Acute kidney injury

What is an acute kidney injury?

Acute kidney injury (AKI) is a term covering a spectrum of injury to the kidneys which can result from a number of causes. It is a clinical syndrome rather than a biochemical diagnosis. It is characterised by a decline in renal excretory function over hours or days that can result in failure to maintain fluid, electrolyte, and acid-base homeostasis.[1]

It is detected and monitored by serial serum creatinine readings primarily, which rise acutely. Urine output and eGFR fall, and may also be used for detection and monitoring of the condition.

Acute kidney disease staging

Acute kidney disease staging according to the Kidney Disease: Improving Global Outcomes classification:[2]

- Stage 1:
  - Serum creatinine levels: 1.5-1.9-fold higher than baseline or increase ≥ 3 mg/L.
  - Urine output <0.5 ml/kg/hr for 6-12 hrs.
- Stage 2:
  - Serum creatinine levels: 2-2.9-fold higher than baseline.
  - Urine output <0.5 ml/kg/hr for ≥12 hrs.
- Stage 3:
  - Serum creatinine levels: 3-fold higher than baseline or increase ≥40 mg/L, or initiation of renal replacement therapy.
  - Urine output <0.3 ml/kg/hr for ≥24 hrs or anuria for ≥12 hrs.

Causes of acute kidney injury (aetiology) [1]

The majority of AKI developing in the community is due to a pre-renal state (90% cases), typically hypotension associated with sepsis and/or fluid depletion (eg, vomiting or diarrhoea). This can be further exacerbated by commonly prescribed drugs - eg, angiotensin-converting enzyme (ACE) inhibitors or non-steroidal anti-inflammatory drugs (NSAIDs) - that impair how the kidneys respond to hypotension.

Prerenal

- Volume depletion (eg, haemorrhage, severe vomiting or diarrhoea, burns, inappropriate diuresis).
- Oedematous states: cardiac failure, cirrhosis, nephrotic syndrome.
- Hypotension (eg, cardiogenic shock, sepsis, anaphylaxis).
- Cardiovascular (eg, arrhythmias).
- Renal hypoperfusion: NSAIDs or selective cyclo-oxygenase-2 (COX-2) inhibitors, ACE inhibitors or angiotensin-II receptor antagonists (AIIRAs - commonly called angiotensin receptor blockers (ARBs)), abdominal aortic aneurysm, renal artery stenosis or occlusion, hepatorenal syndrome.

Intrinsic renal problem

- Glomerular disease: glomerulonephritis, thrombosis, haemolytic uraemic syndrome.
- Tubular injury: acute tubular necrosis (ATN) following prolonged ischaemia; nephrotoxins (eg, aminoglycosides, radiocontrast media, myoglobin, cisplatin, heavy metals, light chains in myeloma kidney).
- Acute interstitial nephritis due to drugs (eg, NSAIDs), infection or autoimmune diseases.
- Vascular disease: vasculitis (usually associated with antineutrophil cytoplasmic antibody), cryoglobulinaemia, polyarteritis nodosa, thrombotic microangiopathy, cholesterol emboli, renal artery stenosis, renal vein thrombosis, malignant hypertension.
- Eclampsia.

Postrenal

- Calculus.
- Blood clot.
- Papillary necrosis.
- Urethral stricture.
- Benign prostatic hypertrophy or prostate cancer.
- Bladder tumour.
- Radiation fibrosis.
- Pelvic malignancy.
- Retroperitoneal fibrosis.

How common is acute kidney injury? (Epidemiology)[1]

- Acute kidney injury is very common in acute illness, with stage 1 acute kidney injury occurring in more than 15% of emergency hospital admissions.
- Community-acquired AKI is thought to be up to three times more common than hospital-acquired AKI.
- Hospital Episode Statistics noted AKI in 2.4% of hospital admissions, but the prevalence calculated from standardised estimates was much higher at 14%.
- The incidence of AKI is increasing, possibly as a result of the number of people in the population who are elderly or at-risk with multiple comorbidities. Improved detection of AKI is also likely to have contributed to this rise.

Risk factors[3]

The National Institute for Health and Care Excellence (NICE) recommends investigating for acute kidney injury, by measuring serum creatinine and comparing with baseline:

In adults with acute illness if any of the following are likely or present:

- Chronic kidney disease (people with eGFR less than 60 ml/min/1.73 m2 are at particular risk).
- Heart failure.
- Liver disease.
- Diabetes.
- History of acute kidney injury.
- Oliguria (urine output less than 0.5 ml/kg/hour).
- Neurological or cognitive impairment or disability, which may mean limited access to fluids because of reliance on a carer.
- Hypovolaemia.
- Use of drugs that can cause or exacerbate kidney injury (eg, non-steroidal anti-inflammatory drugs, aminoglycosides, ACE inhibitors, angiotensin II receptor antagonists and diuretics) within the past week, especially if hypovolaemic.
- Use of iodine-based contrast media within the past week.
- Symptoms or history of urological obstruction, or conditions that may lead to obstruction.
- Sepsis.
- Deteriorating early warning scores.
- Age 65 years or over.

In addition children and young people with acute illness should be investigated for acute kidney injury if:

- Young age, neurological or cognitive impairment or disability, which may mean limited access to fluids because of reliance on a parent or carer.
- Deteriorating paediatric early warning score (based on heart rate, respiratory rate, systolic blood pressure, level of consciousness, oxygen saturation, temperature and capillary refill time).

- Severe diarrhoea (children and young people with bloody diarrhoea are at particular risk).
- Symptoms or signs of nephritis (eg, oedema or haematuria).
- Haematological malignancy.
- Hypotension.

Symptoms of acute kidney injury (presentation)

The presentation will depend on the underlying cause and severity of AKI. Clinically, AKI is recognised by decreasing urine volume (oliguria or anuria) and a rise in serum creatinine. NICE recommends detecting acute kidney injury, in line with the (p)RIFLE (paediatric Risk, Injury, Failure, Loss, End stage renal disease), AKIN (Acute Kidney Injury Network) or KDIGO (Kidney Disease: Improving Global Outcomes) definitions, by using any of the following criteria:[3]

- A rise in serum creatinine of 26 micromol/L or greater within 48 hours.
- A 50% or greater rise in serum creatinine known or presumed to have occurred within the previous seven days.
- A fall in urine output to less than 0.5 ml/kg/hour for more than six hours in adults and more than eight hours in children and young people.
- A 25% or greater fall in eGFR in children and young people within the previous seven days.

Symptoms

- Urine output:
    - AKI is usually accompanied by oliguria or anuria. However, polyuria may occur due either to reduced fluid reabsorption by damaged renal tubules, or the osmotic effect of accumulated metabolites.
    - Abrupt anuria suggests an acute obstruction, acute and severe glomerulonephritis, or acute renal artery occlusion.
    - Gradual diminution of urine output may indicate a urethral stricture or bladder outlet obstruction - eg, benign prostatic hyperplasia.
- Nausea, vomiting.
- Dehydration.
- Confusion.

Signs

- Hypertension.
- Abdomen: may reveal a large, painless bladder typical of chronic urinary retention.
- Dehydration with postural hypotension and no oedema.
- Fluid overload with raised jugular venous pressure (JVP), pulmonary oedema and peripheral oedema.
- Pallor, rash, bruising: petechiae, purpura and nosebleeds may suggest inflammatory or vascular disease, emboli or disseminated intravascular coagulation.
- Pericardial rub.

Assessment and investigations

It is important first to identify the cause of AKI, as this will affect management, particularly where there is a potentially treatable cause (for example, obstruction, hypovolaemia, nephrotoxic drugs or glomerulonephritis). Often, however, there are multiple causes and finding the cause will not always dictate specific management.

Cause established by:[4]

History

- Drugs - nephrotoxic drugs, remembering recreational drugs, over-the-counter drugs and herbal remedies.
- Occupational or recreational history - exposure to sewer systems, tropical diseases, rodents.
- Urinary symptoms.
- Past medical history.

Examination

- Signs of infection or sepsis.
- Signs of acute or chronic heart failure.
- Fluid status (dehydration or fluid overload).
- Palpable bladder or abdominal/pelvic mass.
- Features of underlying systemic disease (rashes, arthralgia).

Urinalysis

- Dipstick urine for blood, nitrates, leukocytes, glucose and protein in all patients with suspected AKI. Consider acute nephritis and referral to a nephrologist if there is blood or protein on the dipstick in the absence of urinary infection or trauma due to catheterisation, and no obvious cause for AKI.
- Urine osmolality.

Blood tests

As appropriate to find cause as dictated by history. This could involve:

- FBC, blood film. (Eosinophilia may be present in acute interstitial nephritis, cholesterol embolisation, vasculitis. Thrombocytopenia and red cell fragments suggest thrombotic microangiopathy.)
- U&Es and creatinine.

- Coagulation studies: disseminated intravascular coagulation associated with sepsis.
- Creatine kinase, myoglobinuria: markedly elevated creatine kinase and myoglobinuria suggest rhabdomyolysis.
- C-reactive protein (CRP): nonspecific marker of infection or inflammation.
- Immunology:
    - Serum immunoglobulins, serum protein electrophoresis, Bence Jones' proteinuria: immune paresis, monoclonal band on serum protein electrophoresis, and Bence Jones' proteinuria suggest myeloma.
    - Antinuclear antibody (ANA): ANA positive in systemic lupus erythematosus (SLE) and other autoimmune disorders; anti-double-stranded DNA (anti-dsDNA) antibodies more specific for SLE; anti-dsDNA antibodies; antineutrophil cytoplasmic antibody (ANCA) - associated with systemic vasculitis; classical antineutrophil cytoplasmic antibodies (c-ANCA) and antiproteinase 3 (anti-PR3) antibodies associated with granulomatosis with polyangiitis; protoplasmic-staining antineutrophil cytoplasmic antibodies (p-ANCA) and antimyeloperoxidase (anti-MPO) antibodies present in microscopic polyangiitis), anti-PR3 antibodies, anti-MPO antibodies.
    - Complement concentrations: low in SLE, acute postinfectious glomerulonephritis, cryoglobulinaemia.
    - Antiglomerular basement membrane (anti-GBM) antibodies: present in Goodpasture's syndrome.
    - Antistreptolysin O and anti-DNase B titres: high after streptococcal infection.
- Virology: hepatitis B and C; HIV: (important implications for infection control within dialysis area).

- New biomarkers: creatinine is a poor indicator of renal function and there have been many studies trying to find a more sensitive biomarker. These include cystatin C, neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1) and interleukin-18 (IL-18). None has yet been recommended for routine use.

Ultrasound

When obstruction is suspected or no cause has been identified.

Other radiology

Where appropriate - for example:

- CXR (pulmonary oedema).
- Low-dose non-contrast computed tomography (NCCT) scan is the preferred imaging modality for any non-pregnant adult with suspected renal colic. NCCT has a high sensitivity and specificity. If the patient is pregnant or under 16 years of age, a renal ultrasound is preferred as the initial investigation.[5]
- Contrast studies such as intravenous urogram (IVU) and renal angiography should be avoided because of the risk of contrast nephropathy.
- Doppler ultrasound of the renal artery and veins: assessment of possible occlusion of the renal artery and veins.
- Magnetic resonance angiography: for more accurate assessment of renal vascular occlusion.

Which tests are relevant will vary considerably with the individual. Urinalysis is done in all and ultrasound is often indicated.

Differential diagnosis

- CKD: factors that suggest CKD include:
    - Long duration of symptoms.
    - Nocturia.
    - Absence of acute illness.
    - Anaemia.
    - Hyperphosphataemia, hypocalcaemia (but similar laboratory findings may complicate AKI).
    - Reduced renal size and cortical thickness on renal ultrasound (but renal size is typically preserved in patients with diabetes).
- Acute on chronic kidney disease.

Management of acute kidney injury[1] [3]

There is no specific treatment for AKI so management is largely supportive. It consists of treating the cause where possible, monitoring fluid and electrolyte balance closely and optimising haemodynamic status with appropriate fluid therapy.

Immediate admission or referral to hospital is not needed for all people with acute kidney injury. Individual factors such as age, comorbidities, and the need for carer input should be considered. As a general guide:

- Urgent admission or same day referral for:
    - Likely stage 3 acute kidney injury.
    - An underlying cause that requires urgent secondary care management - eg, when an obstructed, infected kidney is suspected.
    - No identifiable cause for acute kidney injury.
    - A risk of urinary tract obstruction (eg, prostate or bladder disease, abdominal or pelvic cancer, previous hydronephrosis, recurrent urinary tract infections), or other conditions consistent with possible obstruction (eg, anuria, single functioning kidney, or neurogenic bladder).
    - Sepsis.
    - Evidence of hypovolaemia requiring intravenous fluid replacement and monitoring.
    - Deterioration in clinical condition or a need for observation or monitoring of a frequency which is impractical in primary care.
    - A complication of acute kidney injury requiring urgent secondary care management - eg, pulmonary oedema, uraemic encephalopathy or pericarditis, or severe hyperkalaemia.
- Refer anyone with upper tract urological obstruction to a urologist. Refer immediately when one or more of the following present: pyonephrosis, an obstructed solitary kidney, bilateral upper urinary tract obstruction, complications of acute kidney injury caused by urological obstruction.

- Discuss the management of acute kidney injury with a nephrologist as soon as possible and within 24 hours of detection, when one or more of the following is present:
    - Stage 4 or 5 chronic kidney disease.
    - A possible diagnosis that may need specialist treatment - eg, tubulointerstitial nephritis, glomerulonephritis (indicated by haematuria/proteinuria), systemic vasculitis that may also be affecting the kidney, or myeloma.
    - Inadequate response to treatment.
    - Other complications associated with acute kidney injury.
    - A renal transplant.
- For people with stage 1 acute kidney injury, discuss with a general physician or nephrologist if there is uncertainty about the cause or management, or the person is not responding to treatment.

- For people with stage 1 acute kidney injury, who do not have an indication for admission, referral, or specialist input:
    - Manage the cause, if the expertise and resources are available in primary care.
    - Offer supportive measures such as advice on maintaining appropriate hydration.
    - Consider stopping potentially nephrotoxic medications (eg, ACE enzyme inhibitors, angiotensin II receptor antagonists, nonsteroidal anti-inflammatory drugs, and diuretics) or adjusting the doses of medication in relation to renal function. Seek specialist advice if unsure. Information on dose adjustment in renal impairment is available from the BNF (see link in Further Reading section below) or the manufacturers' Summary of Product Characteristics.
    - Monitor creatinine regularly, using clinical judgement to determine frequency. Even small increases in creatinine can be significant.
    - Reconsider the need to admit to hospital or discuss with a specialist if there is deterioration in the person's condition, or an inadequate response to treatment.
- Consider referral to a paediatric nephrologist for children and young people who have recovered from an episode of acute kidney injury but have hypertension, impaired renal function or 1+ or greater proteinuria on dipstick testing of an early morning urine sample.

The NICE guideline (see reference link below) provides further recommendations for management in secondary care and indications for renal replacement therapy. Recommendations for pharmacological management include:

- Do not routinely offer loop diuretics to treat acute kidney injury.
- Consider loop diuretics for treating fluid overload or oedema while awaiting renal replacement therapy or renal function is recovering in anyone not receiving renal replacement therapy.
- Do not offer low-dose dopamine to treat acute kidney injury.

Complications of acute kidney injury

AKI, if unrecognised and allowed to worsen, will result in progressive uraemia (toxic waste accumulation), metabolic acidosis, hyperkalaemia, spontaneous haemorrhage and pulmonary oedema if fluid balance is not carefully monitored.[1] These complications prolong hospitalisation and are associated with increased mortality.

Prognosis[1]

- Any acute change in kidney function often indicates severe systemic derangement and predicts a poor prognosis.
- Early detection is likely to improve prognosis. Up to 30% of deaths from AKI are thought to be preventable by early recognition and management of patient risk factors.
- The prognosis varies depending on clinical setting, the underlying cause, and any comorbidities. There is also evidence that mortality increases with increasing stages of AKI. A UK hospital-based study reported an overall mortality of 23.8% (16.1% for stage 1, 36.1% for stage 3).
- AKI acquired in the community has a lower mortality rate than hospital acquired AKI, but is still associated with increased morbidity and mortality.
- A systematic review studying long-term prognosis after AKI found that in people with chronic kidney disease preceding the episode of AKI there was a four- to five-fold increase in renal outcomes, and mortality outcomes were doubled compared with people with AKI alone.

Prevention of acute kidney injury

The best 'treatment' of AKI is prevention. NICE guidance reflects this, with the emphasis being on identification of patients at risk. Close monitoring of urinary output and creatinine levels for these patients allows early detection. Avoidance of nephrotoxic drugs and iodinated contrast agents in these patients reduces the risk of them developing AKI. All acutely ill patients in hospital should be closely monitored for signs of developing AKI.

At-risk patients who need iodinated contrast agents should be offered intravenous volume expansion with isotonic sodium bicarbonate or 0.9% sodium chloride to reduce the risks of developing AKI.[3]

Further reading

- NKF (National Kidney Federation)
- British National Formulary (BNF); NICE Evidence Services (UK access only)
- Acute kidney injury; NICE Quality Standards, December 2014 - last updated March 2023
- UK Kidney Association
- Peerapornratana S, Manrique-Caballero CL, Gomez H, et al; Acute kidney injury from sepsis: current concepts, epidemiology, pathophysiology, prevention and treatment. Kidney Int. 2019 Nov;96(5):1083-1099. doi: 10.1016/j.kint.2019.05.026. Epub 2019 Jun 7.
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- Levey AS; Defining AKD: The Spectrum of AKI, AKD, and CKD. Nephron. 2022;146(3):302-305. doi: 10.1159/000516647. Epub 2021 Jun 24.

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