Acute kidney injury

Straight to the point of care

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Summary

Commonly associated with sepsis, hypovolaemia, and/or hypotension (pre-kidney AKI and intrinsic AKI); nephrotoxins such as aminoglycoside antibiotics (e.g., gentamicin), intravenous iodinated contrast, ethylene glycol, or rarer forms of AKI such as vasculitis or interstitial nephritis (intrinsic AKI); or urinary outflow obstruction (post-kidney AKI).

Usually occurs in patients with intercurrent illness, without symptoms or signs specific to the kidneys, and is only diagnosed when kidney function tests are performed. Patients may present in many different ways (e.g., with sepsis, hypotension, decreased urine output, lower urinary tract symptoms, or oedema).

Suspect AKI when there is an acute rise in serum creatinine and/or a fall in urine output. More severe AKI can be complicated by hyperkalaemia and acidaemia along with uraemic encephalopathy or pericarditis. Pulmonary oedema can also occur in patients with AKI secondary to obstructive uropathy or renal artery stenosis (flash pulmonary oedema) but is usually iatrogenic due to over-enthusiastic fluid resuscitation.

The mainstay of management is supportive care, with treatment of the underlying cause. Give particular attention to the prompt treatment of sepsis, optimisation of volume status, correction of acidaemia or electrolyte complications, avoidance of nephrotoxins, and relief of any obstruction.

Renal replacement therapy may be needed for severe AKI with complications that do not respond to medical management.

Prompt recognition and treatment is important; AKI occurs in 10% to 20% of emergency admissions and has an inpatient mortality >20% (>35% for stage 3 AKI).

Definition

Acute kidney injury (AKI), previously known as acute renal failure (ARF), is an acute decline in kidney function, leading to a rise in serum creatinine and/or a fall in urine output.[1] The change in terminology emphasises that kidney injury presents as a disease spectrum from mild kidney injury to severe kidney failure.[1][2][3] A standardised definition is important to facilitate clinical care and research.[4] AKI may be due to various insults such as impaired kidney perfusion, exposure to nephrotoxins, outflow obstruction, or intrinsic kidney 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] UK Renal Registry data, covering a population of 9.1 million people in England over a 3 month period in 2017, produced an annual estimated AKI rate of 10,400 per million population (95% CI 10,000 to 10,400).[8] AKI is seen in 10% to 20% of people admitted to hospital as emergencies, with an inpatient mortality >20%.[3] The overall incidence of AKI in the ICU is higher at 20% to 50% and it is associated with mortality over 50%.[11] There is some evidence to suggest that AKI is becoming more common, perhaps because of more aggressive medical and surgical interventions in older patients who are at higher risk of developing AKI as a complication.[13] One study found the incidence of AKI not requiring dialysis among a large population of hospitalised patients to have increased from 323 to 522 per 100,000 person-years between 1996 and 2003.[14] Prediction scores have been developed for outcomes of AKI, but have had variable success.[15] [16]

Acute tubular necrosis (ATN) accounts for 45% of cases of AKI. ATN is caused by sepsis in 19% of ICU patients. Pre-kidney AKI, obstruction, glomerulonephritis, vasculitis, acute interstitial nephritis, acute on chronic kidney disease and atheroembolic injury account for most of the remainder.[17] [18]

The incidence of contrast nephropathy varies, and is reported to be the third most common cause of AKI in hospitalised 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 38 micromols/L (0.5 mg/dL) or more, and 25% of patients with a baseline creatinine of at least 153 micromols/L (2.0 mg/dL) experienced AKI.[19]

Up to 7% of patients hospitalised with AKI require renal replacement therapy.[20] In the ICU, the mortality rate exceeds 50% in patients with multi-organ failure who require dialysis.[17] [18] [20] Minor rises in creatinine (≥26.5 micromols/L [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 kidney failure.

Risk factors

Strong

advanced age

Advanced age is associated with chronic kidney disease, underlying vascular disease of the kidneys, and other comorbid medical conditions that predispose to AKI.

underlying kidney disease

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

diabetes mellitus

AKI incidence rates of 9% to 38% have been reported in patients with diabetes and chronic kidney disease undergoing contrast exposure.[49]

sepsis

May result in acute tubular necrosis, infectious glomerulonephritis, pre-kidney AKI from hypotension, or drug-induced injury from medicines used in treatment. Highest risk with bacteraemia.
iodinated contrast

Intravenous iodinated contrast has previously been reported to cause contrast-induced AKI.\[5\] However, the association has been questioned more recently by large population studies that have failed to demonstrate this risk.\[40\] \[41\] \[42\] Risk of contrast-induced AKI increases with intra-arterial administration and with increasing volume of contrast medium.\[3\]

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

May precede and lead to AKI.\[5\] \[50\] \[51\]

excessive fluid loss

From haemorrhage, vomiting, diarrhoea, or sweating; hospitalised patients may have insufficient replacement fluids.

surgery

May precede AKI from pre-kidney, intrinsic, or post-kidney causes. Cardiothoracic surgery is particularly high risk, although off-pump approaches may limit this risk.\[52\]

haemorrhage

The resulting impaired kidney perfusion supports pre-kidney AKI as cause of AKI or ischaemia resulting in acute tubular necrosis.

recent vascular intervention

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

cardiac arrest

May precede pre-kidney AKI or acute tubular necrosis, especially if there is severe and prolonged kidney ischaemia.

pancreatitis

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

trauma

There may be impaired kidney perfusion causing pre-kidney AKI, rhabdomyolysis predisposing to pigment-induced injury, or ischaemia causing acute tubular necrosis.

malignant hypertension

Malignant hypertension may cause AKI.\[5\]

myeloproliferative disorders, such as multiple myeloma

Intratubular precipitation of light chains in times of volume contraction is associated with kidney injury, especially in cases of contrast exposure with volume contraction in myeloma patients. Hypercalcaemia predisposes to pre-kidney AKI.\[5\] \[53\]
connective tissue disease

May present with AKI (e.g., systemic lupus erythematosus, scleroderma, anti-neutrophil cytoplasmic antibody-associated glomerulonephritis, anti-glomerular 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]

drug overdose

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

nephrolithiasis

May lead to AKI if significant obstruction is present.

Weak

drug abuse

AKI from nephrotoxicity, ischaemia.

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 haemolytic transfusion reaction, deposition of immune complexes.

malignancy

May lead to post-kidney AKI if mass effect is causing outflow obstruction, or AKI may result in association with myeloproliferative disorders or chemotherapy-related toxicities (i.e., tumour 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.[47] Genome-wide searches have found other protective candidates, but much more work is needed to validate these findings.[48]

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.[54]
Acute kidney injury

**Theory**

proton pump inhibitors

Proton pump inhibitors may increase risk of AKI; however, more studies are needed to clarify this association.[55]

herbal therapy

Case reports suggest that herbs and dietary supplements could potentially contribute to kidney injuries.[56]

Aetiology

Aetiology of AKI may be multifactorial, generally classified into pre-kidney, intrinsic, and post-kidney causes.[21]

- Pre-kidney AKI can be due to various causes of reduced kidney perfusion, such as hypovolaemia, haemorrhage, sepsis, third spacing of fluid (such as in severe pancreatitis), overdiuresis, or other causes of reduced kidney perfusion such as heart failure. Hepatorenal syndrome, a form of pre-kidney AKI 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 kidney failure may be multifactorial. ATN, rapidly progressive glomerulonephritis, and interstitial nephritis are the most common aetiologies. Vascular diseases, including haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura, scleroderma renal crisis, atheromatous embolisation, and thrombosis, are also potential causes. Severe ischaemic injury may result in cortical necrosis.

- Post-kidney AKI results from mechanical obstruction of the urinary outflow tract. Retroperitoneal fibrosis, lymphoma, tumour, prostate hyperplasia, strictures, renal calculi, ascending urinary infection (including pyelonephritis), and urinary retention are common causes.

Pathophysiology

Pre-kidney AKI results from impaired kidney perfusion and the changes seen are appropriate physiological responses. The kidney’s response to a lower perfusion pressure is to enhance sodium and water re-absorption. 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 re-absorption, concentrating the urine.

Acute tubular necrosis (ATN) due to prolonged or severe ischaemia, the most common form of AKI, is preceded by impaired kidney perfusion and tissue hypoxaemia, yielding direct microvascular endothelial injury and tubular ischaemia typically most severe in the early proximal tubule and the outer medullary segments.[22] [23] Hypoxaemia results in increased reactive oxygen species, reduction in available adenosine triphosphate, and cellular dysfunction and death.[24] Additionally, complement system activation, direct neutrophil activation, membrane attack complex activation, cytokines, chemokines, and vasoactive hormones have been studied and may be contributory.[25] [26] [27] [28] [29] [30] [31] [32] [33] ATN may also result from exposure to drugs, endotoxins, or radiocontrast media. Animal models suggest direct cytotoxic
effects of the contrast as well as vasoconstriction in the kidney resulting in impaired medullary blood flow, increased viscosity, and hypoxaemia. However, the association with radiocontrast exposure is controversial, as population studies do not replicate risk.

Kidney injury associated with obstruction results from increased intratubular pressure yielding tubular ischaemia and atrophy. Evidence also suggests injury results from an influx of monocytes and macrophages. Cytokines, free radicals, proteases, and tumour necrosis factor-beta are released, causing irreversible tubular injury and fibrosis when obstruction becomes chronic.

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

Classification

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

Any of the following:

- Increase in serum creatinine by ≥26 micromol/L (≥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

- Pre-kidney (pre-renal) AKI: injury due to impaired kidney perfusion.
- Intrinsic AKI: direct injury to the kidney parenchyma.
- Post-kidney (post-renal) AKI: injury due to urinary outflow obstruction.

Case history

Case history #1

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

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 a reduction in urine output. Urinalysis reveals more than 20 white blood cells, more than 20 red blood cells, and red cell casts. Urine culture is negative. Kidney ultrasound is unremarkable. Serum erythrocyte sedimentation rate is elevated.

**Other presentations**

Rarer presentations include AKI secondary to:

- **Vasculitis**
  - AKI may be associated with systemic symptoms such as arthralgia, myalgia, and/or rash. Urinalysis will demonstrate blood and protein.
- **Interstitial nephritis**
  - Patients may present with fever, rash, and/or arthralgia with leucocytes on urinalysis. There may be a history of a new medication being commenced.
- **Atheroembolic injury**
  - AKI may occur following vascular catheterisation or systemic anticoagulation resulting from atheroembolic injury.
- **Obstruction**
  - AKI secondary to abdominal masses or an enlarged bladder may be found on examination or by imaging. Patients may be otherwise asymptomatic.
Recommendations

Urgent

Consider the possibility of AKI whenever a patient presents with an acute illness or shows a deterioration in their early warning scores.[1] [3] [62]

- AKI is **easily missed**; most patients present asymptomatically, with non-specific symptoms or with symptoms solely related to the precipitating illness (e.g., sepsis).
- AKI occurs in **10% to 20% of emergency admissions** and has an **inpatient mortality >20% (>35% in stage 3 AKI).**[3] [9] [10]

**Look for signs of sepsis and manage promptly.** [9] [63]

- Perform a septic screen and implement your local care bundle (e.g., Sepsis Six) if infection is suspected.

**Recognise and treat hypovolaemia promptly with an immediate bolus of crystalloid intravenous fluid.** [1] [62] [13] [64]

**Stop/avoid exposure to any nephrotoxins (e.g., non-steroidal anti-inflammatory drugs [NSAIDs], aminoglycoside antibiotics) and to any other agents that may reduce kidney function (e.g., ACE inhibitors, angiotensin-II receptor antagonists).** [1]

- Review and **adjust dosing** of all other medications in line with the degree of kidney injury.

Key Recommendations

**Definition and staging of AKI**

AKI is diagnosed based on **an acutely rising serum creatinine and/or reduction in urine output.**[4] [1]

- AKI can often be non-oliguric.

AKI is present if any **one or more of the following criteria** is met:[4] [1] [3]

- **A rise in serum creatinine of ≥26 micromol/L (≥0.3 mg/dL) within 48 hours**
- **A rise in serum creatinine to ≥1.5 times baseline**, which is known or presumed to have occurred within the past 7 days (in practice you can use the lowest value from the past 3 months as the baseline for the patient).[62]
- **Urine volume <0.5 ml/kg/hour for at least 6 hours.**

**Stage the AKI** according to the KDIGO staging criteria.[1]

- A higher stage of AKI is associated with a greater risk of death as well as increased likelihood of needing renal replacement therapy (RRT).[13]

**Clinical presentation**

AKI is often asymptomatic so a **high index of suspicion** is vital for prompt recognition and treatment.[62]

A **relevant history** is a key part of the assessment. Check for:
Acute kidney injury

Diagnosis

- **Risk factors**: frail, older people are at particular increased risk, especially those with chronic kidney disease (CKD), heart failure, liver disease, or cognitive impairment.[3] [9] [64] [65]
- **Precipitating insults** to the kidney: the most common causes of AKI are sepsis, nephrotoxins, hypovolaemia, and/or hypotension.[62] [13]

Your examination should prioritise volume status and a sepsis screen.

- Also look for any symptoms and signs that may suggest a specific underlying cause (e.g., fever, rash, and/or joint pain suggest small-vessel vasculitis or interstitial nephritis).[9] [64]

**Causes of AKI**

Establish the underlying cause of AKI as this will determine the correct treatment and the need for onward referral.[5] [17] [52]

The causes of AKI have traditionally been classified as pre-kidney (pre-renal), intrinsic, and post-kidney (post-renal):[5] [21]

- **Pre-kidney AKI** (80% of cases) is usually due to hypovolaemia and/or hypotension:[1] [3] [9] [62]
  - Sepsis (e.g., pneumonia, cellulitis)
  - Fluid loss (e.g., vomiting and diarrhoea, or blood loss)
  - Reduced fluid intake - a particular problem in frail, elderly patients.
- **Intrinsic AKI** is due to cellular damage within the kidneys - seek early specialist input if you suspect an intrinsic cause:[17] [18] [9] [62]
  - Prolonged pre-kidney AKI that progresses to overt cellular damage is the most common cause.
  - Nephrotoxins (e.g., iodinated contrast agents, NSAIDs, aminoglycoside antibiotics).[1] See our Primary prevention section for information about preventing AKI.
  - Rare causes (e.g., vasculitis, glomerulonephritis).
- **Post-kidney AKI** is due to obstruction:[9] [62]
  - Most common in older men with prostatic hyperplasia[4]
  - Other causes include kidney stones and tumours.

**Investigations**

- **Bloods**
  - Urea and electrolytes (including creatinine and bicarbonate) are the key investigations.[1] [62] [13] [64] [65]
  - Also request liver function tests, C-reactive protein, full blood count, and blood cultures if infection suspected.
- **Urinalysis** [3] [9] [62] [64]
  - If positive for both protein and blood (in the absence of a urinary tract infection or catheterisation), consider the possibility of an intrinsic cause (e.g., glomerulonephritis).
  - Nitrites and leukocytes may indicate infection - send urine culture.
- **Routine renal tract ultrasound is not needed** if a clear cause has been identified. Only request it if:[3] [13] [64]
  - There is no clear cause of AKI
• Pyelonephritis or pyonephrosis is suspected (if pyonephrosis is suspected, ensure the patient has an ultrasound within 6 hours because of the risk of septic shock).
• Urinary tract obstruction is suspected (the ultrasound should be performed within 24 hours at the latest).

Further diagnostic tests (e.g., immunology, kidney biopsy) may be indicated according to the suspected cause of AKI.[13] [64]

Full Recommendations

When to check for AKI

AKI is a medical emergency. Prompt recognition and treatment are vital to improve patient outcomes and preserve long-term kidney function.[62]

• Kidney function often does not return to the baseline level after recovery from AKI, especially if the patient has pre-existing CKD.[66]

AKI is often asymptomatic. Consider the possibility of AKI in any patient who is admitted as an emergency or who deteriorates during their hospital stay.[3] [62]

• AKI occurs in 10% to 20% of emergency admissions and has an inpatient mortality >20% (>35% in stage 3 AKI).[3] [9] [10]

Measure serum creatinine to check for AKI whenever an acutely ill patient meets one or more of the following criteria:[3] [9] [62]

• Age ≥ 65 years
• History of any one or more of CKD, heart failure, liver disease, diabetes, dementia
• Previous AKI episode
• Exposure within the previous week to:
  • Iodinated contrast agent
  • Any other nephrotoxin (e.g., NSAID, aminoglycoside antibiotic)
  • Renin-angiotensin-system modifying agent (e.g., ACE inhibitor/angiotensin-II receptor antagonist)
  • Diuretic.
• Symptoms or history of urological obstruction
• Suspected or confirmed sepsis
• Hypovolaemia (with or without hypotension) - may be related to dehydration or over-diuresis
• Hypotension (SBP <90 mmHg or a fall of >40mmHg from baseline BP)
• Oliguria (urine output <0.5ml/kg/hour).

Check for AKI in any patient whose early warning score deteriorates acutely - but never use a reassuring early warning score to rule out AKI.[1] [3]

• Because AKI is so common in acutely ill patients, the UK Royal College of Physicians recommends that a NEWS2 score of 5 or above should prompt a check for AKI (kidney function, fluid balance, and urine output).[62]
• But be aware that some patients with AKI may not have an elevated early warning score. This is because urine output is not included in commonly used scores such as NEWS2 - so oliguria (an indicator of possible AKI) will not trigger any increase in the patient’s score.

Practical tip
AKI is often a ‘silent disease’ so a high index of suspicion is important, particularly in acutely ill patients. [62]

- Most patients with AKI present asymptptomatically, with non-specific symptoms or with symptoms solely related to the precipitating illness (e.g., sepsis).
- A 2009 report from the UK’s National Confidential Enquiry into Patient Outcome and Death (NCEPOD) identified an unacceptable delay in post-admission diagnosis of AKI in 43% of patients who died in hospital from the condition.[67]

Definition of AKI

AKI is diagnosed based on an acute rise in serum creatinine and/or a sustained reduction in urine output. [4]

- Acute kidney injury has replaced the term ‘acute renal failure’.
  - AKI is a sudden reduction in kidney function that makes it difficult to maintain fluid, electrolyte, and acid-base balance.[9]
  - The condition covers the full spectrum of kidney damage ranging from less severe kidney injury through to kidney failure requiring RRT.
  - Evidence has demonstrated that even a minor increase in serum creatinine is associated with a significantly increased mortality. [1] [62]

AKI is present if any one or more of the following criteria is met: [4] [1] [3]

- A rise in serum creatinine of ≥26 micromol/L (≥0.3 mg/dL) within 48 hours
- A rise in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the past 7 days
- Urine volume <0.5 ml/kg/hour for at least 6 hours (at least 8 hours in children/young people).

  - These criteria were defined in the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guideline. [1]
  - One additional criterion for diagnosing AKI applies only to children/young people: a fall in estimated glomerular filtration rate (eGFR) of ≥25% over the past 7 days.

Baseline serum creatinine is best considered clinically as the lowest value over the previous 3 months. [62]

- If no recent creatinine value is available, provided the patient does not have progressive CKD, it is reasonable to assume that creatinine levels will have been stable for some time, so that a measurement from 6 months or even 1 year ago can be used as the baseline. [1]
- If there is no previous serum creatinine within the previous year, and AKI is suspected, consider repeating the creatinine within 12 hours - and certainly within 24 hours.[13]

Practical tip

You may work in an institution with an automatic alert system for AKI that is based on serum creatinine results.

- The algorithm used in the UK NHS alert system for AKI determines baseline serum creatinine as the lowest value in the past 7 days. If there is no creatinine value available from that period, it uses a median value over the previous 12 months.
In England and Wales a system is mandated across both primary and secondary care, whereby an AKI alert is triggered by rises in serum creatinine, based on the KDIGO definition and staging system.

In practice, both the serum creatinine and urine output criteria present diagnostic challenges. [1]

- **Rises in creatinine are delayed** for approximately 24 hours following kidney injury.
- **A reduction in urine output is an earlier indicator** of AKI in some patients but AKI can also present without oliguria.
  - In addition, unless the patient is catheterised, **accurate and timely measurement of urine output is difficult**. Routine catheterisation is not recommended. [1] [68]

**Practical tip**

**It is important to differentiate AKI from a progression of CKD at initial presentation.**
- This can be difficult if there are no recent comparison creatinine values. The clinical context will be important in helping you assess whether a rise in serum creatinine has been acute or occurred over a longer period.
- Features that favour a diagnosis of CKD (although do not exclude AKI) include: [9] [62]
  - Hypocalcaemia
  - Hyperphosphataemia
  - Anaemia
  - Small kidneys on ultrasound (sometimes scarred) - suggestive of advanced CKD.
- If the patient is acutely unwell or hypovolaemic, this points towards AKI. [9]
- Remember that pre-existing CKD is a risk factor for AKI.
- Repeat blood testing along with reference to historical creatinine values is the key to confirming or ruling out AKI.

**Practical tip**

**Beware false positive rises in creatinine, for example:** [1] [9]
- Recent use of trimethoprim can lead to a rise in serum creatinine that does not reflect any change in glomerular filtration rate
- Serum creatinine falls during pregnancy so a rise in creatinine after recent delivery may be a false positive.

**Staging the AKI**

**Stage the severity of AKI according to KDIGO criteria.** [4] [69] [70]

- The stage of AKI is determined by the **extent to which serum creatinine rises or urine output falls**.
- The 2012 KDIGO AKI definition and staging criteria are internationally recognised. They harmonised the earlier RIFLE (Risk, Injury, Failure, Loss of kidney function, and End stage kidney disease) and AKIN (Acute Kidney Injury Network) definitions. [69] [70]

**Stage the AKI using whichever one of serum creatinine or urine output gives the higher stage.** [1] [13]
A higher stage of AKI is associated with a greater risk of death as well as increased likelihood of needing RRT. [13]

<table>
<thead>
<tr>
<th>AKI Stage [1] [62]</th>
<th>Serum creatinine (SCr) criteria*</th>
<th>Urine output criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• SCr rise of ≥26 micromol/L within 48 hours or • SCr increase to 1.5 to 1.9 times baseline</td>
<td>• &lt;0.5 mL/kg/h for at least 6 consecutive hours</td>
</tr>
<tr>
<td>Stage 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• SCr increase to 2 to 2.9 times baseline</td>
<td>• &lt;0.5 mL/kg/h for at least 12 consecutive hours</td>
</tr>
<tr>
<td>Stage 3</td>
<td></td>
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<tr>
<td></td>
<td>• SCr increase to ≥3 times baseline or • SCr rise to ≥354 micromol/L or • Patient initiated on RRT (irrespective of AKI stage at time of initiation)</td>
<td>• &lt;0.3 mL/kg/h for at least 24 consecutive hours or • Anuria for 12 hours</td>
</tr>
</tbody>
</table>

*Baseline SCr is the lowest level in the last 7 days or, if not available, the lowest within the previous 3 months.

Practical tip

Even relatively minor changes in serum creatinine levels are associated with a significant increase in mortality. [62]

- In a person with normal kidney function, a rise of creatinine above the normal range reflects a loss of more than 50% of function and a significant loss in kidney reserve.

Evidence: AKI stage and mortality

Mortality rises sharply with increasing stage of AKI.

AKI during hospital admission is associated with an overall mortality of greater than 20% whereas stage 3 AKI is associated with >35% mortality. [3] [9] [10]

- A comparison of the RIFLE, AKIN, and KDIGO staging systems found they were all good predictors of mortality. [71] Whichever system was used, the key message was that mortality increases with severity as determined by rising serum creatinine.
- One study of more than 20,000 patients showed a nearly linear increase in in-hospital mortality with increasing RIFLE stage. [72]
Patients at Risk (R) had triple the mortality rate of patients without AKI.

Patients with Injury (I) had close to twice the mortality of R.

Patients with Failure (F) had 10 times the mortality rate of inpatients without AKI.

The RIFLE and KDIGO criteria map to each other approximately as:

- R = KDIGO stage 1
- I = KDIGO stage 2
- F = KDIGO stage 3

**Causes of AKI**

AKI can be classified as pre-kidney (or pre-renal), intrinsic, or post-kidney (post-renal).

- In practice, AKI is sometimes multi-factorial.

There are many causes of AKI. The most common are:

- Sepsis, hypovolaemia, and/or hypotension (pre-kidney AKI)
  - Often due to acute illness in a patient with background risk factors
  - In such patients, AKI is a strong indicator of a very sick patient who needs urgent recognition and management

- Exposure to nephrotoxins (intrinsic AKI).
  - If AKI is not secondary to either of these, then consider the possibility of obstruction or a less common intrinsic cause.
It is essential to take all possible steps to determine and record the cause of the patient's AKI, based on the history, examination, and investigations. [5] [17] [1] [52] [13]

- The most appropriate management plan will depend on both the severity of AKI and the underlying cause.[1]

1. **Pre-kidney AKI (80%)**
Pre-kidney AKI is caused by reduced kidney perfusion often resulting from sepsis, excessive fluid loss, and/or hypotension associated with acute illness.

- By definition this is a functional process whereby there is no cellular damage.

**Causes of pre-kidney AKI include:** [1] [62]

- Hypovolaemia/dehydration. For example, due to:
  - Haemorrhage
  - Vomiting and diarrhoea
  - Insufficient maintenance or replacement fluids to cover losses[3]
  - Acute pancreatitis.
- Sepsis
- Hypotension (SBP <90 mmHg or a drop of >40 mmHg from baseline BP)
  - May be related to antihypertensive medications.
- After major surgery
- Ileus (sequestration of fluid)
- High output ileostomy.

2. **Intrinsic AKI (10%-20%)**
Intrinsic AKI occurs when there is cellular damage within the kidneys.

- If you suspect an intrinsic cause (e.g., vasculitis), seek early specialist input.

**Causes of intrinsic AKI include:** [9] [62]

- Prolonged pre-kidney AKI leading to acute tubular injury (the most common cause)
- Nephrotoxins (e.g., iodinated contrast agents, aminoglycoside antibiotics, NSAIDs) - see our Primary prevention section for information on preventing AKI
- Tubulointerstitial nephritis (e.g., triggered by infection or nephrotoxic drugs)
- Acute glomerulonephritis (e.g., post-streptococcal glomerulonephritis)
- Vasculitis (e.g., anti-neutrophil cytoplasmic antibodies [ANCA]-associated vasculitis)
- Haemoglobinuria
- Microangiopathy (e.g., accelerated hypertension, haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura)
- Rhabdomyolysis.

3. **Post-kidney AKI (5%-10%)**
Post-kidney AKI is secondary to urinary outflow obstruction. Causes include: [9] [62]
Acute kidney injury

**Diagnosis**

- Prostatic hyperplasia
- Kidney stones (bilateral or in a single kidney)
- Retroperitoneal fibrosis (associated with malignancy, e.g., lymphoma)
- Papillary necrosis (flank pain and haematuria, e.g., associated with NSAIDs)
- Tumour (e.g., cervical, prostate)

**Clinical presentation**

**History**

AKI is commonly asymptomatic. A comprehensive history is important to identify risk factors or precipitating causes for AKI. You should check for:

- **Risk factors**
  - Age ≥65 years (frail older people are at particular increased risk).
  - History of any one or more of CKD, heart failure, liver disease, diabetes, dementia (or any other neurological/cognitive impairment that may result in limited access to oral fluids).
  - Previous AKI.
  - Myeloproliferative disorder (e.g., multiple myeloma).

- **Precipitating factors**
  - Suspected or confirmed sepsis.
  - Hypovolaemia (with or without hypotension).
  - May be related to haemorrhage or dehydration due to poor fluid intake, over-diuresis, illness (e.g., diarrhoea and vomiting) or insufficient replacement fluids in a hospital inpatient.
  - Hypotension (SBP <90 mmHg or a fall of >40mmHg from baseline BP).
  - Exposure within the previous week to iodinated contrast.
  - Recent surgery (especially cardiac).
  - Acute pancreatitis.
  - History of urinary tract symptoms that might suggest an obstructive cause.
  - Recent vascular intervention - raises the possibility of cholesterol embolisation (livedo reticularis), contrast-induced AKI. See our Primary prevention section for information about preventing AKI.

- **Medication history**
  - NSAID or aminoglycoside antibiotic use (nephrotoxic potential - can cause drug-induced interstitial nephritis).
  - ACE inhibitor/angiotensin-II receptor antagonist.
  - Renin-angiotensin system modifying agents reduce the kidney’s ability to adapt to changes in perfusion pressure by lowering efferent glomerular arteriolar tone, making it more difficult for the kidney to maintain glomerular filtration pressure in the event of hypovolaemia/hypotension.
  - Diuretic or any other antihypertensive - particularly if started (or dose changed) in the last 7 days.
  - These medications increase the risk of hypovolaemia and/or hypotension.
Acute kidney injury

Diagnosis

- Aciclovir, methotrexate, triamterene, indinavir, or sulfonamides (can cause tubular obstruction by forming crystals).[77]
- Recreational drug use.
- Over-the-counter drugs and herbal remedies.

If symptoms do occur they may include:

- **Dizziness**
  - Postural hypotension **secondary to hypovolaemia** suggests pre-kidney AKI.
  - **Thirst** is another common symptom of hypovolaemia.

- **Decreased urine output**
  - Oliguria is **one of the diagnostic criteria** for AKI and is an earlier indicator of impaired kidney function than rising creatinine.
    - Urine output <0.5 ml/kg/hour for at least 6 consecutive hours (at least 8 hours in children/young people) is diagnostic of AKI.[1]
    - But be aware that **patients with AKI are often not oliguric**.
  - **Anuria** suggests either an obstructive cause or severe AKI from a pre-kidney or intrinsic cause.

- **Nausea/vomiting**
  - Vomiting may **cause pre-kidney AKI** or can be a later manifestation of **AKI-related uraemia**.[62]
  - **Lower urinary tract symptoms** (urgency, frequency, nocturia, or hesitancy)
    - Suggestive of an obstructive cause.[4]

- **Altered mental status**
  - Usually secondary to a primary kidney insult (e.g., sepsis) but may also result from **AKI-related uraemia**.

- **Muscle tenderness**
  - Suspect intrinsic AKI secondary to **rhabdomyolysis** and tubular toxicity from myoglobin in the setting of acidosis.

- **Haematuria** (visible or non-visible)
  - May be related to pyelonephritis, kidney stones, papillary necrosis, tumour, or acute glomerulonephritis.

**Less commonly, symptoms of volume overload can be seen at presentation:**

- **Orthopnoea**
  - From **pulmonary oedema** or AKI-related **acidaemia**.

- **Swollen ankles**
  - Suggests salt/water overload - from an obstructive cause or in patients with nephrotic syndrome secondary to glomerulonephritis.

**In rare causes of AKI, the patient may present with:** [9] [64]

- **Fever, rash, and/or joint pain**
Acute kidney injury

**Diagnosis**

- Suspect small-vessel vasculitis (e.g., granulomatosis with polyangiitis, microscopic polyangiitis), or interstitial nephritis.

- **Haemoptysis**
  - Suspect small vessel vasculitis or anti-glomerular basement membrane antibody disease.

- **Hypercalcaemia, hyperuricaemia, bone pain, and lytic lesions**
  - Suspect multiple myeloma.

**Examination**

*Your examination should cover:*

- **Volume status** - signs of hypovolaemia are often present (less commonly, signs of volume overload are seen at presentation). Check:
  - Peripheral perfusion (capillary refill)
  - Pulse rate
  - Blood pressure (BP) - including a check for postural hypotension
  - Jugular venous pressure
  - Dry axillae/mucous membranes
  - Peripheries (oedema)
  - Auscultation of lungs (crackles may suggest pulmonary oedema)
  - Respiratory rate (tachypnoea suggests fluid overload and/or acidosis).

- **Mental status**
  - May be affected by precipitating illness (e.g., sepsis).
  - Confusion can result from encephalopathy in a patient with AKI-related uraemia.

- **Any signs of uraemic syndrome** (e.g., pericardial rub)[13] [65]
  - Acute pericarditis is a complication associated with severe AKI and worsening uraemia.[13] [65]
  - Presence of a pericardial friction rub on clinical examination is an indication for RRT (although it may be absent if there is a significant effusion).[1] [13]
  - **Asterixis** is another possible symptom of uraemia.

*Look for any signs of sepsis and manage promptly.* [9] [64]

- Perform a *septic screen* and implement your local care bundle (e.g., Sepsis Six) if infection is suspected. See our Sepsis topic for more information.

**Clinical findings that may support a specific underlying diagnosis include:** [64]

- **Rash** - for example, petechiae or purpura (intrinsic AKI, e.g., interstitial nephritis, vasculitis, glomerulonephritis)
- **Jaundice** (hepatorenal syndrome)
- **Joint swelling/pain** (vasculitis)
- **Hypertension, pulmonary oedema, and peripheral oedema** (obstructive cause; renal artery stenosis; acute glomerulonephritis)[18] [78] [79] [9]
- **Hypotension** (pre-kidney or intrinsic AKI)[9]
• Note that hypotension might be absolute (SBP < 90 mmHg) or relative (BP fall of > 40 mmHg from the patient’s baseline).
• May be secondary to sepsis and vasodilation and/or hypovolaemia, resulting in reduced kidney perfusion and pre-kidney AKI.
• Prolonged hypotension can then cause cell damage and acute tubular injury, resulting in intrinsic AKI.

  • **Abdominal bruit** (renovascular disease)
  • **Abdominal distension** and/or **palpable bladder** and/or **enlarged prostate** (obstruction).[64]

**Investigations**

**Baseline bloods and urine analysis**

The key investigations in suspected or confirmed AKI are baseline bloods and urine analysis.

**Baseline bloods** [1] [62] [13] [64] [65]

Urea and electrolytes (including creatinine) are essential.

  • The initial **serum creatinine** level, followed by ongoing serum creatinine monitoring, forms the basis of diagnosing, staging, and monitoring the progress of any patient with AKI.[1]
  • An acutely elevated serum creatinine may be the only sign of AKI.
  • **Ensure close monitoring of serum potassium.** [62] [80]

  • Hyperkalaemia is a common complication of AKI.
  • Urgent treatment is required if potassium >6.0 mmol/L and/or ECG changes are seen.
  • For any hospital inpatient with AKI, ensure daily monitoring of urea and electrolytes until the AKI has resolved (i.e., a return to actual or presumed baseline kidney function or the establishment of steady state kidney function).[13]

**Request bicarbonate if it is not part of the standard panel.**

  • Alternatively, if previously taken bloods indicate AKI and bicarbonate was not included, request a **venous blood gas**.
  • Low bicarbonate suggests acidosis.
  • Venous blood gases can help with further evaluation of acidosis.

**Also request:** [13] [64]

  • **Liver function tests** (will aid diagnosis of hepatorenal syndrome)[62]
  • CRP (a marker of inflammation; will be elevated in vasculitis)
  • FBC

  • **Leukocytosis may suggest infection.**

    • **High or low WBC can occur with sepsis.**
  
  • If platelets are low, request a **blood film and lactate dehydrogenase** to check for rare disorders such as haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura, cryoglobulinaemia.[1]
  
    • **Blood cultures** - if infection is suspected[81]
  
    • **Serum creatine kinase** - if rhabdomyolysis is suspected.

**Practical tip**
Do not use the urea:creatinine ratio as an indicator of the cause of AKI. [82]
- An elevated urea: creatinine ratio can occur in AKI.[13] This is because urea and creatinine are both freely filtered at the glomerulus, but urea is reabsorbed by the tubules whereas creatinine is not.
- The urea:creatinine ratio is sometimes suggested as a useful indicator to distinguish pre-kidney AKI from intrinsic or post-kidney causes, with a higher ratio considered to be suggestive of a pre-kidney cause.
- However, there is no reliable evidence to support this and there are multiple confounders that affect the ratio, including gastrointestinal bleeding, drug-induced increases (e.g., corticosteroids) and a high-protein diet.[81]

Urine analysis [1] [3] [62] [64]
Perform urine dipstick testing for specific gravity, blood, protein, leucocytes, nitrites, and glucose as soon as AKI is suspected or diagnosed.
- Use a clean-catch specimen.

Consider the possibility of intrinsic AKI if urinalysis is positive for both blood and protein in the absence of an obvious alternative cause (e.g., urinary tract infection or trauma from urinary catheterisation). [3] [9] [64]
- Proteinuria together with haematuria may indicate an active urinary sediment due to glomerular disease.
  - Patients with glomerular disease typically present with proteinuria and haematuria with hypertension and oedema. An early referral to nephrology is indicated.[3]
  - However, there remains a wide differential diagnosis for blood and protein on dipstick (e.g., infection, trauma, papillary necrosis).
  - Careful microscopy of freshly collected, freshly spun urine for the presence of red cell casts can confirm glomerular origin haematuria. But if this is not available, the absence of catheter trauma or urinary tract infection should raise concerns about glomerular disease.
  - Other causes of an active urinary sediment (dysmorphic red cells and red cell casts) include infection, tumours, calculi, venous thrombosis, and myoglobinuria (rhabdomyolysis).

Send urine culture if clinical features of urinary tract infection are present and/or urinalysis is positive for blood, protein, leukocytes, or nitrites. [64]

Start urine output monitoring (hourly if catheterised, 4-hourly if not). [64]
- **Routine urinary catheterisation is not appropriate** in patients with AKI. Carefully weigh up the **benefits against the risks** for the individual patient.[64]
  - Potential benefits:
    - Oliguria is one of the diagnostic criteria for confirming AKI, but urine output is difficult to measure accurately without catheterisation
    - Urinalysis can be performed on a sample obtained following catheterisation (but be aware that any proteinuria/haematuria might have resulted from catheter-related trauma)
• Hourly urinary output monitoring aids assessment of the patient’s response to treatment
• Catheterisation can be both diagnostic and therapeutic for bladder neck obstruction.

• Potential risks:
  • Infection
  • Trauma
  • Falls risk.

• Catheterisation is indicated:
  • In any case where fluid balance management is crucial
  • If the patient is too ill to use a bottle or commode
  • If bladder neck obstruction is suspected and cannot be quickly ruled out by ultrasound.

Consider requesting urine electrolytes to measure fractional excretion of sodium or urea - but beware the potential pitfalls. [13]

• In principle, calculation of fractional excretion of sodium (FENa) may be helpful in distinguishing pre-kidney from intrinsic AKI. In practice it is rarely performed and results are often difficult to interpret, particularly if loop diuretics have been used within the last 24 hours.
  • Fractional excretion of sodium (FENa) of <1% suggests pre-kidney AKI but may also be seen in glomerulonephritis, hepatorenal syndrome, some cases of obstruction, and even acute tubular necrosis (if tubular function remains intact).

• Fractional excretion of urea (FEUr) is more useful if the patient has received loop diuretics - although results are also difficult to interpret so the test is rarely performed in clinical practice.
  • Urea excretion is not significantly affected by diuretics.
  • A fractional excretion of urea <35% supports a diagnosis of pre-kidney AKI.
  • The fractional excretion of urea is calculated as: 100% X (urine urea x plasma creatinine)/(plasma urea x urine creatinine).

• Urine sodium concentration
  • <20 mmol/L (20 mEq/L) suggests pre-kidney AKI with preserved tubule function/sodium retention.
  • Raised levels are seen in intrinsic AKI where there is tubule damage or in response to diuretics.

Urine osmolality is rarely requested.

• Urine osmolality is the number of moles of solute per kg of solvent and it depends on tubule response to anti-diuretic hormone (ADH).
  • High urine osmolality (>500 mOsm/kg) suggests pre-kidney AKI with preservation of tubule function (assuming no recent administration of iodinated contrast). [1] [83]
  • However this should not be interpreted as confirming pre-kidney AKI because intact tubule function (particularly in the early stages) may be seen in various forms of kidney disease (e.g., glomerulonephritis). [1]
  • Urine osmolality <300 mOsm/kg suggests tubule damage (intrinsic AKI) as urinary concentration is impaired. [83]

Urine microscopy can be useful if there is a finding of blood and protein on urinalysis. [13]
• It is not widely used in the UK but is more commonly performed in other countries (e.g., USA, China).
• It may reveal:
  • Granular casts in acute tubular injury
  • Red cell casts in glomerulonephritis/vasculitis
  • Oxalate crystals - suggestive of ethylene glycol poisoning.[84]

Urinary eosinophil counts may be of some use in patients with pyuria.

• A result above 5% to 7% supports a diagnosis of acute allergic interstitial nephritis but is not diagnostic because of low sensitivity and specificity.[85] The test is dependent on the expertise of the microscopist.
• It has a negative predictive value of >90% for patients with AKI and may be useful in excluding the disease process.[86]
• Eosinophiluria may be seen with atheroembolic disease as well.

Practical tip

• All the urine investigations above, if available, can aid the diagnosis of AKI, but they all have their own limitations and vary in sensitivity and specificity.
• A single investigation will not be enough on its own to draw any firm conclusions.[13] [87]

Other initial tests

Request a chest x-ray. [65] It may demonstrate signs of:

• Infection
• Pulmonary oedema
• Haemorrhage (e.g., ANCA-associated vasculitis, Goodpasture syndrome [pulmonary haemorrhage, rapidly progressive glomerulonephritis, and anti-glomerular basement membrane antibodies])
• Cardiomegaly.

Request an ECG.

• It may demonstrate features consistent with severe hyperkalaemia (peaked T waves, increased PR interval, widened QRS, atrial arrest, deterioration to a sine wave pattern).

Investigations to consider

Kidney imaging

If pyonephrosis (an infected/obstructed renal tract) is suspected, ensure the patient has an ultrasound - and if indicated a nephrostomy - within 6 hours, due to the risk of septic shock. [3] [64]

Renal tract ultrasound is not routinely required. Only request it if no obvious cause for the AKI can be found or if obstruction, pyelonephritis, or pyonephrosis is suspected. [3] [13]

• The presence of dilated renal calyces suggests obstruction and hydronephrosis.
• Ensure the ultrasound is performed within 24 hours if no obvious cause for the AKI can be identified or a urinary tract obstruction is suspected.[3] [64]
• Ultrasound has high sensitivity (90%-98%) but lower specificity (65%-84%) for diagnosing upper tract obstruction, although this may not be the case in the early stages (first 8 hours).[13]
• Repeat the ultrasound after 24 hours if:
• There is a high index of suspicion for hydronephrosis (as it may take several hours for this to develop due to initial non-compliance of the pelvi-caliceal system)
• The patient has oliguric acute tubular necrosis with superimposed obstruction (because urine is needed to dilate the kidneys).

If prior creatinine values are not available to give a baseline, ultrasound can sometimes be helpful in distinguishing AKI from CKD. [62] [13]

• Ultrasound may demonstrate small (sometimes scarred) kidneys consistent with advanced CKD (such changes are unlikely to be seen in less severe CKD).
• Be aware that an ultrasound finding consistent with CKD does not exclude the possibility of AKI on a background of CKD.[13]

Consider requesting a CT or MRI if obstruction is suggested on ultrasound (e.g., possible masses or stones). [13]

• These are not routinely needed - the decision will depend on the degree of obstruction.
• Be cautious with intravenous iodinated contrast CT scans in patients with AKI. MRI is preferred (although note that gadolinium may be needed for MRI enhancement).

Nuclear renal flow scans can sometimes be useful to evaluate for obstruction in cases of mild hydronephrosis, when the diagnosis of mechanical obstruction is uncertain.

• The scan is performed before and after a dose of loop diuretic.
  • Impaired tracer excretion is suggestive of acute tubular necrosis.
  • Poor blood flow is suggestive of obstructed blood supply.
  • Normal blood flow and tracer excretion with tracer accumulation in the collecting system is suggestive of obstruction of the urine outflow tract.

Other tests

Further diagnostic tests may be determined by the suspected cause of AKI. Examples include: [13] [64]

• Immunological tests
  • Anti-nuclear antibodies (ANA) and anti-DNA antibody (lupus nephritis).
  • Complement (lupus nephritis, post-infectious glomerulonephritis).
  • Anti-glomerular basement membrane antibodies (Goodpasture syndrome, anti-glomerular basement membrane syndrome).
  • Anti-neutrophil cytoplasmic antibodies (ANCA-associated vasculitis).
  • Serum/urine electrophoresis and urinary Bence Jones protein (myeloma).
    • Myeloma is an important potential cause of AKI and should be considered in a patient >40 years who presents with hypercalcaemia, hyperuricaemia, or pathological fracture.[9] [64]
    • Serum electrophoresis will show a paraprotein (monoclonal immunoglobulin).
    • Urine electrophoresis will detect Bence Jones proteins (free light chains) which are not detected on urinalysis.
  • Acute hepatitis profile: hepatitis B, C, and D (glomerulonephritis).
• HIV test (glomerulonephritis or drug-induced AKI).
• Cryoglobulins (glomerulonephritis).
• Complement mutations (haemolytic uraemic syndrome).
• Anti-streptolysin O titres (post-streptococcal glomerulonephritis).

• **Kidney biopsy**
  - May be performed to diagnose rarer forms of AKI (e.g., interstitial nephritis, glomerulonephritis, or vasculitis).

• **Cystoscopy**
  - May be requested to identify the cause of obstructive AKI (e.g., ureteric stenosis, bladder tumour).

### History and exam

#### Key diagnostic factors

**hypotension (common)**

Hypotension and/or hypovolaemia is a common cause of reduced kidney perfusion and resulting pre-kidney AKI. [9] [62]

- Often due to acute illness (e.g., sepsis and vasodilatation; haemorrhage; vomiting and diarrhoea), particularly in a patient with background risk factors.
- Can also result from dehydration due to poor fluid intake, over-diuresis, or insufficient replacement fluids in a hospital inpatient. [3]
  
  - Hypovolaemia due to reduced fluid intake is a particular risk for frail, older patients especially those with cognitive or neurological impairment. [9]

Hypotension may be absolute (SBP <90 mmHg) or relative to the patient’s usual BP (a drop of >40 mmHg from baseline).

- May be related to antihypertensive medications.

**Assessing volume status is a crucial part of your initial examination - signs of hypovolaemia are often present.** [9] [64] Check:

- Peripheral perfusion (capillary refill)
- Pulse rate
- Blood pressure (including a check for postural hypotension)
- Jugular venous pressure
- Dry axillae/mucous membranes.

Treat hypovolaemia promptly with an immediate bolus of crystalloid intravenous fluid. [1] [62] [13] [64]

Prolonged hypotension can cause pre-kidney AKI to progress to cell damage and acute tubular injury (intrinsic AKI).
risk factors (common)

AKI is commonly asymptomatic so is easily missed. Whenever a patient presents with an acute illness, ensure your history covers characteristics that increase the risk of AKI. Check for: [17] [18] [67] [9]

- **Risk factors** [3] [9] [64]
  - Age ≥65 years (frail older people are at particular increased risk).[65]
  - History of any one or more of chronic kidney disease (CKD), heart failure, liver disease, diabetes, dementia (or any other neurological/cognitive impairment that may result in limited access to oral fluids).
  - Previous AKI.
  - Myeloproliferative disorder (e.g., multiple myeloma).[5] [53]

**Medication history** [3] [9] [62]

- Non-steroidal anti-inflammatory drug (NSAID) or aminoglycoside antibiotic use (nephrotoxic potential - can cause drug-induced interstitial nephritis).
- ACE inhibitor/angiotensin-II receptor antagonist use.
  - Renin-angiotensin system modifying agents reduce the kidney’s ability to adapt to changes in perfusion pressure by lowering efferent glomerular arteriolar tone, making it more difficult for the kidney to maintain glomerular filtration pressure in the event of hypovolaemia/hypotension.[9]
  - Diuretic or any other antihypertensive - particularly if started (or dose changed) in the last 7 days.
  - These medications increase the risk of hypovolaemia and/or hypotension.
  - Aciclovir, methotrexate, triamterene, indinavir, or sulfonamides (can cause tubular obstruction by forming crystals).[77]
  - Recreational drug use.
  - Over-the-counter drugs and herbal remedies.

**Practical tip**

AKI is often a ‘silent disease’ so a high index of suspicion is important, particularly in acutely ill patients. [62]

- Most patients with AKI present asymptptomatically, with non-specific symptoms or with symptoms solely related to the precipitating illness (e.g., sepsis).
- A 2009 report from the UK’s National Confidential Enquiry into Patient Outcome and Death (NCEPOD) identified an unacceptable delay in post-admission diagnosis of AKI in 43% of patients who died in hospital from the condition.[67]

**kidney insults (common)**

Many cases of AKI are precipitated by a kidney insult, particularly in patients with underlying risk factors. Examples include :[1] [3] [9] [62]
• Sepsis or other acute illness (e.g., acute pancreatitis, burns)
  • Perform a septic screen and implement your local care bundle (e.g., Sepsis Six) if infection is suspected.[9] [63]
• Hypovolaemia (with or without hypotension)
• Nephrotoxins
  • Exposure within the previous week to iodinated contrast agent
  • Use of an NSAID or aminoglycoside antibiotic[1]
• Recent surgery (especially cardiac)
• Recent vascular intervention - raises the possibility of cholesterol embolisation (livedo reticularis), contrast-induced AKI.[52] [64]

reduced urine production (common)

Oliguria is one of the diagnostic criteria for AKI and is an earlier indicator of impaired kidney function than rising creatinine. [1]

• Confirm a diagnosis of AKI if urine output <0.5 ml/kg/hour for at least 6 consecutive hours (at least 8 hours in children/young people).
• But be aware that patients with AKI are often not oliguric .

Anuria suggests either an obstructive cause or severe AKI from a pre-kidney or intrinsic cause.

AKI can also be staged according to the extent to which urine output falls (or serum creatinine rises). [1]

• Stage the AKI using whichever one of serum creatinine or urine output gives the higher stage.[1] [13]
  • Stage 1 AKI: urine output <0.5 mL/kg/h for at least 6 consecutive hours
  • Stage 2 AKI: urine output <0.5 mL/kg/h for at least 12 consecutive hours
  • Stage 3 AKI: urine output <0.3 mL/kg/h for at least 24 consecutive hours or anuria for 12 hours
• A higher stage of AKI is associated with a greater risk of death as well as increased likelihood of needing renal replacement therapy (RRT). [13]

In practice, accurate and timely measurement of urine output is difficult unless the patient is catheterised.

• Routine catheterisation is not recommended.[1] [68]

lower urinary tract symptoms (common)

Lower urinary tract symptoms such as urgency, frequency, or hesitancy are suggestive of a urinary tract obstruction.

• Prostatic hyperplasia is a common cause of obstructive AKI in older men.[4]
symptoms of volume overload/pulmonary oedema\(^\text{#}(uncommon)\)

Symptoms and signs of volume overload may be seen at presentation if the patient has obstructive AKI or any form of AKI against a background of pre-existing heart failure.

- Otherwise the most common cause of volume overload is overenthusiastic fluid resuscitation.\(^{[1]}\)\(^{[13]}\)

Symptoms of volume overload that may be reported at presentation include:

- **Orthopnoea**
  - From **pulmonary oedema** or AKI-related **acidosis**
  - **Swollen ankles/other signs of peripheral oedema**
    - From an obstructive cause or in patients with nephrotic syndrome secondary to glomerulonephritis.

Examination signs in a patient with volume overload might include:

- **Crackles** on auscultation of lungs (suggests pulmonary oedema)
- **Tachypnoea** (suggests fluid overload and/or acidosis).\(^{[64]}\)

vomiting/nausea (uncommon)

Vomiting may cause pre-kidney AKI or can be a later manifestation of AKI-related uraemia.\(^{[62]}\)

fever, rash, and/or arthralgia (uncommon)

If present, suspect small-vessel vasculitis (e.g., granulomatosis with polyangiitis, microscopic polyangiitis), or interstitial nephritis.\(^{[64]}\)

haematuria (visible or non-visible) (uncommon)

Can occur with kidney stones, papillary necrosis, infection, tumour, or acute glomerulonephritis.

palpable bladder and/or enlarged prostate and/or abdominal distension (uncommon)

Point to an obstructive cause of AKI.\(^{[13]}\)\(^{[64]}\)\(^{[65]}\)

Other diagnostic factors

dizziness and orthostatic symptoms (common)

Orthostatic symptoms and postural hypotension confirmed on blood pressure monitoring are consistent with hypovolaemia and **suggest pre-kidney AKI**.

- **Thirst** is another common symptom of hypovolaemia.

hypertension (uncommon)
May be seen in AKI secondary to renal artery stenosis or a rapidly progressive glomerulonephritis. [18] [78] [79] [9]

**altered mental status** (uncommon)

A change in mental status is usually secondary to a primary kidney insult (e.g., sepsis) that precipitated AKI.

Confusion can also result from encephalopathy in a patient with AKI-related uraemia. [13]

**pericardial/pleural rub (uncommon)**

Acute pericarditis is a complication associated with severe AKI and worsening uraemia (most often on a background of pre-existing CKD). [13] [65]

- The presence of a pericardial friction rub on examination is an indication for renal replacement therapy (although it may be absent if there is a significant effusion).[1] [13]
- **Asterixis** is another possible symptom of uraemia.

**muscle tenderness (uncommon)**

Suspect intrinsic AKI secondary to rhabdomyolysis and tubular toxicity from myoglobin in the setting of acidosis.

**haemoptysis (uncommon)**

Suspect an intrinsic cause of AKI (e.g., small vessel vasculitis or anti-glomerular basement membrane antibody disease). [64]

**abdominal bruit (uncommon)**

Suspect renovascular disease.
# Investigations

## 1st test to order

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>basic metabolic profile (including urea and creatinine and liver</td>
<td>• acutely elevated serum creatinine, high serum potassium, metabolic</td>
</tr>
<tr>
<td>function tests)</td>
<td>acidosis</td>
</tr>
<tr>
<td><strong>Creatinine for AKI diagnosis</strong></td>
<td>• confirm the diagnosis of AKI if there is:</td>
</tr>
<tr>
<td><strong>AKI is often asymptomatic so is easily missed.</strong> [62]</td>
<td>[4] [1]</td>
</tr>
<tr>
<td>* An acutely rising creatinine may be the only sign.</td>
<td>[3]</td>
</tr>
<tr>
<td>* Rises in creatinine are delayed for approximately 24 hours</td>
<td>[9]</td>
</tr>
<tr>
<td>following kidney injury.</td>
<td>[62]</td>
</tr>
<tr>
<td>Measure serum creatinine to check for AKI whenever an acutely ill</td>
<td>• a rise in serum creatinine of ≥26 micromol/L (≥0.3 mg/dL) within 48</td>
</tr>
<tr>
<td>patient meets one or more of the following criteria:</td>
<td>hours</td>
</tr>
<tr>
<td>• Age ≥65 years</td>
<td>OR</td>
</tr>
<tr>
<td>• History of any one or more of chronic kidney disease (CKD),</td>
<td>• a rise in serum creatinine to ≥1.5 times baseline,</td>
</tr>
<tr>
<td>heart failure, liver disease, diabetes, dementia</td>
<td>which is known or presumed to have occurred within the past 7 days</td>
</tr>
<tr>
<td>• Previous AKI episode</td>
<td>• LFTs will be deranged in hepatorenal syndrome</td>
</tr>
<tr>
<td>• Exposure within the previous week to:</td>
<td></td>
</tr>
<tr>
<td>• Iodinated contrast agent</td>
<td></td>
</tr>
<tr>
<td>• Any other nephrotoxin (e.g., non-steroidal anti-inflammatory</td>
<td></td>
</tr>
<tr>
<td>drug [NSAID], aminoglycoside antibiotic)</td>
<td></td>
</tr>
<tr>
<td>• Renin-angiotensin-system modifying agent (e.g., ACE inhibitor/</td>
<td></td>
</tr>
<tr>
<td>angiotensin-II receptor antagonist)</td>
<td></td>
</tr>
<tr>
<td>• Diuretic.</td>
<td></td>
</tr>
<tr>
<td>• Symptoms or history of urological obstruction</td>
<td></td>
</tr>
<tr>
<td>• Suspected or confirmed sepsis</td>
<td></td>
</tr>
<tr>
<td>• Hypovolaemia (with or without hypotension) - may be related to</td>
<td></td>
</tr>
<tr>
<td>dehydration or over-diuresis[9]</td>
<td></td>
</tr>
<tr>
<td>• Hypotension (SBP &lt;90 mmHg or a fall of &gt;40 mmHg from baseline</td>
<td></td>
</tr>
<tr>
<td>BP)</td>
<td></td>
</tr>
<tr>
<td>• Oliguria (urine output &lt;0.5 ml/kg/hour)</td>
<td></td>
</tr>
<tr>
<td>• Acute rise in early warning score (e.g., NEWS2 &gt;5).</td>
<td></td>
</tr>
<tr>
<td>**AKI is diagnosed based on an acute rise in serum creatinine and/or</td>
<td></td>
</tr>
<tr>
<td>a sustained reduction in urine output. [1]</td>
<td></td>
</tr>
<tr>
<td>**Baseline serum creatinine is best considered clinically as the</td>
<td></td>
</tr>
<tr>
<td>lowest value over the previous 3 months. [62]</td>
<td></td>
</tr>
<tr>
<td>* If no recent creatinine value is available, provided the patient</td>
<td></td>
</tr>
<tr>
<td>does not have CKD it is reasonable to assume that creatinine</td>
<td></td>
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<tr>
<td>levels will have been stable for some time, so that a measurement</td>
<td></td>
</tr>
<tr>
<td>from 6 months or even 1 year ago can be used as the baseline. [1]</td>
<td></td>
</tr>
</tbody>
</table>
### Test | Result
---|---
- If there is no previous serum creatinine within the previous year, and AKI is suspected, consider repeating the creatinine within 12 hours - and certainly within 24 hours.\[13\]

#### Practical tip

**It is important to differentiate AKI from a progression of CKD at initial presentation.**

- This can be difficult if there are no recent comparison creatinine values. The clinical context will be important in helping you assess whether a rise in serum creatinine has been acute or occurred over a longer period.
- Features that favour a diagnosis of CKD (although do not exclude AKI) include:\[9\] \[62\]
  - Hypocalcaemia
  - Hyperphosphataemia
  - Anaemia
  - Small kidneys on ultrasound (sometimes scarred) - suggestive of advanced CKD.
- If the patient is acutely unwell or hypovolaemic, this points towards AKI.\[9\]
- Remember that pre-existing CKD is a risk factor for AKI.
- Repeat blood testing along with reference to historical creatinine values is the key to confirming or ruling out AKI.

#### Practical tip

**Beware false positive rises in creatinine, for example:** \[1\] \[9\]

- Recent use of trimethoprim can lead to a rise in serum creatinine that does not reflect any change in glomerular filtration rate.
- Serum creatinine falls during pregnancy so a rise in creatinine after recent delivery may be a false positive.

### Creatinine for AKI staging

**Stage the AKI using whichever one of serum creatinine or urine output gives the higher stage.** \[1\] \[13\]

- A higher stage of AKI is associated with a greater risk of death as well as increased likelihood of needing renal replacement therapy (RRT).\[13\]

**For any hospital inpatient with AKI, ensure daily monitoring of urea and electrolytes until the AKI has resolved, as indicated by:** \[13\]

- A return to actual or presumed baseline kidney function
<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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</thead>
<tbody>
<tr>
<td>or</td>
<td>The establishment of steady state kidney function.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AKI Stage [1] [62]</th>
<th>Serum creatinine (SCr) criteria*</th>
</tr>
</thead>
</table>
| Stage 1            | • SCr rise of ≥26 micromol/L within 48 hours  
or  • SCr increase to 1.5 to 1.9 times baseline |
| Stage#2            | • SCr increase to 2 to 2.9 times baseline |
| Stage#3            | • SCr increase to ≥3 times baseline  
or  • SCr rise to ≥354 micromol/L  
or  • Patient initiated on RRT (irrespective of AKI stage at time of initiation) |

*Baseline SCr is the lowest level in the last 7 days or, if not available, the lowest within the previous 3 months.

**Practical tip**

*Even relatively minor changes in serum creatinine levels are associated with a significant increase in mortality.* [62]

• In a person with normal kidney function, a rise of creatinine above the normal range reflects a loss of more than 50% of function and a significant loss in kidney reserve.

**Evidence: AKI stage and mortality**

*Mortality rises sharply with increasing stage of AKI*

AKI during hospital admission is associated with an overall mortality of greater than 20%, whereas stage 3 AKI is associated with >35% mortality. [3] [9] [68]
A comparison of the RIFLE, AKIN, and KDIGO staging systems found they were all good predictors of mortality.[71] Whichever system was used, the key message was that mortality increases with severity as determined by rising serum creatinine.

One study of more than 20,000 patients showed a nearly linear increase in in-hospital mortality with increasing RIFLE stage.[72]

- Patients at Risk (R) had triple the mortality rate of patients without AKI.
- Patients with Injury (I) had close to twice the mortality of R.
- Patients with Failure (F) had 10 times the mortality rate of inpatients without AKI.

The RIFLE and KDIGO criteria map to each other approximately as:

- R = KDIGO stage 1
- I = KDIGO stage 2
- F = KDIGO stage 3

More info

**KDIGO diagnostic and staging criteria**

The international KDIGO guideline group harmonised the previous definitions and staging criteria for AKI to produce a widely accepted consensus.[1]

Prior to the 2012 KDIGO definitions, there were a large number of different definitions of AKI.

- The best known were the 2004 RIFLE criteria and the subsequent modification of these to produce the 2007 AKIN criteria.[70] [69] [73]

In one study of 50,000 patients that compared the incidence of AKI using the RIFLE, AKIN, and KDIGO criteria, 11.6% of hospitalised patients were diagnosed as having AKI with the KDIGO criteria and 11.0% with the RIFLE criteria, whereas only 4.8% were classified as having AKI under the AKIN criteria.[74]

A comparison of the RIFLE definition with the modified AKIN definition demonstrated that there were subsets of patients defined as having AKI by each definition that were not detected by the other.[75]

- The RIFLE criteria failed to detect 9% of cases that were detected by AKIN criteria.
### Test

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>serum potassium</strong>&lt;br&gt;<strong>Ensure close monitoring of serum potassium.</strong> [62] [80]</td>
<td>elevated in hyperkalaemia&lt;br&gt;• 5.5 to 5.9 mmol/L indicates mild hyperkalaemia&lt;br&gt;• 6.0 to 6.4 mmol/L indicates moderate hyperkalaemia&lt;br&gt;• ≥6.5 mmol/L indicates severe hyperkalaemia</td>
</tr>
<tr>
<td><strong>Hyperkalaemia is a common complication of AKI.</strong>&lt;br&gt;• Urgent treatment is required if potassium &gt;6.0 mmol/L and/or ECG changes are seen.</td>
<td></td>
</tr>
</tbody>
</table>

| FBC | anaemia, leukocytosis, thrombocytopenia<br>**Leukocytosis may suggest infection.**<br>• High or low WBC can occur with sepsis.<br>**If platelets are low, request a blood film and lactate dehydrogenase:** [62] | |
| **Use to check for rare disorders such as haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura, cryoglobulinaemia.**[1] | |
| **Anaemia can occur in AKI secondary to haemolytic uraemic syndrome, myeloma, or vasculitis.** | |

| bicarbonate | low bicarbonate suggests acidosis<br>**Request bicarbonate if it is not part of the standard panel.** [62] [64] [65] | |
| **Alternatively, if previously taken bloods indicate AKI and bicarbonate was not included, request a venous blood gas.**<br>**Venous blood gases can help with further evaluation of acidosis.** | |

| C-reactive protein | elevated in infection and also in vasculitis<br>**Request in all patients.** [64] [65] | |

| blood culture | positive for bacterial pathogen<br>**Request if infection is suspected.** [62] [81] [64] | |

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### Acute kidney injury

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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</thead>
<tbody>
<tr>
<td><strong>Sepsis is a common cause of AKI.</strong> [9] [63]</td>
<td><strong>• Perform a septic screen and implement your local care bundle (e.g., Sepsis Six) if infection is suspected.</strong></td>
</tr>
<tr>
<td><strong>urinalysis</strong></td>
<td><strong>• Use a clean-catch specimen.</strong></td>
</tr>
<tr>
<td><strong>Perform urine dipstick testing for specific gravity, blood, protein, leucocytes, nitrites, and glucose as soon as AKI is suspected or diagnosed.</strong> [3] [62]</td>
<td><strong>• Proteinuria together with haematuria may indicate an active urinary sediment due to glomerular disease.</strong></td>
</tr>
<tr>
<td><strong>Consider the possibility of intrinsic AKI if urinalysis is positive for both blood and protein in the absence of an obvious alternative cause (e.g., urinary tract infection [UTI] or trauma from urinary catheterisation).</strong> [3] [9] [64]</td>
<td><strong>• Patients with glomerular disease typically present with proteinuria and haematuria with hypertension and oedema. An early referral to nephrology is indicated.</strong> [3]</td>
</tr>
<tr>
<td><strong>• However, there remains a wide differential diagnosis for blood and protein on dipstick (e.g., infection, trauma, papillary necrosis).</strong></td>
<td><strong>• Careful microscopy of freshly collected, freshly spun urine for the presence of red cell casts can confirm glomerular origin haematuria, but if this is not available then the absence of catheter trauma or UTI should raise concerns about glomerular disease.</strong></td>
</tr>
<tr>
<td><strong>• Other causes of an active urinary sediment (dysmorphic red cells and red cell casts) include infection, tumours, calculi, venous thrombosis, myoglobinuria (rhabdomyolysis).</strong></td>
<td><strong>• Other causes of an active urinary sediment (dysmorphic red cells and red cell casts) include infection, tumours, calculi, venous thrombosis, myoglobinuria (rhabdomyolysis).</strong></td>
</tr>
<tr>
<td><strong>urine culture</strong></td>
<td><strong>bacterial growth with antibiotic sensitivity</strong></td>
</tr>
<tr>
<td><strong>Send urine culture if clinical features of urinary tract infection are present and/or urinalysis is positive for blood, protein, leucocytes, or nitrites.</strong> [64]</td>
<td><strong>• confirm a diagnosis of AKI if urine output &lt;0.5 ml/kg/hour for at least 6 consecutive hours (at least 8 hours in children/young people).</strong></td>
</tr>
<tr>
<td><strong>urine output monitoring</strong></td>
<td><strong>• In practice, accurate monitoring can be difficult if the patient is not catheterised.</strong></td>
</tr>
<tr>
<td><strong>Start urine output monitoring in any patient diagnosed with AKI (hourly if catheterised, 4-hourly if not).</strong> [64]</td>
<td><strong>• In practice, accurate monitoring can be difficult if the patient is not catheterised.</strong></td>
</tr>
</tbody>
</table>
### Test

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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<tbody>
<tr>
<td><strong>Routine urinary catheterisation is not appropriate</strong> in patients with AKI. Carefully weigh up the <strong>benefits against the risks</strong> for the individual patient.[64]</td>
<td><strong>if catheterisation is considered appropriate:</strong></td>
</tr>
<tr>
<td>Potential benefits:</td>
<td>• significant urine volume released after catheter placement points to bladder outlet obstruction</td>
</tr>
<tr>
<td>• A sustained fall in urine output is one of the diagnostic criteria for confirming AKI, but urine output is difficult to measure accurately without catheterisation[1]</td>
<td>• minimal residual urine after catheter placement suggests a non-obstructive cause of AKI or higher level urinary tract obstruction</td>
</tr>
<tr>
<td>• Urinalysis can be performed on a sample obtained following catheterisation (but be aware that any proteinuria/haematuria might have resulted from catheter-related trauma)</td>
<td></td>
</tr>
<tr>
<td>• Hourly urinary output monitoring aids assessment of the patient’s response to treatment</td>
<td></td>
</tr>
<tr>
<td>• Catheterisation can be both diagnostic and therapeutic for bladder neck obstruction.</td>
<td></td>
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<tr>
<td>Potential risks:</td>
<td></td>
</tr>
<tr>
<td>• Infection</td>
<td></td>
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<tr>
<td>• Trauma</td>
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<td>• Falls risk.</td>
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**Catheterisation is indicated:**

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<tbody>
<tr>
<td>• In any case where fluid balance management is crucial</td>
</tr>
<tr>
<td>• If the patient is too ill to use a bottle or commode</td>
</tr>
<tr>
<td>• If bladder neck obstruction is suspected and cannot be quickly ruled out by ultrasound.</td>
</tr>
</tbody>
</table>

**fluid challenge**

* A good response to a fluid challenge supports a diagnosis of pre-kidney AKI.

**venous blood gases**

* Can be requested to assess acid/base status. [64]

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<table>
<thead>
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<tbody>
<tr>
<td>• An anion gap acidosis is seen in AKI due to impaired excretion of non-volatile acids.</td>
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**CXR**

* Request a chest x-ray. [65] It may demonstrate signs of: #

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<tbody>
<tr>
<td>• Infection</td>
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<tr>
<td>• Pulmonary oedema</td>
</tr>
<tr>
<td>• Haemorrhage (e.g., ANCA-associated vasculitis, Goodpasture syndrome [pulmonary haemorrhage, rapidly progressive)</td>
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</thead>
<tbody>
<tr>
<td>• may show signs of infection, fluid, cardiomegaly, or haemorrhage</td>
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</tbody>
</table>

  **DIAGNOSIS**

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<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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</thead>
<tbody>
<tr>
<td>glomerulonephritis, and anti-glomerular basement membrane antibodies</td>
<td></td>
</tr>
<tr>
<td>• Cardiomegaly.</td>
<td>ECG changes associated with hyperkalaemia: peaked T waves, increased PR interval, widened QRS, atrial arrest, and deterioration to a sine wave pattern</td>
</tr>
<tr>
<td><strong>ECG</strong></td>
<td></td>
</tr>
<tr>
<td>An ECG is important to assess for hyperkalaemia.</td>
<td></td>
</tr>
<tr>
<td>• Hyperkalaemia is a common complication of AKI.</td>
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</tbody>
</table>
## Other tests to consider

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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</thead>
<tbody>
<tr>
<td>renal tract ultrasound</td>
<td>• presence of dilated renal calyces suggests obstruction and hydronephrosis</td>
</tr>
<tr>
<td>If pyonephrosis (an infected/obstructed renal tract) is suspected, ensure the patient has an ultrasound - and if indicated a nephrostomy - within 6 hours due to the risk of septic shock. [3] [13] [64]</td>
<td></td>
</tr>
<tr>
<td>Renal tract ultrasound is not routinely required. Only request it if no obvious cause for the AKI can be found or if obstruction, pyelonephritis, or pyonephrosis is suspected. [3] [13]</td>
<td></td>
</tr>
<tr>
<td>• Ensure the ultrasound is performed <strong>within 24 hours</strong> if no obvious cause for the AKI can be identified or a urinary tract obstruction is suspected.</td>
<td></td>
</tr>
<tr>
<td>• Ultrasound has high sensitivity (90%-98%) but lower specificity (65%-84%) for diagnosing upper tract obstruction, although this may not be the case in the early stages (first 8 hours). [13]</td>
<td></td>
</tr>
<tr>
<td>• <strong>Repeat the ultrasound after 24 hours if:</strong></td>
<td></td>
</tr>
<tr>
<td>• There is a high index of suspicion for hydronephrosis (as it may take several hours for this to develop due to initial non-compliance of the pelvi-caliceal system)</td>
<td></td>
</tr>
<tr>
<td>• The patient has oliguric acute tubular necrosis with superimposed obstruction (because urine is needed to dilate the kidneys).</td>
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</tr>
<tr>
<td>If prior creatinine values are not available to give a baseline, ultrasound can sometimes be helpful in distinguishing AKI from CKD. [62] [13]</td>
<td></td>
</tr>
<tr>
<td>• Ultrasound may demonstrate small (sometimes scarred) kidneys consistent with advanced CKD (such changes are unlikely to be seen in less severe CKD).</td>
<td></td>
</tr>
<tr>
<td>• Be aware that an ultrasound finding consistent with CKD does not exclude the possibility of AKI on a background of CKD. [13]</td>
<td></td>
</tr>
<tr>
<td>abdominal CT or MRI scan</td>
<td>image of mass or stone may be present</td>
</tr>
<tr>
<td>Consider requesting a CT or MRI if obstruction is suggested on ultrasound (e.g., possible masses or stones). [13]</td>
<td></td>
</tr>
<tr>
<td>• These are not routinely needed - the decision will depend on the degree of obstruction.</td>
<td></td>
</tr>
<tr>
<td>• Be cautious with intravenous iodinated contrast CT scans in patients with AKI. MRI is preferred (although note that gadolinium may be needed for MRI enhancement).</td>
<td></td>
</tr>
<tr>
<td>nuclear renal flow scan</td>
<td>normal scan reveals appropriate kidney perfusion, tracer uptake, and excretion</td>
</tr>
<tr>
<td>Nuclear renal flow scans can sometimes be useful to evaluate for obstruction in cases of mild hydronephrosis,</td>
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### Test

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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<tbody>
<tr>
<td>when the diagnosis of mechanical obstruction is uncertain. [13]</td>
<td>abnormal scan may demonstrate:</td>
</tr>
<tr>
<td>• The scan is performed before and after a dose of loop diuretic.</td>
<td>• impaired tracer excretion (supportive of acute tubular necrosis)</td>
</tr>
<tr>
<td></td>
<td>• poor blood flow (supportive of obstruction of blood supply)</td>
</tr>
<tr>
<td></td>
<td>• normal blood flow and tracer excretion with tracer accumulation</td>
</tr>
<tr>
<td></td>
<td>in the collecting system (supportive of obstruction of the urine</td>
</tr>
<tr>
<td></td>
<td>outflow tract)</td>
</tr>
<tr>
<td><strong>urine osmolality</strong></td>
<td><strong>urine osmolality</strong></td>
</tr>
<tr>
<td><strong>Urine osmolality is rarely requested. [13]</strong></td>
<td>• urine osmolality &gt;500 mOsm/kg (in the absence of recent administration of iodinated contrast) suggests pre-kidney AKI with preservation of tubule function</td>
</tr>
<tr>
<td>• Urine osmolality is the number of moles of solute per kg of solvent and it depends on tubule response to anti-diuretic hormone (ADH).</td>
<td>• urine osmolality &lt;300 mOsm/kg suggests tubule damage</td>
</tr>
<tr>
<td>• High urine osmolality suggests pre-kidney AKI with preservation of tubule function (assuming no recent administration of iodinated contrast).[1] [83]</td>
<td></td>
</tr>
<tr>
<td>• However this should not be interpreted as confirming pre-kidney AKI because intact tubule function (particularly in the early stages) may be seen in various forms of kidney disease (e.g., glomerulonephritis).[1]</td>
<td></td>
</tr>
<tr>
<td>• Low urine osmolality suggests tubule damage (intrinsic AKI) as urinary concentration is impaired.[83]</td>
<td></td>
</tr>
<tr>
<td><strong>urine sodium concentration</strong></td>
<td>urinary sodium &lt;20 mmol/L suggests avid sodium retention in pre-kidney AKI</td>
</tr>
<tr>
<td><strong>In pre-kidney AKI the urinary sodium is typically low (&lt;20 mmol/L). [13]</strong></td>
<td></td>
</tr>
<tr>
<td>• This is dependent on preserved tubule function.</td>
<td>• a fractional excretion of sodium (<strong>FENa</strong>) of &lt;1% supports pre-kidney AKI, as long as tubular function remains intact</td>
</tr>
<tr>
<td><strong>Urinary sodium is raised in intrinsic AKI when there is tubule damage, or in response to diuretics.</strong></td>
<td></td>
</tr>
<tr>
<td><strong>fractional excretion of sodium/urea</strong></td>
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</table>
### Test

<table>
<thead>
<tr>
<th><strong>Test</strong></th>
<th><strong>Result</strong></th>
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<tbody>
<tr>
<td><strong>urinary eosinophil count</strong>&lt;br&gt;Urinary eosinophil counts may be of some use in patients with pyuria. [85] [13] [64]&lt;br&gt;- A result above 5% to 7% supports a diagnosis of acute allergic interstitial nephritis but is not diagnostic because of low sensitivity and specificity.[85] The test is dependent on the expertise of the microscopist.&lt;br&gt;- It has a negative predictive value of &gt;90% among patients with AKI and may be useful in excluding the disease process.[86]&lt;br&gt;- Eosinophiluria may be seen with atheroembolic disease as well.</td>
<td><strong>- &gt;5% to 7% supports a diagnosis of acute allergic interstitial nephritis but is not diagnostic because of low sensitivity and specificity[85]&lt;br&gt;- has a negative predictive value of &gt;90% for patients with AKI and may be useful in excluding the disease process[86]</strong></td>
</tr>
<tr>
<td><strong>serum creatine kinase</strong>&lt;br&gt;Request if rhabdomyolysis is suspected. [62] [13] [64]</td>
<td>markedly elevated in rhabdomyolysis</td>
</tr>
<tr>
<td><strong>ANA (anti-nuclear antibodies)</strong>&lt;br&gt;A broad screening test for a range of autoimmune diseases (e.g., kidney manifestations of systemic lupus erythematosus [SLE]). [13] [64] [65]</td>
<td>normal or elevated</td>
</tr>
<tr>
<td><strong>anti-dsDNA</strong>&lt;br&gt;Elevated titre supports the diagnosis of SLE, which often includes the kidney. [13] [64] [65]</td>
<td>normal or elevated</td>
</tr>
<tr>
<td><strong>complement (C3, C4, CH50)</strong>&lt;br&gt;Low complement levels support an active disease process such as SLE. [13] [64] [65]&lt;br&gt;- Reduced levels are also seen in infectious endocarditis.</td>
<td>normal or depressed</td>
</tr>
<tr>
<td><strong>anti-glomerular basement membrane antibody</strong>&lt;br&gt;Elevated in anti-glomerular basement membrane antibody disease and Goodpasture syndrome. [13] [64] [65]</td>
<td>normal or elevated</td>
</tr>
</tbody>
</table>
### Acute kidney injury

#### Diagnosis

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>anti-neutrophil cytoplasmic antibodies (ANCA)</td>
<td>Elevated titres are seen in small vessel vasculitic syndromes such as: [13] [64] [65]</td>
</tr>
<tr>
<td></td>
<td>- Granulomatosis with polyangiitis</td>
</tr>
<tr>
<td></td>
<td>- Eosinophilic polyangiitis</td>
</tr>
<tr>
<td></td>
<td>- Microscopic polyangiitis</td>
</tr>
<tr>
<td></td>
<td>normal or elevated titres</td>
</tr>
<tr>
<td>acute hepatitis profile</td>
<td>Positive serology in active hepatitis B or C is associated with kidney conditions such as membranoproliferative glomerulonephritis and cryoglobulinaemia.</td>
</tr>
<tr>
<td>HIV serology</td>
<td>Relevant with regard to HIV-associated nephropathy and nephrotoxicity of some of the medications used to manage HIV.</td>
</tr>
<tr>
<td>cryoglobulins</td>
<td>The presence of cryoglobulins in a patient with AKI supports a diagnosis of cryoglobulin-associated glomerulonephritis.</td>
</tr>
<tr>
<td>anti-streptolysin-O antibody</td>
<td>An elevated titre supports but is not diagnostic of post-streptococcal glomerulonephritis as the cause of AKI. [13]</td>
</tr>
<tr>
<td>serum/urine electrophoresis</td>
<td>Myeloma is an important potential cause of AKI and should be considered in a patient aged &gt;40 years who presents with hypercalcaemia, hyperuricaemia, or pathological fracture. [9] [64] [65]</td>
</tr>
<tr>
<td></td>
<td>- Serum electrophoresis will show a paraprotein (monoclonal immunoglobulin).</td>
</tr>
<tr>
<td></td>
<td>- Urine electrophoresis will detect Bence Jones proteins (free light chains) which are not detected on urinalysis.</td>
</tr>
<tr>
<td></td>
<td>normal or elevated</td>
</tr>
<tr>
<td>cystoscopy</td>
<td>May be requested to identify cause of obstruction (e.g., ureteric stenosis, bladder tumour).</td>
</tr>
<tr>
<td>kidney biopsy</td>
<td>Kidney biopsy may be required to further investigate positive serological studies and confirm the cause of AKI. [13]</td>
</tr>
<tr>
<td></td>
<td>changes associated with rarer forms of intrinsic AKI</td>
</tr>
<tr>
<td>HIV serology</td>
<td>positive or negative</td>
</tr>
<tr>
<td>cryoglobulins</td>
<td>positive or negative serology</td>
</tr>
<tr>
<td>anti-streptolysin-O antibody</td>
<td>normal or elevated</td>
</tr>
<tr>
<td>serum/urine electrophoresis</td>
<td>• paraprotein identified on serum electrophoresis</td>
</tr>
<tr>
<td></td>
<td>• Bence Jones protein detected on urine electrophoresis</td>
</tr>
</tbody>
</table>

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Emerging tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>novel serum and urinary biomarkers</td>
<td>not in current clinical use</td>
</tr>
</tbody>
</table>

Various novel serum and urinary biomarkers have been studied in the earlier diagnosis of AKI\cite{88} and as predictors of mortality after AKI.\cite{89} \cite{90} More robust studies are required to determine the role of the biomarkers.\cite{91} \cite{92} \cite{93} \cite{94} \cite{95}
## Differentials

<table>
<thead>
<tr>
<th>Condition</th>
<th>Differentiating signs / symptoms</th>
<th>Differentiating tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic kidney disease</td>
<td>• Reduced kidney function with elevation of creatinine is chronic (&gt;3 months), although there may be acute on chronic kidney disease.</td>
<td>• An acutely elevated serum creatinine is diagnostic of AKI and indicative of reduced clearance. The clinical context is important in differentiating AKI from a progression of CKD at initial presentation if there are no recent comparison creatinine values available for the patient. Features that favour a diagnosis of CKD (although do not exclude AKI) include hypocalcaemia, hyperphosphataemia, anaemia, and small kidneys (sometimes scarred) on ultrasound.[9][62] • 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 kidney function; the use of 131-I iothalamate is the definitive test for this purpose.</td>
</tr>
<tr>
<td>Increased muscle mass</td>
<td>• Any elevation of creatinine is minor and typically non-acute.</td>
<td>• 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 kidney function.</td>
</tr>
</tbody>
</table>
**Drug side effect**

- Certain medicines such as cimetidine or trimethoprim may lead to an elevation of creatinine that is minor and non-acute.
- Discontinuing the medicine should result in normalising 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 ≥26 micromol/L (≥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
  - ≥26 micromol/L (≥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 or longer
- **Stage 3**
  - Creatinine increased ≥3.0 times; or
  - Increase in creatinine to ≥354 micromol/L (≥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[69]**

Laboratory test indicates reduced kidney 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).

**National Institute for Health and Care Excellence: detecting acute kidney injury[3]**

Detect AKI, in line with the RIFLE, Acute Kidney Injury Network (AKIN), or KDIGO definitions, by using any of the following criteria:

- A rise in serum creatinine of 26 micromol/L (0.3 mg/dL) or greater within 48 hours; or
- A 50% or greater rise in serum creatinine known or presumed to have occurred within the past 7 days; or
- A fall in urine output to <0.5 mL/kg/hour for more than 6 hours in adults and more than 8 hours in children and young people; or
- A 25% or greater fall in estimated GFR in children and young people within the past 7 days.
Urgent

Immediate management is supportive and guided by the cause.

- In most patients with AKI, the priority is to treat hypovolaemia and correct electrolyte imbalances.[13]

Use a simple care bundle - STOP AKI is a good option although others are available:[62] [64]

- Sepsis - perform an urgent septic screen and implement your local care bundle (e.g., Sepsis Six) within 1 hour if infection is suspected. See our Sepsis in adults topic for more information.
- Toxins - identify and stop (or avoid exposure to):[1] [13]
  - Nephrotoxic drugs (e.g., non-steroidal anti-inflammatory drugs [NSAIDs], aminoglycoside antibiotics, iodinated contrast agents).[1]
  - Nephrotoxins (a contributor in 20%-30% of cases of AKI).[1]
- Optimise volume status and blood pressure (BP).
  - If hypovolaemic, give an immediate intravenous bolus of crystalloid (choose a balanced crystalloid unless hyperkalaemia is confirmed or suspected, in which case use normal saline).[62] [65]
  - Withhold drugs that may exacerbate AKI, particularly ACE inhibitors or angiotensin-II receptor antagonists.
  - Consider withholding diuretics and other antihypertensive medications.
  - Escalate to critical care for consideration of vasopressors if the patient remains severely hypotensive despite adequate volume resuscitation.
- Prevent harm
  - Identify and treat reversible causes (e.g., relief of any urinary tract obstruction).
  - Treat life-threatening complications (e.g., hyperkalaemia and acidosis).
  - Review and modify doses of all medications in line with the degree of kidney injury.[13] [64]

Refer the following life-threatening complications for emergency renal replacement therapy (RRT):[13] [64]

- Refractory hyperkalaemia (potassium >6.5 mmol/L)
- Refractory metabolic acidosis (pH <7.15)
- Refractory volume overload with or without pulmonary oedema
- End-organ complications of uraemia (e.g., pericarditis, encephalopathy, uraemic bleeding) or other end-organ involvement (e.g., neuropathy, myopathy)
- Severe AKI and poisoning /drug overdose (e.g., ethylene glycol, lithium).
Key Recommendations

It is crucial to identify the cause and severity of the AKI when formulating your management plan for the patient.[1] [62]

In most patients, successful management consists of:[1] [62] [13] [64] [65]

- **Supportive therapy with close ongoing monitoring** of volume status and electrolytes
- Prompt identification and management of the underlying cause (e.g., sepsis, nephrotoxic medication, urinary tract obstruction)
- Early recognition and correction of life-threatening complications (e.g., hyperkalaemia, acidosis, volume overload).

Most patients with AKI do not need referral to nephrology. [62] Do refer if there is:[3] [64]

- Uncertainty about the cause or a poor response to treatment or complications that fail to respond to medical management
- A specific diagnosis that might need specialist treatment (e.g., vasculitis, glomerulonephritis, myeloma)
- **Stage 3 AKI** or AKI in a patient with pre-existing CKD stage 4 or 5
- A history of kidney transplant.

Management of volume status

Prompt correction of volume depletion or volume overload can often reverse or improve AKI.

**Hypovolaemia** is common at presentation.

- Start **immediate intravenous fluid resuscitation** to improve kidney perfusion but take care to use close monitoring to avoid volume overload.[1] [62] [13] [64]
- Give a **500 mL intravenous bolus of crystalloid over 15 minutes** and then continue with goal-directed fluid therapy.
- Escalate for **senior review** if no improvement after two boluses.[62] [96]

If the patient is volume overloaded, consider the need for a loop diuretic or RRT - consult the nephrology team.[1] [13]

- **Never use loop diuretics in AKI without specialist supervision.**

Specific treatment of the underlying cause

No specific treatment has been shown to be effective in pre-kidney AKI that is secondary to hypovolaemia and/or sepsis.[13]

- A key principle is to correct the haemodynamic status of the patient to improve kidney perfusion.[62] [64]

Specific management of intrinsic AKI depends on the aetiology and is led by the nephrology team so early referral is important.[62] For example:

- Interstitial nephritis - stop causative drugs and manage with a corticosteroid.
- Acute glomerulonephritis/vasculitis - managed with a cytotoxic or immunomodulating agent.
Acute kidney injury

Management

In obstructive AKI, relief of the obstruction is key.[9][64]

- Insert a bladder catheter if obstruction is suspected clinically and cannot be quickly ruled out by ultrasound. Input from the urology and/or radiology team will be needed.
- Refer immediately to urology and/or radiology if the patient has pyonephrosis (ensure an ultrasound within 6 hours), an obstructed single kidney, bilateral upper urinary tract obstruction, or complications secondary to obstruction.[3]

Management of complications

Hyperkalaemia - management depends on the severity but may include:

- Immediate cardiac protection with intravenous calcium chloride or calcium gluconate - ensure ongoing ECG monitoring
- Adjunctive therapy to drive potassium intracellularly with intravenous insulin/glucose (beware the risk of hypoglycaemia) and nebulised salbutamol
- Treatment to remove potassium from the body with a cation-exchange resin (e.g., calcium polystyrene sulfonate)
- Withholding culprit medications (e.g., ACE inhibitor, angiotensin-II receptor antagonist, potassium-sparing diuretics)
- RRT is indicated for severe refractory hyperkalaemia.

Acidosis - severe metabolic acidosis may need treatment with intravenous sodium bicarbonate (only under expert supervision due to the risk of volume overload and/or hypernatraemia).

- RRT is indicated for refractory acidosis.

Pulmonary oedema - often results from overzealous fluid resuscitation in a patient who presented with hypovolaemic AKI. For immediate management:[62][64]

- Sit the patient upright
- Give high-flow oxygen and intravenous glyceryl trinitrate
- Seek senior support
- A loop diuretic may be used to manage associated volume overload but only with specialist supervision
- Never allow these holding measures to delay initiation of RRT if indicated.[13]

Full Recommendations

Principles for managing AKI

Determine the cause and severity of AKI when formulating your management plan for the patient.[1][62]

- Monitor electrolytes and acid-base balance and correct any abnormalities. Tailor the frequency of monitoring to individual patient risk factors and the severity (stage) of AKI.

In most patients, successful management of AKI consists of: [1][62][13][64][65]

- Supportive therapy and close ongoing monitoring of volume status and electrolytes.
• Focus in particular on giving **adequate intravenous** fluids to ensure rapid correction of **hypovolaemia** if present (e.g., from haemorrhage, gastrointestinal losses, inadequate fluid intake) - but take care to avoid **volume overload**.

• **Prompt identification and treatment of any reversible underlying cause**, for example:
  - **Sepsis** - perform an urgent septic screen and implement your local care bundle (e.g., Sepsis Six) within one hour if infection is suspected. See our Sepsis in adults topic for more information.
  - **Discontinuation/avoidance of nephrotoxic medications** or any other drugs that might cause indirect harm to kidney function.
  - **Relief of any urinary tract obstruction** - refer urgently to urology and/or radiology as appropriate.

• **Recognition and management of life-threatening complications** (e.g., hyperkalaemia, acidosis, pulmonary oedema, uraemia).

**RRT is indicated in patients who have refractory volume overload or other complications that fail to improve with medical management.** [1] [3] [13] [64]

In rarer forms of intrinsic AKI, more specific management interventions will be needed. [13]

**Practical tip**

The UK Royal College of Physicians suggests the use of the **STOP AKI** acronym as an aide-memoire to recall the immediate steps needed for management of AKI: [62]

• **Sepsis** - implement the your local care bundle (e.g., Sepsis Six) within 1 hour if sepsis is suspected or confirmed. Identify and treat the source of infection.
• **Toxins** - stop/avoid nephrotoxins (e.g., NSAIDs, aminoglycoside antibiotics, iodinated contrast agents).[1]
• **Optimise volume status/BP** - assess volume status and give intravenous fluids as needed; hold antihypertensive medication and diuretics; consider vasopressors if patient does not respond.[3]
• **Prevent harm** - treat complications; identify and treat the cause of AKI; review all medications and adjust doses appropriately; closely monitor intravenous fluid therapy.

**Specialist referral**

Most patients with AKI do not need referral to nephrology. [62]

• Do not refer if there is a clear cause and the AKI is responding to medical management.[3] [97] [98] Refer immediately to critical care and/or nephrology if:

  • The patient meets (or is anticipated to meet) the criteria for RRT[3] [64]
  • There are severe complications that cannot be managed medically (such as hyperkalaemia, pulmonary oedema, acidosis, or uraemia)[64]
  • The patient remains haemodynamically unstable after appropriate supportive care and/or there are signs of multi-organ failure.[64]
Check local protocols for referral criteria and pathways.

Refer for urgent discussion with nephrology (as soon as possible and within 24 hours at the latest) if any one or more of the following is present: [3] [64]

- **Uncertainty about the cause** of AKI or a **poor response** to treatment
- A **possible diagnosis that may need specialist treatment** (e.g., vasculitis, glomerulonephritis, tubulointerstitial nephritis, myeloma)
- **Complications** associated with AKI that are **not responding to medical treatment**
- **Stage 3** AKI
- AKI in a patient with **pre-existing chronic kidney disease (CKD) stage 4 or 5**
- The patient has a **kidney transplant**.

Refer to urology and/or radiology if the patient has an upper urological tract obstruction. [3]

- Refer immediately in any case of pyonephrosis, an obstructed solitary kidney, bilateral upper urinary tract obstruction, or complications of AKI associated with obstruction.

After recovery from an episode of AKI, consider referral to nephrology if: [3]

- Estimated glomerular filtration rate (eGFR) is ≤30 mL/min/1.73 m$^2$
- There is hypertension or proteinuria (1+) on an early morning urine dipstick (particularly in a child or young person).

### Evidence: Speed of referral to nephrology

*There is little evidence available to support routine referral to the nephrology team for every patient with stage 2 AKI.*

Evidence is lacking on whether outcomes are improved by routine rapid referral to nephrology (within 12 hours) for all patients with stage 2 or 3 AKI that does not need critical care input. [3]

- The large number of AKI cases among patients admitted acutely to hospital makes it impractical to refer every patient with suspected or confirmed AKI to nephrology.
- Initial management for most patients encompasses identification and treatment of sepsis, avoidance of nephrotoxins, fluid replacement, and correction of hypotension. These steps can be commenced by any medical or surgical team.
- Potential benefits of routine nephrology referral include a faster diagnosis in patients with primary kidney disease, prevention of progressive AKI and the potential need for RRT, avoidance of a delayed transfer to critical care, improved chances of kidney recovery, and a shorter hospital stay.
- However, there is very little evidence to support routine nephrology referral for all patients with stage 2 or 3 AKI.[3]

- Very low quality evidence from one large retrospective study suggested that for non-critically ill patients with AKI, early compared with delayed referral to nephrology may
Volume status monitoring and management

An assessment of the patient’s volume status is a crucial part of your initial examination. [1] [62] [13] [64]

- Prompt correction of volume depletion or volume overload (especially if associated with worsening cardiac output) can reverse or improve AKI.
- Both hypovolaemia and volume overload are associated with worse outcomes, so careful management of fluid balance is vital.[1]

Pre-kidney AKI (80% of all cases) is most often caused by hypovolaemia and/or hypotension

- A key principle is to improve the haemodynamic status of the patient and restore kidney perfusion .[62] [64]

Look for signs of hypovolaemia. Your assessment should cover: [62] [13]

- Peripheral perfusion (capillary refill time)
- Pulse rate
- BP (including a check for postural hypotension) - taking into account the patient’s baseline BP
- Jugular venous pressure
- Dry axillae/mucous membranes
- Skin turgor.

Practical tip

An early fluid challenge can be both diagnostic and therapeutic for pre-kidney AKI.

- In AKI that is secondary to hypovolaemia, kidney function may improve rapidly in response to administration of intravenous fluids.

Signs of volume overload are less common at presentation; for example: [64]

- Respiratory rate - tachypnoea suggests fluid overload and/or acidosis
- Crackles on auscultation of lungs may suggest pulmonary oedema
- Peripheral oedema.

Ensure at least daily ongoing monitoring of volume status for any patient with established AKI or at risk of AKI, via: [13] [64]

- Review of haemodynamic status, including postural BP
- Weight monitoring
- Fluid input/output chart

- Routine urinary catheterisation is not appropriate, so weigh up the benefits and risks (in particular, infection and trauma) for the individual patient.[64] Catheterisation is indicated if fluid balance management is crucial in an acutely unwell patient (e.g., hourly monitoring of fluid balance is needed) or if the patient is too ill or frail to use a bottle or commode.
Management of hypovolaemia

Fluid resuscitation

If the patient is hypovolaemic, start immediate intravenous fluid resuscitation to improve kidney perfusion - but take care to avoid volume overload. [1] [62] [13] [64]

- Give a 500 mL intravenous bolus of fluid over 15 minutes.
- Use a wide bore cannula to allow adequate fluid resuscitation.
- A crystalloid fluid is preferred. [1] [62] [13] [64]
- A smaller bolus (e.g., 250 mL) may be more appropriate if the patient has a history of cardiac failure. [65]

Use a balanced crystalloid unless hyperkalaemia is suspected or confirmed. [62] [65]

- Balanced crystalloid options include Hartmann’s solution, Ringer’s acetate, or Plasma-Lyte 148® (a solution of sodium chloride, sodium gluconate, sodium acetate trihydrate, potassium chloride, and magnesium chloride hexahydrate).
- Use normal saline (0.9% sodium chloride) instead if hyperkalaemia is present (potassium >5.5 mmol/L) or suspected (e.g., rhabdomyolysis). This is because balanced crystalloids all contain potassium.
  - Once hyperkalaemia has been treated and resolved, switch to a balanced crystalloid due to the risk of hyperchloremic metabolic acidosis associated with excessive use of normal saline. [62]

Reassess haemodynamic status after the initial fluid bolus and consider whether further 250 to 500 mL boluses are required.

- Goal-directed fluid therapy is recommended. [13]
- Reassess the patient's response to each fluid challenge through careful clinical examination (ABCDE approach) and monitoring of: [96]
  - BP
  - Pulse rate
  - Jugular venous pressure
  - Capillary refill time
  - Signs of pulmonary oedema
  - Urine output.

- If no improvement is seen after two fluid challenges, escalate the patient for senior review. [62] [96]

  - If the patient has already had ≥2 L of fluid, or is in shock, seek immediate senior help so that critical care involvement for vasopressor support can be considered. [62]
  - In a patient with profound sepsis it can take >24 hours for antibiotics to act and the vascular permeability to reverse and BP to respond to intravenous fluids.
Acute kidney injury

Management

As soon as haemodynamic stability is restored and the patient is euvolaemic, review and adjust the intravenous fluid prescription to match the patient’s ongoing fluid requirements. [62] [96]

- It is vital to recognise when to de-escalate intravenous fluid therapy. Failure to do so can result in volume overload and precipitate pulmonary oedema.
  - There is a particular risk from over-aggressive fluid resuscitation if the patient is oliguric/anuric or has a history of heart failure. [13] [96]

Practical tip

Passive leg raising can help predict fluid responsiveness in critically ill patients. [62] [13]

- In the context of acute hypovolaemia, passive leg raising can improve the venous return and the response in BP can be recorded.
- A rise in BP confirms hypovolaemia and the need for further fluid resuscitation. [62]
- Passive leg raising is most commonly practised on critical care units.

Practical tip

Always be clear about the purpose of the intravenous fluid therapy you are prescribing.

- The UK National Institute for Health and Care Excellence (NICE) has categorised these as Resuscitation, Replacement, or Routine maintenance. [100]

  - **Resuscitation fluid therapy** is aimed at re-establishing haemodynamic stability by restoring intravascular volume.
  - **Replacement fluid therapy** provides daily maintenance water and electrolyte requirements and replaces any ongoing abnormal fluid losses.
  - **Maintenance fluid therapy** must provide daily ongoing water and electrolyte requirements (i.e., sodium 1 mmol/kg, potassium 1 mmol/kg, and water 25-35 mL/kg)

    - Never give maintenance fluids at a rate of >100 mL/hour.

Never prescribe intravenous fluid therapy for more than 24 hours at once due to the risk of causing volume overload.

Blood transfusion will be indicated if hypovolaemia is secondary to significant blood loss.

- This is generally not given unless more than one unit is anticipated, based on local guidelines and the clinical assessment of the patient. [5]
- Note that this may worsen hyperkalaemia.

Vasoactive drugs

Vasopressor support is recommended if the patient remains severely hypotensive despite adequate volume resuscitation (e.g., in septic/hypovolaemic shock). [1] [62] [13] [96]
Acute kidney injury

Management

• Escalate to critical care. Vasopressors should only be used with continuous haemodynamic monitoring in place.

• A reasonable goal is to maintain mean arterial pressure (MAP) ≥65 mmHg, but this target may need adjusting according to the patient’s baseline BP.[1][13][64]

• In the setting of vasomotor shock where the patient has persistent hypotension despite optimisation of intravascular volume through aggressive fluid resuscitation, preservation and improvement of kidney perfusion can only be achieved by the use of systemic vasopressors.[1]

Noradrenaline (norepinephrine) is the usual vasopressor of choice, with the addition of vasopressin if needed.

• There is little good evidence available to guide the choice of vasopressor in patients with AKI and septic shock.[1][13]

• Do not use low-dose dopamine to treat AKI.[1][3][13]

  • There is no evidence to support its use and it can worsen kidney perfusion in patients with AKI.

Consider the potential need for an inotrope (e.g., dobutamine) to optimise cardiac output if kidney hypoperfusion is caused by impaired cardiac function due to poor left ventricular systolic function.[13]

Evidence: Evidence is scarce to guide the choice of vasopressor

It is not known which vasopressor agent is most effective for prevention or treatment of AKI and septic shock.

There is insufficient evidence to say that one vasoactive agent is better than another in preventing or treating AKI.[1]

• Small open-label studies have shown improvement in creatinine clearance after a 6- to 8-hour infusion of noradrenaline.[101]

• Vasopressin, when compared with noradrenaline in one RCT, was found to increase BP and enhance diuresis, but has not yet been proven to enhance survival or reduce the need for RRT.[102]

  • A post-hoc analysis of the same RCT used the RIFLE criteria for AKI to compare the effects of vasopressin versus noradrenaline.[103] Vasopressin was associated with a trend to a lower rate of progression of the AKI, and a lower rate of use of RRT.

  • According to the Kidney Disease: Improving Global Outcomes (KDIGO) guideline group, this study suggests that vasopressin may reduce progression to kidney failure and mortality in patients with septic shock who have or are at risk of AKI.[1]

• Dopamine has no significant clinical benefits in patients with AKI.[13]

  • A large randomised controlled trial (RCT) comparing dopamine with noradrenaline as the initial vasopressor in patients with shock showed no significant differences between groups with regard to kidney function or mortality.[104]
• However, there were more arrhythmic events among the patients treated with dopamine than among those treated with noradrenaline, and dopamine was associated with an increased rate of death at 28 days among the patients with cardiogenic shock.

• Both the NICE and KDIGO guidelines include a recommendation not to offer low-dose dopamine to treat AKI.\[1\] [3]

Management of volume overload

Volume overload in a patient with AKI can occur as a result of:

• Overaggressive fluid resuscitation in a patient who initially presented with hypovolaemic pre-kidney AKI. This is most commonly seen in patients with sepsis.

• Oliguria in intrinsic or post-kidney AKI.

If the patient is volume overloaded, consider the potential need for a diuretic or RRT. Discuss with the nephrology team.

• Patients with volume overload need careful monitoring and management to reduce the risk of a poor outcome.

• Failure to manage volume overload can lead to complications including pulmonary oedema.\[62\]

In critically ill patients, a positive fluid balance (>5% body weight) has been found to be associated with an increase in mortality at up to 1 year follow-up when compared to neutral or negative (<5%) fluid balance.\[13\]

• Management of volume overload may include:

  • Sodium restriction
  • Cautious use of a loop diuretic under specialist supervision\[1\] [13]
  • RRT - immediate RRT is indicated for refractory volume overload or volume overload associated with severe complications of AKI.\[62\] [13] [64] For more details, see the section further down on Indications for RRT.

Consider a loop diuretic (under specialist supervision) to treat volume overload.\[1\] [13]

• A loop diuretic such as furosemide may be useful in achieving euvoalaemia in a patient with fluid overload (with or without pulmonary oedema).\[1\] This must be done with caution and under the supervision of the nephrology team.

  • Note that there is no evidence to support the routine use of loop diuretics for management of AKI in the absence of volume overload.\[1\] [3] [13]
  • Never use a loop diuretic if the patient is hypovolaemic or hypotensive. The diuretic will exacerbate the haemodynamic instability.

• Do not allow the use of loop diuretics to delay more definitive management of volume overload.

  • Careful monitoring of response is important (e.g., urine output). Stop the diuretic if there is no response.
Acute kidney injury
Management

- Proceed without delay to more definitive management with RR T if the response to diuretics is unsuccessful.[64]

Evidence: The role of loop diuretics in patients with AKI

Loop diuretics have no routine role in the management of AKI. They should be reserved for specific indications (such as volume overload) and only used under specialist supervision.

There is no evidence for any benefits from the routine use of loop diuretics in patients with AKI - but there is some evidence to suggest harm.

- The theoretical rationale for the use of loop diuretics to treat AKI is based on their potential to reduce oxygen consumption in the ascending loop of Henle, thereby reducing any ischaemic damage to the kidneys. They may also be used to convert oliguric AKI to non-oliguric AKI.[1] [13]

- However, diuretics can also excessively reduce circulating volume and so cause a pre-kidney insult that could worsen established AKI. Hence an evaluation of the available evidence is vital to determine their appropriate role.

- There is no evidence to support the use of loop diuretics in routine treatment of AKI.

- One RCT found furosemide to be ineffective in treating AKI and epidemiological data suggest the use of loop diuretics may increase mortality in patients with critical illness and AKI.[105] [106]

- Two systematic reviews on the use of furosemide to prevent or treat AKI found no significant effect on in-hospital mortality, risk for requiring RRT, the number of dialysis sessions needed, or even the proportion of patients with persistent oliguria.[107] [108]

- Prophylactic furosemide has been shown to increase the risk of AKI when given to prevent AKI in patients having cardiac surgery.[109]

- There is no evidence to support the use of loop diuretics for managing AKI-associated hyperkalaemia.[110]

- However, in practice their use may be considered (with specialist supervision) as an adjunct to other therapies provided the patient is fluid replete.

Medication review

Whenever AKI is suspected or confirmed, review all medications and stop/avoid any nephrotoxic drugs and other drugs that may affect kidney function. [13] [64] [65]

- Common nephrotoxic drugs include aminoglycoside antibiotics, NSAIDs, and iodinated contrast agents.[1] Consult a pharmacist for a full list of nephrotoxic drugs.

- ACE inhibitors, angiotensin-II receptor antagonists, and other renin-angiotensin modifying agents can exacerbate AKI by reducing the kidney’s ability to adapt to changes in perfusion pressure.[9]

- Diuretics or other antihypertensives increase the risk of hypovolaemia/hypotension.
Management

- If there are overriding reasons why a potentially harmful drug must be continued, seek specialist pharmacist advice to minimise negative effects (e.g., dose adjustment, keep the treatment course as short as possible, monitor blood levels of the drug if feasible).

Review and adjust doses of all other medications in line with the patient’s degree of kidney injury. [13] [64]

- Any medication that is cleared via the kidneys has the potential to accumulate during an episode of AKI. Dose adjustment is therefore important to prevent toxicity and patient harm.
- Inappropriate drug dosing in patients with AKI is an important cause of adverse drug events. [13]

When restarting drugs after an episode of AKI, ensure:

- Any medications that were used for the treatment of pre-existing heart failure are re-started as soon as clinically reasonable and re-titrated to achieve the best control of fluid balance and blood pressure[13]
- All medications are reviewed before discharge and a plan is put in place to reintroduce any medications that have been withheld, at an appropriate time, with re-titration to the optimum dose continued in primary care as appropriate[96]
  - Ensure a process is in place for measurement of serum creatinine and potassium 1 to 2 weeks later. This may need to be part of discharge planning.[13]

Specific treatment for the underlying cause of AKI

Alongside supportive therapy and management of any complications, it is important to identify and treat the specific underlying cause of AKI.

Pre-kidney AKI

No specific pharmacological treatment has been proven to treat AKI that is secondary to hypovolaemia and/or sepsis. [13]

- Pre-kidney AKI is most often caused by hypovolaemia and/or hypotension.
- A key principle is to improve the haemodynamic status of the patient and restore kidney perfusion through careful administration of intravenous fluid resuscitation (plus vasopressor therapy if needed).[62] [64]

Intrinsic AKI

Specific management of intrinsic AKI depends on the aetiology and is led by the nephrology team. [62]

- Immunological tests and kidney biopsy are needed to confirm acute glomerulonephritis, ANCA-associated vasculitis, anti–glomerular basement membrane (anti-GBM) antibody disease (Goodpasture syndrome if associated with pulmonary hypertension), and lupus nephritis.
  - Treatment will require corticosteroids, cytotoxic agents, immunomodulating drugs, and/or plasma exchange.
• Acute kidney injury

Management

• Atypical haemolytic uraemic syndrome (HUS) is treated with the monoclonal antibody eculizumab or plasma exchange.[111]
• Thrombotic thrombocytopenic purpura (TTP) is treated with plasma exchange.[112]
• Acute allergic interstitial nephritis is treated with a corticosteroid (after excluding infection) and stopping potential causative medications (e.g., proton-pump inhibitors, NSAIDs, antibiotics).[113]

Obstructive AKI

Relief of the obstruction is key in the management of obstructive AKI. [9] [64]

• Insert a bladder catheter in any case of AKI when bladder outlet obstruction is suspected clinically and cannot be quickly ruled out by ultrasound.
  • Refer to urology within 24 hours if obstruction is confirmed on ultrasound.[3] [64]

Refer immediately to urology and/or radiology if one of more of the following is present: [3]

• Pyonephrosis - if pyonephrosis is suspected, ensure the patient has an ultrasound within 6 hours (because of the risk of septic shock)[3]
• Obstructed single kidney
• Bilateral upper urinary tract obstruction
• Complications of AKI secondary to urological obstruction.

Refer to urology and/or radiology for ureteral stenting, urinary diversion, debulking procedures, or other case-specific requirements. [64]

• Nephrostomy or ureteral stenting must be undertaken as quickly as possible and at the latest within 12 hours of diagnosis.[3]
• Ureteral stenting may be indicated if there is a ureteral stricture, stone, or extrinsically obstructing mass.
• Lithotripsy or surgical removal may be needed if obstruction is caused by stones at the ureteropelvic junction.
• Exploratory laparotomy may be indicated if a compressing tumour is suspected that may require surgical removal; this may be done following ureteral stenting.
• 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.

RRT may be needed while the underlying obstruction is being addressed if there is severe acidosis, volume overload, or electrolyte or uraemic complications.

Management of complications of AKI

Hyperkalaemia [62]

Hyperkalaemia is a common complication of AKI. It can lead to:

• Muscle weakness
Acute kidney injury

**Management**

- Cardiac arrhythmias (e.g., bradycardia, bundle branch block, ventricular tachycardia, ventricular fibrillation, asystole).

Treatment depends on the severity and presence of muscular and/or cardiac complications. The principles of treatment are: [110]

- **Immediate cardiac protection** with intravenous calcium chloride or calcium gluconate
- **Adjunctive therapy to drive potassium intracellularly**
  - Intravenous insulin/glucose
  - Nebulised salbutamol
- **Removal of potassium from the body**
  - Cation-exchange resin (e.g., calcium polystyrene sulfonate)
- **Correction of exacerbating factors:**
  - Manage the AKI
  - Withhold culprit medications (e.g., ACE inhibitor, angiotensin-II receptor antagonist, potassium-sparing diuretics)
  - Restrict dietary intake - avoid potassium-rich foods and fluids[80]
  - Close ongoing monitoring of potassium and glucose.

Refer for RRT if the patient has moderate or severe hyperkalaemia that fails to respond to medical management. [13] [64]

Check your local protocols - many hospitals have institutional guidelines for managing hyperkalaemia.

**Management of mild hyperkalaemia (potassium 5.5 to 5.9 mmol/L)** [62] [80]

In mild hyperkalaemia, always look for and treat the underlying cause.

- **Review medications** that might be responsible (e.g., ACE inhibitor, angiotensin-II receptor antagonist, potassium-sparing diuretics).

  - Treatment of hyperkalaemia only results in a temporary intracellular shift of potassium so the cause of hyperkalaemia must be identified and corrected.[62]
  - Consult a pharmacist for a full list of medications that can cause hyperkalaemia.

A cation-exchange resin can be considered. [110]

- This will help remove potassium from the body.[80]
- Do not use if the patient has obstructive bowel disease.

**Management of moderate hyperkalaemia (potassium 6.0 to 6.4 mmol/L)** [62] [80]

Check for any acute ECG changes:

- Features of hyperkalaemia include peaked t waves, flattened p waves, broad QRS complexes.
If there are ECG changes consistent with hyperkalaemia, treat in the same way as severe hyperkalaemia (see below).

If there are no acute ECG changes consistent with hyperkalaemia:

- Give an infusion of insulin/glucose to push potassium intracellularly [62] [80]
  - Give over 15 minutes
  - Acts within 10 to 20 minutes
  - Lasts 4 to 6 hours
  - Monitor hourly for hypoglycaemia
- Consider further adjunctive treatment with nebulised salbutamol if necessary
  - Decide whether this is needed based on the ECG and the rate of rise of serum potassium[80]
  - Use caution if there is a history of ischaemic heart disease and avoid if there is a history of tachyarrhythmias.[62] [80]

Always look for and treat the underlying cause.

Management of severe hyperkalaemia (potassium ≥6.5 mmol/L) [62] [80]

Check for any acute ECG changes.

If the patient has severe hyperkalaemia or moderate hyperkalaemia with associated ECG changes: [80]

- Seek expert advice from the nephrology or ICU team to consider whether immediate RRT may be needed
  - RRT is indicated if severe hyperkalaemia (potassium ≥6.5 mmol/L) fails to respond quickly to medical management [13]
  - Monitor the patient in a high-dependency area. [62]

Give immediate intravenous calcium for cardiac protection. [62] [80]

- Give over 5 to 10 minutes, then repeat the ECG and consider a further dose if ECG changes persist.[80]
  - Use a wide bore cannula and avoid extravasation.
  - Ensure cardiac monitoring.
  - Intravenous calcium antagonises the cardiac membrane excitability and so protects the heart against arrhythmias. [110]
  - Effective within 3 minutes and lasts 30 to 60 minutes.
  - Seek senior advice if the ECG fails to normalise after one dose. [62]

Give an immediate infusion of insulin/glucose to push potassium intracellularly: [62] [80]

- Give over 15 minutes
Acute kidney injury

Management

- Acts within 10 to 20 minutes
- Lasts 4 to 6 hours
- Monitor hourly for hypoglycaemia.

Give further adjunctive treatment with nebulised salbutamol. [80]

- Use caution if there is a history of ischaemic heart disease and avoid if there is a history of tachyarrhythmias. [62]

Always look for and treat the underlying cause.

Routine use of sodium bicarbonate is not recommended.

- Sodium bicarbonate is often used to treat acute hyperkalaemia in clinical practice although there is little evidence to support its use. [110]
- It can be considered in the setting of hyperkalaemia with hypovolaemia and acidosis.

  - Use only with expert supervision due to the risk of causing volume overload and/or hypernatraemia.

There is no evidence to support the use of loop diuretics for managing AKI-associated hyperkalaemia. [110]

- However, in practice their use may sometimes be considered as an adjunct to other therapies, provided the patient is fluid replete (but only with supervision from the nephrology team).

**Debate: Loop diuretics**

*The role of loop diuretics in the management of AKI-associated hyperkalaemia remains controversial.*

- Loop diuretics may be used under specialist supervision for volume management in patients with AKI and there is a theoretical rationale to suggest they could be beneficial in managing hyperkalaemia. [1]
  - Loop diuretics promote potassium excretion in the urine through their action in inhibiting the Na⁺-K⁺-2Cl⁻ co-transporter on the ascending limb of Henle, thereby reducing uptake of potassium (as well as sodium and chloride).
  - However, the 2014 UK Renal Association guideline on acute hyperkalaemia concluded that there is no evidence to support the use of diuretics in the management of AKI-associated hyperkalaemia. [110]
  - Both the NICE and KDIGO guidelines are clear that loop diuretics should not be used routinely to manage AKI. [1] [3] The use of loop diuretics is indicated (under specialist supervision) only if a patient with AKI-associated hyperkalaemia also has volume overload (which is a clear indication for their use). [3]

**Acidosis (pH <7.25)** [62] [64]

Metabolic acidosis is a common metabolic disturbance in AKI.
Acute kidney injury

Management

- It occurs primarily due to impaired excretion of the normal load of metabolic acid in the setting of a low glomerular filtration rate (GFR).
- Other factors may also contribute (e.g., increased production of lactic acid in patients with sepsis).
- Note that there will be relative resistance to vasopressors in the presence of severe metabolic acidosis.

If the patient has severe acidosis, seek expert supervision as intravenous sodium bicarbonate may be needed. [64]

- Severe metabolic acidosis (\(\text{pH} < 7.2\)) is an indication for intravenous sodium bicarbonate.
- This should only be given under expert supervision due to the risk of causing volume overload and/or hypernatraemia.
  - Consider referring to ICU.
  - Sodium bicarbonate should only be used if venous bicarbonate is <16 mmol/L with no signs of volume overload.[64]
    - Ionised Ca\(^{2+}\) falls with rapid correction and this can trigger tetany, seizures and cardiac instability. Prior to administration of sodium bicarbonate, correct low ionised Ca\(^{2+}\) via a different intravenous route due to the incompatibility of bicarbonate and calcium solutions.[64]

Refer for RRT if the patient has: [13] [64]

- Refractory acidosis (\(\text{pH} < 7.15\)) that is not responding to initial management
- Severe acidosis in the setting of volume overload (hence sodium bicarbonate must not be given).

Pulmonary oedema [62] [64]

Pulmonary oedema may occur:

- As a result of overzealous intravenous fluid resuscitation in a patient who presented with hypovolaemic pre-kidney AKI[96]
- At presentation in some types of AKI, for example:
  - Renal artery stenosis - flash pulmonary oedema
  - Renal tract obstruction - salt and water retention
  - Cardiac failure with AKI.

Mortality is high in acute pulmonary oedema so emergency management is vital.

For immediate management of pulmonary oedema: [62] [64]

- Sit the patient upright
- Give high-flow oxygen (15 L/minute via a reservoir mask) and, if available, consider continuous positive airway pressure ventilation
- Give intravenous glyceryl trinitrate - titrate the dose upwards, aiming to maintain systolic BP (SBP) >95mmHg
Acute kidney injury

Management

• Consider a loop diuretic (under specialist supervision) provided the patient is haemodynamically stable and well filled intravascularly [1] [62] [13]

• For more details, see the section on Management of volume overload above

• Seek senior support.

Refractory pulmonary oedema is an indication for emergency RRT. [13] [64]

• The use of an intravenous nitrate and a loop diuretic such as furosemide can be a useful holding measure but do not delay proceeding to definitive management with kidney support if needed.

Renal replacement therapy

Indications for RRT

Renal replacement therapy (RRT) is the cornerstone for treatment of severe AKI with complications that are not responding to medical management.

• It can be used to manage refractory hyperkalaemia, restore metabolic homeostasis, and correct volume overload.[3]

Refer immediately to the nephrology team for consideration of RRT if a patient with AKI has any one or more of the following indications for emergency kidney support: [13] [64]

• Refractory hyperkalaemia (potassium >6.5 mmol/L)
• Refractory metabolic acidosis  (pH <7.15)
• Refractory volume overload  with or without pulmonary oedema
• End-organ complications of uraemia (e.g., pericarditis, encephalopathy, uraemic bleeding) or other end-organ involvement (e.g., neuropathy, myopathy)
• Severe AKI and poisoning /drug overdose (e.g., ethylene glycol, lithium).

The decision to start RRT must be based on the patient’s overall condition and not on any isolated urea, creatinine, or potassium value .[1] [3]

• The potential metabolic and fluid benefits of earlier initiation of RRT must be balanced with the potential harm for the individual patient (e.g., complications related to line insertion, anticoagulation).[13]

• In the absence of any of the emergency indications for RRT listed above, there is little clear evidence available to guide decisions on whether and when to start RRT , with individual studies reaching conflicting findings and meta-analyses hampered by varied definitions of ‘early’ and ‘late’ initiation.[13]

• In practice, the decision to start RRT is based on a combination of clinical, physiological, and laboratory parameters used to assess the patient’s fluid, electrolyte, and metabolic status .[1] [13]

• Factors to consider include: [13]

  • The trend as well as the absolute values of biochemical parameters (e.g., potassium, pH, urea)
• The uraemic solute burden (which is increased in tumour lysis syndrome, rhabdomyolysis, and hypercatabolic states)
• The need for intravascular space to allow administration of therapeutic interventions such as blood products or nutrition
• The degree and duration of oliguria
• Whether or not the underlying kidney insult has resolved
• Any signs of organ dysfunction (which will affect the patient’s ability to tolerate uraemic complications)
• The presence of any other electrolyte disturbances that may be corrected by RRT (e.g., hypercalcaemia).

There may be some patients with pre-existing comorbidities for whom RRT will not offer any realistic benefits. [114] [13]

• This needs to be a shared decision between the patient and their family members/carers after discussion with the multidisciplinary team.

Pre-assessment for RRT requires careful consideration and must include: [114]

• Clinical preparation
• Discussion with the patient around the types of RRT that are available and the acute process (it must be made clear that RRT is supportive treatment that is doing the work of the kidneys)
• If it is unclear whether the patient has a reversible form of AKI, discussion about the longer term options and the impact they may have on the patient’s life
• Psychological assessment and support.

Choice of RRT modality

The nephrology team will select the best modality of RRT after assessment of the patient’s overall medical condition and comorbidities. [63]

• Various options exist for supporting kidney function.
• There is no evidence that one modality is better than another in terms of outcomes among patients with AKI. [115]
• If your patient is in a non-renal centre and is too unwell to transfer, the critical care team will lead the decision-making.

The choice of RRT modality depends on several factors, including: [63]

• Individual patient factors:

  • Haemodynamic stability (and hence the patient’s physiologic reserve to tolerate metabolic shifts and fluctuations in fluid status) is a key determinant of the most appropriate RRT modality [13]
  • Severity of electrolyte and acid base balance disorders
  • Risk of ongoing catabolism with cellular breakdown and acidosis.
  • Any need for rapid poison removal (e.g., lithium or ethylene glycol)

• Availability of modality and staff skill mix.

The options for RRT include: [115] [13]
• Intermittent haemodialysis (IHD) - usually the preferred option in haemodynamically stable AKI patients, but generally avoided in haemodynamically unstable patients, as it often precipitates hypotensive events.[1]
  
  • Duration up to 4 hours so the patient can participate in active rehabilitation.
  • Fast removal of toxins (e.g., urea, ethylene glycol). In the case of lithium, rebound can occur after IHD as the drug redistributes from the intracellular to extracellular compartment.
  • May risk dialysis disequilibrium syndrome through over-rapid solute removal and attendant osmolar shifts.
  • Fast correction of acidosis/hyperkalaemia with risk of rebound following the treatment.
  • Hybrid versions of IHD include:
    • Sustained low-efficiency dialysis (SLED)
    • Extended daily dialysis (EDD)[116]
    • Prolonged intermittent renal replacement therapy (PIRRT).

• Continuous renal replacement therapy (CRRT) - preferred in haemodynamically unstable patients. [117][118][119]
  
  • Duration 24 to 72 hours, depending on blood circuit clotting.
  • Slower blood flow.
  • Slower but continual removal of toxins allowing more gradual restoration of metabolic homeostasis and avoidance of rebound (e.g., lithium toxicity).#
  • Slows patient rehabilitation when recovering.
  • There are several different types of CRRT but no evidence to support one form over another in terms of better outcomes:
    • Continuous venovenous haemofiltration (CVVH)[120] [121] [122]
    • Continuous venovenous haemodialysis (CVVHD)
    • Continuous venovenous haemodiafiltration (CVVHDF).[116] [117] [118] [119]

• Peritoneal dialysis - rarely used in the developed world except in paediatric patients.

RRT (whether IHD or CRRT) is performed through a large double lumen catheter placed into the central venous system, such as the internal jugular or femoral vein.

Evidence: Choice of RRT modality

CRRT and IHD have similar outcomes in AKI.

Mortality outcomes are similar in critically ill AKI patients treated with CRRT and IHD.

• Several RCTs have compared CRRT to IHD in AKI patients, including the Hemodiafe study, the SHARF study, the CONVINT study and the OUTCOMEREA study. None has found any survival advantage from one modality over the other.[13]
• A Cochrane systematic review that analysed 15 RCTs in 1550 AKI patients concluded that outcomes were similar in the CRRT and IHD groups in terms of hospital mortality, ICU mortality, length of hospitalisation, and kidney recovery.[123]
Peritoneal dialysis has generally been thought ineffective in adults with AKI and hypercatabolic states, although some studies now suggest equal effectiveness in appropriate subjects. [124] [125]

- However, one study was stopped early because there was a significant benefit to patients being on CRRT rather than PD. [126]
- In practice, PD is rarely used in adult patients in high-income countries although it is an option for children with AKI. [13]

### 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 (summary)**

<table>
<thead>
<tr>
<th>Hypovolaemic</th>
<th>1st</th>
<th>fluid resuscitation</th>
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<tbody>
<tr>
<td></td>
<td>plus</td>
<td>review medications and stop nephrotoxins</td>
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<tr>
<td></td>
<td>plus</td>
<td>identify and treat underlying cause of AKI</td>
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<tr>
<td></td>
<td>consider</td>
<td>vasoactive drug</td>
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<tr>
<td></td>
<td>consider</td>
<td>blood transfusion</td>
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<tr>
<td></td>
<td>consider</td>
<td>specialist referral</td>
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<tr>
<td>with mild hyperkalaemia (potassium 5.5 to 5.9 mmol/L)</td>
<td>plus</td>
<td>identify and treat underlying cause of hyperkalaemia</td>
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<tr>
<td></td>
<td>consider</td>
<td>cation-exchange resin</td>
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<tr>
<td>with moderate hyperkalaemia (potassium 6.0 to 6.4 mmol/L) and no associated ECG changes</td>
<td>plus</td>
<td>insulin/glucose</td>
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<td></td>
<td>consider</td>
<td>salbutamol</td>
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<tr>
<td></td>
<td>plus</td>
<td>calcium</td>
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<tr>
<td>with severe hyperkalaemia (potassium ≥6.5 mmol/L) OR moderate hyperkalaemia (potassium 6.0 to 6.4 mmol/L) and associated ECG changes</td>
<td>plus</td>
<td>insulin/glucose</td>
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<td></td>
<td>plus</td>
<td>salbutamol</td>
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<td></td>
<td>plus</td>
<td>identify and treat underlying cause of hyperkalaemia</td>
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<tr>
<td>with metabolic acidosis</td>
<td>consider</td>
<td>sodium bicarbonate</td>
</tr>
<tr>
<td>with uraemia, refractory severe hyperkalaemia, or refractory metabolic acidosis</td>
<td>consider</td>
<td>renal replacement therapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypervolaemic</th>
<th>1st</th>
<th>loop diuretic (only under specialist supervision) and sodium restriction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>plus</td>
<td>identify and treat the underlying cause of AKI</td>
</tr>
<tr>
<td>Acute</td>
<td>( summary )</td>
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<tr>
<td>with pulmonary oedema</td>
<td>consider renal replacement therapy plus upright positioning plus high-flow oxygen plus glyceryl trinitrate</td>
<td></td>
</tr>
<tr>
<td>with mild hyperkalaemia (potassium 5.5 to 5.9 mmol/L)</td>
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<td></td>
</tr>
<tr>
<td>with severe hyperkalaemia (potassium ≥6.5 mmol/L) OR moderate hyperkalaemia (potassium 6.0 to 6.4 mmol/L) and associated ECG changes</td>
<td>plus calcium plus insulin/glucose plus salbutamol plus identify and treat underlying cause of hyperkalaemia</td>
<td></td>
</tr>
<tr>
<td>with metabolic acidosis</td>
<td>plus seek specialist advice from the renal team</td>
<td></td>
</tr>
</tbody>
</table>
**Treatment algorithm**

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Acute kidney injury

### Management

#### 1st fluid resuscitation

- Pre-kidney AKI (80% of all cases) is most often caused by hypovolaemia and/or hypotension.
  - A key principle is to improve the haemodynamic status of the patient.\[62\] \[64\]
  - Prompt correction of volume depletion can reverse or improve AKI.

- If the patient is hypovolaemic, start immediate intravenous fluid resuscitation to improve kidney perfusion - but take care to avoid volume overload. \[1\] \[62\] \[13\] \[64\]
  - Give a 500 mL bolus of intravenous fluid over 15 minutes.
  - Use a wide bore cannula to allow adequate fluid resuscitation.
  - A crystalloid fluid is preferred. \[1\] \[62\] \[13\] \[64\]
  - A smaller bolus (e.g., 250 mL) may be more appropriate if the patient has a history of cardiac failure.\[65\]

- Use a balanced crystalloid unless hyperkalaemia is suspected or confirmed. \[62\] \[65\]
  - Balanced crystalloid options include Hartmann’s solution, Ringer’s acetate, or Plasma-Lyte 148® (a solution of sodium chloride, sodium gluconate, sodium acetate trihydrate, potassium chloride, and magnesium chloride hexahydrate).

- Use normal saline (0.9% sodium chloride) instead if hyperkalaemia is present (potassium >5.5 mmol/L) or suspected (e.g., rhabdomyolysis).
  - This is because balanced crystalloids all contain potassium.
  - Once hyperkalaemia has been treated and resolved, switch to a balanced crystalloid due to the risk of hyperchloremic metabolic acidosis associated with excessive use of normal saline.\[62\]

- Reassess haemodynamic status after the initial fluid bolus and consider
Management

Acute

whether further 250 to 500 mL boluses are required.

- **Goal-directed** fluid therapy is recommended.[13]
- Reassess the patient’s response to each fluid challenge through careful clinical examination (ABCDE approach) and monitoring of:[96]
  - Capillary refill time
  - Pulse rate
  - Blood pressure (BP)
  - Jugular venous pressure
  - Signs of pulmonary oedema
  - Urine output.

- If no improvement is seen after two fluid challenges, escalate the patient for senior review. [62] [96]
  - If the patient has already had ≥2 L of fluid, or is in shock, seek immediate senior help so that critical care involvement for vasopressor support can be considered.[62]
  - In a patient with profound sepsis it can take >24 hours for antibiotics to act and the vascular permeability to reverse and BP to respond to intravenous fluids.

**Practical tip**

An early fluid challenge can be both diagnostic and therapeutic for pre-kidney AKI.
- In AKI that is secondary to hypovolaemia, kidney function may improve rapidly in response to administration of intravenous fluids.

**Practical tip**

Passive leg raising can help predict fluid responsiveness in critically ill patients. [62] [13]
- In the context of acute hypovolaemia, passive leg raising can improve the venous return and the response in blood pressure can be recorded.
As soon as haemodynamic stability is restored and the patient is euvoalaemic, review and adjust the intravenous fluid prescription to match the patient’s ongoing fluid requirements. [62] [96]

- It is vital to recognise when to de-escalate intravenous fluid therapy. Failure to do so can result in volume overload and precipitate pulmonary oedema.

- There is a particular risk from over-aggressive fluid resuscitation if the patient is oliguric/anuric or has a history of heart failure. [13] [96]

**Practical tip**

Always be clear about the purpose of the intravenous fluid therapy you are prescribing.

- The UK National Institute for Health and Care Excellence (NICE) has categorised these as **Resuscitation, Replacement or Routine maintenance**. [100]

- **Resuscitation fluid therapy** is aimed at re-establishing haemodynamic stability by restoring intravascular volume.

- **Replacement fluid therapy** provides daily maintenance water and electrolyte requirements and replaces any ongoing abnormal fluid losses.

- **Maintenance fluid therapy** must provide daily ongoing water and electrolyte requirements (i.e., sodium 1 mmol/kg, potassium 1 mmol/kg, and water 25-35 mL/kg)

- Never give maintenance fluids at a rate of >100 mL/hour.
Acute kidney injury

Management

Never prescribe intravenous fluid therapy for more than 24 hours at once due to the risk of causing volume overload.

» Ensure at least daily ongoing monitoring of volume status for any patient with established AKI or at risk of AKI, via: [13] [64]

- Review of haemodynamic status, including postural BP
- Weight monitoring
- Fluid input/output chart

- Routine urinary catheterisation is not appropriate, so weigh up the benefits and risks (in particular, infection and trauma) for the individual patient. [64] Catheterisation is indicated if fluid balance management is crucial in an acutely unwell patient (e.g., hourly monitoring of fluid balance is needed) or if the patient is too ill or frail to use a bottle or commode

- Urea and electrolytes.

Plus review medications and stop nephrotoxins

Treatment recommended for ALL patients in selected patient group

» Whenever AKI is suspected or confirmed, review all medications and stop/avoid any nephrotoxic drugs and other drugs that may affect kidney function. [13] [64] [65]

- Common nephrotoxic drugs include aminoglycoside antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), and iodinated contrast agents. [1] Consult a pharmacist for a full list of nephrotoxic drugs.
- ACE inhibitors, angiotensin-II receptor antagonists, and other renin-angiotensin modifying agents can exacerbate AKI by reducing the kidney’s ability to adapt to changes in perfusion pressure. [9]
- Diuretics or other antihypertensives increase the risk of hypovolaemia/hypotension.
Acute kidney injury

Management

• If there are overriding reasons why a potentially harmful drug must be continued, seek specialist pharmacist advice on steps to minimise negative effects (e.g., dose adjustment, keep the treatment course as short as possible, monitor blood levels of the drug if feasible).

> Review and adjust doses of all other medications in line with the patient’s degree of kidney injury. [13] [64]

• Any medication that is cleared via the kidneys has the potential to accumulate during an episode of AKI. Dose adjustment is therefore important to prevent toxicity and patient harm.

• Inappropriate drug dosing in patients with AKI is an important cause of adverse drug events.[13]

> When restarting drugs after an episode of AKI, ensure:

• Any medications that were used for the treatment of pre-existing heart failure are re-started as soon as clinically reasonable and re-titrated to achieve the best control of fluid balance and blood pressure[13]

• All medications are reviewed before discharge and a plan is put in place to reintroduce any medications that have been withheld, at an appropriate time, with re-titration to the optimum dose continued in primary care as appropriate[96]

  • Ensure a process is in place for measurement of serum creatinine and potassium 1 to 2 weeks after restarting. This may need to be part of discharge planning.[13]

plus identify and treat underlying cause of AKI

Treatment recommended for ALL patients in selected patient group

> Determine the cause and severity of AKI when formulating your management plan for the patient. [1] [62]

> Pre-kidney AKI (80% of cases) is usually due to hypovolaemia and/or hypotension and is often associated with acute illness,
Acute kidney injury particularly in a patient with background risk factors. Common causes are: [1] [3] [9] [62]

- **Sepsis** (e.g., pneumonia, cellulitis) - perform a **septic screen** and implement your local care bundle (e.g., Sepsis Six) if infection is suspected [9] [63]
  - See our Sepsis in adults topic for more information
- **Fluid loss** (e.g., vomiting and diarrhoea, or blood loss)
- Reduced fluid intake - a particular problem in frail, elderly patients in the community. May also be due to insufficient maintenance or replacement fluids to replace losses in a hospital inpatient.

» In acutely ill patients, AKI is a strong indicator of a very sick patient who needs urgent recognition and management.

**Practical tip**

The UK Royal College of Physicians suggests the use of the STOP AKI acronym as an aide-memoire to recall the immediate steps needed for management of AKI: [62]

- **Sepsis** - implement your local care bundle (e.g., Sepsis Six) within 1 hour if sepsis is suspected or confirmed. Identify and treat the source of infection.
- **Toxins** - stop/avoid nephrotoxins (e.g., NSAIDs, aminoglycoside antibiotics, iodinated contrast agents). These are a contributory cause in 20% to 30% of patients with AKI. [1]
- **Optimise volume status/BP** - assess volume status and give intravenous fluids as needed; hold antihypertensive medication and diuretics; consider vasopressors if patient does not respond. [3]
- **Prevent harm** - treat complications; identify and treat the cause of AKI; review all medications and adjust doses appropriately; closely monitor intravenous fluid therapy.

**consider vasoactive drug**

Treatment recommended for SOME patients in selected patient group
Acute kidney injury

Management

Primary options

» noradrenaline (norepinephrine): 0.4 to 0.8 mg/hour intravenous infusion initially, adjust dose according to response
  Dose refers to noradrenaline base.

OR

» noradrenaline (norepinephrine): 0.4 to 0.8 mg/hour intravenous infusion initially, adjust dose according to response
  Dose refers to noradrenaline base.
  -and-
  » vasopressin: 0.01 units/minute intravenous infusion initially, adjust dose according to response, maximum 0.03 units/minute

OR

» dobutamine: 2.5 to 10 micrograms/kg/minute intravenous infusion initially, adjust dose according to response, maximum 40 micrograms/kg/minute

» Vasopressor support is recommended if the patient remains severely hypotensive despite adequate volume resuscitation (e.g., in septic/hypovolaemic shock). [1] [62] [13] [96]

- Escalate to critical care. Vasopressors should only be used with continuous haemodynamic monitoring in place.
- A reasonable goal is to maintain mean arterial pressure (MAP) ≥65 mmHg, but this target may need adjusting according to the patient’s baseline BP. [1] [13] [64]
- In the setting of vasomotor shock where the patient has persistent hypotension despite optimisation of intravascular volume through aggressive fluid resuscitation, preservation and improvement of kidney perfusion can only be achieved by the use of systemic vasopressors. [1]

» Noradrenaline (norepinephrine) is the usual vasopressor of choice, with the addition of vasopressin if needed.

- There is little good evidence available to guide the choice of vasopressor in patients with AKI and septic shock. [1] [13]
• **Do not use low-dose dopamine** to treat AKI.\[1\] [3] [13]

  • There is no evidence to support its use and it can **worsen kidney perfusion** in patients with AKI.

**Evidence: Evidence is scarce to guide the choice of vasopressor**

*It is not known which vasopressor agent is most effective for prevention or treatment of AKI and septic shock.*

**There is insufficient evidence to say that one vasoactive agent is better than another in preventing or treating AKI.** [1]

• Small open-label studies have shown improvement in creatinine clearance after a 6- to 8-hour infusion of noradrenaline.\[101\]

• Vasopressin, when compared with noradrenaline in one RCT, was found to increase blood pressure and enhance diuresis, but has not yet been proven to enhance survival or reduce the need for RRT.\[102\]

• A post-hoc analysis of the same RCT used the RIFLE criteria for AKI to compare the effects of vasopressin versus noradrenaline.\[103\] Vasopressin was associated with a trend to a lower rate of progression of the AKI, and a lower rate of use of RRT.

• According to the Kidney Disease: Improving Global Outcomes (KDIGO) guideline group, this study suggests that vasopressin may reduce progression to kidney failure and mortality in patients with septic shock who have or are at risk of AKI.\[1\]

**Dopamine has no significant clinical benefits in patients with AKI.** [13]

• A large RCT comparing dopamine with noradrenaline as the initial vasopressor in patients with shock showed no significant differences between groups.
Acute kidney injury

Management

Acute

with regard to kidney function or mortality.[104]

• However, there were more arrhythmic events among the patients treated with dopamine than among those treated with noradrenaline, and dopamine was associated with an increased rate of death at 28 days among the patients with cardiogenic shock.

• Both the NICE and KDIGO guidelines include a recommendation not to offer low-dose dopamine to treat AKI.[1] [3]

Consider the need for an inotrope (e.g., dobutamine) to optimise cardiac output if kidney hypoperfusion is caused by impaired cardiac function due to poor left ventricular systolic function. [13]

consider blood transfusion

Treatment recommended for SOME patients in selected patient group

» Blood transfusion is indicated if hypovolaemia is secondary to significant blood loss.

• This is generally not given unless more than one unit is anticipated, based on local guidelines and the clinical assessment of the patient.[5]

• Note that this may worsen hyperkalaemia.

consider specialist referral

Treatment recommended for SOME patients in selected patient group

» Most patients with AKI do not need referral to nephrology. [62]

• Do not refer if there is a clear cause and the AKI is responding to medical management.[3] [97] [98]

» Refer immediately to critical care and/or nephrology if:

• The patient meets (or is anticipated to meet) the criteria for RRT[3] [64]
• There are severe complications that cannot be managed medically (such
<table>
<thead>
<tr>
<th>Acute Kidney Injury (AKI) Management</th>
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</table>

- **Management**

  - **Acute**: as hyperkalaemia, pulmonary oedema, acidosis, or uraemia [64]
  - **The patient remains haemodynamically unstable after appropriate supportive care and/or there are signs of multi-organ failure.** [64]

  Check local protocols for referral criteria and pathways.

  **» Refer for urgent discussion with nephrology (as soon as possible and within 24 hours at the latest) if any one or more of the following is present:** [3] [64]

  - **Uncertainty about the cause of AKI or a poor response to treatment**
  - **A possible diagnosis that may need specialist treatment** (e.g., vasculitis, glomerulonephritis, tubulointerstitial nephritis, myeloma)
  - **Complications** associated with AKI that are **not responding to medical treatment**
  - **Stage 3 AKI**
  - **AKI in a patient with pre-existing chronic kidney disease (CKD) stage 4 or 5**
  - **The patient has a kidney transplant**.

**Evidence: Speed of referral to nephrology**

*There is little evidence available to support routine referral to the nephrology team for every patient with stage 2 AKI.*

**Evidence is lacking on whether outcomes are improved by routine rapid referral to nephrology (within 12 hours) for all patients with stage 2 or 3 AKI that does not need critical care input.** [3]

- **The large number of AKI cases among patients admitted acutely to hospital makes it impractical to refer every patient with suspected or confirmed AKI to nephrology.**
- **Initial management for most patients encompasses identification and treatment of sepsis, avoidance of nephrotoxins, fluid replacement, and correction of hypotension. These steps**
### Acute Kidney Injury

**Management**

Acute kidney injury (AKI) can be commenced by any medical or surgical team.

- Potential benefits of routine nephrology referral include a faster diagnosis in patients with primary kidney disease, prevention of progressive AKI and the potential need for renal replacement therapy, avoidance of a delayed transfer to critical care, improved chances of kidney recovery, and a shorter hospital stay.

- However, there is very little evidence to support routine nephrology referral for all patients with stage 2 or 3 AKI.[3]

  - Very low quality evidence from one large retrospective study suggested that for non-critically ill patients with AKI, early compared with delayed referral to nephrology may reduce in-hospital mortality, the number of patients needing RRT, and length of hospital stay.[99]

### Treatment for Hyperkalaemia

**with mild hyperkalaemia (potassium 5.5 to 5.9 mmol/L)**

- **plus** identify and treat underlying cause of hyperkalaemia

Treatment recommended for ALL patients in selected patient group

- **Always look for the underlying cause of hyperkalaemia and treat it.** [62]

  - **Review medications** that might be responsible (e.g., ACE inhibitors, angiotensin-II receptor antagonists, potassium-sparing diuretics).

  - Treatment of hyperkalaemia only results in a temporary intracellular shift of potassium so the cause of hyperkalaemia must be identified and corrected.[62]

  - Consult a pharmacist for a full list of medications that can cause hyperkalaemia.

  - **Restrict dietary intake - avoid potassium-rich foods and fluids.** [80]

  - **Ensure close ongoing monitoring of potassium and glucose.**
Acute kidney injury (AKI) is a common complication of AKI. It can lead to:

- Muscle weakness
- Cardiac arrhythmias (e.g., bradycardia, bundle branch block, ventricular tachycardia, ventricular fibrillation, asystole).

Check your local protocols - many hospitals have institutional guidelines for managing hyperkalaemia. Consider a cation-exchange resin, treatment recommended for some patients in selected patient groups.

Primary options

- **Calcium polystyrene sulfonate**: 15 g orally three to four times daily; 30 g rectally once daily (as a retention enema retained for 9 hours followed by irrigation to remove resin from colon).
  

- **A cation-exchange resin (e.g., calcium polystyrene sulfonate)** can be considered. [110]
  
  - This will help remove potassium from the body. [80]
  - Do not use if the patient has obstructive bowel disease.
  - Can be administered orally or rectally. The rectal route should be reserved for patients who are vomiting or have upper gastrointestinal conditions (e.g., paralytic ileus).
  - Administer the oral formulation 3 hours before or after other oral medications (consider a 6-hour separation in patients with gastroparesis). Check potential
Acute kidney injury

Management

Acute

• Drug-drug interactions before use (e.g., digoxin).
  • May cause constipation. Administer a suitable laxative during treatment. [80] Magnesium-containing laxatives and sorbitol are not recommended due to the risk of alkalosis and intestinal necrosis, respectively.
  • Monitor serum electrolyte levels during treatment and stop once potassium levels fall to 5 mmol/L.

with moderate hyperkalaemia (potassium 6.0 to 6.4 mmol/L) and no associated ECG changes

plus

identify and treat underlying cause of hyperkalaemia

Treatment recommended for ALL patients in selected patient group

» Look for the underlying cause of hyperkalaemia and treat it. [62]

• Review medications that might be responsible (e.g., ACE inhibitors, angiotensin-II receptor antagonists, potassium-sparing diuretics).
  • Treatment of hyperkalaemia only results in a temporary intracellular shift of potassium so the cause of hyperkalaemia must be identified and corrected. [62]
  • Consult a pharmacist for a full list of medications that can cause hyperkalaemia.

• Restrict dietary intake - avoid potassium-rich foods and fluids. [80]
  • Ensure close ongoing monitoring of potassium and glucose.

» Check for any acute ECG changes.

• Features of hyperkalaemia include peaked t waves, flattened p waves, broad QRS complexes.
  • If there are ECG changes consistent with hyperkalaemia, treat in the same way as severe hyperkalaemia.

» Hyperkalaemia is a common complication of AKI. It can lead to:
  • Muscle weakness
  • Cardiac arrhythmias (e.g., bradycardia, bundle branch block, ventricular...

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**Acute kidney injury**

**Management**

> tachycardia, ventricular fibrillation, asystole).

> **Check your local protocols - many hospitals have institutional guidelines for managing hyperkalaemia.**

**plus insulin/glucose**

Treatment recommended for ALL patients in selected patient group

**Primary options**

» **insulin neutral**: 10 units by intravenous infusion over 15 minutes

-and-

» **glucose**: 25 g (50 mL of a 50% solution or 125 mL of a 20% solution) by intravenous infusion over 15 minutes

- **Give an infusion of soluble (neutral) insulin and glucose to push potassium intracellularly:** [62] [80]
  
  • Give over 15 minutes
  • Acts within 10 to 20 minutes
  • Lasts 4 to 6 hours.

- **Monitor hourly for hypoglycaemia.**

**consider salbutamol**

Treatment recommended for SOME patients in selected patient group

**Primary options**

» **salbutamol inhaled**: 10-20 mg inhaled via nebuliser as a single dose


- **Consider further adjunctive treatment with nebulised salbutamol to drive potassium intracellularly if necessary.** [62]
  
  • Decide whether this is needed based on the ECG and the rate of rise of serum potassium.[80]
  • Use with caution if there is a history of ischaemic heart disease (a lower dose is recommended), and avoid if there is a history of tachyarrhythmias.[62] [80]
Acute kidney injury

**Management**

**Acute with severe hyperkalaemia** (potassium ≥6.5 mmol/L) OR **moderate hyperkalaemia** (potassium 6.0 to 6.4 mmol/L) and associated ECG changes

**plus calcium**

Treatment recommended for ALL patients in selected patient group

**Primary options**

- **calcium chloride**: 6.8 mmol (10 mL of a 10% solution) intravenously over 5-10 minutes; may repeat if ECG changes persist; consult local protocols for further guidance on dose

**OR**

- **calcium gluconate**: 6.8 mmol (30 mL of a 10% solution) intravenously over 5-10 minutes; may repeat if ECG changes persist; consult local protocols for further guidance on dose

- **Give immediate intravenous calcium for cardiac protection.** [62] [80]

  - Give over 5 to 10 minutes, then repeat the ECG and consider a further dose if ECG changes persist.[80]

    • Use a wide bore cannula and avoid extravasation.
    • Ensure cardiac monitoring.
    • Intravenous calcium antagonises the cardiac membrane excitability and so protects the heart against arrhythmias.[110]

    • Effective within 3 minutes and lasts 30 to 60 minutes.
    • Seek senior advice if the ECG fails to normalise after one dose.[62]

**plus insulin/glucose**

Treatment recommended for ALL patients in selected patient group

**Primary options**

- **insulin neutral**: 10 units by intravenous infusion over 15 minutes
- **glucose**: 25 g (50 mL of a 50% solution or 125 mL of a 20% solution) by intravenous infusion over 15 minutes
Acute kidney injury

Management

MANAGEMENT

Acute

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plus 

salbutamol

Treatment recommended for ALL patients in selected patient group

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» Consider further adjunctive treatment with nebulised salbutamol to drive potassium intracellularly if necessary. [62]
  
  • Decide whether this is needed based on the ECG and the rate of rise of serum potassium.[80]
  • Use with caution if there is a history of ischaemic heart disease (a lower dose is recommended), and avoid if there is a history of tachyarrhythmias.[62] [80]

plus 

identify and treat underlying cause of hyperkalaemia

Treatment recommended for ALL patients in selected patient group

» Look for the underlying cause of hyperkalaemia and treat it. [62]
  
  • Review medications that might be responsible (e.g., ACE inhibitors, angiotensin-II receptor antagonists, potassium-sparing diuretics).
    
    • Treatment of hyperkalaemia only results in a temporary intracellular shift of potassium so the cause of hyperkalaemia must be identified and corrected.[62]
Consult a pharmacist for a full list of medications that can cause hyperkalaemia.

**Hyperkalaemia is a common complication of AKI. It can lead to:**

- Muscle weakness
- Cardiac arrhythmias (e.g., bradycardia, bundle branch block, ventricular tachycardia, ventricular fibrillation, asystole).

**Check your local protocols - many hospitals have institutional guidelines for managing hyperkalaemia.**

**There is no evidence to support the use of loop diuretics for managing AKI-associated hyperkalaemia.**[110]

- However, in practice their use may sometimes be considered by the nephrology team as an adjunct to other therapies provided the patient is fluid replete (but only with close specialist supervision).

**Debate: Loop diuretics**

The role of loop diuretics in the management of AKI-associated hyperkalaemia remains controversial.

- Loop diuretics may be used under specialist supervision for volume management in patients with AKI and there is a theoretical rationale to suggest they could be beneficial in managing hyperkalaemia.[1]

- Loop diuretics promote potassium excretion in the urine through their action in inhibiting the Na⁺-K⁺-2Cl⁻ co-transporter on the ascending limb of Henle, thereby reducing uptake of potassium (as well as sodium and chloride).

- However, the 2014 UK Renal Association guideline on acute hyperkalaemia concluded that there...
### Acute kidney injury

#### Management

**Acute**

- is no evidence to support the use of diuretics in the management of AKI-associated hyperkalaemia.[110]
  - Both the NICE and KDIGO guidelines are clear that loop diuretics should not be used routinely to manage AKI.[1][3] The use of loop diuretics is indicated (under specialist supervision) only if a patient with AKI-associated hyperkalaemia also has volume overload (which is a clear indication for their use).[3]

<table>
<thead>
<tr>
<th>with metabolic acidosis</th>
<th>consider</th>
<th>sodium bicarbonate</th>
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<tbody>
<tr>
<td>Treatment recommended for SOME patients in selected patient group</td>
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</table>

**Primary options**

- **sodium bicarbonate**: consult local protocols for guidance on dose
  - If the patient has severe acidosis, seek senior input as intravenous sodium bicarbonate may be needed. [64]
    - Severe metabolic acidosis (pH < 7.2) is an indication for intravenous sodium bicarbonate.
    - This should only be given under expert supervision due to the risk of causing volume overload and/or hypernatraemia.
      - Consider referring to ICU.
      - Sodium bicarbonate should only be used if venous bicarbonate is < 16 mmol/L with no signs of volume overload.[64]
        - Ionised Ca$^{2+}$ falls with rapid correction and this can trigger tetany, seizures, and cardiac instability. Prior to administration of sodium bicarbonate, correct low ionised Ca$^{2+}$ with intravenous calcium via a different intravenous route due to the incompatibility of bicarbonate and calcium solutions.[64]

- **Metabolic acidosis is a common metabolic disturbance in AKI.**
  - It occurs primarily due to impaired excretion of the normal load of metabolic
### Acute kidney injury

#### Management

Acute kidney injury (AKI) is defined as a decrease in kidney function over a short period of time. It is a medical emergency and requires immediate attention to prevent further deterioration of kidney function or complications such as hyperkalaemia, acidosis, and uraemia.

- **Acute acid in the setting of a low glomerular filtration rate (GFR).**
  - Other factors may also contribute (e.g., increased production of lactic acid in patients with sepsis).
  - Note that there will be relative resistance to vasopressors in the presence of severe metabolic acidosis.

  > Sodium bicarbonate can also be considered in the setting of **hyperkalaemia with hypovolaemia and acidosis**.

  - Use only with expert supervision due to the risk of causing volume overload and/or hypernatraemia.

- **Use renal replacement therapy** in selected patient group considering the presence of:
  
  - End-organ complications of uraemia (e.g., pericarditis, encephalopathy, uraemic bleeding)
  - Severe hyperkalaemia (potassium ≥ 6.5 mmol/L) that fails to respond quickly to medical management

  * If the patient has **severe hyperkalaemia (or moderate hyperkalaemia with associated ECG changes)**, seek expert advice from the nephrology or ICU team to consider whether RRT may be needed.

  * Refractory acidosis (pH < 7.15) that is not responding to initial management.

  > RRT is the cornerstone for treatment of **severe AKI with complications** that are not responding to medical management.

  > There may be some patients with pre-existing comorbidities for whom RRT will not offer any realistic benefits.

  - This needs to be a shared decision between the patient and their family.

---

**With uraemia, refractory severe hyperkalaemia, or refractory metabolic acidosis consider renal replacement therapy**

Treatment recommended for SOME patients in selected patient group

> Refer immediately to the renal team for emergency initiation of RRT if the patient has:

* End-organ complications of uraemia (e.g., pericarditis, encephalopathy, uraemic bleeding)
* Severe hyperkalaemia (potassium ≥ 6.5 mmol/L) that fails to respond quickly to medical management

> If the patient has **severe hyperkalaemia (or moderate hyperkalaemia with associated ECG changes)**, seek expert advice from the nephrology or ICU team to consider whether RRT may be needed.

> Refractory acidosis (pH < 7.15) that is not responding to initial management.

> RRT is the cornerstone for treatment of severe AKI with complications that are not responding to medical management.

> There may be some patients with pre-existing comorbidities for whom RRT will not offer any realistic benefits.

> This needs to be a shared decision between the patient and their family.
Acute kidney injury

**Management**

Acute members/carers after discussion with the multidisciplinary team.

» **Pre-assessment for RRT requires careful consideration and must include:** [114]

- Clinical preparation
- Discussion with the patient around the types of RRT that are available and the acute process (it must be made clear that RRT is supportive treatment that is doing the work of the kidneys)
- If it is unclear whether the patient has a reversible form of AKI, discussion about the longer term options and the impact they may have on the patient’s life
- Psychological assessment and support.

**Choice of RRT modality**

The renal team will select the best modality of RRT after assessment of the patient’s overall medical condition and comorbidities. [63]

- Various options exist for supporting kidney function.
- There is no evidence that one modality is better than another in terms of outcomes among patients with AKI. [115]
- If your patient is in a non-renal centre and is too unwell to transfer, the critical care team will lead the decision-making.

The choice of RRT modality depends on several factors, including: [63]

- **Individual patient factors:**
  - Haemodynamic stability (and hence the patient’s physiologic reserve to tolerate metabolic shifts and fluctuations in fluid status) is a key determinant of the most appropriate RRT modality [13]
  - Severity of electrolyte and acid base balance disorders
  - Risk of ongoing catabolism with cellular breakdown and acidosis
Acute kidney injury

Management

The options for RRT include: [115] [13]

- **Intermittent haemodialysis (IHD)** - usually the preferred option in haemodynamically stable AKI patients, but generally avoided in haemodynamically unstable patients, as it often precipitates hypotensive events.[1]

  - Duration up to **4 hours** so the patient can participate in active rehabilitation.
  - **Fast removal of toxins** (e.g., urea, ethylene glycol). In the case of lithium, rebound can occur after IHD as the drug redistributes from the intracellular to extracellular compartment.
  - May risk **dialysis disequilibrium syndrome** through over-rapid solute removal and attendant osmolar shifts.
  - **Fast correction of acidosis/hyperkalaemia** with risk of rebound following the treatment.
  - Hybrid versions of IHD include:
    - Sustained low-efficiency dialysis (SLED)
    - Extended daily dialysis (EDD)[116]
    - Prolonged intermittent renal replacement therapy (PIRRT).

- **Continuous renal replacement therapy (CRRT)** - preferred in haemodynamically unstable patients. [117] [118] [119]

  - Duration **24 to 72 hours**, depending on blood circuit clotting.
  - **Slower blood flow.**
  - **Slower but continual removal of toxins** allowing more gradual restoration of metabolic homeostasis and **avoidance of rebound** (e.g., lithium toxicity).
Acute kidney injury

Management

Acute

- Slows patient rehabilitation when recovering.
- There are several different types of CRRT but no evidence to support one form over another in terms of better outcomes:
  - Continuous venovenous haemofiltration (CVVH)\[120\][121][122]
  - Continuous venovenous haemodialysis (CVVHD)
  - Continuous venovenous haemodiafiltration (CVVHDF).\[116\][117][118][119]

- Peritoneal dialysis - rarely used in the developed world except in paediatric patients.

RRT (whether IHD or CRRT) is performed through a large double lumen catheter placed into the central venous system, such as the internal jugular or femoral vein.

Evidence: Choice of RRT modality

CRRT and IHD have similar outcomes in AKI.

Mortality outcomes are similar in critically ill AKI patients treated with CRRT and IHD.

- Several RCTs have compared CRRT to IHD in AKI patients, including the Hemodiafe study, the SHARF study, the CONVINT study and the OUTCOMEREA study. None has found any survival advantage from one modality over the other.[13]
- A Cochrane systematic review that analysed 15 RCTs in 1550 AKI patients concluded that outcomes were similar in the CRRT and IHD groups in terms of hospital mortality, ICU mortality, length of hospitalisation, and kidney recovery.[123]

Peritoneal dialysis has generally been thought ineffective in adults with AKI and hypercatabolic states, although some studies now suggest equal effectiveness in appropriate subjects.\[124\][125]
Management

Acute

• However, one study was stopped early because there was a significant benefit to patients being on CRRT rather than PD.\[126\]
• In practice, PD is rarely used in adult patients in high-income countries although it is an option for children with AKI.\[13\]

hypovolaemic

1st loop diuretic (only under specialist supervision) and sodium restriction

Primary options

» furosemide: consult specialist for guidance on dose

» Volume overload in a patient with AKI can occur as a result of:

• Overaggressive fluid resuscitation in a patient who initially presented with hypovolaemic pre-kidney AKI. This is most commonly seen in patients with sepsis.
• Oliguria in intrinsic or post-kidney AKI.

» Consider a loop diuretic (under specialist supervision) to treat volume overload. [1] [13]

• A loop diuretic such as furosemide may be useful in achieving euvoalaemia in a patient with fluid overload (with or without pulmonary oedema).[1] This must be done with caution and under the supervision of the nephrology team.

• Note that there is no evidence to support the routine use of loop diuretics for management of AKI in the absence of volume overload.[1] [3] [13]
• Never use a loop diuretic if the patient is hypovolaemic or hypotensive. The diuretic will exacerbate the haemodynamic instability,

• Do not allow the use of loop diuretics to delay more definitive management of volume overload.

• Careful monitoring of response is important (e.g., urine output). Stop the diuretic if there is no response.
Acute kidney injury

**MANAGEMENT**

- **Acute**
  - Proceed without delay to more definitive management with RRT if the response to diuretics is unsuccessful.[64]

  » **Sodium restriction** may also be required.

  » **Patients with volume overload need** careful monitoring and management to reduce the risk of a poor outcome.

  - Failure to manage volume overload can lead to complications including **pulmonary oedema**.[62] In critically ill patients, a positive fluid balance (>5% body weight) has been found to be associated with an increase in mortality at up to 1 year follow-up when compared to neutral or negative (<5%) fluid balance.[13]

<table>
<thead>
<tr>
<th>Evidence: The role of loop diuretics in patients with AKI</th>
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<tr>
<td>Loop diuretics have no routine role in the management of AKI. They should be reserved for specific indications (such as volume overload) and only used under specialist supervision.</td>
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<tr>
<td>There is no evidence for any benefits from the routine use of loop diuretics in patients with AKI - but there is some evidence to suggest harm.</td>
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</table>
  
  - The theoretical rationale for the use of loop diuretics to treat AKI is based on their potential to reduce oxygen consumption in the ascending loop of Henle, thereby reducing any ischaemic damage to the kidneys. They may also be used to convert oliguric AKI to non-oliguric AKI.[1][13]

  - However, diuretics can also excessively reduce circulating volume and so cause a pre-kidney insult that could worsen established AKI. Hence an evaluation of the available evidence is vital to determine their appropriate role.
### Acute

<p>| | |</p>
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|   | • There is no evidence to support the use of loop diuretics in routine treatment of AKI.  
  • One RCT found furosemide to be ineffective in treating AKI and epidemiological data suggest the use of loop diuretics may increase mortality in patients with critical illness and AKI.  
  • Two systematic reviews on the use of furosemide to prevent or treat AKI found no significant effect on in-hospital mortality, risk for requiring RRT, the number of dialysis sessions needed, or even the proportion of patients with persistent oliguria.  
  • Prophylactic furosemide has been shown to increase the risk of AKI when given to prevent AKI in patients having cardiac surgery.  
  
  There is no evidence to support the use of loop diuretics for managing AKI-associated hyperkalaemia.  
  • However, in practice their use may be considered (with specialist supervision) as an adjunct to other therapies provided the patient is fluid replete. |
|   | plus| Identify and treat the underlying cause of AKI  
Treatment recommended for ALL patients in selected patient group  

### Obstructive AKI

**Relief of the obstruction is key in the management of obstructive AKI.** [9] [64]

• **Insert a bladder catheter** in any case of AKI when bladder outlet obstruction is suspected clinically and cannot be quickly ruled out by ultrasound.
• Refer to urology within 24 hours if urinary tract obstruction is confirmed on ultrasound.[3] [64]

Refer immediately to urology and/or radiology if one of more of the following is present:[3]

- **Pyonephrosis** - if pyonephrosis is suspected, ensure the patient has an ultrasound within 6 hours (because of the risk of septic shock)[3]
- **Obstructed single kidney**
- **Bilateral** upper urinary tract obstruction
- Complications of AKI secondary to urological obstruction.

Arrangements for ureteral stenting, urinary diversion, debulking procedures, or other case-specific requirements will be made by the specialist urology or radiology team. [64]

• Nephrostomy or ureteral stenting must be undertaken as quickly as possible and at the latest within 12 hours of diagnosis.[3]
• Ureteral stenting is indicated if there is a ureteral stricture, stone, or extrinsically obstructing mass.
• Lithotripsy or surgical removal may be needed if obstruction is caused by stones at the ureteropelvic junction.
• Exploratory laparotomy may be indicated if a compressing tumour is suspected that may require surgical removal; this may be done following ureteral stenting.
• 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.

Renal replacement therapy may be needed while the underlying obstruction is being addressed if there is severe acidosis, volume overload, or electrolyte or uraemic complications.
Acute Kidney Injury

Management

Intrinsic AKI

Intrinsic AKI is due to cellular damage within the kidneys – seek early specialist input from nephrology if you suspect an intrinsic cause (e.g., vasculitis). Causes include:

- Prolonged pre-kidney AKI that progresses to overt cellular damage (the most common cause of intrinsic AKI)
- Nephrotoxins (e.g., iodinated contrast agents, non-steroidal anti-inflammatory drugs [NSAIDs], aminoglycoside antibiotics)[1]
- Rare causes (e.g., vasculitis, glomerulonephritis).

Consider the possibility of intrinsic AKI if urinalysis is positive for both blood and protein in the absence of an obvious alternative cause for this (e.g., urinary tract infection or trauma from urinary catheterisation). [3] [9] [64]

Specific management of intrinsic AKI depends on the aetiology and is led by the nephrology team. [62]

- Immunological tests and kidney biopsy are needed to confirm acute glomerulonephritis, anti-neutrophil cytoplasmic antibodies [ANCA]-associated vasculitis, anti–glomerular basement membrane (anti-GBM) antibody disease (Goodpasture syndrome if associated with pulmonary hypertension) and lupus nephritis.

  - Treatment will require corticosteroids, cytotoxic agents, immunomodulating drugs, and/or plasma exchange.

- Atypical haemolytic uraemic syndrome (HUS) is treated with the monoclonal antibody eculizumab or plasma exchange.[111]

- Thrombotic thrombocytopenic purpura (TTP) is treated with plasma exchange.[112]

- Acute allergic interstitial nephritis is treated with a corticosteroid (after excluding infection) and stopping potential causative medications (e.g., proton-pump inhibitors, NSAIDs, antibiotics).[113]
**Medication review**

Whenever AKI is suspected or confirmed, review all medications and stop/avoid any nephrotoxic drugs and other drugs that may affect kidney function. [13] [64] [65]

- Common nephrotoxic drugs include **aminoglycoside antibiotics, NSAIDs, and iodinated contrast agents**. Consult a pharmacist for a full list of nephrotoxic drugs.
- **ACE inhibitors, angiotensin-II receptor antagonists**, and other renin-angiotensin modifying agents can exacerbate AKI by reducing the kidney’s ability to adapt to changes in perfusion pressure. [9]
- **Diuretics** or other antihypertensives increase the risk of hypovolaemia/hypotension.
- If there are overriding reasons why a potentially harmful drug must be continued, seek specialist **pharmacist advice** to minimise negative effects (e.g., dose adjustment, keep the treatment course as short as possible, monitor blood levels of the drug if feasible).

**Review and adjust doses of all other medications in line with the patient’s degree of kidney injury.** [13] [64]

- Any medication that is cleared via the kidneys has the potential to accumulate during an episode of AKI. Dose adjustment is therefore important to prevent toxicity and patient harm.
- Inappropriate drug dosing in patients with AKI is an important cause of adverse drug events. [13]

**consider renal replacement therapy**

Treatment recommended for SOME patients in selected patient group

» **Immediate RRT is indicated for refractory volume overload or volume overload associated with severe complications of AKI.** [62] [13] [64]

- Refractory volume overload typically includes pulmonary oedema.
- However, RRT may also be needed in a patient with gross peripheral oedema.
Acute kidney injury

Management

Acute (without pulmonary oedema) that fails to respond to a loop diuretic. Such patients will usually have oliguric AKI.

» The decision to start RRT must be based on the patient’s overall condition and not on any isolated urea or creatinine value.[1]

- The potential metabolic and fluid benefits of earlier initiation of RRT must be balanced with the potential harm for the individual patient (e.g., complications related to line insertion, anticoagulation).[13]
- In the absence of an emergency indication for RRT (e.g., severe refractory hyperkalaemia, acidosis or volume overload, or end-organ complications of uraemia), there is little clear evidence available to guide decisions on whether and when to start RRT.

- Individual studies have reached conflicting findings and meta-analyses have been hampered by varied definitions of ‘early’ and ‘late’ initiation of RRT.[13]
- In practice, the decision to start RRT is based on a combination of clinical, physiological, and laboratory parameters used to assess the patient’s fluid, electrolyte, and metabolic status.[1][13]
- Factors to consider include:[13]

  - The trend as well as the absolute values of biochemical parameters (e.g., potassium, pH, urea)
  - The uraemic solute burden (which is increased in tumour lysis syndrome, rhabdomyolysis, and hypercatabolic states)
  - The need for intravascular space to allow administration of therapeutic interventions such as blood products or nutrition
  - The degree and duration of oliguria
  - Whether or not the underlying kidney insult has resolved
Acute kidney injury

Management

**MANAGEMENT**

- Any signs of organ dysfunction (which will affect the patient’s ability to tolerate uraemic complications)
- The presence of any other electrolyte disturbances that may be corrected by RRT (e.g., hypercalcaemia).

» **There may be some patients with pre-existing comorbidities for whom RRT will not offer any realistic benefits.** [114] [13]

  - This needs to be a shared decision between the patient and their family members/carers after discussion with the multidisciplinary team.

» **Pre-assessment for RRT requires careful consideration and must include:** [114]

  - Clinical preparation
  - Discussion with the patient around the types of RRT that are available and the acute process (it must be made clear that RRT is supportive treatment that is doing the work of the kidneys)
  - If it is unclear whether the patient has a reversible form of AKI, discussion about the longer term options and the impact they may have on the patient’s life
  - Psychological assessment and support.

**Choice of RRT modality**

The nephrology team will select the best modality of RRT after assessment of the patient’s overall medical condition and comorbidities. [63]

- Various options exist for supporting kidney function.
- There is **no evidence that one modality is better than another in terms of outcomes** among patients with AKI. [115]
- If your patient is in a non-renal centre and is too unwell to transfer, the critical care team will lead the decision-making.

The choice of RRT modality depends on several factors, including: [63]
Acute kidney injury

Management

Individually, the patient factors:

- **Haemodynamic stability** (and hence the patient’s physiologic reserve to tolerate metabolic shifts and fluctuations in fluid status) is a key determinant of the most appropriate RRT modality[13]
- Severity of electrolyte and acid base balance disorders
- Risk of ongoing catabolism with cellular breakdown and acidosis
- Any need for rapid poison removal (e.g., lithium or ethylene glycol)

Availability of modality and staff skill mix.

The options for RRT include: [115] [13]

- **Intermittent haemodialysis (IHD)** - usually the preferred option in haemodynamically stable AKI patients, but generally avoided in haemodynamically unstable patients, as it often precipitates hypotensive events.[1]
  - Duration up to **4 hours** so the patient can participate in active rehabilitation.
  - **Fast removal of toxins** (e.g., urea, ethylene glycol). In the case of **lithium**, rebound can occur after IHD as the drug redistributes from the intracellular to extracellular compartment.
  - May risk **dialysis disequilibrium syndrome** through over-rapid solute removal and attendant osmolar shifts.
  - **Fast correction of acidosis/hyperkalaemia** with risk of rebound following the treatment.
  - Hybrid versions of IHD include:
    - Sustained low-efficiency dialysis (SLED)
    - Extended daily dialysis (EDD)[116]
    - Prolonged intermittent renal replacement therapy (PIRRT).

- **Continuous renal replacement therapy (CRRT)** - preferred in
Acute kidney injury

Management

**Acute**

- **haemodynamically unstable patients.** [117] [118] [119]
  - Duration 24 to 72 hours, depending on blood circuit clotting.
  - Slower blood flow.
  - **Slower but continual removal of toxins** allowing more gradual restoration of metabolic homeostasis and **avoidance of rebound** (e.g., lithium toxicity).
  - Slows patient rehabilitation when recovering.
  - There are several different types of CRRT but no evidence to support one form over another in terms of better outcomes:
    - Continuous venovenous haemofiltration (CVVH) [120] [121] [122]
    - Continuous venovenous haemodialysis (CVVHD)
    - Continuous venovenous haemodiafiltration (CVVHDF). [116] [117] [118] [119]
    - Peritoneal dialysis - rarely used in the developed world except in paediatric patients.

RRT (whether IHD or CRRT) is performed through a large double lumen catheter placed into the central venous system, such as the internal jugular or femoral vein.

**Evidence: Choice of RRT modality**

**CRRT and IHD have similar outcomes in AKI.**

**Mortality outcomes are similar in critically ill AKI patients treated with CRRT and IHD.**

- Several RCTs have compared CRRT to IHD in AKI patients, including the Hemodiafe study, the SHARF study, the CONVINT study and the OUTCOMEREA study. None has found any survival advantage from one modality over the other.[13]
- A Cochrane systematic review that analysed 15 RCTs in 1550 AKI patients...
Acute kidney injury

Management

Acute concluded that outcomes were similar in the CRRT and IHD groups in terms of hospital mortality, ICU mortality, length of hospitalisation, and kidney recovery.\[123\]

Peritoneal dialysis has generally been thought ineffective in adults with AKI and hypercatabolic states, although some studies now suggest equal effectiveness in appropriate subjects.\[124\] \[125\]

- However, one study was stopped early because there was a significant benefit to patients being on CRRT rather than PD.\[126\]
- In practice, PD is rarely used in adult patients in high-income countries although it is an option for children with AKI.\[13\]

## with pulmonary oedema plus upright positioning

Treatment recommended for ALL patients in selected patient group

» Sit the patient upright. [62] [64]

» Pulmonary oedema may occur:

- As a result of overzealous intravenous fluid resuscitation in a patient who presented with hypovolaemic pre-kidney AKI\[96\]

- At presentation in some types of AKI, for example:

  - Renal artery stenosis - flash pulmonary oedema
  - Renal tract obstruction - salt and water retention
  - Cardiac failure with AKI.

» Mortality is high in acute pulmonary oedema so emergency management is vital.

plus high-flow oxygen

Treatment recommended for ALL patients in selected patient group

» Give high-flow oxygen: [62]

  - 15 L/minute via a reservoir mask.
<table>
<thead>
<tr>
<th>Acute</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute</strong></td>
<td>If available, consider continuous positive airway pressure ventilation. [64] plus <strong>glyceryl trinitrate</strong></td>
</tr>
<tr>
<td>Treatment recommended for ALL patients in selected patient group</td>
<td></td>
</tr>
<tr>
<td><strong>Primary options</strong></td>
<td>Glyceryl trinitrate: 10 micrograms/minute intravenous infusion initially, increase gradually according to response, maximum 400 micrograms/minute. An alternative regimen recommended by the Royal College of Physicians in the UK is 2 mg/hour initially, titrated up to 20 mg/hour according to response maintaining systolic BP &gt;95 mmHg. Royal College of Physicians. Acute care toolkit 12: acute kidney injury and intravenous fluid therapy. October 2015 [internet publication]. <a href="https://www.rcplondon.ac.uk/guidelines-policy/acute-care-toolkit-12-acute-kidney-injury-and-intravenous-fluid-therapy">https://www.rcplondon.ac.uk/guidelines-policy/acute-care-toolkit-12-acute-kidney-injury-and-intravenous-fluid-therapy</a></td>
</tr>
<tr>
<td><strong>Give intravenous glyceryl trinitrate.</strong> [62] [64]</td>
<td></td>
</tr>
<tr>
<td>• Titrate the dose upwards, aiming to maintain systolic BP &gt;95 mmHg. [62]</td>
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<tr>
<td><strong>with mild hyperkalaemia</strong> (potassium 5.5 to 5.9 mmol/L)</td>
<td>plus <strong>identify and treat underlying cause of hyperkalaemia</strong></td>
</tr>
<tr>
<td>Treatment recommended for ALL patients in selected patient group</td>
<td></td>
</tr>
<tr>
<td><strong>Always look for the underlying cause of hyperkalaemia and treat it.</strong> [62]</td>
<td></td>
</tr>
<tr>
<td>• Review medications that might be responsible (e.g., ACE inhibitors, angiotensin-II receptor antagonists, potassium-sparing diuretics).</td>
<td></td>
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<tr>
<td>• Treatment of hyperkalaemia only results in a temporary intracellular shift of potassium so the cause of hyperkalaemia must be identified and corrected. [62]</td>
<td></td>
</tr>
<tr>
<td>• Consult a pharmacist for a full list of medications that can cause hyperkalaemia.</td>
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<tr>
<td>• Restrict dietary intake — avoid potassium-rich foods and fluids. [80]</td>
<td></td>
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<tr>
<td>• Ensure close ongoing monitoring of potassium and glucose.</td>
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</tbody>
</table>
Acute kidney injury

Management

Acute

» Hyperkalaemia is a common complication of AKI. It can lead to:

- Muscle weakness
- Cardiac arrhythmias (e.g., bradycardia, bundle branch block, ventricular tachycardia, ventricular fibrillation, asystole).

» Check your local protocols - many hospitals have institutional guidelines for managing hyperkalaemia.

consider cation-exchange resin

Treatment recommended for SOME patients in selected patient group

Primary options

» calcium polystyrene sulfonate: 15 g orally three to four times daily; 30 g rectally once daily (as a retention enema retained for 9 hours followed by irrigation to remove resin from colon)


» A cation-exchange resin (e.g., calcium polystyrene sulfonate) can be considered. [110]

- This will help remove potassium from the body.[80]
- Do not use if the patient has obstructive bowel disease.
- Can be administered orally or rectally. The rectal route should be reserved for patients who are vomiting or have upper gastrointestinal conditions (e.g., paralytic ileus).
- Administer the oral formulation 3 hours before or after other oral medications (consider a 6-hour separation in patients with gastroparesis). Check potential
Acute kidney injury

Management

**Acute**

| Drug-drug interactions before use (e.g., digoxin).
| May cause constipation. Administer a suitable laxative during treatment. [80] Magnesium-containing laxatives and sorbitol are not recommended due to the risk of alkalosis and intestinal necrosis, respectively.
| Monitor serum electrolyte levels during treatment and stop once potassium levels fall to 5 mmol/L.

**with moderate hyperkalaemia** (potassium 6.0 to 6.4 mmol/L) and no associated ECG changes

| plus | Identify and treat underlying cause of hyperkalaemia
| Treatment recommended for ALL patients in selected patient group

> Look for the underlying cause of hyperkalaemia and treat it. [62]

- Review medications that might be responsible (e.g., ACE inhibitors, angiotensin-II receptor antagonists, potassium-sparing diuretics).
  - Treatment of hyperkalaemia only results in a temporary intracellular shift of potassium so the cause of hyperkalaemia must be identified and corrected. [62]
  - Consult a pharmacist for a full list of medications that can cause hyperkalaemia.

- Restrict dietary intake – avoid potassium-rich foods and fluids. [80]
- Ensure close ongoing monitoring of potassium and glucose.

> Check for any acute ECG changes.

- Features of hyperkalaemia include peaked t waves, flattened p waves, broad QRS complexes.
  - If there are ECG changes consistent with hyperkalaemia, treat in the same way as severe hyperkalaemia.

> Hyperkalaemia is a common complication of AKI. It can lead to:

- Muscle weakness
- Cardiac arrhythmias (e.g., bradycardia, bundle branch block, ventricular
Acute kidney injury

Management

tachycardia, ventricular fibrillation, asystole).

» Check your local protocols – many hospitals have institutional guidelines for managing hyperkalaemia.

plus insulin/glucose

Treatment recommended for ALL patients in selected patient group

Primary options

» insulin neutral: 10 units by intravenous infusion over 15 minutes
  -and-
  » glucose: 25 g (50 mL of a 50% solution or 125 mL of a 20% solution) by intravenous infusion over 15 minutes

» Give an infusion of soluble (neutral) insulin and glucose to push potassium intracellularly. [62] [80]
  • Give over 15 minutes
  • Acts within 10 to 20 minutes
  • Lasts 4 to 6 hours.

» Monitor hourly for hypoglycaemia.

consider salbutamol

Treatment recommended for SOME patients in selected patient group

Primary options

» salbutamol inhaled: 10-20 mg inhaled via nebuliser as a single dose

» Consider further adjunctive treatment with nebulised salbutamol to drive potassium intracellularly if necessary. [62]
  • Decide whether this is needed based on the ECG and the rate of rise of serum potassium.[80]
  • Use with caution if there is a history of ischaemic heart disease (a lower dose is recommended), and avoid if there is a history of tachyarrhythmias.[62] [80]
Acute kidney injury

Management

**Acute with severe hyperkalaemia (potassium ≥6.5 mmol/L) OR moderate hyperkalaemia (potassium 6.0 to 6.4 mmol/L) and associated ECG changes**

+ calcium

Treatment recommended for ALL patients in selected patient group

**Primary options**

- **Calcium chloride:** 6.8 mmol (10 mL of a 10% solution) intravenously over 5-10 minutes; may repeat if ECG changes persist; consult local protocols for further guidance on dose

**OR**

- **Calcium gluconate:** 6.8 mmol (30 mL of a 10% solution) intravenously over 5-10 minutes; may repeat if ECG changes persist; consult local protocols for further guidance on dose

**Give immediate intravenous calcium for cardiac protection. [62][80]**

- Give over 5 to 10 minutes, then repeat the ECG and consider a further dose if ECG changes persist.[80]
  - Use a wide bore cannula and avoid extravasation.
  - Ensure cardiac monitoring.
  - Intravenous calcium antagonises the cardiac membrane excitability and so protects the heart against arrhythmias .[110]
  - Effective within 3 minutes and lasts 30 to 60 minutes.
  - **Seek senior advice** if the ECG fails to normalise after one dose .[62]

+ **Insulin/glucose**

Treatment recommended for ALL patients in selected patient group

**Primary options**

- **Insulin neutral:** 10 units by intravenous infusion over 15 minutes
  - **Glucose:** 25 g (50 mL of a 50% solution or 125 mL of a 20% solution) by intravenous infusion over 15 minutes
Acute kidney injury: Management

**Acute**

- Give an infusion of soluble (neutral) insulin and glucose to push potassium intracellularly. \[62\] \[80\]
  - Give over 15 minutes
  - Acts within 10 to 20 minutes
  - Lasts 4 to 6 hours.
- Monitor hourly for hypoglycaemia.

**plus** salbutamol

Treatment recommended for ALL patients in selected patient group

**Primary options**

- **salbutamol inhaled:** 10-20 mg inhaled via nebuliser as a single dose
- Consider further adjunctive treatment with nebulised salbutamol to drive potassium intracellularly if necessary. \[62\]
  - Decide whether this is needed based on the ECG and the rate of rise of serum potassium.\[80\]
  - Use with caution if there is a history of ischaemic heart disease (a lower dose is recommended), and avoid if there is a history of tachyarrhythmias.\[62\] \[80\]

**plus** identify and treat underlying cause of hyperkalaemia

Treatment recommended for ALL patients in selected patient group

- Look for the underlying cause of hyperkalaemia and treat it. \[62\]
  - Review medications that might be responsible (e.g., ACE inhibitors, angiotensin-II receptor antagonists, potassium-sparing diuretics).
  - Treatment of hyperkalaemia only results in a temporary intracellular shift of potassium so the cause of hyperkalaemia must be identified and corrected.\[62\]
Acute kidney injury

Management

• Consult a pharmacist for a full list of medications that can cause hyperkalaemia.

» Hyperkalaemia is a common complication of AKI. It can lead to:
  • Muscle weakness
  • Cardiac arrhythmias (e.g., bradycardia, bundle branch block, ventricular tachycardia, ventricular fibrillation, asystole).

» Check your local protocols – many hospitals have institutional guidelines for managing hyperkalaemia.

» There is no evidence to support the use of loop diuretics for managing AKI-associated hyperkalaemia. [110]

  • However, in practice their use may sometimes be considered by the nephrology team as an adjunct to other therapies provided the patient is fluid replete (but only with close specialist supervision).

Debate: Loop diuretics

The role of loop diuretics in the management of AKI-associated hyperkalaemia remains controversial.

• Loop diuretics may be used under specialist supervision for volume management in patients with AKI and there is a theoretical rationale to suggest they could be beneficial in managing hyperkalaemia. [1]

  • Loop diuretics promote potassium excretion in the urine through their action in inhibiting the Na⁺-K⁺-2Cl⁻ co-transporter on the ascending limb of Henle, thereby reducing uptake of potassium (as well as sodium and chloride).

  • However, the 2014 UK Renal Association guideline on acute hyperkalaemia concluded that there
is no evidence to support the use of diuretics in the management of AKI-associated hyperkalaemia.[110]

- Both the NICE and KDIGO guidelines are clear that loop diuretics should not be used routinely to manage AKI.[1] [3] The use of loop diuretics is indicated (under specialist supervision) only if a patient with AKI-associated hyperkalaemia also has volume overload (which is a clear indication for their use).[3]

- with metabolic acidosis plus seek specialist advice from the renal team

Treatment recommended for ALL patients in selected patient group

- Once any obstruction has been relieved and diuresis is progressing satisfactorily, the renal team will decide whether or not sodium bicarbonate is indicated, based on an assessment of benefits and risks.
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 ischaemic pre-conditioning appeared to hold promise to prevent AKI, but two systematic reviews (including more than 28 randomised controlled trials) cast doubt on the value of the treatment.

Primary prevention

Prevention of contrast-induced AKI

Intravenous iodinated contrast has previously been reported to cause contrast-induced AKI (CI-AKI). However, the association has been questioned more recently by large population studies that have failed to demonstrate this risk. The evidence regarding the prevention of CI-AKI is weak, and often conflicting.

The patient’s kidney function must be measured within 3 months of offering iodinated contrast for non-emergency imaging.

In 2019, the UK National Institute for Health and Care Excellence (NICE) recommendations on preventing CI-AKI were updated. The updated guidance now recommends that you should encourage oral hydration, rather than previously recommended intravenous volume expansion, before and after procedures using intravenous iodinated contrast agents in adults at increased risk of contrast-induced AKI.

Patients at increased risk of CI-AKI include those people with:

- Chronic kidney disease (eGFR <40 mL/min/1.73 m$^2$). Consider temporarily stopping ACE inhibitors and angiotensin-II receptor antagonists if the patient has an eGFR <40 mL/min/1.73 m$^2$.
- Diabetes, but only if the patient has concomitant chronic kidney disease (eGFR <40 mL/min/1.73 m$^2$).
- Heart failure
- Kidney transplant
- Age ≥75 years
- Hypovolaemia
- Increasing volume of iodinated contrast agent
- Intra-arterial administration of contrast agent with first pass kidney exposure (e.g., contrast injected into the left side of the heart or directly into the renal arteries).

However, it is important to stress that risk assessment should not delay emergency imaging. Consider intravenous volume expansion with either isotonic sodium bicarbonate or normal saline (0.9% sodium chloride) for inpatients having iodinated contrast agents if they have particularly high risk factors, including:

- eGFR <30 mL/min/1.73 m$^2$
Acute kidney injury

Management

- Kidney transplant
- Large volume of contrast agent
- Intra-arterial administration of contrast agent.

Discuss patients on renal replacement therapy or with a kidney transplant with the renal team before offering iodinated contrast but do not delay emergency imaging.

Do not use N-acetylcysteine to prevent contrast-induced AKI.[59] [60] [61]

Prevention of perioperative AKI

Identify patient risk factors for AKI prior to surgery, including:

- Sepsis
- Hypovolaemia
- Intraperitoneal surgery
- Chronic kidney disease (eGFR <60 ml/min/1.73 m²)
- Diabetes
- Heart failure
- Age ≥65 years
- Liver disease
- Nephrotoxins (e.g., NSAIDs, aminoglycoside antibiotics such as gentamicin).

Secondary prevention

Patient discussions

Inform the patient if they have an episode of AKI; give information on what the cause was and what measures they can take to avoid a further episode (e.g., avoiding getting dehydrated during an intercurrent illness).

The UK National Institute for Health and Care Excellence (NICE) recommends:[3]

- Involving parents and carers in the discussion if appropriate
- Discussing immediate treatment options, monitoring, and prognosis; and long-term treatment options, monitoring, self-management, and support in collaboration with a multidisciplinary team appropriate to the person’s individual needs
- Providing information to people needing renal replacement therapy after discharge, including what preparation might be needed (such as having a fistula or peritoneal catheter) and the frequency and length of dialysis sessions
- Discussing the risk of developing future AKI, particularly with people who have chronic kidney disease with an eGFR <60 ml/min/1.73 m², or neurological or cognitive impairment or disability, and who may have limited access to fluids.

- Emphasise the risk associated with conditions leading to dehydration (for example, diarrhoea and vomiting) and drugs that can cause or worsen kidney injury (including over-the-counter NSAIDs).
**Monitoring**

If recovery of function is complete and a normal glomerular filtration rate is re-established with no evidence of residual kidney injury, no kidney 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.[226]

The National Kidney Foundation KDOQI guidelines include recommendations regarding the management of patients who have developed CKD subsequent to AKI.[227] Management of chronic intrinsic kidney 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>hyperphosphataemia</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. Haemodialysis 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>
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</tbody>
</table>

| uraemia                       | long term | medium     |
| Uraemic toxins accumulate with severe and untreated kidney failure, resulting in lethargy, confusion, and obtundation. Dialysis is required for management of uraemia. |

| hyperkalaemia                 | variable  | high       |
| Results from impaired excretion of potassium, cell lysis, or tissue breakdown. Severe hyperkalaemia may result in muscle weakness and classic ECG findings of peaked T waves, increased PR interval, widened QRS, atrial arrest, and deterioration to a sine wave pattern. If hyperkalaemia is confirmed or suspected, use normal saline (0.9% sodium chloride) rather than a balanced crystalloid for fluid balance.[222] [63] Treatment depends on the severity and presence of muscular and/or cardiac complications. Check your local protocols - many hospitals have institutional guidelines for managing hyperkalaemia. See the Treatment algorithm section of this topic for information on managing mild, moderate and severe hyperkalaemia. |

| chronic progressive kidney disease | variable  | medium     |
| AKI may leave the patient with prolonged kidney 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 kidney disease that may progress to end-stage kidney disease.[223] [224] Patients with partial or no recovery from AKI are at increased risk for congestive heart failure and acute myocardial infarction.[225] |

| end-stage kidney disease       | variable  | medium     |

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FOLLOW UP

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### Prognosis

Recovery for AKI is variable and depends on cause of injury and the severity and duration of AKI.[213]

There is an independent association of AKI with a higher risk of death.[214] [213] [215] In-hospital mortality rates associated with AKI vary from 6% to 80%, and there is increased long-term mortality in those with AKI surviving hospitalisation.[215]

Up to 6% of patients admitted to the intensive care unit have AKI requiring renal replacement therapy.[20] [213] [216] In hospital, when AKI requires dialysis, mortality exceeds 50%; those with multi-organ failure are at greatest risk.[17] [20] [216] 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).[217]

AKI is irreversible in approximately 5% to 7% of adults and as many as 16% of older adult patients.[218] 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.[219] [220] [221]
## Diagnostic guidelines

### Europe

<table>
<thead>
<tr>
<th>Title</th>
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<td>Acute kidney injury (AKI)</td>
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## Treatment guidelines

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*Last published:* 2012

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**Management of acute kidney injury: core curriculum 2018**

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

**KDOQI US commentary on the 2012 KDIGO clinical practice guideline for acute kidney injury**

*Published by:* The National Kidney Foundation  
*Last published:* 2013
Key articles


• Royal College of Physicians. Acute care toolkit 12: acute kidney injury and intravenous fluid therapy. October 2015 [internet publication]. Full text

References


8. Think Kidneys. Reporting the rate of acute kidney injury (AKI) within England – the current state of the NHS AKI Master Patient Index and Registry. January 2018 [internet publication]. Full text


64. Think Kidneys. Recommended minimum requirements of a care bundle for patients with AKI in hospital. December 2015 [internet publication]. Full text


Acute kidney injury


137. Fritz Z, Slowther AM, Perkins GD. Resuscitation policy should focus on the patient, not the decision. BMJ. 2017 Feb 28;356:j813 Full text Abstract


156. Pendlebury ST, Klaus SP, Mather M, et al. Routine cognitive screening in older patients admitted to acute medicine: abbreviated mental test score (AMTS) and subjective memory complaint versus Montreal Cognitive Assessment and IQCODE. Age Ageing. 2015 Oct 13;44(6):1000-5 Full text Abstract


161. Nova Scotia Health Authority. This is not my Mom. 2012 [internet publication]  Full text


187. National Centre for smoking cessation and training. Smoking cessation and mental health. 2014 [internet publication]. Full text


References


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5-digit numerals: 10,000
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numerals < 1: 0.25

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