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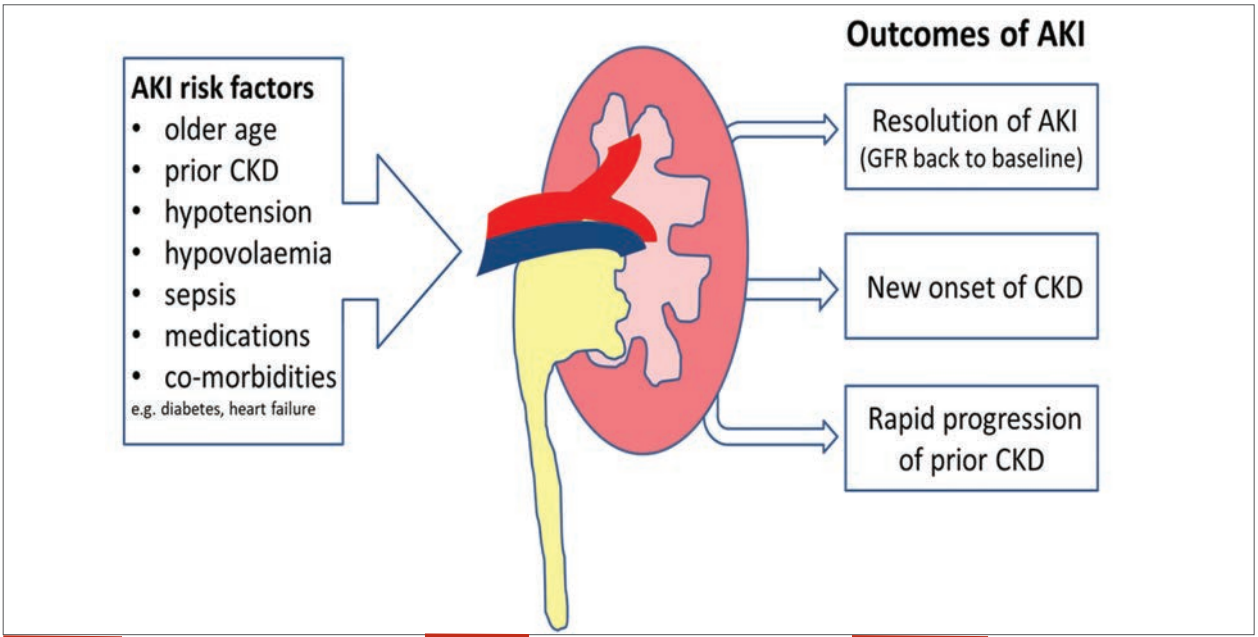


FIGURE 1
Acute kidney injury: common risk factors and potential outcomes

What are the risk factors for acute kidney injury?

ACUTE KIDNEY INJURY (AKI) IS A COMMON COMPLICATION IN HOSPITALISED PATIENTS AND IS ASSOCIATED WITH an increased risk of chronic kidney disease (CKD) and higher mortality.[1,2]

Approximately two thirds of AKI cases develop in the community, prior to hospital admission.[3] AKI may be challenging to recognise because it is typically asymptomatic, hence the opportunities for prevention of AKI are often missed.[4] AKI is a potentially reversible process so improvements in timely recognition and earlier interventions could have a substantial impact on patient outcomes.[4] GPs play an important role in identifying AKI.[5]

AKI is a major risk factor for the development of CKD.[6] This relationship is bidirectional; patients with CKD are at substantially higher risk of AKI.[7] As a result, AKI is frequently superimposed on CKD, and can contribute significantly to progression of CKD. With the increasing burden of CKD worldwide, effective management of AKI is crucial.[7,8]

How should patients be assessed?

IDENTIFICATION

In patients with AKI an acute reduction in kidney function typically occurs within hours to days with resulting impairment in toxin removal and associated disturbance of fluid, electrolyte and acid-base balance. As the glomerular filtration rate (GFR) is falling a single estimated GFR (eGFR) measurement is not a reliable indicator of the current level of kidney function.

AKI is usually detected incidentally in the setting of other illness when a urea & electrolytes (U&E) test has been ordered and a rise in serum creatinine from baseline is identified. Most laboratories now issue electronic AKI alerts, which flag changes in serum creatinine indicative of AKI, helping to identify patients at an earlier stage.[9,10] AKI may also be associated with a reduction in urine output but this is difficult to detect in community settings.

'AKI is a major risk factor for CKD and patients with CKD are at substantially higher risk of AKI'

Which patients should be referred?

RISK FACTORS

There are multiple background risk factors that make some individuals more vulnerable to AKI particularly when they become acutely unwell.[3,4] Recognising these risk factors may lead to earlier and more frequent testing of U&E in adults during any acute illness such as diarrhoea, vomiting, reduced fluid intake, and worsening of underlying conditions.

In adults with acute illness, the risk of AKI is high if any of the features listed in box 1, p12, are present.

It is important to note that in patients with CKD and no clear precipitating illness, a rise in creatinine may still indicate AKI rather than progression of the underlying CKD.[11]

There could be potentially reversible factors contributing to an acute rise in »

serum creatinine e.g. nephrotoxicity from a newly introduced drug or urological symptoms (hesitancy, poor stream, frequency) that indicate superimposed bladder outlet obstruction. AKI may be present in individuals who develop a rash after drug exposure e.g. antibiotics (penicillin and its derivatives, cephalosporins) or proton pump inhibitors.[12]

COMMON CAUSES

AKI can result from abnormal perfusion to a structurally normal kidney (pre-renal AKI), injury to the nephrons (renal AKI) or obstruction to urinary flow (post-renal AKI). Common causes of AKI are shown in box 2, below.

Restoring fluid volume to optimal levels may reverse pre-renal AKI. However, prolonged pre-renal AKI can lead to kidney cell damage known as acute tubular necrosis (ATN) which is not fluid volume responsive. Recovery may be slow and the patient's renal function may not recover to its previous baseline.

AKI due to acute glomerular disease is far less common than pre-renal AKI in the community.

If the patient has a fever, rash, joint pains or pulmonary infiltrates on chest X-ray a less common aetiology for AKI should be considered. Proteinuria and/or haematuria on urine dipstick may indicate an underlying glomerular disease.

Box 1

Risk factors for acute kidney injury (AKI)

- Past history of CKD (adults with eGFR < 60 ml/min/1.73 m^2)
- Older age (≥ 65 years old)
- Sepsis
- Comorbidities such as diabetes, heart failure, liver disease
- Past history of AKI
- Hypovolaemia
- Drugs e.g. NSAIDs, ACE inhibitors, ARBs, diuretics especially if hypovolaemic
- Use of iodine-based contrast media within the past week
- Symptoms or history of urological obstruction
- Neurological or cognitive impairment or disability, which may limit access to fluids
- Deteriorating early warning scores (in hospital patients)

DIAGNOSIS

If an unexpected rise in serum creatinine is observed, a careful assessment of the patient's history should be carried out to establish if any of the more common AKI risk factors are present (see box 1, below). This should be accompanied by a thorough clinical examination, a review of prescribed medication and baseline renal function (where known).

AKI might be suspected where there is reduced fluid intake and/or increased fluid losses, worsening urinary tract symptoms and recent drug ingestion.

'Patients with heart or liver failure are at particular risk of AKI especially when the underlying disease becomes decompensated'

The presence of other clinical features such as fever, rash, joint pains, haemoptysis and non-specific malaise may indicate AKI secondary to a systemic disease.

Clinical examination includes assessment of fluid volume status, which is guided by clinical signs including heart rate, blood pressure, jugular venous pressure, peripheral perfusion (capillary refill time), skin turgor and mucous membranes. It is important to remember that postural changes in pulse and blood pressure are more sensitive indicators of hypovolaemia than supine observations.

Patients with heart or liver failure are at particular risk of AKI especially when the underlying disease becomes decompensated. Of note, the presence of fluid overload (peripheral oedema or ascites) does not prevent AKI developing.

A urine dipstick test for blood, protein, leucocytes, nitrites and glucose is helpful if AKI is suspected or detected. Proteinuria and haematuria (2+ to 4+) on urinalysis raises the possibility that an acute glomerulonephritis is causing AKI and this indicates the need for more urgent referral to hospital.[11]

A high specific gravity (> 1.020) suggests fluid volume depletion and increased oral fluid intake may be needed.

Box 2

Classification of acute kidney injury (AKI)

Classification of AKI	Common causes
Pre-renal AKI **Abnormal perfusion to a structurally normal kidney**	**Hypovolaemia** ● Vomiting and diarrhoea ● Dehydration ● Blood loss **Hypotension** ● Sepsis ● Cardiac failure ● Liver failure ● Medication
Renal AKI **Injury to nephrons (glomeruli and/or tubules), known as intrinsic renal disease**	**Prolonged pre-renal AKI insults** ● Acute tubular necrosis (ATN) due to: — Prolonged pre-renal AKI — Drugs/toxins ● Rapidly progressive glomerulonephritis (e.g. post-infectious or associated with ANCA-vasculitis) ● Allergic interstitial nephritis: — Drug-induced (commonly antibiotics) — Infection-associated ● Vascular damage e.g. malignant hypertension
Post-renal AKI **Obstruction to urinary flow**	**Obstruction** ● Ureteric stones ● Pelvic malignancy ● Prostate hypertrophy

key points

SELECTED BY

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Acute kidney injury (AKI) is a common complication in hospitalised patients and is associated with an increased risk of chronic kidney disease (CKD) and higher mortality. Two thirds of AKI cases develop in the community prior to hospital admission. The relationship with CKD is bidirectional: patients with CKD are at much higher risk of AKI and AKI can contribute significantly to the progression of CKD.

AKI can result from abnormal perfusion to a structurally normal kidney (pre-renal AKI), injury to the nephrons (renal AKI) or obstruction to urinary flow (post-renal AKI). Restoring fluid volume to optimal levels may reverse pre-renal AKI. However, prolonged pre-renal AKI can lead to kidney cell damage known as acute tubular necrosis which is not fluid volume responsive. Recovery may be slow and incomplete.

AKI may be challenging to recognise because it is typically asymptomatic. It is usually detected incidentally in the setting of another illness when a rise in serum creatinine from baseline is identified. AKI may also be associated with a reduction in urine output but this is difficult to detect in community settings. Risk factors for AKI include age ≥ 65, diabetes, CKD, neurological or cognitive impairment, heart failure and the use of potentially nephrotoxic medications. Recognition of those at risk should prompt earlier and more frequent testing of U&E during any acute illness.

If an unexpected rise in serum creatinine is observed, a careful assessment of the patient's history, and a medication review, should be carried out to establish if any of the more common AKI risk factors are present. If the patient has a fever, rash, joint pains or pulmonary infiltrates on chest X-ray a less common aetiology for AKI should be considered. Proteinuria and/or haematuria on urine dipstick testing may indicate glomerular disease. Urological symptoms may indicate bladder outlet obstruction. Clinical examination should include an assessment of fluid volume status. Patients with heart or liver failure are at particular risk of AKI especially when decompensation occurs. Fluid overload (peripheral oedema or ascites) does not prevent AKI developing.

Direct same day contact with a nephrology team is advised for those patients who may require urgent dialysis for AKI complications such as hyperkalaemia, metabolic acidosis, and/or pulmonary oedema. NICE also recommends urgent referral for those patients suspected to have urinary tract obstruction; AKI and sepsis; hypovolaemia with the need for IV fluids and individuals with no identifiable cause for AKI. Management of AKI should be discussed with a nephrologist if the patient has one or more of the following: a renal transplant; a possible diagnosis requiring specialist investigation and treatment e.g. glomerulonephritis, vasculitis, myeloma; or AKI occurring in a patient with advanced CKD. If there is a clear cause for the AKI and it is responding to management in the community, referral is not necessary.

If the cause of AKI is readily apparent then an ultrasound of the urinary tract is not necessary.[11] If an infected and obstructed kidney is suspected then an immediate ultrasound of the urinary tract is needed to help plan management including drainage and antibiotics.[11] When individuals have no obvious cause for AKI or may be at risk of urinary tract obstruction urgent ultrasound of the urinary tract is recommended (within 24 hours of assessment).[11]

Basic laboratory investigations for AKI include: U&E (results should be compared with baseline values whenever possible); full blood count; CRP; liver function tests; glucose and a bone profile.

Immunological tests for rarer causes of AKI may be required such as: antineutrophil cytoplasmic antibodies (for vasculitis); anti-glomerular basement membrane (GBM) antibody (for anti-GBM disease); autoantibody screen including anti-dsDNA titres and complement levels (for SLE and lupus nephritis); serum free light chains, serum immunoglobulins, plasma protein electrophoresis (for myeloma).

Box 3

Drugs that may complicate the management of acute kidney injury

Drugs interfering with renal perfusion
- ACE inhibitors and ARBs
- NSAIDs
- All antihypertensives
- Diuretics
- Nitrates
- Nicorandil

Drugs requiring dose reduction or cessation
- Low molecular weight heparins
- Opiates
- Penicillin-based antibiotics
- Metformin
- Sulphonylurea-based hypoglycaemic agents
- Aciclovir
- High-dose statins

Drugs requiring close monitoring
- Warfarin

Drugs aggravating hyperkalaemia
- Digoxin
- Beta-blockers
- Trimethoprim
- Potassium-sparing diuretics e.g. eplerenone, spironolactone, amiloride

MANAGEMENT

The focus of AKI management is the identification of modifiable risk factors and management of the conditions contributing to renal dysfunction.

The fluid volume status of patients with AKI must be accurately assessed by taking a careful history and examination. If the patient is hypovolaemic or dehydrated increased oral intake of fluids should be encouraged. However, it is important to avoid inadvertent fluid overload. Monitoring their weight may help patients assess their fluid volume status.

Individuals with suspected sepsis should be referred to hospital for blood cultures, antibiotics and fluid resuscitation. Early treatment of infections that may be contributing to hypotension is advised.

Drugs that may induce, exacerbate or complicate AKI should be stopped, at least temporarily. Diuretics, angiotensin receptor blockers (ARBs), ACE inhibitors, and NSAIDs will exacerbate hypoperfusion of the kidneys and should be withheld until the patient has recovered and AKI has resolved. Drugs that can complicate the management of AKI are shown in box 3, below.

Medications are often co-factors in the development of AKI. Furthermore, because of a sudden decrease in renal function associated with AKI, many drugs will need their dosage reduced to avoid serious side effects. It is important to review all the patient's regular medications (see box 3, left).

If medications which might aggravate hyperkalaemia are being commenced in patients with advanced CKD, who are already at risk, careful monitoring of potassium is paramount.

Urgent referral to a urologist for relief of urinary tract or bladder outlet obstruction is crucial.

REFERRAL

Not all patients with AKI need to be referred to hospital. If there is a clear cause for the AKI and it is responding to management in the community referral is not necessary.

Direct same day contact with a nephrology team is advised for those patients who may require urgent dialysis for AKI complications such as hyperkalaemia, metabolic acidosis, and/or pulmonary oedema.[11] NICE also recommends urgent referral to hospital for those patients suspected to have urinary tract obstruction; AKI and sepsis; hypovolaemia with the need for IV fluids and individuals with no identifiable cause for AKI.[11] »

Box 4

Medicine sick day rules for patients that may reduce the risk of AKI

When you are unwell with any of the following:
- Vomiting or diarrhoea
- Fevers, sweats or shaking

Then stop the drugs listed below. Restart these drugs when you are well (after 24-48 hours eating and drinking normally)

Medications to stop temporarily
- ACE inhibitors: (drug names ending in 'pril')
- ARBs: (drug names ending in 'sartan')
- NSAIDs: anti-inflammatory painkillers; e.g. ibuprofen, diclofenac, naproxen
- Diuretics: e.g. bendroflumethiazide, furosemide, spironolactone
- Metformin

Management of AKI should be discussed with a nephrologist if the patient has one or more of the following:
- A renal transplant
- A possible diagnosis requiring specialist investigation and treatment e.g. glomerulonephritis, vasculitis, myeloma
- AKI without an obvious cause
- AKI occurring in a patient with advanced CKD (where the baseline eGFR is < 30 ml/min/1.73m^2)

If a patient seems to have recovered from their AKI but still has an eGFR < 30 ml/min/1.73m^2 or significant proteinuria (urinary albumin:creatinine ratio > 50 mg/mmol) referral to nephrology should be considered.[11]

PREVENTION

Providing information and support to high-risk patients and carers can help to prevent AKI. Some nephrologists advocate discussing the risk of AKI in the setting of acute illness and the use of sick day rules i.e. temporary cessation of certain drugs (diuretics, ACE inhibitors, ARBs, metformin, NSAIDs) in adults with diarrhoea, vomiting or sepsis until their condition has improved and stabilised, see box 4, above. Although such sick day rules advice for AKI has been widely adopted there is still limited evidence for its effectiveness.[13,14,15]

CONCLUSION

AKI can result in prolonged hospitalisation and is associated with an increased risk of CKD and higher mortality. It is a common but potentially reversible condition. Identifying those at risk of AKI, and educating them about the condition, in particular the potential harm from prescribed drugs, may limit the frequency and severity of AKI.

GPs play a key role in the early identification and management of patients with AKI in the community. Good communication between primary and secondary care teams and timely access to appropriate investigations and treatment are critical to reducing the impact of AKI.

Competing interests: None

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