



Be vigilant for acute kidney injury in primary care

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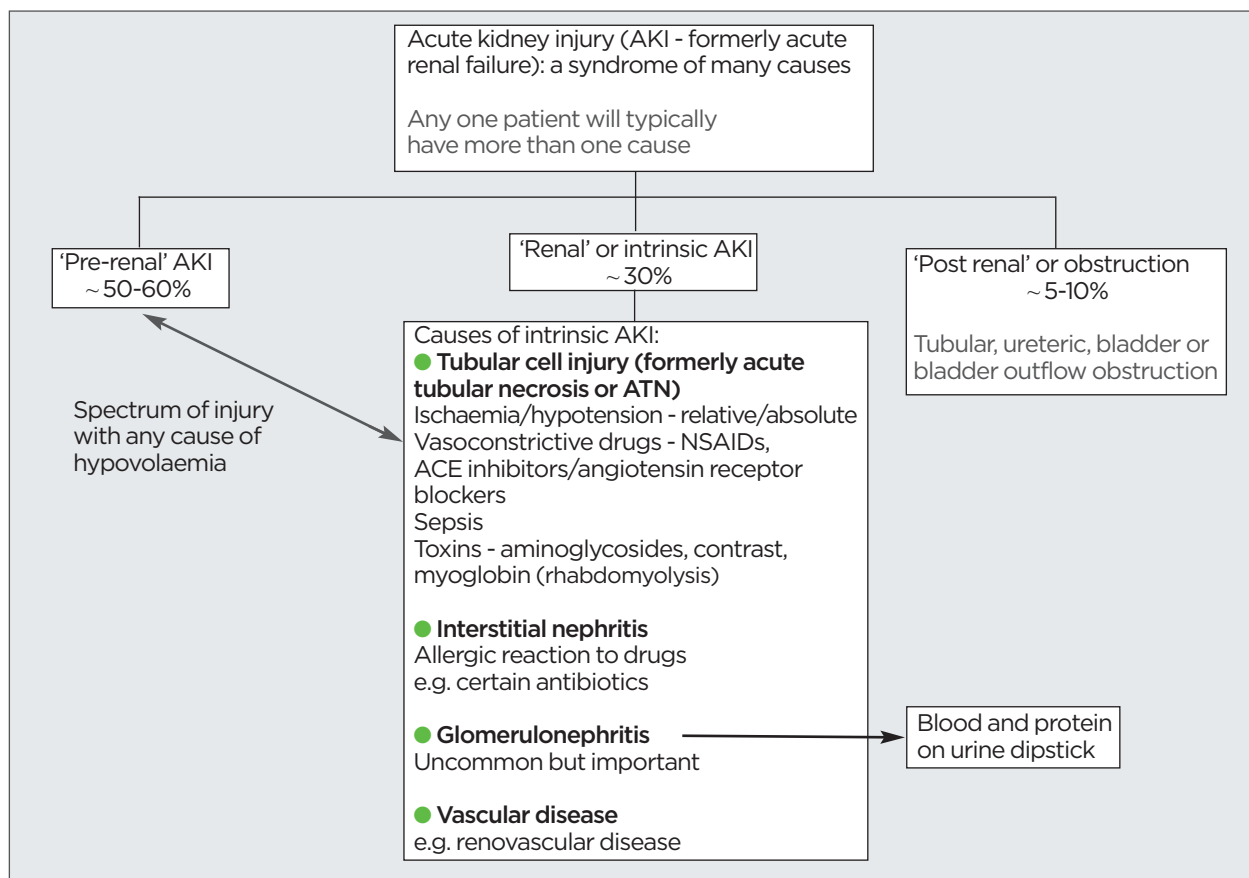


FIGURE 1

Causes of acute kidney injury (AKI). Note that AKI is now regarded as a spectrum of injury ranging from minimal to devastating

What are the risk factors for AKI?

How should diagnosis be made?

Which patients should be referred?



ACUTE KIDNEY INJURY (AKI) HAS BEEN THE CINDERELLA OF ACUTE ORGAN INJURIES.

Large studies have found that about 20% of all adult emergency admissions are affected by AKI.¹⁻⁵ The mortality rate for AKI is almost 25%.^{5,6} As this condition is both frequent and devastating it has a major impact on patient health and NHS costs.⁷ One conservative estimate from an NHS Kidney Care study is that AKI, excluding AKI in the community, causes more than 10,000 preventable deaths a year in England alone.³

AKI was previously called acute

renal failure.⁸ It was regarded as uncommon, with patients typically managed by nephrologists. However, it is now accepted that AKI represents a wide spectrum of injury to the kidneys, not just kidney failure. It is a common problem among the increasingly elderly patients who are admitted to hospital.

A report published by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD)⁹ described systemic deficiencies in the care of adult patients dying from AKI. It became clear that clinicians needed to improve their recognition and management of this condition.

It is not a problem confined to acute hospitals, the vast majority of AKI cases start with an illness in the community. In our study, 67% of AKI cases were identified on blood samples from the A&E department, admission areas or the community.¹⁰ The NCEPOD report led to the commissioning of the NICE clinical guideline on AKI published in August this year.¹¹

PATHOPHYSIOLOGY

In AKI, loss of kidney function contributes to morbidity and mortality. Patients die from AKI rather than with AKI as a complication of an underlying illness. Even when comorbidities are >>

SPECIAL REPORT

ACUTE KIDNEY INJURY

Box 1

Risk factors predisposing to acute kidney injury in the community, adapted from the NICE guideline on AKI¹¹

- Older age – especially over 65 years
- Chronic kidney disease (CKD)²⁷ – especially CKD stage 4 or worse (GFR < 30 ml/min/1.73m²)
- Diabetes – a substantial proportion of type 2 diabetes patients will suffer AKI²³
- The deteriorating patient who is ill for any reason
- Hypovolaemia
- Sepsis
- Other organ failure – notably heart and liver failure
- Nephrotoxic medication use in the community within the past week, especially if hypovolaemic
 - ACE inhibitors or angiotensin receptor blockers
 - NSAIDs – prescribed or over the counter
 - Hypotensive agents including all diuretics
 - Lithium
- Symptoms or history of urological obstruction, or conditions that may lead to obstruction
- Limited access to fluid because of neurological or cognitive impairment or disability
- Previous AKI

Box 2

The detection and staging of acute kidney injury in adults, adapted from the Kidney Disease: Improving Global Outcomes (KDIGO) guideline²⁸

AKI should be diagnosed when any of these criteria are met:

- creatinine rises by $\geq 26 \mu\text{mol/L}$ over 48 hours or less
- creatinine is known or presumed to have risen by $\geq 50\%$ over 7 days or less
- urine output falls to $< 0.5 \text{ ml/kg/hour}$ for ≥ 6 hours

AKI is staged when the creatinine has peaked – which may be obvious only in retrospect. A simplified version of the KDIGO staging is shown below:

Stage	Creatinine rise
1	Rise $\geq 26 \mu\text{mol/L}^\dagger$ within 48 hours or 50–99% rise from baseline within 7 days* (1.50–1.99 $\times$ baseline)
2	100–199% rise from baseline within 7 days* (2.00–2.99 $\times$ baseline)
3	$\geq 200\%$ rise from baseline within 7 days* ($\geq 3.00 \times$ baseline) or any requirement for renal replacement therapy

[†] Equivalent to 0.3 mg/dL

* Known or presumed (based on history) to have occurred over 7 days or less

taken into account, AKI has an independent effect on mortality.¹⁰ This may be because AKI is a pro-inflammatory state that induces distant organ dysfunction: so-called organ crosstalk.¹²

The metabolic work of the kidney tubule imposes major energy demands, especially on the proximal tubule and medullary thick ascending limb. At the same time the tubule normally operates under conditions of borderline oxygen supply, especially in the outer medulla.¹³ If the blood supply to the kidney is compromised, this part of the kidney can fall off a 'hypoxic cliff.' In our ageing, hypertensive society, the kidney is used to a blood pressure in a certain, relatively higher range.¹⁴ In the development of AKI, the typical patient will suffer a surprisingly modest fall in blood pressure of about

15–20 mmHg.¹⁵ It is this relative or absolute hypotension that can lead to a range of tubular injury.

'Patients die from AKI rather than with AKI as a complication of an underlying illness'

Traditionally tubular injury has been divided simplistically into either pre-renal AKI (reversible ischaemia of tubules) or frank acute tubular necrosis. However, the kidney shows various pathologies in AKI, including tubular injury, tubular obstruction,

tubular cell necrosis, apoptosis, and inflammation.^{16,17} Thus acute tubular necrosis is no longer a useful term. The pre-renal – tubular cell injury spectrum is best viewed as just that, a complex spectrum with a wide range of injury. This view has been reinforced by the finding that even small rises in creatinine, indicating AKI, are independently associated with increased mortality.^{7,8,19}

CAUSES

The causes of AKI have traditionally been divided into pre-renal, intrinsic renal, and post-renal or obstructive see figure 1, p23.

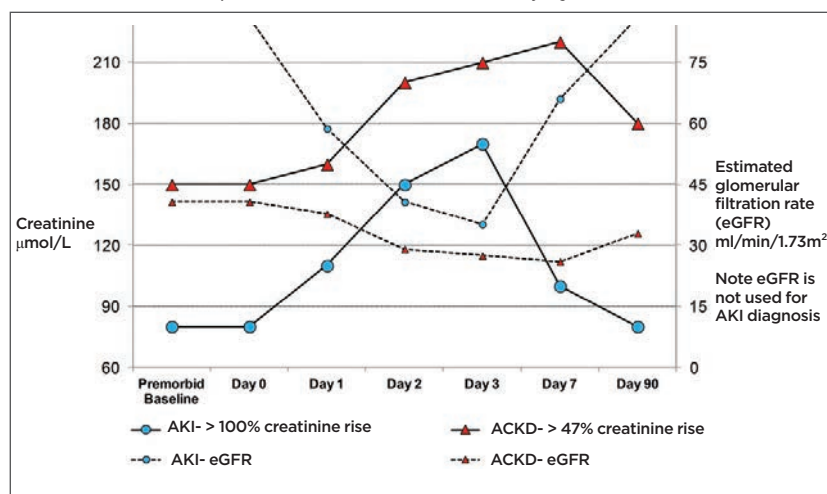
Any cause of hypovolaemia or reduced effective circulating volume can inflict ischaemic tubular injury. These include fluid loss (diarrhoea, vomiting, etc), and blood loss, and other causes of hypotension (relative or absolute, including pump or cardiac failure). Intrinsic renal causes of AKI can be thought of as conditions manifested as direct injury to the glomerulus, the tubule, the interstitium, or the vasculature, see figure 1, p23.

Post-renal AKI refers to any obstruction within the tubule itself, ureters, bladder or the bladder outflow/urethra. Prostatic hyperplasia is a common cause of the latter form of obstruction,²⁰ so AKI in any older man should raise the suspicion of this condition.

The clinician should be aware of the risk factors and conditions that predispose to the development of AKI, see box 1, above. Thus a patient

FIGURE 2

Acute kidney injury (AKI) and acute on chronic kidney disease (ACKD). The graph shows one patient (in blue) with AKI and $>100\%$ rise in creatinine over three days, and another patient (in red) with pre-existing CKD, who has a superimposed episode of AKI, i.e. ACKD



Box 3

Focused assessment of the sick patient with possible acute kidney injury

History

Ask the patient whether they have been passing a normal volume of urine; check past medical and drug history

Early warning score observations

Look for relative hypotension

● Remember ≥ 30 bpm rise in standing heart rate (HR) is the most sensitive sign of hypovolaemia²⁹ (so do lying and standing HR as well as BP)

● Hypernatraemia in the elderly is best indicated by reduced consciousness and/or loss of forearm/subclavicular skin turgor (recoil takes ≥ 3 sec after 3 sec of pinching)³⁰

Cardiovascular examination

Check for oedema

Chest examination

Assess for infection or pulmonary oedema

Abdominal examination

Check for abdominal mass or palpable bladder

Be alert for signs of other organ disease

Signs may indicate multisystem disease (e.g. non-blanching purpuric rash in vasculitis)

Urinalysis

If possible check for presence of blood and protein ($> 1+$ of both on dipstick), indicative of glomerulonephritis

Weight

Box 4

Indications for referral to hospital in acute kidney injury, adapted from the NICE AKI guideline¹¹

- Patient reported oliguria
- Any requirement for (intravenous) fluid resuscitation or any sepsis
- Possible diagnosis that may need specialist treatment e.g. vasculitis, glomerulonephritis, tubulointerstitial nephritis or myeloma
- Acute kidney injury with no clear cause
- Complications associated with acute kidney injury, e.g. hyperkalaemia, uraemia, or fluid overload
- Stage 3 acute kidney injury ($\geq 200\%$ rise in creatinine) – consider referral for stage 1-2 (see box 2, p24) if not improving
- Renal transplant
- AKI in known chronic kidney disease stage 4 or 5 (ACKD) – little room for manoeuvre

Indications for management at home with monitoring

- Stage 1 acute kidney injury likely to respond safely to management in the community e.g. cessation/suspension of nephrotoxic medications, limited oral rehydration
- End of life care with support at home using the Gold Standard Framework

with chronic kidney disease (CKD) may be stable and appropriately treated with an ACE inhibitor for hypertension, until an episode of diarrhoea, vomiting, hypotension and AKI occurs.

AKI SYNDROMES

The diagnosis of AKI is currently based on a rise in creatinine, and/or reduced urine output. Oliguria is detectable occasionally on history taking, but AKI in the community is most often diagnosed on the basis of a rise in creatinine, see box 2, p24. Estimated glomerular filtration rate (eGFR) is not used in the diagnosis of AKI,²¹ and is shown in figure 2, p24 for information only.

During AKI, after a single defined insult to the kidneys, creatinine may rise over a few days before reaching a plateau, see figure 2, p24.²² Creatinine is a by-product of muscle energy metabolism. In patients with low muscle mass, AKI may only be seen as a small rise in creatinine. The rise in creatinine needs to be on a short, acute timescale to distinguish it from the slower steady rise of progressive CKD.

Clinicians should be aware of certain AKI subgroups, shown in schematic form in figure 2, p24. The graph shows one patient with AKI and $>100\%$ rise in creatinine over three days and another patient with pre-existing CKD, who has a superimposed episode of AKI, called acute on chronic kidney disease (ACKD).

‘The diagnosis of AKI is currently based on a rise in creatinine, and/or reduced urine output’

It is increasingly recognised that episodes of AKI can fail to recover fully, particularly in patients with more severe AKI or with prior CKD. Each episode of AKI is another blow to the kidneys, potentially leading to cumulative damage.^{23,24} An episode of AKI is often the final straw for a patient with CKD resulting in end stage renal disease and the need for dialysis.

The recognised international guidance for the detection and staging of AKI is shown in box 2, p24, in simplified form. It has recently been recognised that subtle degrees of AKI with small rises in creatinine ≥ 26 $\mu\text{mol/L}$

independently affect mortality.^{7,18,19} These small rises have therefore been incorporated into the definition of AKI. In the near future it should be standard for all UK laboratory urea, creatinine and electrolyte (U&E) results to include an alert warning for any possible AKI.²⁵

‘Patients should be advised to suspend ACE inhibitors and angiotensin receptor blockers immediately during an episode of vomiting and/or diarrhoea’

INITIAL ASSESSMENT

A key step in the initial assessment is to identify the likely cause(s) of kidney injury, as AKI is a syndrome and not a diagnosis, see box 3, left. In most cases there will be multiple causes.

Not all patients need immediate referral to hospital, see box 4, left. Other factors such as age, the number and severity of comorbidities, and availability of carers will impact on any decision regarding referral.

For example, the following patient could potentially be managed at home.

A 30-year-old man with no associated comorbidities who is generally fit and well develops diarrhoea, after a night out, with no red flag symptoms. Blood tests showed a significant rise in creatinine suggestive of stage 1 AKI. He remains clinically well and is able to keep up his fluid intake. He continues to pass urine as normal. His condition and kidney function should be monitored within 48 to 72 hours of the original detection of AKI, and the latter followed up every 48 to 72 hours over the next two weeks to ensure full recovery.

There has been little research on the assessment of sick patients in the community to determine whether hospital admission is needed. It has been advocated that the National Early Warning Score (NEWS) should be used for this purpose.²⁶

When possible all the major causes »

key points

SELECTED BY

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About 20% of all adult emergency admissions are affected by acute kidney injury (AKI) and the mortality rate is almost 25%. One estimate is that AKI, excluding AKI in the community, causes more than 10,000 preventable deaths a year in England.

AKI represents a wide spectrum of injury to the kidneys, not just kidney failure, the vast majority of AKI cases start with an illness in the community. The diagnosis of AKI is currently based on a rise in creatinine, and/or reduced urine output, eGFR is not used in the diagnosis of AKI. AKI may only be seen as a small rise in creatinine. The rise needs to be on a short, acute timescale to distinguish it from the slower steady rise of progressive chronic kidney disease (CKD). AKI episodes are common in patients with CKD. Such episodes are an important factor in the progression of CKD.

In AKI, loss of kidney function contributes to morbidity and mortality. Patients die from AKI rather than with AKI as a complication of an underlying illness. The metabolic work of the kidney tubule imposes major energy demands and the tubule normally operates under conditions of borderline oxygen supply. A modest fall in blood pressure of about 15–20 mmHg can lead to a range of tubular injury. The definition of AKI now includes any adult with $\geq 26 \mu\text{mol/L}$ rise in creatinine from baseline over 48 hours or less, or $\geq 50\%$ rise in creatinine from baseline known or presumed to have occurred over seven days or less.

The causes of AKI have traditionally been divided into pre-renal, intrinsic renal, and post-renal or obstructive. Any cause of hypovolaemia or reduced effective circulating volume can inflict ischaemic tubular injury. Intrinsic renal causes of AKI can be thought of as conditions manifested as direct injury to the glomerulus, the tubule, the interstitium, or the vasculature. Post-renal AKI refers to any obstruction within the tubule itself, ureters, bladder or the bladder outflow/urethra. A key step in the initial assessment is to identify the likely cause of AKI. Following an episode of AKI, focus of care should switch to monitoring and prevention of further episodes.

In patients with known or suspected AKI all nephrotoxic drugs should be suspended. The use of NSAIDs should be avoided, ACE inhibitors and angiotensin receptor blockers should be suspended during any episode of vomiting and/or diarrhoea.

Useful information

NICE CG169. Acute kidney injury

Different versions of the guideline are available including Information for the public
www.nice.org.uk

Acute kidney injury

<http://www.patient.co.uk/doctor/acute-kidney-injury-pro>

of AKI should be rapidly treated. This may include using antibiotics for tackling infection (where sepsis is not a concern) and cessation/suspension of all nephrotoxic medications.

FOLLOW-UP

At discharge following an episode of AKI, the focus of care should switch to monitoring and prevention of further episodes. Patients and carers should be given information about the cause(s) of the AKI, treatment, monitoring and prognosis.¹¹

It is important to arrange to recheck the kidney function, for example at 1–2 weeks after discharge. In patients with known CKD, further insults to the kidneys should be avoided if at all possible (see risk factors for AKI, box 1, p24). In particular the use of NSAIDs or iodinated contrast should be avoided. When prescribed potentially nephrotoxic drugs, patients should be educated about the AKI risk associated with dehydration and infection.

Although evidence in this area is limited, patients should be advised to suspend ACE inhibitors and angiotensin receptor blockers temporarily.¹¹ In particular, these drugs should be suspended immediately during an episode of vomiting and/or diarrhoea until the patient is clearly improving. This may be done without reference to a doctor at the time, but we advise that the drugs should be restarted in a timely fashion, as they offer cardiovascular and renal protection.

CONCLUSION

AKI is common and has a serious impact on outcomes across the spectrum of affected patients. It is important to be vigilant for AKI, and act promptly if you find it. The failings identified in the NICEPOD report should be consigned to history.

Disclaimer

Both authors contributed to the NICE guideline development group for AKI. The views expressed are the opinions of the authors and do not necessarily represent the opinions of NICE.

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