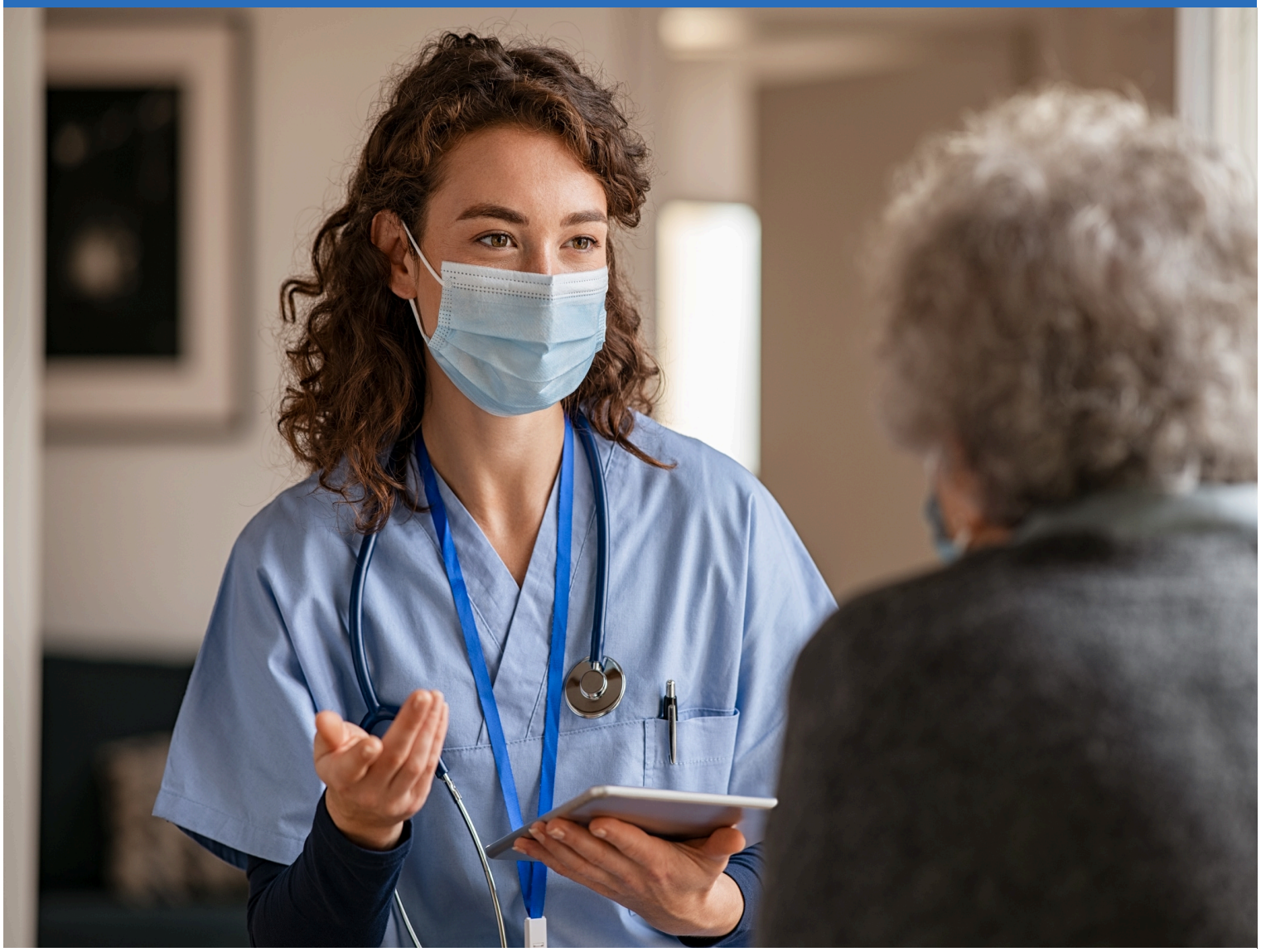
BMJ Best Practice

Acute kidney injury

Straight to the point of care



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Summary

Acute kidney injury (AKI) is commonly associated with sepsis, hypovolaemia, and/or hypotension (pre-kidney AKI and intrinsic AKI); nephrotoxins such as aminoglycoside antibiotics (e.g., gentamicin) and non-steroidal anti-inflammatory drugs (intrinsic AKI); or urinary outflow obstruction (post-kidney AKI). Rarer causes of AKI include vasculitis or interstitial nephritis (intrinsic AKI).

Usually occurs in patients with intercurrent illness, without symptoms or signs specific to the kidneys, and is only identified 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 inappropriate fluid resuscitation (e.g., when excessive fluid is given to patients who are oliguric and/or have heart failure).

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 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. This topic covers acute kidney injury in adults.

THEORY

Epidemiology

The reported incidences of AKI vary, and are confounded by differences in diagnosis, definition criteria, or hospital discharge coding.[6][7] UK Renal Registry data for England showed that in 2018, the unadjusted rate for AKI was 12,300 per million population.[8] [9] AKI is seen in 10% to 20% of people admitted to hospital as emergencies, with an inpatient mortality >20%.[3] [8][10] [11] The overall incidence of AKI in the ICU is higher at 20% to 50% and it is associated with mortality over 50%.[12] [13] 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.[14] 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.[15] Prediction scores have been developed for outcomes of AKI, but have had variable success.[16] [17]

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.[18] [19]

The incidence of contrast nephropathy varies, and there is ongoing uncertainty regarding the causal nature of the association between contrast use and AKI.[20]

US data show that patients with diabetes were hospitalised with AKI at a greater than 2-fold higher rate compared to those without diabetes, and patients with chronic kidney disease (CKD) and diabetes were hospitalised with AKI at a more than 7.5-fold higher rate compared to patients with neither pre-existing condition.[6]

Up to 7% of patients hospitalised with AKI require renal replacement therapy.[21] In the ICU, the mortality rate exceeds 50% in patients with multi-organ failure who require dialysis.[18] [19] [21] Minor rises in creatinine (≥26.5 micromols/L [0.3 mg/dL]) are associated with an increased risk of hospital mortality, increased risk of CKD, 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. Older patients with frailty appear to be at particular risk for AKI.[48]

underlying kidney disease

Associated with increased susceptibility to 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.[50] COVID-19, which is caused by infection with the SARS-CoV-2 virus, is strongly associated with AKI via several proposed pathophysiological mechanisms, some similar to those of non-COVID sepsis.[51]

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

May precede and lead to AKI.[5] [52] [53] [54]

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.[55]

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.[56]

malignant hypertension

Malignant hypertension may cause AKI.[5]

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.[57]

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.[46] Genome-wide searches have found other protective candidates, but much more work is needed to validate these findings.[47]

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.[58] Patients previously taking renin-angiotensin system inhibitors should restart them following an episode of AKI, as there is evidence that they lower risk of death in this group.[59]

proton pump inhibitors

Proton pump inhibitors may increase risk of AKI; however, more studies are needed to clarify this association.[60] [61]

herbal therapy

Case reports suggest that herbs and dietary supplements could potentially contribute to kidney injuries.[62]

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.[38] [39] [40] Risk of contrast-induced AKI increases with intra-arterial administration and with increasing volume of contrast medium.[3]

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] [63]

Aetiology

Aetiology of AKI may be multifactorial, generally classified into pre-kidney, intrinsic, and post-kidney causes.[22]

- 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 usually presents as hypertension and chronic kidney disease but may result in acute tubular necrosis (ATN) and AKI, for example when ACE-inhibitors are prescribed to patients with severe bilateral renal artery stenosis or severe renal artery stenosis of a single functioning kidney.
- 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 reabsorption 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.[23] [24] Hypoxaemia results in increased reactive oxygen species, reduction in available adenosine triphosphate, and cellular dysfunction and death.[25] Additionally, complement system activation, direct neutrophil activation, membrane attack complex activation, cytokines, chemokines, and vasoactive hormones have been studied and may be contributory.[26] [27] [28] [29] [30] [31] [32] [33] [34] 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.[35][36] [37] However, the association with radiocontrast exposure is controversial, as these findings are not replicated in human population studies: use of contrast may be a marker rather than a mediator of risk.[38] [39] [40] [41]

Kidney injury associated with obstruction results from increased intratubular pressure yielding reductions in filtration pressure and potential 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.[42] [43] [44] [45]

There is preliminary evidence that a genetic predisposition for AKI may exist, especially with apolipoprotein E (APO-E) genes.[46] Genome-wide searches have found other protective candidates, but much more work is needed to validate these findings.[47]

Classification

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

Classification based on pathophysiology[5]

- 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] [75]

- 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] [10] [11]

Think **'Could this be sepsis?'** based on acute deterioration in an adult patient in whom there is clinical evidence or strong suspicion of infection.[76] [77] [78]

- Use a systematic approach, alongside your clinical judgement, for assessment; urgently consult a senior clinical decision-maker (e.g., ST4 level doctor in the UK) if you suspect sepsis.[77] [78] [79] [80]
- Refer to local guidelines for the recommended approach at your institution for assessment and management of the patient with suspected sepsis.

Recognise and treat hypovolaemia promptly with an immediate bolus of crystalloid intravenous fluid.[1][14] [75] [81]

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 in the context of hypotension and/or dehydration).[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 identified based on **an acutely rising serum creatinine and/or reduction in urine output**.[1] [4]

- AKI can often be non-oliguric.

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

- 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)[75]
- 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).[14]

Clinical presentation

AKI is often asymptomatic so a high index of suspicion is vital for prompt recognition and treatment.[75]

A relevant history is a key part of the assessment. Check for:

- **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] [10][48] [82]
- **Precipitating insults** to the kidney: the most common causes of AKI are sepsis, nephrotoxins, hypovolaemia, and/or hypotension.[14] [75]

Your examination should prioritise volume statusand 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).[10] [81]

Causes of AKI

Establish the underlying cause of AKI as this will determine the correct treatment and the need for onward referral.[5] [18] [55]

The causes of AKI have traditionally been classified as **pre-kidney** (pre-renal), **intrinsic**, and **post-kidney** (post-renal):[5] [22]

- **Pre-kidney AKI**(80% of cases) is usually due to hypovolaemia and/or hypotension:[1] [3] [10] [51] [75][83]
    - 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:[10] [18] [19][75]
    - 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 Primary prevention for information about preventing AKI.
    - Rare causes (e.g., vasculitis, glomerulonephritis).
- **Post-kidney AKI**is due to obstruction:[10] [75]
    - 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] [14] [75][81] [82]
- Also request liver function tests, C-reactive protein, full blood count, and blood cultures if infection suspected.

- **Urinalysis** [3] [10] [75] [81]
  - 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] [14] [81]
  - 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.[14] [81]

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.[75]

- Kidney function often does not return to the baseline level after recovery from AKI, especially if the patient has pre-existing CKD.[84]

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] [75]

- AKI occurs in 10% to 20% of emergency admissions and has an inpatient mortality >20% (>35% in stage 3 AKI).[3] [10] [11]

Measure serum creatinine to check for AKI whenever an acutely ill patient meets one or more of the following criteria: [3] [10] [75]

- Age ≥ 65 years (frail older people are at particular increased risk)[48] [82]
- History of any one or more of CKD, heart failure, liver disease, diabetes, dementia
- Previous AKI episode
- Exposure within the previous week to:
  - Any nephrotoxin (e.g., NSAID, aminoglycoside antibiotic)
  - Iodinated contrast agent
  - Renin-angiotensin-system modifying agent (e.g., ACE inhibitor/angiotensin-II receptor antagonist) and/or diuretic, especially if hypovolaemic or hypotensive

- 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).[75]
- 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 often presents 'silently' so a high index of suspicion is important, particularly in acutely ill patients. [75]

- Most patients with AKI present asymptomatically, 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 recognition of AKI in 43% of patientswho died in hospital with the condition.[85]

Definition of AKI

AKI is identified 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.[10]
    - 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 significantly increased mortality [1] [75]

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

- 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 corresponds to the level when the patient was most recently in a clinically stable condition; often this is considered the lowest creatinine reading within the last 3 months (the UK Royal College of Physicians also recommends using the lowest reading within the last 7 days, if available). [75]

- 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.[14]

Practical tip

You may work in an institution with a laboratory-based automated AKI warning system that is based on serum creatinine results.

- The UK NHS England AKI algorithm compares a patient's current creatinine value to their baseline level, using the lowest value within the last 7 days as baseline creatinine, where available. If there is no creatinine value available from that period, it uses a median value over the previous 12 months.[86]
- This AKI warning system is mandated by laboratories in England and Wales across both primary and secondary care, whereby an AKI warning alert is triggered by rises in serum creatinine.

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.
- 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] [87]

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:[10] [75]
  - Hypocalcaemia
  - Hyperphosphataemia and hyperparathyroidism
  - Anaemia
  - Small kidneys on ultrasound (sometimes scarred) - suggestive of advanced CKD.
  - If the patient is acutely unwell or hypovolaemic, this points towards AKI.[10]
- These features can be remembered using the **ABCS** mnemonic: **A**naemia, **B**one chemistry [abnormal], **C**linical tolerance of uraemia, **S**mall kidneys.
- Repeat blood testing along with reference to historical creatinine values is the key to confirming or ruling out AKI.
- Remember that pre-existing CKD is a risk factor for AKI.

Practical tip

Beware false positive rises in creatinine, for example: [1] [10]

- Recent use of trimethoprim can lead to a rise in serum creatinine that does not reflect any change in glomerular filtration rate (most commonly in patients with pre-existing CKD)
- 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] [88] [89]

- 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 and replaced the earlier RIFLE (Risk, Injury, Failure, Loss of kidney function, and End stage kidney disease) and AKIN (Acute Kidney Injury Network) definitions.[88] [89]

Stage the AKI using whichever one of serum creatinine or urine output gives the higher stage. [1] [14]

A higher stage of AKI is associated with a greater risk of death as well as increased likelihood of needing RRT. [14]

AKI Stage [1] [75]	Serum creatinine (SCr) criteria*	Urine output criteria
Stage 1	• SCr rise of ≥26 micromol/L within 48 hours **or** • SCr increase to 1.5 to 1.9 times baseline	• <0.5 mL/kg/h for at least 6 consecutive hours
Stage 2	• SCr increase to 2 to 2.9 times baseline	• <0.5 mL/kg/h for at least 12 consecutive hours
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)	• <0.3 mL/kg/h for at least 24 consecutive hours **or** • Anuria for 12 hours
**Baseline SCr is the lowest level in the last 7 days or, if not available, the lowest within the previous 3 months.*		

AKI staging criteria

More info: 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] [10] [11]
- Even relatively minor changes in serum creatinine levels are associated with a significant increase in mortality.[75]
- 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.

Causes of AKI

AKI can be classified as pre-kidney (or pre-renal), intrinsic, or post-kidney (post-renal). [5] [22]

- In practice, AKI is often multi-factorial.[82]

- **AKI is not a diagnosis.** It is important to establish the underlying cause of AKI, as this will help determine the patient's underlying diagnoses and guide treatment.

The most common causes of AKI are: [10] [75]

- **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, e.g., NSAIDs (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. [1] [5] [14][18][55]

- 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] [75]

- 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 exacerbated by 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: [10] [75]

- Prolonged pre-kidney AKI leading to acute tubular injury (the most common cause)
- Nephrotoxins (e.g., aminoglycoside antibiotics, NSAIDs) - see Primary prevention for information on preventing AKI
- Tubulointerstitial nephritis (e.g., triggered by infection or medication, such as proton pump inhibitors [PPIs] or antibiotics)
- Acute glomerulonephritis (e.g., post-infectious glomerulonephritis)
- Vasculitis (e.g., anti-neutrophil cytoplasmic antibodies [ANCA]-associated vasculitis)
- Haemoglobinuria
- Microangiopathy (e.g., accelerated hypertension, haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura)
- Rhabdomyolysis
- Multiple myeloma.[5] [63]

3. Post-kidney AKI (5%-10%)

Post-kidney AKI is secondary to urinary outflow obstruction. Causes include: [10] [75]

- Prostatic hyperplasia
- Kidney stones (bilateral or in a single kidney)
- Retroperitoneal fibrosis (which can be associated with malignancy, e.g., lymphoma)[90]
- Papillary necrosis (flank pain and haematuria, e.g., associated with NSAIDs)
- Tumour (e.g., cervical, prostate).[82]

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: [10] [18] [19] [85]

- **Risk factors** [3] [10]
  - Age ≥65 years (frail older people are at particular increased risk).[48] [82]
  - 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.
- **Precipitating factors** [1] [3] [10] [75]
  - 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).
- 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.[81] [55] See Primary prevention for information about preventing AKI.

- **Medication history** [3] [10] [75]
  - NSAID or aminoglycoside antibiotic use (nephrotoxic potential - can cause drug-induced interstitial nephritis).[1]
  - ACE inhibitor/angiotensin-II receptor antagonist, in the context of hypotension and/or dehydration.
    - 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.[10]
  - 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).[91]
  - 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.[75]

- **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.
- **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: [10] [81]

- **Fever, rash, and/or joint pain**
  - 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: [10] [81]

- **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)[14] [82]
  - Acute pericarditis is a complication associated with severe AKI and worsening uraemia.[14] [82]
  - 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] [14]
  - **Asterixis** is another possible sign of uraemia. This is a negative myoclonus, detected by extending the arms, dorsiflexing the wrist, and spreading the fingers (flapping tremor).

Think **'Could this be sepsis?'** based on acute deterioration in an adult patient in whom there is clinical evidence or strong suspicion of infection.[76] [77] [78]

- Use a systematic approach, alongside your clinical judgement, for assessment; urgently consult a senior clinical decision-maker (e.g., ST4 level doctor in the UK) if you suspect sepsis.[77] [78] [79] [80]
- Refer to local guidelines for the recommended approach at your institution for assessment and management of the patient with suspected sepsis.
- See Sepsis in adults .

Clinical findings that may support a specific underlying diagnosis include: [81]

- **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)[10] [19] [92] [93]
- **Hypotension**(pre-kidney or intrinsic AKI)[10]
  - 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).[81]

Investigations

Baseline bloods and urine analysis

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

Baseline bloods [1] [14][75][81] [82]

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.** [75] [94]
  - 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).[14]

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 metabolic acidosis.
- Venous blood gases can help with further evaluation of acidosis.

Also request: [14] [81]

- **Liver function tests** (will aid diagnosis of hepatorenal syndrome)[75]
  - Often abnormal in clinical scenarios consistent with presence of AKI (e.g., circulatory failure causing pre-renal AKI and ischaemic hepatitis, infections, drug toxicity); concomitant AKI and liver failure confers a poor prognosis.[95]
  - Aids diagnosis of hepatorenal syndrome.[75]
- **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]
- Anaemia can occur in AKI secondary to haemolytic uraemic syndrome, myeloma, or vasculitis, or may occur in AKI secondary to the underlying cause (e.g., gastrointestinal haemorrhage).

- **Blood cultures -** if infection is suspected
- **Serum creatine kinase** - if rhabdomyolysis is suspected.

Practical tip

Do not use the urea:creatinine ratio as an indicator of the cause of AKI. [96]
- An elevated urea: creatinine ratio can occur in AKI.[14] 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.[14]

Urine analysis [1] [3] [75] [81]

Perform urine dipstick testing for specific gravity, blood, protein, leucocytes, nitrites, and glucose as soon as AKI is suspected or confirmed.

- Use a clean-catch specimen.

Consider the possibility of intrinsic AKI especially 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] [10] [81]

- 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.[81]

Start urine output monitoring (hourly if catheterised, 4-hourly if not).[81]

- **Routine urinary catheterisation is not appropriate** in patients with AKI. Carefully weigh up the benefits against the risks for the individual patient.[81]
  - 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.[14]

- 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 (typically <0.2%), some cases of obstruction, and even acute tubular necrosis (if tubular function remains intact).[97]
- **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 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] [98]
- 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.[98]

Urine microscopy can be useful if there is a finding of blood and protein on urinalysis. [14]

- 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.[99]

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.[100] The test is dependent on the expertise of the microscopist.
- It has a negative predictive value of >90% for patients with AKI so may be useful in excluding the disease process.[101]
- Eosinophiluria is not specific to interstitial nephritis and may be seen with atheroembolic disease as well.
- Some guidelines (e.g., American Association for Clinical Chemistry) advise against the routine use of urinary eosinophils in the evaluation of AKI.[97]

Practical tip

- All the urine investigations above, if available, can aid the identification 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.[14] [102]

Other initial tests

Request a chest x-ray. [82] **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] [81]

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] [14]

- 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] [81]
- 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).[14]
- **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. [14] [75]

- 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.[14]

Consider requesting a CT or MRI if obstruction is suggested on ultrasound (e.g., possible masses or stones). [14]

- 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: [14] [81]

- **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 electrophoresis with serum free light chain assay or urinary Bence Jones protein (myeloma).[103]
        - 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.[10] [81]
        - Serum electrophoresis will show a paraprotein (monoclonal immunoglobulin), with monoclonal excess of light chains in serum or urine.
    - 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-infectious 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 . [10] [75]

- 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.[10]

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 . [10] [81] **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] [14][75][81]

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: [10] [18] [19] [85]

- **Risk factors** [3] [10]
  - Age ≥65 years (frail older people are at particular increased risk).[82] [48]
  - 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.

- **Medication history** [3] [10] [75]
  - 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, in the context of hypovolaemia or hypotension.
    - 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.[10]
  - 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).[91]
  - Recreational drug use.
  - Over-the-counter drugs and herbal remedies.

Practical tip

AKI often presents 'silently' so a high index of suspicion is important, particularly in acutely ill patients. [75]

- Most patients with AKI present asymptomatically, 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 recognition of AKI in 43% of patients who died in hospital with the condition.[85]

kidney insults (common)

Many cases of AKI are precipitated by a kidney insult, particularly in patients with underlying risk factors. Examples include:[1] [3] [10] [75] [105]

- Sepsis or other acute illness (e.g., acute pancreatitis, burns, severe COVID-19)

- **Perform a septic screen** and implement your local **care bundle (e.g., Sepsis Six)**if infection is suspected.[10]

- Hypovolaemia (with or without hypotension)
- Nephrotoxins
  - 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.[81] [55]

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 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] [14]
  - 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)**.[14]

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

- Routine catheterisation is not recommended.[1] [87]

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 (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 inappropriate fluid resuscitation (for example, when excessive fluid is given to patients who are oliguric and/or have heart failure).[1] [14]

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).[81]

vomiting/nausea (uncommon)

Vomiting may cause pre-kidney AKI or can be a later manifestation of AKI-related uraemia. [75]

fever, rash, and/or arthralgia (uncommon)

If present, suspect small-vessel vasculitis (e.g., granulomatosis with polyangiitis, microscopic polyangiitis), or interstitial nephritis. [81]

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. [14] [81] [82]

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. [10] [19] [92] [93]

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. [14]

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). [14] [82]

- 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] [14]
- **Asterixis** is another possible sign of uraemia (negative myoclonus, detected by extending the arms, dorsiflexing the wrist, and spreading the fingers [flapping tremor]).

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). [81]

abdominal bruit (uncommon)

Suspect renovascular disease.

Investigations

1st test to order

Test	Result

basic metabolic profile (including urea and creatinine and liver function tests)
Creatinine for AKI diagnosis
AKI is often asymptomatic so is easily missed. [75]
• An acutely rising creatinine may be the only sign.
• **Rises in creatinine are delayed** for approximately 24 hours following kidney injury.
Measure serum creatinine to check for AKI whenever an acutely ill patient meets one or more of the following criteria: [3] [10] [75]
• Age ≥65 years (frail older people are at particular increased risk).[48] [82]
• History of any one or more of chronic kidney disease (CKD), heart failure, liver disease, diabetes, dementia
• Previous AKI episode
• Exposure within the previous week to:
  • Any nephrotoxin (e.g., non-steroidal anti-inflammatory drug [NSAID], aminoglycoside antibiotic)
  • Iodinated contrast agent
  • Renin-angiotensin-system modifying agent (e.g., ACE inhibitor/angiotensin-II receptor antagonist) and/or diuretic, especially if hypovolaemic or hypotensive.
• Symptoms or history of urological obstruction
• Suspected or confirmed sepsis
• Hypovolaemia (with or without hypotension) - may be related to dehydration or over-diuresis[10]
• Hypotension (SBP <90 mmHg or a fall of >40mmHg from baseline BP)
• Oliguria (urine output <0.5ml/kg/hour)
• Acute rise in early warning score (e.g., NEWS2 >5).
AKI is identified based on an acute rise in serum creatinine and/or a sustained reduction in urine output. [1]
Baseline serum creatinine corresponds to the level when a patient was most recently in a clinically stable condition; often this is considered the lowest creatinine reading within the last 3 months (the UK Royal College of Physicians also recommends using the lowest reading within the last 7 days, if available).[75]
	• acutely elevated serum creatinine, high serum potassium, metabolic acidosis
	• confirm AKI if there is: [1] [3] [4]
	  • a rise in serum creatinine of ≥26 micromol/L (≥0.3 mg/dL) within 48 hours
	  OR
	  • a rise in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the past 7 days
	• LFTs will be deranged in hepatorenal syndrome

Test	Result
• If no recent creatinine value is available, provided the patient does not have CKD it is reasonable to assume that creatinine levels will have been stable for some time, so thata 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.[14]	

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:[10] [75]
  - Hypocalcaemia
  - Hyperphosphataemia and hyperparathyroidism
  - Anaemia
  - Small kidneys on ultrasound (sometimes scarred) - suggestive of advanced CKD.
  - If the patient is acutely unwell or hypovolaemic, this points towards AKI.[10]
- These features can be remembered using the **ABCS** mnemonic: **A**naemia, **B**one chemistry [abnormal], **C**linical tolerance of uraemia, **S**mall kidneys.
- Repeat blood testing along with reference to historical creatinine values is the key to confirming or ruling out AKI.
- Remember that pre-existing CKD is a risk factor for AKI.

Practical tip

Beware false positive rises in creatinine, for example: [1] [10]

- Recent use of trimethoprim can lead to a rise in serum creatinine that does not reflect any change in glomerular filtration rate (most commonly in patients with pre-existing CKD).
- Serum creatinine falls during pregnancy so a rise in creatinine after recent delivery may be a false positive.

Test	Result

Creatinine for AKI staging

Stage the AKI using whichever one of serum creatinine or urine output gives the higher stage. [1] [14]

- A higher stage of AKI is associated with a greater risk of death as well as increased likelihood of needing renal replacement therapy (RRT).[14]

For any hospital inpatient with AKI, ensure daily monitoring of urea and electrolytes until the AKI has resolved, as indicated by: [14]

- A return to actual or presumed baseline kidney function

or

- The establishment of steady state kidney function.

AKI Stage [1] [75]	Serum creatinine (SCr) criteria*
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.*	

Test	Result
AKI staging criteria **More info: 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] [10] [11] • Even relatively minor changes in serum creatinine levels are associated with a significant increase in mortality.[75] • 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. **LFTs** Often abnormal in clinical scenarios consistent with presence of AKI (e.g., circulatory failure causing pre-renal AKI and ischaemic hepatitis, infections, drug toxicity); concomitant AKI and liver disease confers a poor prognosis. Aids diagnosis of hepatorenal syndrome.[75]	
serum potassium **Ensure close monitoring of serum potassium.** [75] [94] • Hyperkalaemia is a common complication of AKI. • Urgent treatment is required if potassium >6.0 mmol/L and/or ECG changes are seen.	elevated in hyperkalaemia • 5.5 to 5.9 mmol/L indicates mild hyperkalaemia • 6.0 to 6.4 mmol/L indicates moderate hyperkalaemia • ≥6.5 mmol/L indicates severe hyperkalaemia
FBC **Leukocytosis may suggest infection.** • High or low WBC can occur with sepsis. If platelets are low, request a blood film and lactate dehydrogenase:[75] • 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, or may occur in AKI secondary to the underlying cause (e.g., gastrointestinal haemorrhage).	anaemia, leukocytosis, thrombocytopenia

Test	Result
bicarbonate **Request bicarbonate if it is not part of the standard panel.** [75] [81] [82] • Alternatively, if previously taken bloods indicate AKI and bicarbonate was not included, request a **venous blood gas**. • Venous blood gases can help with further evaluation of acidosis.	low bicarbonate suggests metabolic acidosis
C-reactive protein **Request in all patients.** [81] [82]	elevated in infection and also in vasculitis
blood culture **Request if infection is suspected.** [75][81] **Sepsis is a common cause of AKI.** [10] • Perform a septic screen and implement your local care bundle (e.g., Sepsis Six) if infection is suspected.	positive for bacterial pathogen
urinalysis **Perform urine dipstick testing for specific gravity, blood, protein, leucocytes, nitrites, and glucose as soon as AKI is suspected or confirmed.** [3] [75] • Use a clean-catch specimen. Consider the possibility of intrinsic AKI especially 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).[3] [10] [81] • 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 then the absence of catheter trauma or UTI should raise concerns about glomerular disease.	RBCs, WBCs, cellular casts, proteinuria, positive nitrite, and leukocyte esterase

Test	Result
• Other causes of an active urinary sediment (dysmorphic red cells and red cell casts) include infection, tumours, calculi, venous thrombosis, myoglobinuria (rhabdomyolysis).	
urine culture Send urine culture if clinical features of urinary tract infection are present and/or urinalysis is positive for blood, protein, leukocytes, or nitrites.[81]	bacterial growth with antibiotic sensitivity
urine output monitoring **Start urine output monitoring in any patient with AKI (hourly if catheterised, 4-hourly if not).** [81] • In practice, accurate monitoring can be difficult if the patient is not catheterised. • **Routine urinary catheterisation is not appropriate** in patients with AKI. Carefully weigh up the benefits against the risks for the individual patient.[81] • Potential benefits: • 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] • 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	• confirm AKI if urine output <0.5 ml/kg/hour for at least 6 consecutive hours (at least 8 hours in children/young people) • if catheterisation is considered appropriate: • significant urine volume released after catheter placement points to bladder outlet obstruction • minimal residual urine after catheter placement suggests a non-obstructive cause of AKI or higher level urinary tract obstruction

DIAGNOSIS

Test	Result
• If bladder neck obstruction is suspected and cannot be quickly ruled out by ultrasound.	
fluid challenge **A good response to a fluid challenge supports a diagnosis of pre-kidney AKI.**	kidney function improves rapidly in pre-kidney AKI
venous blood gases **Can be requested to assess acid/base status.** • An anion gap acidosis is seen in AKI due to impaired excretion of non-volatile acids.	an anion gap acidosis occurs in a number of different scenarios
CXR **Request a chest x-ray.** [82] **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.	may show signs of infection, fluid, cardiomegaly, or haemorrhage
ECG **An ECG is important to assess for hyperkalaemia.** • Hyperkalaemia is a common complication of AKI.	ECG changes associated with hyperkalaemia: peaked T waves, increased PR interval, widened QRS, atrial arrest, and deterioration to a sine wave pattern

Other tests to consider

Test	Result

renal tract ultrasound
 	
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] [14] [81]
 	
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] [14]
 	
• 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] [81]
• 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).[14]
• **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.[75] [14]
 	
• Be aware that an ultrasound finding consistent with CKD does not exclude the possibility of AKI on a background of CKD.[14]
	• presence of dilated renal calyces suggests obstruction and hydronephrosis
	• normal kidney size in the setting of AKI and unclear cause and positive serology suggests a rarer cause
	• reduced corticomedullary differentiation and/or small and scarred kidneys is consistent with CKD
	• may demonstrate small (sometimes scarred) kidneys consistent with advanced CKD (such changes are unlikely to be seen in less severe CKD)

abdominal CT or MRI scan **Consider requesting a CT or MRI If obstruction is suggested on ultrasound (e.g., possible masses or stones).** [14] • 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).	image of mass or stone may be present
nuclear renal flow scan **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.** [14]	normal scan reveals appropriate kidney perfusion, tracer uptake, and excretion

DIAGNOSIS

Test	Result
• The scan is performed before and after a dose of loop diuretic.	abnormal scan may demonstrate: • impaired tracer excretion (supportive of acute tubular necrosis) • poor blood flow (supportive of obstruction of blood supply) • normal blood flow and tracer excretion with tracer accumulation in the collecting system (supportive of obstruction of the urine outflow tract)
urine osmolality **Urine osmolality is rarely requested.** [14] • 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 suggests pre-kidney AKI with preservation of tubule function (assuming no recent administration of iodinated contrast).[1] [98] • 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] • Low urine osmolality suggests tubule damage (intrinsic AKI) as urinary concentration is impaired.[98]	• urine osmolality >500 mOsm/kg (in the absence of recent administration of iodinated contrast) suggests pre-kidney AKI with preservation of tubule function • urine osmolality <300 mOsm/kg suggests tubule damage
urine sodium concentration **In pre-kidney AKI the urinary sodium is typically low.** [14] • This is dependent on preserved tubule function. **Urinary sodium is raised in intrinsic AKI when there is tubule damage, or in response to diuretics.**	urinary sodium <20 mmol/L suggests avid sodium retention in pre-kidney AKI
fractional excretion of sodium/urea	• a fractional excretion of sodium (FENa) of <1% supports pre-kidney AKI, as long as tubular function remains intact

Test	Result
	• invalid if the patient has received diuretics • typically <0.2% in hepatorenal syndrome[97] • a fractional excretion of urea of <35% supports a diagnosis of pre-kidney AKI
urinary eosinophil count **Urinary eosinophil counts may be of some use in patients with pyuria.** [14] [100] • The test is dependent on the expertise of the microscopist. • Eosinophiluria is not specific to interstitial nephritis and may be seen with atheroembolic disease as well. • Some guidelines (e.g., American Association for Clinical Chemistry) advise against the routine use of urinary eosinophils in the evaluation of AKI.[97]	• >5% to 7% supports a diagnosis of acute interstitial nephritis but is not diagnostic because of low sensitivity and specificity[100] • has a negative predictive value of >90% for patients with AKI so may be useful in excluding the disease process[101]
serum creatine kinase **Request if rhabdomyolysis is suspected.** [14] [75][81]	markedly elevated in rhabdomyolysis
ANA (anti-nuclear antibodies) **A broad screening test for a range of autoimmune diseases (e.g., kidney manifestations of systemic lupus erythematosus [SLE]).**[14] [81] [82]	normal or elevated
anti-dsDNA **Elevated titre supports the diagnosis of SLE, which often includes the kidney.** [14] [81] [82]	normal or elevated
complement (C3, C4, CH50) **Low complement levels support an active disease process such as SLE.** [14] [81] [82] • Reduced levels are also seen in infectious endocarditis.	normal or depressed
anti-glomerular basement membrane antibody **Elevated in anti-glomerular basement membrane antibody disease and Goodpasture syndrome.** [14] [81] [82]	normal or elevated

Test	Result
anti-neutrophil cytoplasmic antibodies (ANCA) **Elevated titres are seen in small vessel vasculitic syndromes such as:** [14] [81] [82] • Granulomatosis with polyangiitis • Eosinophilic polyangiitis • Microscopic polyangiitis.	normal or elevated titres
acute hepatitis profile **Positive serology in active hepatitis B or C is associated with kidney conditions such as membranoproliferative glomerulonephritis and cryoglobulinaemia.**	positive or negative serology
HIV serology **Relevant with regard to HIV-associated nephropathy and nephrotoxicity of some of the medications used to manage HIV.**	positive or negative
cryoglobulins **The presence of cryoglobulins in a patient with AKI supports a diagnosis of cryoglobulin-associated glomerulonephritis.**	positive or negative serology
anti-streptolysin-O antibody **An elevated titre supports but is not diagnostic of post-infectious glomerulonephritis as the cause of AKI.**[14]	normal or elevated
serum/urine electrophoresis **Myeloma is an important potential cause of AKI and should be considered in a patient aged >40 years who presents with hypercalcaemia, hyperuricaemia, or pathological fracture.** [10] [81] [82] • Serum electrophoresis will show a paraprotein (monoclonal immunoglobulin), with monoclonal excess of light chains in serum or urine.[103]	• paraprotein identified on serum electrophoresis • serum free light chains (sFLC) or urinary Bence Jones detected
cystoscopy **May be requested to identify cause of obstruction (e.g., ureteric stenosis, bladder tumour).**	direct visualisation and treatment of ureteral stenosis if present
kidney biopsy **Kidney biopsy may be required to further investigate positive serological studies and confirm the cause of AKI.** [14]	changes associated with rarer forms of intrinsic AKI

Emerging tests

Test	Result
novel serum and urinary biomarkers Various novel serum and urinary biomarkers have been studied in the earlier identification of AKI and as predictors of mortality after AKI.[106] [107] [108] [109] More robust studies are required to determine the role of the biomarkers.[110] [111] [112] [113] [114]	not in current clinical use

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Chronic kidney disease	• Reduced kidney function with elevation of creatinine is chronic (>3 months), although there may be acute on chronic kidney disease.	• 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.[10] [75] • 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.
Increased muscle mass	• Any elevation of creatinine is minor and typically non-acute.	• 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.

Condition	Differentiating signs / symptoms	Differentiating tests
Drug side effect	• Certain medicines such as cimetidine or trimethoprim may lead to an elevation of creatinine that is minor and non-acute (most commonly in patients with pre-existing CKD).	• 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.

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

Detect AKI, in line with KDIGO and previous 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.

Recommendations

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**.[14]

Use a simple care bundle - a number are available; **STOP AKI** is one option:[75] [81]

- **Sepsis** - perform an urgent septic screen and implement your local care bundle (e.g., Sepsis Six) within 1 hour if infection is suspected. See Sepsis in adults .
- **Toxins** - identify and stop (or avoid exposure to):[1] [14]
  - Nephrotoxic drugs (e.g., non-steroidal anti-inflammatory drugs [NSAIDs], aminoglycoside antibiotics)[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).[75] [82]
  - Withhold drugs that may exacerbate AKI, particularly ACE inhibitors or angiotensin-II receptor antagonists if hypotension and/or dehydration are present.
  - 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.[14] [81]
  - Avoid inappropriate fluid resuscitation (e.g., when excessive fluid is given to patients who are oliguric and/or have heart failure).

Refer the following life-threatening complications for emergency renal replacement therapy (RRT): [14] [81]

- **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] [75]

In most patients, successful management consists of:[1] [14] [75][81] [82]

- **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. [75] **Do refer** if there is:[3] [81]

- **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] [14] [75][81]
- 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.[75] [115]

If the patient is volume overloaded, consider the need for a loop diuretic or RRT - consult the nephrology team.[1] [14]

- Use loop diuretics with caution in patients with AKI. Seek input from renal or heart failure teams if necessary, but do not delay initiation of loop diuretics in patients who are clearly volume overloaded (especially in the presence of pulmonary oedema).

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.[14]

- A **key principle is to correct the haemodynamic status** of the patient to improve kidney perfusion.[75] [81]

Specific **management of intrinsic AKI**depends on the aetiology and is led by the nephrology team so early referral is important.[75] For example:

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

In **obstructive AKI** relief of the obstruction is key.[10] [81]

- Insert a bladder catheterif 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/polymer (e.g., calcium polystyrene sulfonate, sodium zirconium cyclosilicate, patiromer)
- Withholding culprit medications especially in the presence of hypotension and/or dehydration (e.g., ACE inhibitor, angiotensin-II receptor antagonist, potassium-sparing diuretics)
- RRT (also referred to as kidney replacement therapy [KRT] in some regions) 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 and/or ionised hypocalcaemia).

- **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**:[75] [81]

- **Sit the patient upright**
- Give **high-flow oxygen** and intravenous **glyceryl trinitrate**
- Seek **senior support**
- A **loop diuretic** should be used to manage associated volume overload

- Use with caution in patients with AKI and seek input from renal or heart failure teams if necessary, but do not delay initiation of loop diuretics in patients who are clearly volume overloaded (especially in the presence of pulmonary oedema)

- Never allow these holding measures to delay initiation of RRT if indicated.[14]

Full Recommendations

Principles for managing AKI

Determine the cause and severity of AKI when formulating your management plan for the patient. [1] [75]

- 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] [14] [75][81] [82]

- **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.[3]

- **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] [14] [81]

In rarer forms of intrinsic AKI, more specific management interventions will be needed. [14]

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: [75]

- **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).[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 and avoid inappropriate fluid resuscitation (e.g., when excessive fluid is given to patients who are oliguric and/or have heart failure).

Practical tip

Think **'Could this be sepsis?'** based on acute deterioration in an adult patient in whom there is clinical evidence or strong suspicion of infection.[76] [77] [78]

- Use a systematic approach, alongside your clinical judgement, for assessment; urgently consult a senior clinical decision-maker (e.g., ST4 level doctor in the UK) if you suspect sepsis.[77] [78] [79] [80]
- Refer to local guidelines for the recommended approach at your institution for assessment and management of the patient with suspected sepsis.
- See Sepsis in adults .

Specialist referral

Most patients with AKI do not need referral to nephrology. [75]

- Do not refer if there is a clear cause and the AKI is responding to medical management.[3] [116] [117]

Refer immediately to critical care and/or nephrology if:

- The patient meets (or is anticipated to meet) the criteria for RRT[3] [81]
- There are severe complications that cannot be managed medically (such as hyperkalaemia, pulmonary oedema, acidosis, or uraemia)[81]
- The patient remains haemodynamically unstable after appropriate supportive care and/or there are signs of multi-organ failure.[81]

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] [81]

- 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 reduce in-hospital mortality, the number of patients needing RRT, and length of hospital stay.[118]

Volume status monitoring and management

An assessment of the patient's volume status is a crucial part of your initial examination. [1] [14] [75][81]

- 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.[75] [81]

Look for signs of hypovolaemia. Your assessment should cover: [14] [75]

- 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: [81]

- 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: [14] [81]

- 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.[81] 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.

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] [14] [75][81]

- 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] [14] [75][81]
- A smaller bolus (e.g., 250 mL) may be more appropriate if the patient has a history of cardiac failure.[82]

Use a balanced crystalloid unless hyperkalaemia is suspected or confirmed. [75] [82]

- 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 hyperchloraemic metabolic acidosis associated with excessive use of normal saline.[75]

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.[14]
- Reassess the patient's response to each fluid challenge through careful clinical examination (ABCDE approach) and monitoring of:[115]
    - 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.** [75] [115]
    - 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.[75]

- 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.

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. [75] [115]

- 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.[14] [115]

Practical tip

Passive leg raising can help predict fluid responsiveness in critically ill patients. [14] [75]

- 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.[75]
- 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**:[119]
  - **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] [14] [75][115]

- 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] [14] [81]
- 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] [14]
- Do not use low-dose dopamine to treat AKI.[1] [3] [14]
    - 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. [14]

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.[120]
- 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.[121]
    - A post-hoc analysis of the same RCT used the RIFLE criteria for AKI to compare the effects of vasopressin versus noradrenaline.[122] Vasopressin was associated with a trend to a lower rate of progression of the AKI, and a lower rate of use of RRT. The study pre-dated publication of the 2012 KDIGO criteria.
    - 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.** [14]
    - 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.[123]
        - 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.[75] 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.[14]
- Management of volume overload may include:
    - **Sodium and fluid restriction**
    - **Cautious use of a loop diuretic** [1] [14]
    - **RRT -**immediate RRT is indicated for refractory volume overload or volume overload associated with severe complications of AKI.[14] [75][81] For more details, see the section further down on *Indications for RRT*.

Consider a loop diuretic to treat volume overload.[1] [14]

- A loop diuretic such as **furosemide may be useful in achieving euvolaemia in a patient with fluid overload** (with or without pulmonary oedema).[1]
    - Use loop diuretics with caution and seek input from renal or heart failure teams if necessary, but do not delay initiation of loop diuretics in patients who are clearly volume overloaded (especially in the presence of pulmonary oedema).
    - 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] [14]
    - 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.
    - **Proceed without delay to more definitive management with RR T** if the response to diuretics is unsuccessful.[81]

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 used with caution.

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] [14]
    - 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.[124] [125]
    - 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.[126] [127]
    - Prophylactic furosemide has been shown to increase the risk of AKI when given to prevent AKI in patients having cardiac surgery.[128]
- Loop diuretics may be a useful adjunct (with specialist supervision) for the treatment of chronic hyperkalaemia in patients who are non-oliguric and volume replete.[94]

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. [14] [81] [82]

- 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.[10]
- 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. [14] [81]

- 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. Common and important examples include insulin, opioids, digoxin, and gabapentin (though all drug doses should be reviewed). Consult a drug formulary or with a pharmacist, if required.
- Inappropriate drug dosing in patients with AKI is an important cause of adverse drug events.[14]

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[14]
- 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[115]
    - 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.[14]

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. [14]

- 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).[75] [81]

Intrinsic AKI

Specific management of intrinsic AKI depends on the aetiology and is led by the nephrology team. [75]

- 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.
- **Atypical haemolytic uraemic syndrome (HUS)** is treated with the monoclonal antibody eculizumab or plasma exchange.[129] [130]
- **Thrombotic thrombocytopenic purpura (TTP)** is treated with plasma exchange.[131]

- **Acute allergic interstitial nephritis** is treated with a corticosteroid (after excluding infection) and stopping potential causative medications (e.g., proton-pump inhibitors, NSAIDs, antibiotics).[132]

Obstructive AKI

Relief of the obstruction is key in the management of obstructive AKI. [10] [81]

- **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] [81]

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. [81]

- 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 [75]

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).

Treatment depends on the severity and presence of muscular and/or cardiac complications. The principles of treatment are: [94]

- **Immediate cardiac protection** with intravenous calcium chloride or calcium gluconate
- **Adjunctive therapy to drive potassium intracellularly**
    - Intravenous insulin/glucose, ensuring blood sugars are monitored to avoid hypoglycaemia
    - Nebulised salbutamol as adjuvant therapy
- **Removal of potassium from the body**
    - Cation-exchange resins/polymers (e.g., calcium polystyrene sulfonate, sodium zirconium cyclosilicate, patiromer)
- **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[94]
- **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. [14] [81]

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

Practical tip

The role of calcium polystyrene sulfonate for hyperkalaemia

The UK Kidney Association updated their guidance in 2023 and advised that calcium polystyrene sulfonate is **no longer routinely recommended** first line in an acute setting for treating hyperkalaemia in the context of AKI, recommending that sodium zirconium cyclosilicate or patiromer be considered instead.[94]

In current clinical practice **calcium polystyrene sulfonate remains an effective treatment for hyperkalaemia** and is routinely used for this purpose.

- Calcium polystyrene sulfonate is a drug which all staff in acute settings will be familiar with and can access easily. Other cation-exchange resins/polymers may be less readily available and medical staff may be less familiar with their use
- Hyperkalaemia during AKI can be a medical emergency and **delaying effective treatment** could have **life-threatening consequences**, therefore choice of therapy should take into consideration availability, clinical experience and be given **without delay**
- Patiromer and sodium zirconium cyclosilicate have a **stronger evidence base for efficacy and more favourable adverse-effect profiles**, therefore as they become more routinely available in future they will likely have an increased role in clinical practice
- The UKKA continues to recommend calcium polystyrene sulfonate in the community for non-hospitalised patients who do not meet the criteria for other potassium binders.[94]

Management of mild hyperkalaemia (potassium 5.5 to 5.9 mmol/L) [75] [94]

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.[75]
    - Consult a pharmacist for a full list of medications that can cause hyperkalaemia.
- **A cation-exchange resin/polymer can be considered.**
    - This will help remove potassium from the body.
    - Do not use if the patient has obstructive bowel disease.

Management of moderate hyperkalaemia (potassium 6.0 to 6.4 mmol/L) [75] [94]

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** [75] [94]
  - Give over 15 minutes
  - Acts within 15 minutes
  - Lasts 2 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[94]
  - Use caution if there is a history of ischaemic heart disease and avoid if there is a history of tachyarrhythmias.[75] [94]
  - **A cation-exchange resin/polymer can be considered.** [94]
    - This will help remove potassium from the body.
    - Consider calcium polystyrene sulfonate or sodium zirconium cyclosilicate or patiromer for moderate hyperkalaemia.

Always look for and treat the underlying cause.

Management of severe hyperkalaemia (potassium ≥6.5 mmol/L) [75] [94]

Check for any acute ECG changes.

If the patient has severe hyperkalaemia or moderate hyperkalaemia with associated ECG changes: [94]

- 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[14]
- Monitor the patient in a high-dependency area.[75]

Give immediate intravenous calcium for cardiac protection. [75] [94]

- Give over 5 to 10 minutes, then repeat the ECG and consider a further dose if ECG changes persist.[94]
  - 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.[94]

- Effective within 3 minutes and lasts 30 to 60 minutes.

- Seek senior advice if the ECG fails to normalise after one dose.[75]

Give an immediate infusion of insulin/glucose to push potassium intracellularly: [75] [94]

- Give over 15 minutes
- Acts within 15 minutes
- Lasts 2 hours
- Monitor hourly for hypoglycaemia.

Give further adjunctive treatment with nebulised salbutamol. [94]

- Use caution if there is a history of ischaemic heart disease and avoid if there is a history of tachyarrhythmias.[75]

Consider use of a cation-exchange resin/polymer. [94]

- This will help remove potassium from the body.
- The UK Kidney Association recommends patiromer or sodium zirconium cyclosilicate for acute severe hyperkalaemia.[94] However, you should consider availability for prompt treatment and clinical experience in your choice of drug.

Practical tip

Be aware of the risk of underdosing with calcium gluconate in severe hyperkalaemia.[133]

- Calcium chloride and calcium gluconate are not dose-equivalent.
- If calcium gluconate is used instead of calcium chloride, there is a risk of inadvertent underdosing.
- Verify the calcium salt details before administration.[133]

Always look for and treat the underlying cause.

Routine use of sodium bicarbonate is not recommended.[94]

- Sodium bicarbonate is often used to treat acute hyperkalaemia in clinical practice although there is little evidence to support its use.[94]
- 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.

Loop diuretics may be a useful adjunct for the treatment of chronic hyperkalaemia in patients with AKI.[94]

- In practice, loop diuretics may be considered as an adjunct to other therapies, provided the patient is non-oliguric and 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 with caution for volume management in patients with AKI who are clearly volume overloaded, 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).
- 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) [75] [81]

Metabolic acidosis is a common metabolic disturbance in AKI.

- 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. [81]

- 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.[81]
  - Prior to administration of sodium bicarbonate, it is imperative to correct low ionised Ca^{2+}. Ionised Ca^{2+} falls with rapid correction of acidosis and this can trigger tetany, seizures, and cardiac instability. If necessary, intravenous calcium should be administered via a different

intravenous route to intravenous sodium bicarbonate due to the incompatibility of bicarbonate and calcium solutions.[81]

Refer for RRT if the patient has: [14] [81]

- Refractory acidosis (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 [75] [81]

Pulmonary oedema may occur:

- **As a result of overzealous intravenous fluid resuscitatio**n in a patient who presented with hypovolaemic pre-kidney AKI[115]
- **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: [75] [81]

- **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) >95 mmHg
- **Consider a loop diuretic provided the patient is haemodynamically stable and well filled intravascularly** [1] [14] [75]
  - For more details, see the section on *Management of volume overload* above
- **Seek senior support.**

Refractory pulmonary oedema is an indication for emergency RRT. [14] [81]

- 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; also referred to as kidney replacement therapy [KRT] in some regions) 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: [14] [81]

- **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).[14]
- 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.[14] [134]
- 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] [14]
- Factors to consider include:[14]
    - 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. [14] [135]

- 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: [135]

- 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 (or critical care) team will select the best modality of RRT after assessment of the patient's overall medical condition and comorbidities. [1] [136]

- 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.[137]
- 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:[136]

- **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[14]
    - 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: [14] [137]

- **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)[138]
    - Prolonged intermittent renal replacement therapy (PIRRT).

- **Continuous renal replacement therapy (CRRT) - preferred in haemodynamically unstable patients.** [139] [140] [141]
    - 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)[142] [143] [144]
        - Continuous venovenous haemodialysis (CVVHD)
        - Continuous venovenous haemodiafiltration (CVVHDF).[138] [139] [140] [141]

- **Peritoneal dialysis** - rarely used in the developed world except in paediatric patients.[145]

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.[14]
- 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.[146]

Peritoneal dialysis has generally been thought ineffective in adults with AKI and hypercatabolic states, although some studies now suggest equal effectiveness in appropriate subjects. [147] [148]

- However, one study was stopped early because there was a significant benefit to patients being on CRRT rather than PD.[149]
- In practice, PD is rarely used in adult patients in high-income countries although it is an option for children with AKI.[14]

Treatment algorithm overview

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

Acute (summary)		
hypovolaemic		
	1st	fluid resuscitation
	plus	review medications and stop nephrotoxins
	plus	identify and treat underlying cause of AKI
	consider	vasoactive drug
	consider	blood transfusion
	consider	specialist referral
■ with mild hyperkalaemia (potassium 5.5 to 5.9 mmol/L)	plus	identify and treat underlying cause of hyperkalaemia
	consider	cation-exchange resin/polymer
■ with moderate hyperkalaemia (potassium 6.0 to 6.4 mmol/L) and no associated ECG changes	plus	identify and treat underlying cause of hyperkalaemia
	plus	insulin/glucose
	consider	salbutamol
	consider	cation-exchange resin/polymer
■ 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
	plus	insulin/glucose
	plus	salbutamol
	plus	identify and treat underlying cause of hyperkalaemia
	consider	cation-exchange resin/polymer
■ with metabolic acidosis	consider	sodium bicarbonate
■ with uraemia, refractory severe hyperkalaemia,	consider	renal replacement therapy

Acute (summary)

or refractory metabolic acidosis		
hypervolaemic		
	1st	loop diuretic (only under specialist supervision) and sodium and fluid restriction
	plus	identify and treat the underlying cause of AKI
	consider	renal replacement therapy
■ with pulmonary oedema	plus	upright positioning
	plus	high-flow oxygen
	plus	glyceryl trinitrate
■ with mild hyperkalaemia (potassium 5.5 to 5.9 mmol/L)	plus	identify and treat underlying cause of hyperkalaemia
	consider	cation-exchange resin/polymer
■ with moderate hyperkalaemia (potassium 6.0 to 6.4 mmol/L) and no associated ECG changes	plus	identify and treat underlying cause of hyperkalaemia
	plus	insulin/glucose
	consider	salbutamol
	consider	cation-exchange resin/polymer
■ 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
	plus	insulin/glucose
	plus	salbutamol
	plus	identify and treat underlying cause of hyperkalaemia
	consider	cation-exchange resin/polymer
■ with metabolic acidosis	plus	seek specialist advice from the nephrology team

Treatment algorithm

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

Acute

hypovolaemic

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.[75] [81]
- 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] [14] [75][81]

- 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] [14] [75] [81]
- A smaller bolus (e.g., 250 mL) may be more appropriate if the patient has a history of cardiac failure.[82]

» **Use a balanced crystalloid unless hyperkalaemia is suspected or confirmed.** [75] [82]

- 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.

Acute

- Once hyperkalaemia has been treated and resolved, switch to a balanced crystalloid due to the risk of hyperchloraemic metabolic acidosis associated with excessive use of normal saline.[75]

» **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.[14]
- Reassess the patient's response to each fluid challenge through careful clinical examination (ABCDE approach) and monitoring of:[115]
  - 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.** [75] [115]
  - 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.[75]
  - 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

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. [14] [75]

- In the context of acute hypovolaemia, passive leg raising can improve the venous return and the response in blood pressure can be recorded.
- A rise in blood pressure confirms hypovolaemia and the need for further fluid resuscitation.[75]
- Passive leg raising is most commonly practised on critical care units.

» **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.** [75] [115]

- 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.[14] [115]

Acute

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.** [119]
  - **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.

» **Ensure at least daily ongoing monitoring of volume status for any patient with established AKI or at risk of AKI, via:** [14] [81]

- 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.[81] Catheterisation

Acute

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.** [14] [81] [82]

- 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.[10]
- 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 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 .** [14] [81]

- 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.

Acute

Common and important examples include insulin, opioids, digoxin, and gabapentin (though all drug doses should be reviewed). Consult a drug formulary or with a pharmacist, if required.

- Inappropriate drug dosing in patients with AKI is an important cause of adverse drug events.[14]

» **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[14]
- 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[115]
    - 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.[14]

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] [75]

» **Pre-kidney AKI (80% of cases) is usually due to hypovolaemia and/or hypotension and is often associated with acute illness, particularly in a patient with background risk factors. Common causes are:** [1] [3] [10] [75]

- **Sepsis** (e.g., pneumonia, cellulitis) - perform a **septic screen** and implement your local care bundle (e.g., Sepsis Six) if infection is suspected[10]
- **Fluid loss**(e.g., vomiting and diarrhoea, or blood loss)
- Reduced fluid intake - a particular problem in frail, elderly patients in the

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Acute

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: [75]

- **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). 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 and avoid inappropriate fluid resuscitation (e.g., when excessive fluid is given to patients who are oliguric and/or have heart failure).

Acute

Practical tip

Think **'Could this be sepsis?'** based on acute deterioration in an adult patient in whom there is clinical evidence or strong suspicion of infection.[76] [77] [78]

- Use a systematic approach, alongside your clinical judgement, for assessment; urgently consult a senior clinical decision-maker (e.g., ST4 level doctor in the UK) if you suspect sepsis. [77] [78] [79] [80]
- Refer to local guidelines for the recommended approach at your institution for assessment and management of the patient with suspected sepsis.
- See Sepsis in adults .

consider **vasoactive drug**

Treatment recommended for SOME patients in selected patient group

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] [14] [75][115]

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- 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] [14] [81]
- 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] [14]
- Do not use low-dose dopamine to treat AKI.[1] [3] [14]
  - 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.[120]
- 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.[121]

Acute

- A post-hoc analysis of the same RCT used the RIFLE criteria for AKI to compare the effects of vasopressin versus noradrenaline.[122] Vasopressin was associated with a trend to a lower rate of progression of the AKI, and a lower rate of use of RRT. The study pre-dated publication of the 2012 KDIGO criteria.
- 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. [14]

- A large 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.[123]
  - 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.** [14]

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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.** [75]

- Do not refer if there is a clear cause and the AKI is responding to medical management.[3] [116] [117]

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

- The patient meets (or is anticipated to meet) the criteria for RRT[3] [81]
- There are severe complications that cannot be managed medically (such as hyperkalaemia, pulmonary oedema, acidosis, or uraemia)[81]
- The patient remains haemodynamically unstable after appropriate supportive care and/or there are signs of multi-organ failure.[81]

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] [81]

- 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)

Acute

- 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 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

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to nephrology may reduce in-hospital mortality, the number of patients needing RRT, and length of hospital stay.[118]

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.** [75]

- **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.[75]
  - Consult a pharmacist for a full list of medications that can cause hyperkalaemia.
- **Restrict dietary intake - avoid potassium-rich foods and fluids.** [94]
- **Ensure close ongoing monitoring of potassium and glucose.**

» **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/polymer

Treatment recommended for SOME patients in selected patient group

Primary options

Acute

» 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)
Adjust dose according to serum electrolyte levels.

» **A cation-exchange resin/polymer (e.g., calcium polystyrene sulfonate) can be considered.** [94]

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

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.** [75]

- **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.[75]
  - Consult a pharmacist for a full list of medications that can cause hyperkalaemia.
- Restrict dietary intake - avoid potassium-rich foods and fluids.[94]
- 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.

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- 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 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:** [75] [94]

- Give over 15 minutes
- Acts within 15 minutes
- Lasts 2 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
A lower dose of 10 mg is recommended in patients with ischaemic heart disease.[94]

» **Consider further adjunctive treatment with nebulised salbutamol to drive potassium intracellularly if necessary.** [75]

Acute

- Decide whether this is needed based on the ECG and the rate of rise of serum potassium.[94]
- 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.[75] [94]

consider **cation-exchange resin/polymer**

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)
Adjust dose according to serum electrolyte levels.

OR

» patiromer: 8.4 g orally once daily initially, adjust dose according to response and serum potassium levels, maximum 25.2 g/day

OR

» sodium zirconium cyclosilicate: 10 g orally three times daily for up to 72 hours initially, followed by 5 g once daily, adjust dose according to response and serum potassium levels (usual maintenance dose 5 g every other day to 10 g once daily)

» **A cation-exchange resin/polymer can be considered.** [94]

- This will help remove potassium from the body.[94]
- Consider calcium polystyrene sulfonate or sodium zirconium cyclosilicate or patiromer for moderate hyperkalaemia.[94]
- Do not use if the patient has obstructive bowel disease or hypercalcemia.

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Acute

Practical tip

The role of calcium polystyrene sulfonate for hyperkalaemia

The UK Kidney Association updated their guidance in 2023 and advised that calcium polystyrene sulfonate is **no longer routinely recommended** as first line in an acute setting for treating hyperkalaemia in the context of AKI, recommending that sodium zirconium cyclosilicate or patiromer be considered instead.[94]
In current clinical practice **calcium polystyrene sulfonate remains an effective treatment for hyperkalemia** and is routinely used for this purpose.

- Calcium polystyrene sulfonate is a drug which all staff in acute settings will be familiar with and can access easily. Other cation-exchange resins/ polymers may be less readily available and medical staff may be less familiar with their use
- Hyperkalaemia during AKI can be a medical emergency and **delaying effective treatment** could have **life-threatening consequences**, therefore choice of therapy should take into consideration availability, clinical experience and be given **without delay**
- Patiromer and sodium zirconium cyclosilicate have a **stronger evidence base for efficacy and more favourable adverse-effect profiles**, therefore as they become more routinely available in future they will likely have an increased role in clinical practice
- The UKKA continues to recommend calcium polystyrene sulfonate in the community for non-hospitalised patients who do not meet the criteria for novel potassium binders.[94]

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

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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.** [75] [94]

- Give over 5 to 10 minutes, then repeat the ECG and consider a further dose if ECG changes persist.[94]
  - 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.[94]
  - Effective within 3 minutes and lasts 30 to 60 minutes.
- Seek senior advice if the ECG fails to normalise after one dose.[75]

Practical tip

Be aware of the risk of underdosing with calcium gluconate in severe hyperkalaemia. [133]

- Calcium chloride and calcium gluconate are not dose-equivalent.
- If calcium gluconate is used instead of calcium chloride, there is a risk of inadvertent underdosing.
- Verify the calcium salt details before administration.[133]

plus **insulin/glucose**

Treatment recommended for ALL patients in selected patient group

Primary options

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» 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:** [75] [94]

- Give over 15 minutes
- Acts within 15 minutes
- Lasts 2 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
A lower dose of 10 mg is recommended in patients with ischaemic heart disease.[94]

» **Consider further adjunctive treatment with nebulised salbutamol to drive potassium intracellularly if necessary.** [75]

- Decide whether this is needed based on the ECG and the rate of rise of serum potassium.[94]
- 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.[75] [94]

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.** [75]

- **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

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hyperkalaemia must be identified and corrected.[75]

- 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.**

» **Loop diuretics may be a useful adjunct** for the treatment of chronic hyperkalaemia in patients with AKI.[94]

- In practice loop diuretics may be considered by the nephrology team as an adjunct to other therapies provided the patient is non-oliguric and 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 with caution for volume management in patients with AKI who are clearly volume overloaded, 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

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potassium (as well as sodium and chloride).

- 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]

consider **cation-exchange resin/polymer**

Treatment recommended for SOME patients in selected patient group

Primary options

» patiromer: 8.4 g orally once daily initially, adjust dose according to response and serum potassium levels, maximum 25.2 g/day

OR

» sodium zirconium cyclosilicate: 10 g orally three times daily for up to 72 hours initially, followed by 5 g once daily, adjust dose according to response and serum potassium levels (usual maintenance dose 5 g every other day to 10 g once daily)

» **Consider use of a cation-exchange resin/polymer.** [94]

- This will help remove potassium from the body.
- Consider patiromer or sodium zirconium cyclosilicate for acute severe hyperkalaemia.[94]
- You should consider availability for prompt treatment and clinical experience in your choice of drug.

with metabolic acidosis **consider** **sodium bicarbonate**

Treatment recommended for SOME patients in selected patient group

Primary options

» sodium bicarbonate: consult local protocols for guidance on dose

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» **If the patient has severe acidosis, seek senior input as intravenous sodium bicarbonate may be needed.** [81]

- 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.[81]
    - Prior to administration of sodium bicarbonate, it is imperative to correct low ionised Ca^{2+}. Ionised Ca^{2+} falls with rapid correction of acidosis and this can trigger tetany, seizures, and cardiac instability. If necessary, intravenous calcium should be administered via a different intravenous route to intravenous sodium bicarbonate due to the incompatibility of bicarbonate and calcium solutions.[81]

» **Metabolic acidosis is a common metabolic disturbance in AKI.**

- 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.

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

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

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 nephrology team for emergency initiation of RRT if the patient has:** [14] [81]

- **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[94]
- **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.** [14] [135]

- 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:** [135]

- 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 (or critical care) team will select the best modality of RRT after assessment of the patient's overall medical condition and comorbidities. [136]

- 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.[137]
- 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: [136]

- **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[14]
  - 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: [14] [137]

- **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]

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- 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)[138]
    - Prolonged intermittent renal replacement therapy (PIRRT).

- **Continuous renal replacement therapy (CRRT) - preferred in haemodynamically unstable patients.** [139] [140] [141]
    - 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:

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- Continuous venovenous haemofiltration (CVVH)[142] [143] [144]
- Continuous venovenous haemodialysis (CVVHD)
- Continuous venovenous haemodiafiltration(CVVHDF).[138] [139] [140] [141]

- **Peritoneal dialysis** - rarely used in the developed world except in paediatric patients.[145]

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.[14]
- 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.[146]

Peritoneal dialysis has generally been thought ineffective in adults with AKI and hypercatabolic states, although some studies now suggest equal effectiveness in appropriate subjects. [147] [148]

- However, one study was stopped early because there was a significant benefit to patients being on CRRT rather than PD.[149]

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- In practice, PD is rarely used in adult patients in high-income countries although it is an option for children with AKI.[14]

hypervolaemic

1st **loop diuretic (only under specialist supervision) and sodium and fluid 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 to treat volume overload.** [1] [14]

- A loop diuretic such as furosemide may be useful in achieving euvolaemia in a patient with fluid overload (with or without pulmonary oedema).[1]
  - Use loop diuretics with caution and seek input from renal or heart failure teams if necessary, but do not delay initiation of loop diuretics in patients who are clearly volume overloaded (especially in the presence of pulmonary oedema).
  - 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] [14]
  - 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.**

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- Careful monitoring of response is important (e.g,. urine output). Stop the diuretic if there is no response.
- **Proceed without delay to more definitive management with RRT** if the response to diuretics is unsuccessful.[81]

» **Sodium and fluid 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.[75] 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.[14]

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] [14]
    - However, diuretics can also excessively reduce circulating volume and so cause a pre-kidney insult that could worsen established AKI. Hence an

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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.[124] [125]
  - 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.[126] [127]
  - Prophylactic furosemide has been shown to increase the risk of AKI when given to prevent AKI in patients having cardiac surgery.[128]
- Loop diuretics may be a useful adjunct (with specialist supervision) for the treatment of chronic hyperkalaemia in patients who are non-oliguric and volume replete.[94]

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. [10] [81]

- Insert a bladder catheter in any case of AKI when bladder outlet obstruction is suspected clinically and cannot be quickly ruled out by ultrasound.

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- Refer to urology within 24 hours if urinary tract obstruction is confirmed on ultrasound.[3] [81]

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. [81]

- 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.

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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:[10] [18] [19] [75]

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

Consider the possibility of intrinsic AKI especially 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] [10] [81]

Specific management of intrinsic AKI depends on the aetiology and is led by the nephrology team. [75]

- 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.[129] [130]
- **Thrombotic thrombocytopenic purpura (TTP)** is treated with plasma exchange.[131]
- **Acute allergic interstitial nephritis** is treated with a corticosteroid (after excluding infection) and stopping potential

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causative medications (e.g., proton-pump inhibitors, NSAIDs, antibiotics).[132]

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. [14] [81] [82]

- 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.[10]
- 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. [14] [81]

- 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. Common and important examples include insulin, opioids, digoxin, and gabapentin (though all drug doses should be reviewed). Consult a drug formulary or with a pharmacist, if required.
- Inappropriate drug dosing in patients with AKI is an important cause of adverse drug events.[14]

consider renal replacement therapy

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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.** [14] [75] [81]

- Refractory volume overload typically includes pulmonary oedema.
- However, RRT may also be needed in a patient with gross peripheral oedema (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] [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).[14]
- 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.[14] [134]
- 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] [14]
- Factors to consider include [14]
    - The trend as well as the absolute values of biochemical parameters (e.g., potassium, pH, urea)

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- 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.** [14] [135]

- 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:** [135]

- 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.

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Choice of RRT modality

The nephrology (or critical care) team will select the best modality of RRT after assessment of the patient's overall medical condition and comorbidities. [136]

- 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.[137]
- 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: [136]

- **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[14]
  - 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: [14] [137]

- **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

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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)[138]
    - Prolonged intermittent renal replacement therapy (PIRRT).

- **Continuous renal replacement therapy (CRRT) - preferred in haemodynamically unstable patients.** [139] [140] [141]
    - 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)[142] [143] [144]
        - Continuous venovenous haemodialysis (CVVHD)
        - Continuous venovenous haemodiafiltration

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(CVVHDF).[138] [139] [140] [141]

- **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

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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.[14]
- 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.[146]

Peritoneal dialysis has generally been thought ineffective in adults with AKI and hypercatabolic states, although some studies now suggest equal effectiveness in appropriate subjects. [147] [148]

- However, one study was stopped early because there was a significant benefit to patients being on CRRT rather than PD.[149]
- In practice, PD is rarely used in adult patients in high-income countries although it is an option for children with AKI.[14]

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with pulmonary oedema **plus** **upright positioning**

Treatment recommended for ALL patients in selected patient group

» **Sit the patient upright.** [75] [81]

» **Pulmonary oedema may occur:**

- **As a result of overzealous intravenous fluid resuscitation** in a patient who presented with hypovolaemic pre-kidney AKI[115]
- **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:** [75]

- 15 L/minute via a reservoir mask.

» **If available, consider continuous positive airway pressure ventilation.** [81]

plus **glyceryl trinitrate**

Treatment recommended for ALL patients in selected patient group

Primary options

» 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 >95 mmHg.[75]

» **Give intravenous glyceryl trinitrate.** [75] [81]

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- Titrate the dose upwards, aiming to maintain systolic BP >95 mmHg.[75]

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.** [75]

- **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.[75]
  - Consult a pharmacist for a full list of medications that can cause hyperkalaemia.
- Restrict dietary intake – avoid potassium-rich foods and fluids.[94]
- Ensure close ongoing monitoring of potassium and glucose.

» **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/polymer

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)

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Adjust dose according to serum electrolyte levels.

» **A cation-exchange resin/polymer (e.g., calcium polystyrene sulfonate) can be considered.** [94]

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

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.** [75]

- **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.[75]
  - Consult a pharmacist for a full list of medications that can cause hyperkalaemia.
- Restrict dietary intake – avoid potassium-rich foods and fluids.[94]
- 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**:

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- 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.**

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**:[75] [94]

- Give over 15 minutes
- Acts within 15 minutes
- Lasts 2 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
A lower dose of 10 mg is recommended in patients with ischaemic heart disease.[94]

» **Consider further adjunctive treatment with nebulised salbutamol to drive potassium intracellularly if necessary.** [75]

- Decide whether this is needed based on the ECG and the rate of rise of serum potassium.[94]
- 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.[75] [94]

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consider **cation-exchange resin/polymer**

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)
Adjust dose according to serum electrolyte levels.

OR

» patiromer: 8.4 g orally once daily initially, adjust dose according to response and serum potassium levels, maximum 25.2 g/day

OR

» sodium zirconium cyclosilicate: 10 g orally three times daily for up to 72 hours initially, followed by 5 g once daily, adjust dose according to response and serum potassium levels (usual maintenance dose 5 g every other day to 10 g once daily)

» **A cation-exchange resin/polymer can be considered.** [94]

- This will help remove potassium from the body.[94]
- Consider calcium polystyrene sulfonate or sodium zirconium cyclosilicate or patiromer for moderate hyperkalaemia.[94]
- Do not use if the patient has obstructive bowel disease or hypercalcaemia.

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Practical tip

The role of calcium polystyrene sulfonate for hyperkalaemia

The UK Kidney Association updated their guidance in 2023 and advised that calcium polystyrene sulfonate is **no longer routinely recommended** as first line in an acute setting for treating hyperkalaemia in the context of AKI, recommending that sodium zirconium cyclosilicate or patiromer be considered instead.[94]
In current clinical practice **calcium polystyrene sulfonate remains an effective treatment for hyperkalemia** and is routinely used for this purpose.

- Calcium polystyrene sulfonate is a drug which all staff in acute settings will be familiar with and can access easily. Other cation-exchange resins/ polymers may be less readily available and medical staff may be less familiar with their use
- Hyperkalaemia during AKI can be a medical emergency and **delaying effective treatment** could have **life-threatening consequences**, therefore choice of therapy should take into consideration availability, clinical experience and be given **without delay**
- Patiromer and sodium zirconium cyclosilicate have a**stronger evidence base for efficacy and more favourable adverse-effect profiles**, therefore as they become more routinely available in future they will likely have an increased role in clinical practice
- The UKKA continues to recommend calcium polystyrene sulfonate in the community for non-hospitalised patients who do not meet the criteria for novel potassium binders.[94]

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

Acute

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.** [75] [94]

- Give over 5 to 10 minutes, then repeat the ECG and consider a further dose if ECG changes persist.[94]
  - 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.[94]
  - Effective within 3 minutes and lasts 30 to 60 minutes.
- Seek senior advice if the ECG fails to normalise after one dose.[75]

Practical tip

Be aware of the risk of underdosing with calcium gluconate in severe hyperkalaemia. [133]

- Calcium chloride and calcium gluconate are not dose-equivalent.
- If calcium gluconate is used instead of calcium chloride, there is a risk of inadvertent underdosing.
- Verify the calcium salt details before administration.[133]

plus **insulin/glucose**

Treatment recommended for ALL patients in selected patient group

Primary options

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» 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**:[75] [94]

- Give over 15 minutes
- Acts within 15 minutes
- Lasts 2 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
A lower dose of 10 mg is recommended in patients with ischaemic heart disease.[94]

» **Consider further adjunctive treatment with nebulised salbutamol to drive potassium intracellularly if necessary.** [75]

- Decide whether this is needed based on the ECG and the rate of rise of serum potassium.[94]
- 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.[75] [94]

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.** [75]

- **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

Acute

hyperkalaemia must be identified and corrected.[75]

- 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.**

» **Loop diuretics may be a useful adjunct** for the treatment of chronic hyperkalaemia in patients with AKI.[94]

- In practice loop diuretics may be considered by the nephrology team as an adjunct to other therapies provided the patient is non-oliguric 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 with caution for volume management in patients with AKI who are clearly volume overloaded, 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

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potassium (as well as sodium and chloride).

- 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]

consider **cation-exchange resin/polymer**

Treatment recommended for SOME patients in selected patient group

Primary options

» patiromer: 8.4 g orally once daily initially, adjust dose according to response and serum potassium levels, maximum 25.2 g/day

OR

» sodium zirconium cyclosilicate: 10 g orally three times daily for up to 72 hours initially, followed by 5 g once daily, adjust dose according to response and serum potassium levels (usual maintenance dose 5 g every other day to 10 g once daily)

» **Consider use of a cation-exchange resin/polymer.** [94]

- This will help remove potassium from the body.
- Consider patiromer or sodium zirconium cyclosilicate for acute severe hyperkalaemia.[94]
- You should consider availability for prompt treatment and clinical experience in your choice of drug.

with metabolic acidosis **plus** **seek specialist advice from the nephrology team**

Treatment recommended for ALL patients in selected patient group

» Once any obstruction has been relieved and diuresis is progressing satisfactorily, the nephrology team will decide whether or not

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sodium bicarbonate is indicated, based on an assessment of benefits and risks.

Emerging

Novel therapeutic agents

The use of novel therapeutic agents, including atrial natriuretic peptide, theophylline, insulin-like growth factor, epidermal growth factor, free radical oxygen scavengers, antibodies to adhesion molecules, and prostaglandins, has been reviewed. None have shown clear benefit in human AKI.[22] [153] The protective effect of statins (administered either pre-intervention or chronically) is debated, but results from recent studies are disappointing.[114] [154] [155] [156] [157] [158] Controlled hypothermia and recombinant alkaline phosphatase infusion may be of benefit.[159] [160] 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.[161] [162] 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.[163] [164] [165]

Primary prevention

Prevention of AKI in high-risk patients

Acutely ill patients in hospital are at increased risk of AKI, particularly if they have risk factors (e.g., chronic kidney disease, diabetes mellitus, heart failure, or advanced age). You should:[3]

- Use early warning scores (e.g., NEWS2) to help identify patients at risk of AKI because their clinical condition is deteriorating or they are at risk of deteriorating.
- Ensure patients at risk of AKI who are admitted to hospital have their serum creatinine level monitored, with a system in place to recognise and respond to acute creatinine changes which meet criteria for AKI.[64]
- Ensure a system of urine output monitoring is in place to recognise and respond to oliguria (urine output <0.5 ml/kg/hour)
- Seek advice from a pharmacist about optimising medicines and drug dosing for patients with or at risk of AKI.[3]

Prevention of contrast-induced AKI

Intravenous iodinated contrast has previously been reported to cause contrast-induced AKI (CI-AKI).[5] However, the association has been questioned by large population studies that have failed to demonstrate this risk.[38] [39] [40] The evidence regarding the prevention of CI-AKI is weak, and often conflicting.[65] [66]

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

- Measure kidney function within 3 months of offering iodinated contrast for non-emergency imaging in adults assessed as being at increased risk of kidney injury.
- Encourage oral hydration before and after procedures using intravenous iodinated contrast agents in adults at increased risk of CI-AKI (e.g., CKD, diabetes, heart failure, and advanced age [≥75 years]).
- Consider intravenous volume expansion only if the patient is particularly high risk (e.g., eGFR less than 30 ml/min/1.73 m^2, kidney transplant).
- Do not delay emergency imaging to undertake a risk assessment.

In 2023, the UK Royal College of Radiologists and Royal College of Emergency Medicine issued the following joint recommendations in relation to emergency iodinated intravenous contrast CT scans:[67]

- Measurement of renal function or administration of intravenous fluid should not be considered prerequisites for emergency imaging.
- Age, pre-existing renal disease, diabetes mellitus, or medications such as metformin should not delay emergency scanning.

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

Drugs evaluated for prevention of CI-AKI include N-acetylcysteine, high-dose statins, probucol, allopurinol, and alprostadil, but benefits remain uncertain and such therapies should not be used routinely.[68][69][70][71][72][73][74]

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 m^2)
- Diabetes
- Heart failure
- Age ≥65 years
- Liver disease
- Nephrotoxins (e.g., NSAIDs, aminoglycoside antibiotics such as gentamicin).

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 m^2, 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).

FOLLOW UP

Monitoring

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, nephrologist follow-up is recommended with interventions based on stage of CKD.[182]

The National Kidney Foundation KDOQI guidelines include recommendations regarding the management of patients who have developed CKD subsequent to AKI.[183] 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

Complications	Timeframe	Likelihood
hyperphosphataemia	**long term**	**high**
A late complication usually arising several days after glomerular filtration falls. Treatment includes dietary restriction and the administration of phosphate binders, such as calcium acetate, calcium carbonate, sevelamer, or lanthanum carbonate. 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.		
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.[177] 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.[178] [179] Patients with partial or no recovery from AKI are at increased risk for congestive heart failure and acute myocardial infarction.[180] [181]		

FOLLOW UP

Complications	Timeframe	Likelihood
end-stage kidney disease	**variable**	**medium**
Some patients may not recover from severe kidney injury, especially those with underlying kidney disease or other comorbid medical conditions. Chronic renal replacement therapy may be required.[172]		

Prognosis

Recovery for AKI is variable and depends on cause of injury and the severity and duration of AKI.[166] [167]

There is an independent association of AKI with a higher risk of death.[166] [168][169] 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.[169]

Up to 6% of patients admitted to the intensive care unit have AKI requiring renal replacement therapy.[21] [166] [170] In hospital, when AKI requires dialysis, mortality exceeds 50%; those with multi-organ failure are at greatest risk.[18] [21] [170] 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).[171]

AKI is irreversible in approximately 5% to 7% of adults and as many as 16% of older adult patients.[172] There is controversy as to whether prior AKI is a major risk factor leading to future chronic kidney disease, but there is increasing evidence of strong association.[173] [174] [175] [176]

Diagnostic guidelines

United Kingdom

Acute kidney injury: prevention, detection and management

Published by: National Institute for Health and Care Excellence **Last published:** 2023

Acute kidney injury (AKI)

Published by: UK Kidney Association (formerly The Renal Association) **Last published:** 2019

International

Kidney disease: improving global outcomes (KDIGO) clinical practice guideline for acute kidney injury

Published by: International Society of Nephrology **Last published:** 2012

North America

Management of acute kidney injury: core curriculum 2018

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

ACR appropriateness criteria: renal failure

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

Treatment guidelines

United Kingdom

Acute kidney injury: prevention, detection and management

Published by: National Institute for Health and Care Excellence **Last published:** 2023

Acute kidney injury (AKI)

Published by: UK Kidney Association (formerly The Renal Association) **Last published:** 2019

British consensus guidelines on intravenous fluid therapy for adult surgical patients

Published by: BAPEN; Association for Clinical Biochemistry; Association of Surgeons of Great Britain and Ireland; Society of Academic and Research Surgery; Renal Association/Intensive Care Society **Last published:** 2011

Europe

ESPEN guideline on clinical nutrition in hospitalized patients with acute or chronic kidney disease

Published by: European Society for Clinical Nutrition and Metabolism **Last published:** 2021

International

Kidney disease: improving global outcomes (KDIGO) clinical practice guideline for acute kidney injury

Published by: International Society of Nephrology **Last published:** 2012

North America

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

- Kidney disease: improving global outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl. 2012 Mar;2(1):1-138. Full text
- National Institute for Health and Care Excellence. Acute kidney injury: prevention, detection and management. September 2023 [internet publication]. Full text
- Kanagasundaram S, Ashley C, Bhojani S, et al. Renal Association clinical practice guideline acute kidney injury (AKI). August 2019 [internet publication]. Full text
- Royal College of Physicians. Acute care toolkit 12: acute kidney injury and intravenous fluid therapy. October 2015 [internet publication]. Full text

References

1. Kidney disease: improving global outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl. 2012 Mar;2(1):1-138. Full text
2. Palevsky PM, Liu KD, Brophy PD, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for acute kidney injury. Am J Kidney Dis. 2013 May;61(5):649-72. Full text Abstract
3. National Institute for Health and Care Excellence. Acute kidney injury: prevention, detection and management. September 2023 [internet publication]. Full text
4. Thomas ME, Blaine C, Dawnay A, et al. The definition of acute kidney injury and its use in practice. Kidney Int. 2015 Jan;87(1):62-73. Abstract
5. Sharfuddin AA, Weisbord SD, Palevsky PM, et al. Acute kidney injury. In: Taal MW, Chertow GM, Marsden PA, et al, eds. Brenner and Rector's the kidney. 9th ed. Philadelphia, PA: Saunders; 2012.
6. National Institutes of Health; National Institute of Diabetes and Digestive and Kidney Diseases. United States Renal Data System 2023 annual data report: epidemiology of kidney disease in the United States. 2023 [internet publication]. Full text
7. Ali T, Khan I, Simpson W, et al. Incidence and outcomes in acute kidney injury: a comprehensive population-based study. J Am Soc Nephrol. 2007 Apr;18(4):1292-8. Full text Abstract
8. UK Kidney Association (Renal Association). UK Renal Registry: acute kidney injury (AKI) in England - a report on the nationwide collection of AKI warning test scores from 2018. 2020 [internet publication]. Full text
9. 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

REFERENCES

10. Think Kidneys. Acute kidney injury best practice guidance: responding to AKI warning stage test results for adults in primary care. April 2016 [internet publication]. Full text

11. Selby NM, Kolhe NV, McIntyre CW, et al. Defining the cause of death in hospitalised patients with acute kidney injury. PLoS One. 2012 Nov 2;7(11):e48580. Full text Abstract

12. Case J, Khan S, Khalid R, et al. Epidemiology of acute kidney injury in the intensive care unit. Crit Care Res Pract. 2013;2013:479730. Full text Abstract

13. Ronco C, Bellomo R, Kellum JA. Acute kidney injury. Lancet. 2019 Nov 23;394(10212):1949-64. Abstract

14. Kanagasundaram S, Ashley C, Bhojani S, et al. Renal Association clinical practice guideline acute kidney injury (AKI). August 2019 [internet publication]. Full text

15. Hsu CY, McCulloch CE, Fan D, et al. Community-based incidence of acute renal failure. Kidney Int. 2007 Jul;72(2):208-12. Full text Abstract

16. Ohnuma T, Uchino S, Toki N, et al. External validation for acute kidney injury severity scores: a multicenter retrospective study in 14 Japanese ICUs. Am J Nephrol. 2015;42(1):57-64. Abstract

17. Poukkanen M, Vaara ST, Reinikainen M, et al. Predicting one-year mortality of critically ill patients with early acute kidney injury: data from the prospective multicenter FINNAKI study. Crit Care. 2015 Mar 27;19:125. Full text Abstract

18. Mehta R, Pascual MT, Soroko S, et al. Spectrum of acute renal failure in the intensive care unit: the PICARD experience. Kidney Int. 2004 Oct;66(4):1613-21. Abstract

19. Liaño F, Pascual J. Epidemiology of acute renal failure: a prospective, multicenter, community-based study. Madrid Acute Renal Failure Study Group. Kidney Int. 1996 Sep;50(3):811-8. Abstract

20. Rihal CS, Textor SC, Grill DE, et al. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. Circulation. 2002 May 14;105(19):2259-64. Full text Abstract

21. Liangos O, Wald R, O'Bell JW, et al. Epidemiology and outcomes of acute renal failure in hospitalized patients: a national survey. Clin J Am Soc Nephrol. 2006 Jan;1(1):43-51. Full text Abstract

22. Lameire N, Van Biesen W, Vanholder R. Acute renal failure. Lancet. 2005 Jan 29-Feb 4;365(9457):417-30. Abstract

23. Myers BD, Moran SM. Hemodynamically mediated acute renal failure. N Engl J Med. 1986 Jan 9;314(2):97-105. Abstract

24. Brezis M, Rosen S, Silva P, et al. Renal ischemia: a new perspective. Kidney Int. 1984 Oct;26(4):375-83. Abstract

25. Kaushal GP, Basnakian AG, Shah SV. Apoptotic pathways in ischemic acute renal failure. Kidney Int. 2004 Aug;66(2):500-6. Abstract

26. Zhou W, Farrar CA, Abe K, et al. Predominant role for C5b-9 in renal ischemia/reperfusion injury. J Clin Invest. 2000 May;105(10):1363-71. Full text Abstract

27. Thurman J, Lucia MS, Ljubanovic D, et al. Acute tubular necrosis is characterized by activation of the alternative pathway of complement. Kidney Int. 2005 Feb;67(2):524-30. Abstract

28. Bonventre JV, Zuk A. Ischemic acute renal failure: an inflammatory disease? Kidney Int. 2004 Aug;66(2):480-5. Abstract

29. Lien YH, Yong KC, Cho C, et al. S1P(1) selective agonist, SEW2871, ameliorates ischemic-reperfusion injury in acute renal failure. Kidney Int. 2006 May;69(9):1601-8. Abstract

30. Boffa JJ, Arendshorst WJ, et al. Maintenance of renal vascular reactivity contributes to acute renal failure during endotoxemic shock. J Am Soc Nephrol. 2005 Jan;16(1):117-24. Abstract

31. Boffa JJ, Just A, Coffman TM, et al. Thromboxane receptor mediates renal vasoconstriction and contributes to acute renal failure in endotoxemic mice. J Am Soc Nephrol. 2004 Sep;15(9):2358-65. Abstract

32. Khan RZ, Badr KF. Endotoxin and renal function: perspectives to the understanding of septic acute renal failure and toxic shock. Nephrol Dial Transplant. 1999 Apr;14(4):814-8. Abstract

33. Schrier RW, Wang W. Acute renal failure and sepsis. N Engl J Med. 2004 Jul 8;351(2):159-69. Abstract

34. Badr KF, Kelley VE, Rennke HG, et al. Roles for thromboxane A2 and leukotrienes in endotoxin-induced acute renal failure. Kidney Int. 1986 Oct;30(4):474-80. Abstract

35. Persson P, Hansell P, Liss P. Pathophysiology of contrast medium-induced nephropathy. Kidney Int. 2005 Jul;68(1):14-22. Abstract

36. Heyman S, Rosenberger C, Rosen S, et al. Regional alterations in renal haemodynamics and oxygenation: a role in contrast medium-induced nephropathy. Nephrol Dial Transplant. 2005 Feb;20 Suppl 1:i6-11. Abstract

37. Pflueger A, Larson TS, Nath KA, et al. Role of adenosine in contrast media-induced acute renal failure in diabetes mellitus. Mayo Clin Proc. 2000 Dec;75(12):1275-83. Abstract

38. Wilhelm-Leen E, Montez-Rath ME, Chertow G. Estimating the risk of radiocontrast-associated nephropathy. J Am Soc Nephrol. 2017 Feb;28(2):653-9. Full text Abstract

39. Brinjikji W, Demchuk AM, Murad MH, et al. Neurons over nephrons: systematic review and meta-analysis of contrast-induced nephropathy in patients with acute stroke. Stroke. 2017 Jul;48(7):1862-8. Full text Abstract

40. Ehrmann S, Quartin A, Hobbs BP, et al. Contrast-associated acute kidney injury in the critically ill: systematic review and Bayesian meta-analysis. Intensive Care Med. 2017 Jun;43(6):785-94. Abstract

41. Goulden R, Rowe BH, Abrahamowicz M, et al. Association of intravenous radiocontrast with kidney function: a regression discontinuity analysis. JAMA Intern Med. 2021 Jun 1;181(6):767-74. Abstract

42. Schreiner GF, Kohan DE. Regulation of renal transport processes and hemodynamics by macrophages and lymphocytes. Am J Kidney Dis. 1990 Apr;258(4 Pt 2):F761-7. Abstract

43. Klahr S. New insights into the consequences and mechanisms of renal impairment in obstructive nephropathy. Am J Kidney Dis. 1991 Dec;18(6):689-99. Abstract

44. Ophascharoensuk V, Giachelli CM, Gordon K, et al. Obstructive uropathy in the mouse: Role of osteopontin in interstitial fibrosis and apoptosis. Kidney Int. 1999 Aug;56(2):571-80. Abstract

45. Moon JA, Kim HT, Cho IS, et al. IN-1130, a novel transforming growth factor-beta type I receptor kinase (ALK5) inhibitor, suppresses renal fibrosis in obstructive nephropathy. Kidney Int. 2006 Oct;70(7):1234-43. Abstract

46. Lu JC, Coca SG, Patel UD, et al. Searching for genes that matter in acute kidney injury: a systematic review. Clin J Am Soc Nephrol. 2009 Jun;4(6):1020-31. Full text Abstract

47. Zhao B. Genome-wide association study to identify single nucleotide polymorphisms conferring risk for acute kidney injury. Abstract TH-OR028. Paper presented at: Kidney Week 2014. 11-16 Nov 2014. Philadelphia, PA. J Am Soc Nephrol. 2014;25(suppl):7A. Full text

48. Jiesisibieke ZL, Tung TH, Xu QY, et al. Association of acute kidney injury with frailty in elderly population: a systematic review and meta-analysis. Ren Fail. 2019 Nov;41(1):1021-7. Full text Abstract

49. Parfrey PS, Griffiths SM, Barrett BJ, et al. Contrast material induced renal failure in patients with diabetes mellitus, renal insufficiency, or both. A prospective controlled study. N Engl J Med. 1989 Jan 19;320(3):143-9. Abstract

50. Liu J, Xie H, Ye Z, et al. Rates, predictors, and mortality of sepsis-associated acute kidney injury: a systematic review and meta-analysis. BMC Nephrol. 2020 Jul 31;21(1):318. Full text Abstract

51. Legrand M, Bell S, Forni L, et al. Pathophysiology of COVID-19-associated acute kidney injury. Nat Rev Nephrol. 2021 Nov;17(11):751-64. Full text Abstract

52. Giuliano CA, Patel CR, Kale-Pradhan PB. Is the combination of piperacillin-tazobactam and vancomycin associated with development of acute kidney injury? A meta-analysis. Pharmacotherapy. 2016 Dec;36(12):1217-28. Abstract

53. Luther MK, Timbrook TT, Caffrey AR, et al. Vancomycin plus piperacillin-tazobactam and acute kidney injury in adults: a systematic review and meta-analysis. Crit Care Med. 2018 Jan;46(1):12-20. Abstract

54. Bellos I, Karageorgiou V, Pergialiotis V, et al. Acute kidney injury following the concurrent administration of antipseudomonal β-lactams and vancomycin: a network meta-analysis. Clin Microbiol Infect. 2020 Jun;26(6):696-705. Full text Abstract

55. Garg AX, Devereaux PJ, Yusuf S, et al. Kidney function after off-pump or on-pump coronary artery bypass graft surgery: a randomized clinical trial. JAMA. 2014 Jun 4;311(21):2191-8. Full text Abstract

56. Søvik S, Isachsen MS, Nordhuus KM, et al. Acute kidney injury in trauma patients admitted to the ICU: a systematic review and meta-analysis. Intensive Care Med. 2019 Apr;45(4):407-19. Abstract

57. Rojas-Valverde D, Sánchez-Ureña B, Crowe J, et al. Exertional rhabdomyolysis and acute kidney injury in endurance sports: a systematic review. Eur J Sport Sci. 2021 Feb;21(2):261-74. Abstract

58. Bell S, Dekker FW, Vadiveloo T, et al. Risk of postoperative acute kidney injury in patients undergoing orthopaedic surgery - development and validation of a risk score and effect of acute kidney injury on survival: observational cohort study. BMJ. 2015 Nov 11;351:h5639. Full text Abstract

59. Shi H, Peng Q, Zhou XL, et al. Use of angiotensin-converting enzyme inhibitors or receptor blockers is associated with reduced mortality in patients with post-acute kidney injury: meta-analysis. Eur Rev Med Pharmacol Sci. 2021 Aug;25(15):4900-08. Abstract

60. Yang Y, George KC, Shang WF, et al. Proton-pump inhibitors use, and risk of acute kidney injury: a meta-analysis of observational studies. Drug Des Devel Ther. 2017 Apr 24;11:1291-9. Full text Abstract

61. Nochaiwong S, Ruengorn C, Awiphan R, et al. The association between proton pump inhibitor use and the risk of adverse kidney outcomes: a systematic review and meta-analysis. Nephrol Dial Transplant. 2018 Feb 1;33(2):331-42. Full text Abstract

62. Brown AC. Kidney toxicity related to herbs and dietary supplements: Online table of case reports. Part 3 of 5 series. Food Chem Toxicol. 2017 Sep;107(pt a):502-19. Abstract

63. McCarthy CS, Becker JA. Multiple myeloma and contrast media. Radiology. 1992 May;183(2):519-21. Abstract

64. National Institute for Health and Care Excellence. Quality statement 2: identifying acute kidney injury in people admitted to hospital. NICE quality standard QS76: acute kidney injury. March 2023 [internet publication].

65. Barrett BJ, Parfey PS. Clinical practice. Preventing nephropathy induced by contrast medium. N Engl J Med. 2006 Jan 26;354(4):379-86. Abstract

66. Nijssen EC, Rennenberg RJ, Nelemans PJ, et al. Prophylactic hydration to protect renal function from intravascular iodinated contrast material in patients at high risk of contrast-induced nephropathy (AMACING): a prospective, randomised, phase 3, controlled, open-label, non-inferiority trial. Lancet. 2017 Apr 1;389(10076):1312-22. Abstract

67. Royal College of Emergency Medicine; Royal College of Radiologists. Joint advisory statement between Royal College of Radiologists & Royal College Emergency Medicine regarding emergency computed somography scans and the use of intravenous iodinated contrast agents. May 2023 [internet publication]. Full text

68. Weisbord SD, Gallagher M, Jneid H, et al; PRESERVE Trial Group. Outcomes after angiography with sodium bicarbonate and acetylcysteine. N Engl J Med. 2018 Feb 15;378(7):603-14. Full text Abstract

69. Guo Z, Liu J, Lei L, et al. Effect of N-acetylcysteine on prevention of contrast-associated acute kidney injury in patients with STEMI undergoing primary percutaneous coronary intervention: a systematic review and meta-analysis of randomised controlled trials. BMJ Open. 2020 Oct 16;10(10):e039009. Full text Abstract

70. Magner K, Ilin JV, Clark EG, et al. Meta-analytic techniques to assess the association between N-acetylcysteine and acute kidney injury after contrast administration: a systematic review and meta-analysis. JAMA Netw Open. 2022 Jul 1;5(7):e2220671. Abstract

71. Li H, Wang C, Liu C, et al. Efficacy of short-term statin treatment for the prevention of contrast-induced acute kidney injury in patients undergoing coronary angiography/percutaneous coronary intervention: a meta-analysis of 21 randomized controlled trials. Am J Cardiovasc Drugs. 2016 Jun;16(3):201-19. Full text Abstract

72. Xin W, Lin Z, Zhang T, et al. Probucol for the prevention of contrast-induced acute kidney injury in patients undergoing coronary angiography or percutaneous coronary intervention: a meta-analysis of randomized controlled trials. Clin Nephrol. 2019 Jul;92(1):36-43. Full text Abstract

73. Xin W, Lin Z, Zhang T, et al. Effects of allopurinol pretreatment on the risk of contrast-induced acute kidney injury in patients undergoing percutaneous coronary intervention: a meta-analysis of randomized controlled trials. Clin Nephrol. 2020 Jan;93(1):24-33. Abstract

74. Xu H, Wang H, Zhang C, et al. Efficacy of alprostadil in preventing contrast-induced nephropathy: a systematic review and meta-analysis. Angiology. 2021 Oct;72(9):878-88. Abstract

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

76. Royal College of Physicians. National early warning score (NEWS) 2: standardising the assessment of acute-illness severity in the NHS. Dec 2017 [internet publication]. Full text

77. NHS England. Sepsis guidance implementation advice for adults. September 2017 [internet publication]. Full text

78. National Institute for Health and Care Excellence. Sepsis: recognition, diagnosis and early management. September 2017 [internet publication]. Full text

79. Nutbeam T, Daniels R; The UK Sepsis Trust. Clinical tools [internet publication]. Full text

80. Academy of Medical Royal Colleges. Statement on the initial antimicrobial treatment of sepsis V2.0. Oct 2022 [internet publication]. Full text

81. Think Kidneys. Recommended minimum requirements of a care bundle for patients with AKI in hospital. December 2015; reviewed March 2020 [internet publication]. Full text

82. Anathhanam S, Lewington AJ. Acute kidney injury. J R Coll Physicians Edinb. 2013;43(4):323-8; quiz 329. Abstract

83. Selby NM, Forni LG, Laing CM, et al. Covid-19 and acute kidney injury in hospital: summary of NICE guidelines. BMJ. 2020 May 26;369:m1963. Full text Abstract

84. Sawhney S, Mitchell M, Marks A, et al. Long-term prognosis after acute kidney injury (AKI): what is the role of baseline kidney function and recovery? A systematic review. BMJ Open. 2015 Jan 6;5(1):e006497. Full text Abstract

85. National Confidential Enquiry into Patient Outcome and Death. Adding insult to injury: a review of care of patients who died in hospital with a primary diagnosis of acute kidney injury (acute renal failure). 2009 [internet publication]. Full text

86. NHS England. Acute kidney injury (AKI) algorithm [internet publication]. Full text

87. Baum N, Dichoso CC, Carlton CE. Blood urea nitrogen and serum creatinine. Physiology and interpretations. Urology. 1975 May;5(5):583-8. Abstract

88. Bellomo R, Ronco C, Kellum JA, et al. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care. 2004 Aug;8(4):R204-12. Full text Abstract

89. Mehta RL, Kellum JA, Shah SV, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care. 2007;11(2):R31. Full text Abstract

90. Gabardi S, Munz K, Ulbricht C. A review of dietary supplement-induced renal dysfunction. Clin J Am Soc Nephrol. 2007 Jul;2(4):757-65. Full text Abstract

91. Yarlagadda SG, Perazella MA. Drug-induced crystal nephropathy: an update. Expert Opin Drug Saf. 2008 Mar;7(2):147-58. Full text Abstract

92. Feehally J, Gilmore I, Barasi S, et al. RCPE UK consensus conference statement: Management of acute kidney injury: the role of fluids, e-alerts and biomarkers. J R Coll Physicians Edinb. 2013;43(1):37-8. Full text Abstract

93. Academy of Medical Royal Colleges. Acute kidney injury: a competency framework. Defining the role of the expert clinician. November 2011 [internet publication]. Full text

94. UK Kidney Association. Clinical practice guidelines treatment of acute hyperkalaemia in adults. Oct 2023 [internet publication]. Full text

95. Chancharoenthana W, Leelahavanichkul A. Acute kidney injury spectrum in patients with chronic liver disease: where do we stand? World J Gastroenterol. 2019 Jul 28;25(28):3684-703. Full text Abstract

96. Rachoin JS, Daher R, Moussallem C, et al. The fallacy of the BUN:creatinine ratio in critically ill patients. Nephrol Dial Transplant. 2011 Dec 29;27(6):2248-54. Full text Abstract

REFERENCES

97. El-Khoury JM, Hoenig MP, Jones GRD, et al. AACC guidance document on laboratory investigation of acute kidney injury. J Appl Lab Med. 2021 Sep 1;6(5):1316-37. Full text Abstract

98. Agrawal M, Swartz R. Acute renal failure. Am Fam Physician. 2000 Apr 1;61(7):2077-88. Abstract

99. Fogazzi GB. Crystalluria: a neglected aspect of urinary sediment analysis. Nephrol Dial Transplant. 1996 Feb;11(2):379-87. Abstract

100. Muriithi AK, Nasr SH, Leung N. Utility of urine eosinophils in the diagnosis of acute interstitial nephritis. Clin J Am Soc Nephrol. 2013 Nov;8(11):1857-62. Full text Abstract

101. Rossert J. Drug-induced acute interstitial nephritis. Kidney Int. 2001 Aug;60(2):804-17. Abstract

102. Carvounis CP, Nisar S, Guro-Razuman S. Significance of the fractional excretion of urea in the differential diagnosis of acute renal failure. Kidney Int. 2002 Dec;62(6):2223-9. Full text Abstract

103. National Institute for Health and Care Excellence. Myeloma: diagnosis and management. February 2016 [internet publication]. Full text

104. Simundic AM, Bölenius K, Cadamuro J, et al. Joint EFLM-COLABIOCLI recommendation for venous blood sampling. Clin Chem Lab Med 2018;56(12):2015-38. Abstract

105. Folkestad T, Brurberg KG, Nordhuus KM, et al. Acute kidney injury in burn patients admitted to the intensive care unit: a systematic review and meta-analysis. Crit Care. 2020 Jan 2;24(1):2. Full text Abstract

106. Coca SG, Yalavarthy R, Concato J, et al. Biomarkers for the diagnosis and risk stratification of acute kidney injury: a systematic review. Kidney Int. 2008 May;73(9):1008-16. Abstract

107. Ho J, Tangri N, Komenda P, et al. Urinary, plasma, and serum biomarkers' utility for predicting acute kidney injury associated with cardiac surgery in adults: a meta-analysis. Am J Kidney Dis. 2015 Dec;66(6):993-1005. Full text Abstract

108. Erstad BL. Usefulness of the biomarker TIMP-2•IGFBP7 for acute kidney injury assessment in critically ill patients: a narrative review. Ann Pharmacother. 2022 Jan;56(1):83-92. Full text Abstract

109. Ostermann M, Zarbock A, Goldstein S, et al. Recommendations on acute kidney injury biomarkers from the Acute Disease Quality Initiative Consensus Conference: a consensus statement. JAMA Netw Open. 2020 Oct 1;3(10):e2019209. Full text Abstract

110. Vaidya VS, Ferguson MA, Bonventre JV. Biomarkers of acute kidney injury. Annu Rev Pharmacol Toxicol. 2008;48:463-93. Full text Abstract

111. Zhang Z, Lu B, Sheng X, et al. Cystatin C in prediction of acute kidney injury: a systemic review and meta-analysis. Am J Kidney Dis. 2011 Sep;58(3):356-65. [Erratum in: Am J Kidney Dis. 2012 Apr;59(4):590-2.] Abstract

112. Small DM, Gobe GC. Cytochrome c: potential as a noninvasive biomarker of drug-induced acute kidney injury. Expert Opin Drug Metab Toxicol. 2012 Jun;8(6):655-64. Abstract

113. Clerico A, Galli C, Fortunato A, et al. Neutrophil gelatinase-associated lipocalin (NGAL) as biomarker of acute kidney injury: a review of the laboratory characteristics and clinical evidences. Clin Chem Lab Med. 2012 Feb 15;50(9):1505-17. Abstract

114. Pappy R, Stavrakis S, Hennebry TA, et al. Effect of statin therapy on contrast-induced nephropathy after coronary angiography: a meta-analysis. Int J Cardiol. 2011 Sep 15;151(3):348-53. Abstract

115. Royal College of Physicians of Edinburgh, NHS Kidney Care. Acute kidney injury. Mobile application content. February 2013 [internet publication]. Full text

116. Balasubramanian G, Al-Aly Z, Moiz A, et al. Early nephrologist involvement in hospital-acquired acute kidney injury: a pilot study. Am J Kidney Dis. 2011 Feb;57(2):228-34. Abstract

117. Wilson FP, Shashaty M, Testani J, et al. Automated, electronic alerts for acute kidney injury: a single-blind, parallel-group, randomised controlled trial. Lancet. 2015 May 16;385(9981):1966-74. Full text Abstract

118. Meier P, Bonfils RM, Vogt B, et al. Referral patterns and outcomes in noncritically ill patients with hospital-acquired acute kidney injury. Clin J Am Soc Nephrol. 2011 Aug 4;6(9):2215-25. Full text Abstract

119. National Institute for Health and Care Excellence. Intravenous fluid therapy in adults in hospital. Clinical guideline CG174. May 2017 [internet publication]. Full text

120. Redl-Wenzl EM, Armbruster C, Edelmann G, et al. The effects of norepinephrine on hemodynamics and renal function in severe septic shock states. Intensive Care Med. 1993;19(3):151-4. Abstract

121. Russell JA, Walley KR, Singer J, et al. Vasopressin versus norepinephrine infusion in patients with septic shock. N Engl J Med. 2008 Feb 28;358(9):877-87. Full text Abstract

122. Gordon AC, Russell JA, Walley KR, et al. The effects of vasopressin on acute kidney injury in septic shock. Intensive Care Med. 2009 Oct 20;36(1):83-91. Full text Abstract

123. De Backer D, Biston P, Devriendt J, et al. Comparison of dopamine and norepinephrine in the treatment of shock. N Engl J Med. 2010 Mar 4;362(9):779-89. Full text Abstract

124. Mehta RL, Pascual MT, Soroko S, et al. Diuretics, mortality, and nonrecovery of renal function in acute renal failure. JAMA. 2002 Nov 27;288(20):2547-53. Full text Abstract

125. Cantarovich F, Rangoonwala B, Lorenz H, et al. High-dose furosemide for established ARF: a prospective, randomized, double-blind, placebo-controlled, multicenter trial. Am J Kidney Dis. 2004 Sep;44(3):402-9. Abstract

126. Ho KM, Sheridan DJ. Meta-analysis of frusemide to prevent or treat acute renal failure. BMJ. 2006 Jul 21;333(7565):420. Full text Abstract

127. Ho KM, Power BM. Benefits and risks of furosemide in acute kidney injury. Anaesthesia. 2010 Jan 19;65(3):283-93. Full text Abstract

REFERENCES

128. Solomon R, Werner C, Mann D, et al. Effects of saline, mannitol, and furosemide on acute decreases in renal function induced by radiocontrast agents. N Engl J Med. 1994 Nov 24;331(21):1416-20. Full text Abstract

129. National Institute for Health and Care Excellence. Eculizumab for treating atypical haemolytic uraemic syndrome. January 2015 [internet publication]. Full text

130. Cao M, Leite BN, Ferreiro T, et al. Eculizumab modifies outcomes in adults with atypical hemolytic uremic syndrome with acute kidney injury. Am J Nephrol. 2018;48(3):225-33. Abstract

131. Matsumoto M, Fujimura Y, Wada H, et al. Diagnostic and treatment guidelines for thrombotic thrombocytopenic purpura (TTP) 2017 in Japan. Int J Hematol. 2017 May 26;106(1):3-15. Abstract

132. Joyce E, Glasner P, Ranganathan S, et al. Tubulointerstitial nephritis: diagnosis, treatment, and monitoring. Pediatr Nephrol. 2016 May 7;32(4):577-87. Abstract

133. Medicines and Healthcare products Regulatory Agency. Calcium chloride, calcium gluconate: potential risk of underdosing with calcium gluconate in severe hyperkalaemia. June 2023 [internet publication]. Full text

134. Fayad AI, Buamscha DG, Ciapponi A. Timing of kidney replacement therapy initiation for acute kidney injury. Cochrane Database Syst Rev. 2022 Nov 23;11(11):CD010612. Full text Abstract

135. National Institute for Health and Care Excellence. Renal replacement management therapy and conservative management. October 2018. Full text

136. Intensive Care Society. Guidelines for the provision of intensive care services. June 2019 [internet publication]. Full text

137. Lins RL, Elseviers MM, Van der Niepen P, et al. Intermittent versus continuous renal replacement therapy for acute kidney injury patients admitted to the intensive care unit: results of a randomized clinical trial. Nephrol Dial Transplant. 2008 Oct 14;24(2):512-8. Full text Abstract

138. Palevsky PM, Zhang JH, O'Connor TZ, et al; VA/NIH Acute Renal Failure Trial Network. Intensity of renal support in critically ill patients with acute kidney injury. N Engl J Med. 2008 Jul 3;359(1):7-20. Full text Abstract

139. Tolwani AJ, Campbell RC, Stofan BS, et al. Standard versus high-dose CVVHDF for ICU-related acute renal failure. J Am Soc Nephrol. 2008 Jun;19(6):1233-8. Full text Abstract

140. Bellomo R, Cass A, Cole L, et al; RENAL Replacement Therapy Study Investigators. Intensity of continuous renal-replacement therapy in critically ill patients. N Engl J Med. 2009 Oct 22;361(17):1627-38. Full text Abstract

141. Chertow GM, Burdick E, Honour M, et al. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. J Am Soc Nephrol. 2005 Nov;16(11):3365-70. Full text Abstract

142. Ronco C, Bellomo R, Homel P, et al. Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomised trial. Lancet. 2000 Jul 1;356(9223):26-30. Full text Abstract

143. Saudan P, Niederberger M, De Seigneux S, et al. Adding a dialysis dose to continuous hemofiltration increases survival in patients with acute renal failure. Kidney Int. 2006 Jul 19;70(7):1312-7. Full text Abstract

144. Ronco C. Continuous renal replacement therapies for the treatment of acute renal failure in intensive care patients. Clin Nephrol. 1993 Oct;40(4):187-98. Abstract

145. Cullis B, Al-Hwiesh A, Kilonzo K, et al. ISPD guidelines for peritoneal dialysis in acute kidney injury: 2020 update (adults). Perit Dial Int. 2021 Jan;41(1):15-31. Full text Abstract

146. Rabindranath K, Adams J, Macleod AM, et al. Intermittent versus continuous renal replacement therapy for acute renal failure in adults. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD003773. Full text Abstract

147. Ponce D, Balbi AL. Peritoneal dialysis in acute kidney injury: a viable alternative. Perit Dial Int. 2011 Jul-Aug;31(4):387-9. Abstract

148. Ponce D, Berbel MN, Regina de Goes C, et al. High-volume peritoneal dialysis in acute kidney injury: indications and limitations. Clin J Am Soc Nephrol. 2012 Jun;7(6):887-94. Abstract

149. Phu NH, Hien TT, Mai NT, et al. Hemofiltration and peritoneal dialysis in infection-associated acute renal failure in Vietnam. N Engl J Med. 2002 Sep 19;347(12):895-902. Full text Abstract

150. Webster J, Osborne S, Rickard CM, et al. Clinically-indicated replacement versus routine replacement of peripheral venous catheters. Cochrane Database Syst Rev. 2019 Jan 23;1(1):CD007798. Full text Abstract

151. Royal College of Nursing. Catheter care: RCN guidance for health care professionals. Jul 2021 [internet publication]. Full text

152. Royal College of Nursing. Catheter care: guidance for health care professionals. Jul 2021 [internet publication]. Full text

153. Yamada H, Doi K, Tsukamoto T, et al. Low-dose atrial natriuretic peptide for prevention or treatment of acute kidney injury: a systematic review and meta-analysis. Crit Care. 2019 Feb 11;23(1):41. Full text Abstract

154. Zhang T, Shen LH, Hu LH, et al. Statins for the prevention of contrast-induced nephropathy: a systematic review and meta-analysis. Am J Nephrol. 2011;33(4):344-51. Full text Abstract

155. Zhang BC, Li WM, Xu YW. High-dose statin pretreatment for the prevention of contrast-induced nephropathy: a meta-analysis. Can J Cardiol. 2011 Nov-Dec;27(6):851-8. Abstract

156. Giacoppo D, Capodanno D, Capranzano P, et al. Meta-analysis of randomized controlled trials of preprocedural statin administration for reducing contrast-induced acute kidney injury in patients undergoing coronary catheterization. Am J Cardiol. 2014 Aug 15;114(4):541-8. Abstract

157. Gandhi S, Mosleh W, Abdel-Qadir H, et al. Statins and contrast-induced acute kidney injury with coronary angiography. Am J Med. 2014 Oct;127(10):987-1000. Abstract

158. Bangalore S, Fayyad R, Hovingh GK, et al. Statin and the risk of renal-related serious adverse events: Analysis from the IDEAL, TNT, CARDS, ASPEN, SPARCL, and other placebo-controlled trials. Am J Cardiol. 2014 Jun 15;113(12):2018-20. Abstract

159. Susantitaphong P, Alfayez M, Cohen-Bucay A, et al. Therapeutic hypothermia and prevention of acute kidney injury: a meta-analysis of randomized controlled trials. Resuscitation. 2012 Feb;83(2):159-67. Full text Abstract

160. Pickkers P, Heemskerk S, Schouten J, et al. Alkaline phosphatase for treatment of sepsis-induced acute kidney injury: a prospective randomized double-blind placebo-controlled trial. Crit Care. 2012 Jan 23;16(1):R14. Full text Abstract

161. Kim JE, Song SW, Kim JY, et al. Effect of a single bolus of erythropoietin on renoprotection in patients undergoing thoracic aortic surgery with moderate hypothermic circulatory arrest. Ann Thorac Surg. 2016 Feb;101(2):690-6. Abstract

162. Nigwekar SU, Strippoli GF, Navaneethan SD. Thyroid hormones for acute kidney injury. Cochrane Database Syst Rev. 2013 Jan 31;(1):CD006740. Full text Abstract

163. Yang Y, Lang XB, Zhang P, et al. Remote ischemic preconditioning for prevention of acute kidney injury: a meta-analysis of randomized controlled trials. Am J Kidney Dis. 2014 Oct;64(4):574-83. Abstract

164. Menting TP, Wever KE, Ozdemir-van Brunschot DMD, et al. Ischaemic preconditioning for the reduction of renal ischaemia reperfusion injury. Cochrane Database Sys Rev. 2017 Mar 4; (3):CD010777. Full text Abstract

165. Moore PK, Hsu RK, Liu KD. Management of acute kidney injury: core curriculum 2018. Am J Kidney Dis. 2018 Feb 22;72(1):136-48. Full text Abstract

166. Lewington AJ, Cerdá J, Mehta RL. Raising awareness of acute kidney injury: a global perspective of a silent killer. Kidney Int. 2013 Sep;84(3):457-67. Full text Abstract

167. Mehta S, Chauhan K, Patel A, et al. The prognostic importance of duration of AKI: a systematic review and meta-analysis. BMC Nephrol. 2018 Apr 19;19(1):91. Full text Abstract

168. Wang HE, Muntner P, Chertow GM, et al. Acute kidney injury and mortality in hospitalized patients. Am J Nephrol. 2012;35(4):349-55. Full text Abstract

169. Coca SG, Yusuf B, Shlipak MG, et al. Long-term risk of mortality and other adverse outcomes after acute kidney injury: systematic review and meta-analysis. Am J Kidney Dis. 2009 Jun;53(6):961-73. Full text Abstract

170. Tao Li PK, Burdmann EA, Mehta RL. Acute kidney injury: global health alert. Int J Organ Transplant Med. 2013;4(1):1-8. Full text Abstract

171. Rimes-Stigare C, Awad A, Mårtensson J, et al. Long-term outcome after acute renal replacement therapy: a narrative review. Acta Anaesthesiol Scand. 2012 Feb;56(2):138-46. Abstract

172. Bhandari S, Turney JH. Survivors of acute renal failure who do not recover renal function. QJM. 1996 Jun;89(6):415-21. Abstract

173. Rifkin DE, Coca SG, Kalantar-Zadeh K. Does AKI Truly Lead to CKD? J Am Soc Nephrol. 2012 Jun;23(6):979-84. Abstract

174. Leung KC, Tonelli M, James MT. Chronic kidney disease following acute kidney injury: risk and outcomes. Nat Rev Nephrol. 2013 Feb;9(2):77-85. Abstract

175. Bucaloiu ID, Kirchner HL, Norfolk ER, et al. Increased risk of death and de novo chronic kidney disease following reversible acute kidney injury. Kidney Int. 2012 Mar;81(5):477-85. Abstract

176. See EJ, Jayasinghe K, Glassford N, et al. Long-term risk of adverse outcomes after acute kidney injury: a systematic review and meta-analysis of cohort studies using consensus definitions of exposure. Kidney Int. 2019 Jan;95(1):160-72. Full text Abstract

177. Jaber S, Paugam C, Futier E, et al; BICAR-ICU Study Group. Sodium bicarbonate therapy for patients with severe metabolic acidaemia in the intensive care unit (BICAR-ICU): a multicentre, open-label, randomised controlled, phase 3 trial. Lancet. 2018 Jul 7;392(10141):31-40. Abstract

178. Finn W. Recovery from acute renal failure. Acute renal failure: a companion to Brenner and Rector's the kidney. 1st ed. Philadelphia, PA: WB Saunders; 2001:425-50.

179. Shaw NJ, Brocklebank JT, Dickinson DF, et al. Long-term outcome for children with acute renal failure following cardiac surgery. Int J Cardiol. 1991 May;31(2):161-5. Abstract

180. Odutayo A, Wong CX, Farkouh M, et al. AKI and long-term risk for cardiovascular events and mortality. J Am Soc Nephrol. 2017 Jan;28(1):377-87. Full text Abstract

181. Legrand M, Rossignol P. Cardiovascular consequences of acute kidney injury. N Engl J Med. 2020 Jun 4;382(23):2238-47. Abstract

182. Cerdá J, Liu KD, Cruz DN, et al. Promoting kidney function recovery in patients with AKI requiring RRT. Clin J Am Soc Nephrol. 2015 Oct 7;10(10):1859-67. Abstract

183. Kidney Disease: Improving Global Outcomes (KDIGO). 2012 clinical practice guideline for the evaluation and management of chronic kidney disease (CKD). Kidney Int Suppl. 2013 Jan;3(1):1-150. Full text

Images

Clinical assessment:

- Compare with baseline renal function (review series of results).
- Assess fluid status: if intravascularly depleted (jugular venous pulse not visible, postural drop in BP and no oedema), consider cautious intravenous fluids.
- Interpret BP in the context of usual values (low BP does not necessarily mean patient needs fluid).
- Reduce/withdraw RAASI if symptomatic hypotension.
- Repeated clinical and biochemical assessment is vital.
- Presence of moderate or severe hyperkalaemia may override recommendations based on change in renal function.
- In severe renal dysfunction assess for symptoms or uraemia.

	Recommendations for RAAS inhibitors	
Change in renal function compared with baseline	**HFpEF (assuming no other prognostic indication).**	**HFREF.**
Increase in serum creatinine by <30%	Consider stop ACEI/ARB/ARNI Review MRA according to fluid status.	Continue unless symptomatic hypotension.
Increase in serum creatinine 30%–50%	Stop RAAS inhibitor.	Consider reducing dose or temporary withdrawal.*
Increase in serum creatinine >50%	Stop RAAS inhibitor.	Temporarily stop RAAS inhibitor.*
Severe renal dysfunction, for example, eGFR <20	Stop RAAS inhibitor.	Stop RAAS inhibitor if symptomatic uraemia irrespective of baseline function.

*Reinitiate and/or retitrate when renal function improved in patients with HFrEF.
ACEI, ACE inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; eGFR, estimated glomerular filtration rate; HFrEF, heart failure with reduced left ventricular ejection fraction; HFpEF, heart failure with preserved left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonists; RAAS, renin–angiotensin–aldosterone.

Figure 1: Management of RAAS inhibitors in response to change in renal function

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

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DISCLOSURES: JM is co-chair for the UK Kidney Association Acute Kidney Injury Specialist Interest Group, co-chair for the UK Kidney MedTech Research Network, and a member of the Renal Service Transformation Programme Acute Kidney Injury Workstream. JM was a Specialist Committee Member Update to NICE Acute Kidney Injury Quality Standard update, and an Expert Commentator for NICE Medtech Innovation Briefing. JM has co-authored national guidelines for the UK Kidney Association, providing best practice guidance for providing renal support for critically ill patients during the COVID-19 pandemic (published November 2020). JM recently co-authored two articles evaluating technology to enable monitoring of kidney tests; he received no payment and has no vested interest in the technologies used. JM delivered a lecture at the Society for Acute Medicine meeting about acute kidney injury (September 2022) and a lecture about one of the above studies at the Royal College of Physicians, in Edinburgh (April, 2020). JM is due to lead a national acute kidney injury summit meeting in September 2023, within his role as co-chair for the UK Kidney Association Acute Kidney Injury Specialist Interest Group. All roles disclosed above are unpaid.

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