



PRACTICE

RATIONAL TESTING

Investigating acute kidney injury in primary care

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What you need to know

- Acute kidney injury (AKI) in the community is most commonly due to infections such as influenza or gastroenteritis, with associated fluid depletion, but 10% of community cases are due to obstructive uropathy
- AKI is associated with longer inpatient admissions, increased risk of progression to chronic kidney disease (CKD), and higher in-hospital and long term mortality
- After an episode of AKI, review patients in primary care to advise on appropriate management and reintroduction of any medications withheld during an AKI episode and to screen for CKD

A 65 year old obese man with diabetes, hypertension, osteoarthritis, and a two month history of persistent lower urinary tract symptoms attended his general practice with general malaise. Regular medications included metformin, gliclazide, ramipril, and ibuprofen. On examination, his blood pressure was 150/96 mm Hg. Digital rectal examination revealed a smooth enlarged prostate. Urine analysis showed 2+ proteinuria. Blood tests revealed a serum creatinine concentration of 160 $\mu\text{mol/L}$, compared with 78 $\mu\text{mol/L}$ three weeks earlier; his prostate specific antigen (PSA) level had been 6 $\mu\text{g/L}$.

The problem

Acute kidney injury (AKI) is a syndrome characterised by a sudden decline in renal function. To standardise AKI classification, international guidelines were published in 2012 ([table 1](#)).¹

Population incidence of AKI is as high as 0.2%,² and between 8.4% and 17.6% among hospital inpatients.^{3,4} Around two thirds of AKI cases identified in hospital develop in the community

before hospitalisation.⁵ AKI is associated with longer inpatient admissions, increased risk of progression to chronic kidney disease (CKD), and higher mortality (in hospital⁶ and long term).^{3,7} Prompt identification of AKI and early management initiated in primary care is central to improving outcomes.

Identifying AKI in primary care

AKI in the community is most commonly due to infections such as influenza or gastroenteritis, with associated fluid depletion.⁸ Patients generally present with non-specific symptoms; instead patients are identified as being at enhanced risk of developing AKI ([box 1](#)).⁹ AKI may be confirmed either incidentally or through targeted screening showing an elevated serum creatinine level above baseline ([table 1](#)).¹ To support early identification, in the UK, electronic AKI alerts should accompany all blood tests from primary and secondary care, notifying responsible clinicians of an AKI episode,¹⁰ although they only serve to prompt further clinical assessment to determine aetiology. A common problem is that it is impossible to discriminate between AKI and CKD from a single blood test result without baseline values, although other blood and imaging results may strongly suggest underlying CKD ([box 2](#)).^{10,11}

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This series of occasional articles provides an update on the best use of key diagnostic tests in the initial investigation of common or important clinical presentations. The series advisers are Steve Atkin, professor of medicine, Weill Cornell Medical College Qatar; and Eric Kilpatrick, Division Chief, Clinical Chemistry, Sidra Medical and Research Center, Qatar; honorary professor, department of clinical biochemistry, Hull Royal Infirmary, Hull York Medical School. To suggest a topic for this series, please email us at practice@bmj.com.

Box 1: Factors warranting investigation for AKI in acutely ill patients*

- Age >65 years
- Medical history of
 - Chronic kidney disease
 - Prior AKI
 - Heart failure
 - Liver failure
- Exposure to nephrotoxic drugs within previous week
- Exposure to contrast agent within previous week
- Factors predisposing to hypovolaemia (such as reliance on carer)
- Clinical evidence of hypovolaemia
- Sepsis
- History of, predisposing factors for, or symptoms of urological obstruction

*Recommended by National Institute for Health and Care Excellence (NICE)⁹

Box 2: Blood and urine tests to consider when investigating AKI**In all cases**

- Urine analysis
 - Microscopy, culture, and sensitivity if clinical suspicion or urine analysis is positive for nitrites or leucocytes
 - Protein:creatinine ratio if urine analysis is positive for proteinuria or haematuria
- Blood tests
 - Full blood count (normocytic anaemia may suggest underlying CKD)
 - Urea and electrolytes (particularly screen for hyperkalaemia in AKI and CKD)
 - Bone profile (raised serum phosphate levels may suggest underlying CKD)
 - C reactive protein (raised in infection or inflammation)

Suspected intrinsic renal disease*

- Further blood tests
 - Serum bicarbonate and chloride (screen for metabolic acidosis in AKI and CKD)
 - Creatine kinase (may indicate muscle injury, such as rhabdomyolysis)
 - Erythrocyte sedimentation rate (raised in infection or inflammation)
- Immunological tests
 - Antinuclear antibody (raised in many autoimmune conditions)
 - Double stranded DNA antibody (raised in systemic lupus erythematosus (SLE))
 - Antinuclear cytoplasmic antibodies (raised in vasculitis, but also in infection)
 - Antiglomerular basement membrane antibody (raised in anti-GBM disease)
 - Rheumatoid factor (raised in rheumatoid arthritis and cryoglobulinaemia)
 - Complement levels (C3 and C4) (low in active SLE and cryoglobulinaemia)
 - Immunoglobulins/Serum and urine protein electrophoresis (screen for multiple myeloma)
- Serological tests
 - Antistreptolysin O titre (raised after streptococcal infection)
 - Hepatitis B and C serology (hepatitis B surface antigen, hepatitis C antibody)
 - HIV serology (HIV-1 and HIV-2 antibodies)

*May be undertaken in primary care after urgent specialist referral

(table 2).¹⁰ Further investigations will be indicated to determine the cause of AKI (table 3).^{10 14}

Factors warranting earlier review include hyperkalaemia, suspected urinary tract obstruction, suspected intrinsic renal disease, history of CKD or renal transplant, frailty, history of AKI

Urine analysis

Perform dipstick urine analysis in all cases of AKI as a rapid screen for treatable pathology.⁹ Presence of leucocytes and/or nitrites may indicate bacteriuria, urinary tract infection, or pyelonephritis; haematuria and proteinuria alone may suggest glomerulonephritis; leucocytes alone may indicate interstitial nephritis.⁹

Urine microscopy to identify crystals and casts in AKI is not routinely recommended.⁹

Blood tests

Blood tests confirming AKI may reveal abnormalities requiring urgent intervention (such as hyperkalaemia).¹³ Full blood count, C reactive protein assay, and bone profile must be undertaken to screen for infection, inflammation, or electrolyte abnormalities. If there is no clear cause, or intrinsic renal disease is suspected, additional blood tests may be undertaken, accompanying urgent nephrological referral (box 2). Repeat serum creatinine levels should be taken alongside clinical review after an AKI episode (box 2). This will help identify refractory AKI and guide management.^{1 10}

Ultrasound scan

Urinary tract ultrasound scan is the investigation of choice when obstructive uropathy is suspected.⁹ About 10% of AKI cases in the community are due to obstructive uropathy¹⁵; of these, 95% will demonstrate hydronephrosis.¹⁶ Causes for false negative results include early obstruction or extrinsic compression preventing ureteric dilatation. False positive results may occur in pregnancy or vesicoureteric reflux.¹¹ Other common non-obstructive pathologies found on ultrasound include nephrolithiasis, anatomical variants, and altered renal parenchymal echogenicity.¹¹ Ultrasound may help distinguish between AKI and CKD: reduced kidney size and cortical and parenchymal thickness suggest underlying CKD.¹¹

Most ultrasound requests for suspected AKI are normal. One single-centre retrospective study of all ultrasound scans for AKI over three years showed 61.7% of scans were normal; increased renal parenchymal echogenicity was found in 39.5% of patients, 2.6% showed bilateral hydronephrosis, and 2.6% unilateral hydronephrosis.¹⁷ Hydronephrosis was commoner among patients aged >65 years and in those with abdominal malignancy.¹⁷ Another single-centre retrospective study showed that, of 567 ultrasound scans performed for AKI, 10% showed bilateral hydronephrosis and 9% unilateral hydronephrosis.¹⁸

Referral for urgent renal ultrasound

Although the result is often normal, ultrasound imaging remains an important tool in primary care. If available, a post-micturition bladder scan can expedite investigation. However, if obstructive uropathy or pyelonephritis is suspected in relation to AKI, an urgent renal ultrasound scan is needed. A history of abdominal or pelvic malignancy, benign prostatic hyperplasia, neurogenic bladder, nephrolithiasis, and treatments associated with retroperitoneal fibrosis all raise suspicion for obstructive uropathy.¹⁹ Further suggestive features include a history of lower

What is the next investigation?

Early clinical assessment involves reviewing blood parameters to exclude severe complications (hyperkalaemia, uraemia, and hypovolaemia or hypervolaemia^{12 13}). While immediate clinical assessment may not be possible in primary care, appropriate time frames for review will be determined by clinical context

urinary tract symptoms, oligouria or anuria, and a palpable bladder, abdominal mass, or prostate on examination.

Where an ultrasound scan is performed will depend on local service availability and clinical context: If the patient is unwell, this will necessitate secondary care referral to a specialist urologist or nephrologist or to acute medical services.

Current UK guidelines advise ultrasound be performed within 24 hours if obstruction is suspected or there is no identifiable cause.⁹ Features suggestive of pyonephrosis (fever, flank pain, and/or dysuria associated with leucocyturia, nitrite-positive urine analysis, and raised inflammatory blood markers) necessitate ultrasound within six hours, probably through emergency referral to secondary care.⁹

Acting on ultrasound results for AKI in primary care

Urinary catheter placement can immediately relieve confirmed bladder outlet obstruction (in older men this is most commonly due to prostatic enlargement). This may be undertaken either through a local primary care pathway or emergency referral to secondary care. After urgent relief of obstruction, definitive management will be discussed with the urology service.

Where isolated upper urinary tract obstruction is identified, urgent specialist urologist referral is advised to plan further cross sectional imaging (computed tomography or magnetic resonance imaging) to localise the cause of obstruction²⁰ and guide emergent intervention (nephrostomy or ureteric stent placement).¹⁹ If clinical suspicion for obstruction remains high despite a negative ultrasound scan, a repeat ultrasound or cross-sectional imaging may help delineate the cause, after specialist urologist guidance.

Management of AKI

Appropriate management of clinically stable patients with AKI stage 1-2 can be undertaken in primary care or in outpatient clinics, depending on local AKI service availability. It is recommended that patients with AKI are hydrated, infections treated, nephrotoxic medications discontinued, and diuretic and angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) are temporarily withheld.^{1,21} For particular situations, such as concurrent heart failure, a more nuanced approach may be required, recognising a necessary trade-off between cardiac and renal function. Whilst there remains an insufficient evidence in this setting, an important approach is to treat the patient, and not the blood result.¹⁰ Further management depends on aetiology: specialist urology referral will be required for obstructive uropathy.⁹ If AKI stage 3 is identified, urgent nephrological referral is indicated. Such referral is also indicated if there is suspected intrinsic renal disease, no clear cause for AKI identified, refractory AKI, or AKI in renal transplant patients. If a patient is unwell with AKI they may, depending on clinical context, be best managed on an acute medical unit.⁹

To ensure patients are adequately informed, provide patient information leaflets (such as *Understanding Acute Kidney Injury*²²) alongside discussions about AKI.

Management after recovery from AKI

After resolution of AKI, review patients in primary care to advise on appropriate management and reintroduction of drugs withheld during an AKI episode.^{8,23} Regardless of aetiology and management, review all patients with AKI at three months to screen for evolving CKD.¹

Outcome

AKI stage 2 was diagnosed; the patient was re-assessed as clinically stable with no severe complications. His management was continued in primary care: nephrotoxic medications (NSAIDs) were withheld; as were his ACE-inhibitor and metformin, consistent with “sick day rules.”²¹ His lower urinary tract symptoms, alongside clinical examination findings, prompted an urgent outpatient ultrasound scan, which revealed bilateral hydronephrosis (fig 1) and an enlarged prostate compressing the bladder (fig 2). The patient was catheterised and commenced α blockade and finasteride. His serum creatinine level returned to baseline at 80 $\mu\text{mol/L}$. He was subsequently re-challenged with the ACE inhibitor and metformin. Definitive urological management of his prostatic outflow obstruction was then arranged.

Education into practice

- Consider your last patient diagnosed with AKI. How were they managed?
- After reading this article, how would you alter your approach toward investigating and managing AKI?
- Consider the next patient due in clinic. Are they at risk of developing AKI?

How were patients involved in the creation of this article

The article was reviewed and endorsed by a small cohort of patients at our AKI clinic who had recovered from AKI.

Contributors: IKS performed all of the initial literature searches; IKS and NMPA wrote the first draft; AD contributed anonymised clinical images. All authors critically revised all subsequent drafts. NMPA is the guarantor.

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Tables

Table 1 | KDIGO classification of acute kidney injury (AKI)¹

AKI stage	Serum creatinine	Urine output
Stage 1	1.5-1.9 × baseline creatinine* <i>or</i> >26 µmol/L within 24 hours	<0.5 mL/kg/hour for 6 hours
Stage 2	2.0-2.9 × baseline creatinine*	<0.5 mL/kg/hour for 12 hours
Stage 3	3.0 × baseline creatinine* <i>or</i> >353.6 µmol/L* <i>or</i> Initiation of renal replacement therapy <i>or</i> Decrease of eGFR to <35 mL/min in patients <18 years old	<0.3 mL/kg/hour for 24 hours <i>or</i> Anuria for 12 hours

KDIGO = Kidney Disease: Improving Global Outcomes. eGFR = estimated glomerular filtration rate.

* Applicable when creatinine change presumed to have occurred in previous 7 days

Table 2| Recommended timeframe for clinical review after identification of AKI from biochemistry results (adapted from Think Kidneys¹⁰)

AKI stage	Clinically stable patient, low pre-test probability	Acutely ill patient or high pre-test probability
Stage 1	<72 hours	<24 hours
Stage 2	<24 hours	<6 hours
Stage 3	<6 hours, consider admission	Consider immediate admission

Table 3| Causes of AKI (adapted from Think Kidneys^{10 14})

	Specific causes	History	Examination
Sepsis, hypoperfusion, hypovolaemia	<ul style="list-style-type: none"> • Sepsis • Organ failure • Dehydration • Haemorrhage 	<ul style="list-style-type: none"> • Infective symptoms • Oral fluid intake • History of heart failure, renal failure, liver failure 	<ul style="list-style-type: none"> • Blood volume status (capillary refill, jugular venous pressure, pulse, blood pressure) • Source of infection
Medication/Toxicity	<ul style="list-style-type: none"> • Medication contributing to hypovolaemia or hypotension • Nephrotoxic medications • Recent exposure to contrast agent 	<ul style="list-style-type: none"> • Medication history: <ul style="list-style-type: none"> - NSAIDs, diuretics, antihypertensive agents - Drugs that accumulate, causing harm in AKI - New drugs that may cause AKI, such as PPIs 	
Obstruction	<ul style="list-style-type: none"> • Benign prostatic hypertrophy • Prostatic, pelvic, or abdominal malignancy • Kidney or bladder stones • Retroperitoneal fibrosis 	<ul style="list-style-type: none"> • Lower urinary tract symptoms • History of: <ul style="list-style-type: none"> - Malignancy - Kidney stones - Pelvic radiotherapy - Family history of malignancy 	<ul style="list-style-type: none"> • Palpable abdominal or pelvic mass • Palpable bladder • Enlarged prostate
Primary or intrinsic renal disease	<ul style="list-style-type: none"> • Glomerulonephritis • Interstitial nephritis • Myeloma 	<ul style="list-style-type: none"> • Medication history • History of: <ul style="list-style-type: none"> - Shortness of breath or haemoptysis - Rash - Back or bone pain - Weight loss 	<ul style="list-style-type: none"> • Urine analysis • Skin rashes

NSAIDs = non-steroidal anti-inflammatory drugs. PPIs = proton pump inhibitors.

Figures

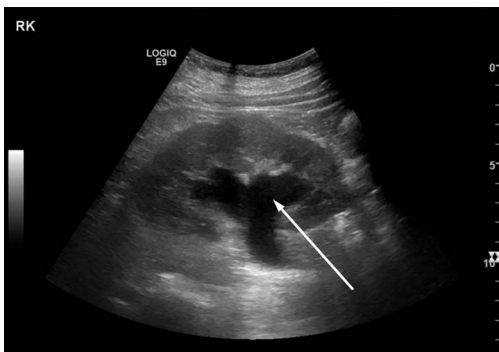


Fig 1 Transverse ultrasound scan of right kidney showing dilatation of pelvicalyceal system (arrow) consistent with hydronephrosis

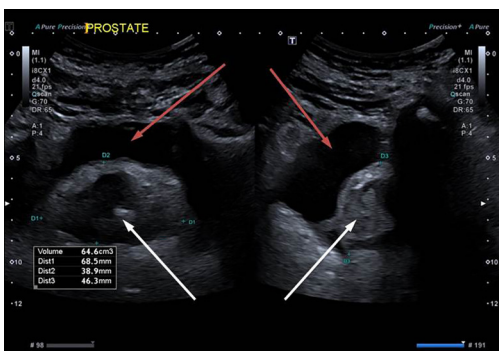


Fig 2 Transabdominal transverse (left) and longitudinal (right) ultrasound scans showing an enlarged prostate (white arrow) compressing the bladder (red arrow)