td><strong>ratio of serum BUN to creatinine</strong></td>
<td>serum BUN to creatinine ratio ≥20:1 supports prerenal azotemia</td>
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<tr>
<td>• Consider other causes of elevated BUN (such as drug-induced elevations or gastrointestinal bleeding) when interpreting results.</td>
<td></td>
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<tr>
<td><strong>urinalysis</strong></td>
<td>red blood cells, WBCs, cellular casts, proteinuria, bacteria, positive nitrite and leukocyte esterase (in cases of infection)</td>
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<td>• Collected as clean-catch specimen.</td>
<td></td>
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<td>• Patients with glomerular disease typically present with proteinuria and microscopic hematuria with hypertension and edema.</td>
<td></td>
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<tr>
<td><strong>urine culture</strong></td>
<td>bacterial or fungal growth may occur</td>
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<tr>
<td>• Collected if there is suspicion of infection on initial urinalysis.</td>
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<td><strong>complete blood count</strong></td>
<td>anemia, leukocytosis, thrombocytopenia</td>
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<tr>
<td>• Anemia is suggestive of possible chronic kidney disease, blood loss.</td>
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<td>• Leukocytosis may support infection.</td>
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<td>• Thrombocytopenia can be seen in rare disorders such as cryoglobulinemia, hemolytic uremic syndrome, or thrombotic microangiopathies.</td>
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<tr>
<td><strong>fractional excretion of sodium</strong></td>
<td>&lt;1% supports prerenal azotemia</td>
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<td>• May also be seen in glomerulonephritis, hepatorenal syndrome, and some cases of obstruction, as long as tubular function remains intact.</td>
<td></td>
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<td>• Increased levels are also caused by diuretics.</td>
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</tr>
<tr>
<td>• The FENa is calculated as follows: (urine sodium x serum creatinine)/(serum sodium x urine creatinine) x 100%.</td>
<td></td>
</tr>
<tr>
<td><strong>fractional excretion of urea</strong></td>
<td>&lt;35% supports prerenal azotemia</td>
</tr>
<tr>
<td>• 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%.</td>
<td></td>
</tr>
<tr>
<td><strong>urinary eosinophil count</strong></td>
<td>&gt;5% to 7% supports a diagnosis of interstitial nephritis</td>
</tr>
<tr>
<td>• Urinary eosinophil counts have low sensitivity and specificity for acute interstitial nephritis, but may be of some use in patients with pyuria.[78]</td>
<td></td>
</tr>
<tr>
<td>• Eosinophiluria may also be seen with atheroembolic disease.</td>
<td></td>
</tr>
<tr>
<td><strong>venous blood gases</strong></td>
<td>diagnostic for metabolic acidosis and certain intoxications</td>
</tr>
<tr>
<td>• Anion gap acidosis seen in acute and chronic renal failure due to impaired excretion of nonvolatile acids.</td>
<td></td>
</tr>
<tr>
<td>• Assists in further evaluation of acidosis, which is often suggested by the low bicarbonate on the basic metabolic profile.</td>
<td></td>
</tr>
<tr>
<td>Test</td>
<td>Result</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>fluid challenge</td>
<td>renal function improves rapidly in prerenal azotemia</td>
</tr>
<tr>
<td>• May be administered with crystalloid or colloid (but not hydroxyethyl starch solutions), and is both diagnostic and therapeutic in suspected prerenal azotemia.</td>
<td></td>
</tr>
<tr>
<td>bladder catheterization</td>
<td>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)</td>
</tr>
<tr>
<td>• Diagnostic and therapeutic for bladder neck obstruction in addition to providing an assessment of residual urine and a sample for analysis.</td>
<td></td>
</tr>
<tr>
<td>urine osmolality</td>
<td>high in prerenal azotemia (the effect of dyes and mannitol must be excluded); close to serum osmolality in acute tubular necrosis</td>
</tr>
<tr>
<td>• Evaluates maintenance of normal tubular function and response to antidiuretic hormone in cases of hypovolemia.</td>
<td></td>
</tr>
<tr>
<td>urine sodium concentration</td>
<td>&lt;20 mEq/L (suggests avid sodium retention in renal hypoperfusion and prerenal azotemia); high level (often with acute tubular necrosis)</td>
</tr>
<tr>
<td>• High levels in acute tubular necrosis not exclusive to the diagnosis.</td>
<td></td>
</tr>
<tr>
<td>renal ultrasound</td>
<td>dilated renal calyces (suggesting obstruction), reduced corticomedullary differentiation, or small and sclerotic-appearing kidneys (suggesting chronic kidney disease)</td>
</tr>
<tr>
<td>• Assists in evaluation of postobstructive causes as well as in the evaluation of renal architecture and size (underlying chronic kidney disease).</td>
<td></td>
</tr>
<tr>
<td>chest x-ray</td>
<td>may show signs of pulmonary edema and cardiomegaly</td>
</tr>
<tr>
<td>• If renal failure is associated with heart failure.</td>
<td></td>
</tr>
<tr>
<td>ECG</td>
<td>peaked T waves, increased PR interval, widened QRS, atrial arrest, and deterioration to a sine wave pattern (if severe hyperkalemia)</td>
</tr>
<tr>
<td>• Changes may occur with severe hyperkalemia.</td>
<td></td>
</tr>
</tbody>
</table>
## Other tests to consider

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>antinuclear antibodies</td>
<td>• Elevated titer is supportive of a diagnosis of systemic lupus erythematosus, which often has renal manifestations. (normal or elevated)</td>
</tr>
<tr>
<td>anti-DNA</td>
<td>• Elevated titer supports the diagnosis of systemic lupus erythematosus, which often has renal manifestations. (normal or elevated)</td>
</tr>
<tr>
<td>complement (C3, C4, CH50)</td>
<td>• Low complement levels support an active disease process, such as systemic lupus erythematosus. (normal or depressed)</td>
</tr>
<tr>
<td>anti-glomerular basement membrane antibodies</td>
<td>• 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)</td>
</tr>
<tr>
<td>antineutrophil cytoplasmic antibodies</td>
<td>• 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)</td>
</tr>
<tr>
<td>acute hepatitis profile</td>
<td>• The presence of positive serology in active hepatitis C is associated with renal conditions such as membranoproliferative glomerulonephritis and cryoglobulinemia. (positive or negative serology)</td>
</tr>
<tr>
<td>HIV serology</td>
<td>• HIV-associated nephropathy and certain medications used in the management of HIV have renal complications. (positive or negative)</td>
</tr>
<tr>
<td>cryoglobulins</td>
<td>• The presence of cryoglobulins support cryoglobulin-associated renal disease, if AKI is present. (positive or negative serology)</td>
</tr>
<tr>
<td>erythrocyte sedimentation rate</td>
<td>• A normal erythrocyte sedimentation rate argues against the presence of inflammatory renal disease or embolic injury. (normal or elevated)</td>
</tr>
<tr>
<td>antistreptolysin-O antibody</td>
<td>• An elevated titer supports but does not make a diagnosis of an infectious glomerulonephritis. (normal or elevated)</td>
</tr>
<tr>
<td>abdominal computed tomography or magnetic resonance imaging scan</td>
<td>• Sometimes required to further evaluate cases of obstruction suggested on ultrasound. (image of mass or stone may be present)</td>
</tr>
<tr>
<td>nuclear renal flow scan</td>
<td>• 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)</td>
</tr>
</tbody>
</table>
### Diagnosis

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>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)</td>
</tr>
<tr>
<td><strong>cystoscopy</strong></td>
<td>direct visualization and treatment of ureteral stenosis if present</td>
</tr>
<tr>
<td></td>
<td>• May be used if obstruction due to stenosis of the ureter is suspected.</td>
</tr>
<tr>
<td><strong>renal biopsy</strong></td>
<td>changes associated with acute tubular necrosis, glomerulonephritis, vasculitis, or other intrinsic renal disease may be present</td>
</tr>
<tr>
<td></td>
<td>• Biopsy is frequently required to further investigate positive serologic studies for suspected glomerulonephritis.</td>
</tr>
<tr>
<td></td>
<td>• Biopsies also done when the cause of kidney injury is unclear.</td>
</tr>
<tr>
<td></td>
<td>• May confirm acute tubular necrosis, but not often performed for this diagnosis.</td>
</tr>
</tbody>
</table>

### Emerging tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>novel serum and urinary biomarkers</strong></td>
<td>results indicative of renal damage</td>
</tr>
<tr>
<td>• 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: [79] [80] [81] however, further studies are needed to determine their clinical utility. [82] [83] [84] [85] [86] [87]</td>
<td></td>
</tr>
</tbody>
</table>
**Conditions, Differentiating signs / symptoms, Differentiating tests**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Differentiating signs / symptoms</th>
<th>Differentiating tests</th>
</tr>
</thead>
</table>
| 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 medications).  
  • 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 131-I iothalamate 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 medications such as cimetidine or trimethoprim may lead to an elevation of creatinine that is minor and nonacute. | Discontinuing the medication should result in normalizing of the serum creatinine.  
  • Twenty-four-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[72]

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.
Acute kidney injury

Diagnosis

• Indicates ESRD:
  
  • ESRD (loss >3 months).
Approach

For updates on diagnosis and management of coexisting conditions during the pandemic, see our topic "Management of coexisting conditions in the context of COVID-19".

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.

Sodium and volume restriction are generally required along with limiting potassium and phosphorus intake.

Dose adjustment of medications is likely required in all cases and should not be overlooked. 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. Early involvement by a nephrologist may be valuable;[90] however, automated electronic alerts to identify AKI have not improved outcomes.[91]

**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 (but not hydroxyethyl starch [HES]) to restore euvolemia.

Crystalloid (normal saline or lactated Ringers) or colloid (considered in cases of significant hypoalbuminemia) fluids are infused, along with packed red blood cells if there is significant anemia.[5] The use of semisynthetic HES is not advised, as mortality appears to be increased.[92]

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) >60 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.)

Management is often difficult if renal hypoperfusion results from impaired cardiac function due to poor left ventricular systolic function. 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]

Vasopressors and inotropic agents should be used only with appropriate hemodynamic monitoring in place.

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.[69] [70] Larger randomized studies remain necessary to alter practice.[70]

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

Removal of offending drugs, when possible, is necessary in cases of interstitial nephritis or drug-induced AKI.

Acute glomerulonephritis and vasculitis management may also require corticosteroids, cytotoxic agents, or other immune-modifying drugs depending on the specific diagnosis, often determined by renal biopsy and serology studies.


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.

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

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), or continuous renal replacement therapy (CRRT).[93] 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).[93] [94] [95] [96]

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.[94] [95] [96]

Early dialysis appeared to reduce mortality compared with a delayed strategy in one small single-center randomized trial of critically ill patients with AKI,[97] but a larger study and meta-analysis found no benefit associated with early initiation of renal replacement therapy.[98] [99]

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.[100] [101] [102]

**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 kidney injury

### Management

#### Acute

<table>
<thead>
<tr>
<th>Type</th>
<th>1st</th>
<th>Adjunct</th>
</tr>
</thead>
<tbody>
<tr>
<td>prerenal azotemia</td>
<td>volume expansion and/or red blood cell transfusion</td>
<td>diuretic</td>
</tr>
<tr>
<td></td>
<td>with severe hypotension plus vasopressor</td>
<td></td>
</tr>
<tr>
<td></td>
<td>with volume overload adjunct diuretic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>with uremia, severe metabolic acidosis, hyperkalemia refractory to medical management, or volume overload unresponsive to diuretics</td>
<td>renal replacement therapy</td>
</tr>
</tbody>
</table>

#### Intrinsic renal failure

<table>
<thead>
<tr>
<th>Type</th>
<th>1st</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>treatment of underlying condition</td>
</tr>
<tr>
<td></td>
<td>with volume overload adjunct diuretic</td>
</tr>
<tr>
<td></td>
<td>with pre-existing prerenal azotemia adjunct volume expansion</td>
</tr>
<tr>
<td></td>
<td>with uremia, severe metabolic acidosis, hyperkalemia refractory to medical management, or volume overload unresponsive to diuretics</td>
</tr>
</tbody>
</table>

#### Obstructive renal failure

<table>
<thead>
<tr>
<th>Type</th>
<th>1st</th>
<th>2nd</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>bladder catheterization</td>
<td>relief of obstruction above bladder neck</td>
</tr>
<tr>
<td></td>
<td>with volume overload adjunct diuretic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>with uremia, severe metabolic acidosis, or hyperkalemia refractory to medical management, or volume overload unresponsive to diuretics</td>
<td>renal replacement therapy</td>
</tr>
</tbody>
</table>
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 kidney injury

Management

**Acute prerenal azotemia**

- **First step**: volume expansion and/or red blood cell transfusion
  - The underlying cause of volume contraction or blood loss must be treated, along with restoring euvoelma and hemodynamic stability.
  - Crystalloid (normal saline or lactated Ringers) is sufficient in most cases for volume expansion. Colloid might be used if there is significant hypoalbuminemia. The use of the semisynthetic hydroxyethyl starch is not advised, as mortality appears to be increased.[92]
  - 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.[53] However, a large study did not show benefit in patients at risk of contrast-induced nephropathy according to current guidelines.[54]
  - As prerenal azotemia predisposes the kidney to injury from other means, such as contrast or nephrotoxins, care should be given to minimize exposures and dose-adjust drugs to maximize recovery potential.
  - Hemorrhage requires blood product replacement.
  - With severe hypotension plus vasopressor

**Primary options**

- **Dopamine**: 1 microgram/kg/min intravenously initially, increase by 5-10 micrograms/kg/min increments until response, maximum 50 micrograms/kg/min
  - OR

- **Epinephrine (adrenaline)**: 1 microgram/min intravenously initially, increase dose according to response, maximum 20 micrograms/min
  - OR

- **Norepinephrine**: 1 microgram/min intravenously initially, increase dose
### Acute Kidney Injury Management

**Acute**

- Vaspressors are recommended for severe hypotension, often with the goal of keeping mean arterial pressure (MAP) >60 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 vaspressors should be used only with appropriate hemodynamic monitoring in place.

- The underlying cause of hypotension needs to be treated alongside restoring euvolemia and hemodynamic stability.

- The septic patient requires hemodynamic support with vaspressors as needed to support MAP and organ perfusion.

- Vasopressin is sometimes used as an adjunct to other vaspressors.

- Management is often difficult if renal hypoperfusion results from impaired cardiac function. It requires optimizing cardiac output and volume status. Inotropes, diuretics, or renal replacement therapy may be required.

### Management of Fluid Overload

**Primary options**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>furosemide</td>
<td>40-80 mg intravenously initially, increase by 20 mg/dose increments every 2 hours as necessary until clinical response</td>
</tr>
</tbody>
</table>

**Secondary options**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>torsemide</td>
<td>20 mg intravenously once daily initially, increase gradually according to response, maximum 200 mg/day</td>
</tr>
<tr>
<td>bumetanide</td>
<td>1-2 mg intravenously initially, may repeat in 2-3 hours for up to 2 doses if necessary, maximum 10 mg/day</td>
</tr>
</tbody>
</table>
Acute kidney injury

**Management**

» 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.

» Patients also require sodium restriction.

» It is important to remove or minimize any nephrotoxins.

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

adjunct 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). 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 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.[93] [94] [95] [96] [104]

» Early dialysis appeared to reduce mortality compared with a delayed strategy in one small single-center randomized trial of critically ill patients with AKI,[97] but a larger study and meta-analysis found no benefit associated with early initiation of renal replacement therapy.[98] [99]
## Acute intrinsic renal failure

<table>
<thead>
<tr>
<th>intrinsic renal failure</th>
<th>1st treatment of underlying condition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>» Management of intrinsic renal failure varies according to etiology. Nephrotoxic agents should be ceased and the patient referred to a nephrologist if specific treatment, such as dialysis, management of fluids/acid-base status, severe hyperkalemia, or immunosuppression is required.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>with volume overload</th>
<th>adjunct diuretic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment recommended for SOME patients in selected patient group</td>
<td></td>
</tr>
</tbody>
</table>

**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. 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.

- It is important to remove or minimize any nephrotoxins.
<table>
<thead>
<tr>
<th>Acute kidney injury</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>with pre-existing prerenal azotemia</td>
<td>volume expansion</td>
</tr>
<tr>
<td>Treatment recommended for SOME patients in selected patient group</td>
<td></td>
</tr>
<tr>
<td>» Crystalloid (normal saline or lactated Ringers) is sufficient in most cases for volume expansion. Colloid might be used if there is significant hypoalbuminemia. The use of the semisynthetic hydroxyethyl starch (HES) is not advised, as mortality appears to be increased.</td>
<td></td>
</tr>
<tr>
<td>» As prerenal azotemia predisposes the kidney to injury from other means, such as contrast or nephrotoxins, care should be given to minimize exposures and dose-adjust drugs to maximize recovery potential.</td>
<td></td>
</tr>
<tr>
<td>with uremia, severe metabolic acidosis, hyperkalemia refractory to medical management, or volume overload unresponsive to diuretics</td>
<td>renal replacement therapy</td>
</tr>
<tr>
<td>Treatment recommended for SOME patients in selected patient group</td>
<td></td>
</tr>
<tr>
<td>» Nephrologist consultation recommended.</td>
<td></td>
</tr>
<tr>
<td>» Conventional hemodialysis is used in hemodynamically stable patients.</td>
<td></td>
</tr>
<tr>
<td>» Other modes of renal replacement include sustained low-efficiency dialysis (SLED), extended daily dialysis (EDD), or continuous renal replacement therapy (CRRT). Major commonly used modalities include continuous venovenous hemofiltration (CVVH), continuous venovenous hemodialysis (CVVHD), and continuous venovenous hemodiafiltration (CVVHDF).</td>
<td></td>
</tr>
<tr>
<td>» 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.</td>
<td></td>
</tr>
<tr>
<td>» Studies have shown that intensive dialysis in critically ill patients with AKI confers no increased benefit.</td>
<td></td>
</tr>
<tr>
<td>» 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 a larger study and meta-analysis found no benefit associated with early initiation of renal replacement therapy.</td>
<td></td>
</tr>
<tr>
<td>obstructive renal failure</td>
<td>1st bladder catheterization</td>
</tr>
</tbody>
</table>
Acute kidney injury

**Management**

Acute

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

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

2nd relief of obstruction above bladder neck

**Primary options**

- **ureteral stenting**: if there is a ureteral stricture, stone or extrinsically obstructing mass

  OR

- **lithotripsy**: stones present at the ureteropelvic junction causing obstruction may require lithotripsy or surgical removal

  OR

- **exploratory laparotomy**: compressing tumors may require surgical removal; may be done following ureteral stenting

  OR

- **percutaneous nephrostomy**: placement of a catheter into the renal pelvis percutaneously for drainage of urine from a distal obstruction may be done by a urologist, surgeon or interventional radiologist

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

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

Surgical consultation may be needed if the cause is tumor with mass effect.

**with volume overload adjunct 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
### Acute Kidney Injury

#### 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.

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.

It is important to remove or minimize any nephrotoxins.

Adjunct 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 continuous renal replacement therapy (CRRT) if the patient is hemodynamically unstable despite full support.

Renal replacement therapy may be required to manage complications of obstruction while surgical interventions are planned and implemented.
Emerging 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. None have been shown to be beneficial in human AKI. The protective effect of statins (administered either pre-intervention or chronically) is debated, but results from recent studies are disappointing. Controlled hypothermia and recombinant alkaline phosphatase infusion may be of benefit. 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. 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 the treatment.

Primary prevention

Exposure to radiocontrast may cause AKI. However, the association is controversial because population studies do not replicate risk. 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. However, a large study did not show benefit in patients at risk of contrast-induced nephropathy according to current guidelines. 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. Probucol, atrial natriuretic peptide, and high-dose statins reduced the risk of contrast-induced AKI in small studies, but remain experimental.

Sodium bicarbonate is unlikely to be superior to saline for the prevention of contrast-induced injury. Studies assessing the efficacy of acetylcysteine administration before contrast exposure show no significant benefit, and this approach should be abandoned.

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.
- 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. These interventions are 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. In a similar patient population, AKI was more common among those randomized to perioperative rosuvastatin than to placebo.
- Levosimendan, a calcium sensitizer used to improve cardiac output, appears to prevent AKI in patients undergoing cardiac surgery.
- 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.
- Compared with on-pump coronary artery bypass grafting, off-pump surgery appears to reduce the risk of postoperative AKI.

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.\[69\] [70] Larger randomized studies remain necessary to alter practice.\[70\]

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.\[71\] 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.
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, a nephrologist follow-up is recommended with interventions based on stage of CKD.[128]

The National Kidney Foundation KDOQI guidelines include recommendations regarding the management of patients who have developed CKD subsequent to AKI.[129] 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

<table>
<thead>
<tr>
<th>Complications</th>
<th>Timeframe</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>hyperphosphatemia</td>
<td>long term</td>
<td>high</td>
</tr>
<tr>
<td>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.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>uremia</td>
<td>long term</td>
<td>medium</td>
</tr>
<tr>
<td>Uremic toxins accumulate with severe and untreated renal failure, resulting in lethargy, confusion, and obtundation. Dialysis is required for management of uremia.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>volume overload (pulmonary edema, peripheral edema)</td>
<td>variable</td>
<td>high</td>
</tr>
<tr>
<td>Impaired volume regulation is common in AKI not occurring from prerenal azotemia. 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.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hyperkalemia</td>
<td>variable</td>
<td>high</td>
</tr>
<tr>
<td>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.</td>
<td></td>
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</tr>
</tbody>
</table>
Acute kidney injury

Follow up

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.[125] [126]

Patients with partial or no recovery from AKI are at increased risk for congestive heart failure and acute myocardial infarction.[127]

**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.[121]

Prognosis

Recovery for AKI is variable and depends on cause of injury and the severity and duration of AKI.[117]

There is an independent association of AKI with a higher risk of death.[9] [117] [118] 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.[118]

Up to 6% of patients admitted to the intensive care unit have AKI requiring renal replacement therapy.[16] [117] [119] In hospital, when AKI requires dialysis, mortality exceeds 50%; those with multiorgan failure are at greatest risk.[13] [16] [119] 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).[120]

AKI is irreversible in approximately 5% to 7% of adults and as many as 16% of older adult patients.[121] There is controversy as to whether prior AKI is a major risk factor leading to future chronic kidney disease, but increasing evidence of strong association mounts.[122] [123] [124]
# Diagnostic guidelines

## International

|---------------------------------------------------------------|--------------------------------------------------|----------------------|

|----------------------------------------------------------------------------------------------------------------|-----------------------------------------------|----------------------|

|----------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|----------------------|

# Treatment guidelines

## International

|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------|----------------------|

|------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|----------------------|

|----------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|----------------------|
Online resources


## 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?**[55]

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 (https://www.nice.org.uk/guidance/ng148/evidence)

**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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Effectiveness (BMJ rating)†</th>
<th>Confidence in evidence (GRADE)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium chloride 0.9% versus no intravenous hydration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CI-AKI</td>
<td>No statistically significant difference</td>
<td>Low</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>No statistically significant difference</td>
<td>Low</td>
</tr>
<tr>
<td>Need for renal replacement therapy: dialysis</td>
<td>No statistically significant difference</td>
<td>Low</td>
</tr>
<tr>
<td>Adverse events</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>Sodium chloride 0.9% versus oral fluids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CI-AKI</td>
<td>No statistically significant difference</td>
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<tbody>
<tr>
<td>Need for renal replacement therapy: dialysis</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>Sodium chloride 0.9% versus sodium chloride 0.45%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CI-AKI</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>Mortality</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>Need for renal replacement therapy: dialysis</td>
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<td>Very Low</td>
</tr>
<tr>
<td>Adverse events</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>Sodium chloride 0.9% versus sodium bicarbonate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CI-AKI</td>
<td>No statistically significant difference</td>
<td>Moderate</td>
</tr>
<tr>
<td>All-cause mortality (30 days)</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>All-cause mortality (&gt;30 days)</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>No statistically significant difference</td>
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<td>Need for renal replacement therapy</td>
<td>No statistically significant difference</td>
<td>Low</td>
</tr>
<tr>
<td>Adverse events</td>
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<td>Low</td>
</tr>
<tr>
<td>Adverse events: heart failure</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>Sodium chloride 0.9% versus oral sodium bicarbonate plus oral fluids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CI-AKI</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
</tbody>
</table>

**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 (https://bestpractice.bmj.com/info/evidence-tables/) 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

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>The authors are very confident that the true effect is similar to the estimated effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>The authors are moderately confident that the true effect is likely to be close to the estimated effect.</td>
</tr>
<tr>
<td>Low</td>
<td>The authors have limited confidence in the effect estimate and the true effect may be substantially different.</td>
</tr>
<tr>
<td>Very Low</td>
<td>The authors have very little confidence in the effect estimate and the true effect is likely to be substantially different.</td>
</tr>
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</table>

BMJ Best Practice EBM Toolkit: What is GRADE? (https://bestpractice.bmj.com/info/toolkit/learn-ebm/what-is-grade/)
Key articles


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Acute kidney injury


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Please note that recommended formulations and doses may differ between drug databases drug names and brands, drug formularies, or locations. A local drug formulary should always be consulted for full prescribing information.

Treatment recommendations in BMJ Best Practice are specific to patient groups. Care is advised when selecting the integrated drug formulary as some treatment recommendations are for adults only, and external links to a pediatric formulary do not necessarily advocate use in children (and vice-versa). Always check that you have selected the correct drug formulary for your patient.

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Regardless of the language in which the content is displayed, numerals are displayed according to the original English-language numerical separator standard. For example 4 digit numbers shall not include a comma nor a decimal point; numbers of 5 or more digits shall include commas; and numbers stated to be less than 1 shall be depicted using decimal points. See Figure 1 below for an explanatory table.

BMJ accepts no responsibility for misinterpretation of numbers which comply with this stated numerical separator standard.

This approach is in line with the guidance of the International Bureau of Weights and Measures Service.

Figure 1 – BMJ Best Practice Numeral Style
Contributors:

// Authors:

Richard A. Lafayette, MD
Professor of Medicine
Nephrology Division, Stanford University Medical Center, Stanford, CA
DISCLOSURES: RAL works as a consultant and researcher for Relypsa, Inc. Although unrelated to this topic area, RAL also works as a consultant for Fibrogen, Inc.; Mallinckrodt, Inc.; and Omeros, Inc.; and as a researcher for Genentech, Inc.; Mallinckrodt, Inc.; GlaxoSmithKline, Inc.; Rigel, Inc.; Aurinia, Inc.; and the NIH.

// Acknowledgements:

Dr Richard A. Lafayette would like to gratefully acknowledge Dr Sandra Sabatini, Dr Neil Kurtzman, and Dr Corey D. Ball, the previous contributors to this topic. SS, NK, and CDB declare that they have no competing interests.

// Peer Reviewers:

Garabed Eknoyan, MD
Professor of Medicine
Section of Nephrology, Department of Medicine, Baylor College of Medicine, Houston, TX
DISCLOSURES: GE declares that he has no competing interests.

Dominic de Takats, MA, MRCP
Consultant Nephrologist
Nephrology, North Staffs Royal Infirmary, University Hospital of North Staffordshire, Stoke-on-Trent, UK
DISCLOSURES: DdT declares that he has no competing interests.