Assessment and initial management of acute kidney injury

Laura Griffiths

Nigel Suren Kanagasundaram

Abstract

Acute kidney injury (AKI) is a common and dangerous complication of hospital admission; even mild degrees of dysfunction reduce the chances of survival. Unfortunately, as confirmed by the UK's National Confidential Enquiry into Patient Outcome and Death (NCEPOD), its recognition is often delayed and management frequently sub-optimal. A failure to recognize relevant risk factors may expose patients, unnecessarily, to the chance of developing AKI. In this review article, we present a structured approach to prevention, diagnosis and initial management that should provide a framework for routine clinical care.

Keywords acute kidney injury; creatinine; morbidity; mortality; nephrotoxic medications; renal replacement therapy; urine output

What's new?

- The term 'acute renal failure' has now been replaced by 'acute kidney injury (AKI)' to reflect the spectrum of disease severity
- AKI is a dangerous condition with increasing severity reducing the chances of survival
- Even mild AKI carries an increased risk of mortality
- A consensus definition for AKI has now emerged, enhancing prospects for comparative research and clinical audit
- Long-term outcomes in survivors of AKI may not be benign, with significant numbers being left with residual renal dysfunction. This, in turn, increases long-term mortality and the risks of progression to end-stage renal disease

Introduction

Acute kidney injury (AKI), formerly known as acute renal failure, is common, affecting around 7% of hospital in-patients[1] and up to 25% of those in critical care.[2] It is also dangerous — even mild disease affects survival.[3–6] Mortality rates increase sharply as AKI worsens[4–7] and may exceed 50% in septic, multi-organ failure.[8] Evidence also suggests that patients are not dying simply with AKI, but because of it.[9]

Laura Griffiths ***MBChB (Hons) MBBS MRCP*** *graduated from the University of Sheffield in 2007 with honours. Having completed her foundation programme in the Northern Deanery she remains in the region as a core medical trainee. She gained her MRCP in 2010. Conflicts of interest: none.*

Nigel Suren Kanagasundaram ***MBChB FRCP MD*** *is an Honorary Clinical Senior Lecturer at the Institute of Cellular Medicine, Newcastle University and Consultant Nephrologist at the Freeman Hospital, Newcastle-upon-Tyne, where he leads the critical care nephrology and chronic haemodialysis services. He was a co-author of the current and past Renal Association clinical practice guideline for AKI and was a member of the expert group of the NCEPOD AKI study. During his time in higher specialist training in Yorkshire, he spent 3 years as the Nakamoto Hemodialysis Research Fellow at the Cleveland Clinic, USA, where NIH-sponsored work on ICU dialysis provision formed the basis of his MD thesis. He maintains an active research programme and has authored a number of textbook chapters and original articles in critical care nephrology — a key area of interest. Conflicts of interest: none.*

Survivors often fail to recover renal function,[7] so that significant numbers need long-term dialysis.[10,11] Long-term survival may be reduced[12] especially in those with persisting renal dysfunction.[10,11] AKI also carries a significant economic impact; severe disease often requires expensive interventions such as dialysis or critical care, but even modest AKI may increase hospital costs.[13]

The management of AKI is often seen as challenging because of its perceived complexity. Ample evidence exists, though, that even the basics of care are often neglected.[14,15] The most recent confirmation has come from the UK's NCEPOD (the National Confidential Enquiry into Patient Outcome and Death)[15] which found systematic failings in the recognition and management of AKI and its complications, and frequent omission of fluid balance, fluid administration and regular blood monitoring. NCEPOD found that shortcomings in practice were worst in those who developed AKI during their hospital stay rather than those admitted with it,[15] suggesting a slackening of surveillance for this common complication of admission.

Bearing in mind the diffidence with which practitioners view AKI and evidence of clear shortcomings in practice, this article provides a structured approach for its prevention, assessment and management in a hospital setting.

Risk factors and prevention

Up to 30% of AKI may be preventable through early recognition and simple management of patient risk factors.[14,16,17]

Common risk factors include increasing age and pre-existing chronic kidney disease (CKD)[18] (see also Table 1).

Certain drugs may be directly nephrotoxic: examples include aminoglycoside antibiotics, such as gentamicin, non-steroidal anti-inflammatory drugs (NSAIDs), chemotherapeutic agents, such as cisplatin, and radio-contrast media. Other drugs, such as angiotensin-converting enzyme (ACE) inhibitors, are not directly nephrotoxic but reduce the glomerular filtration rate through their mechanism of action. When weighing the balance of risk versus benefit for the initiation or continuation of these drugs in the individual patient, consider the presence of other risk factors for AKI and the availability of non-nephrotoxic alternatives.

A wide variety of drugs may cause an acute allergic interstitial nephritis (see 'Intrinsic AKI', below). As these reactions are

Common risk factors for acute kidney injury[19]

- Chronic kidney disease (CKD, eGFR <60 ml/minute/1.73 m^2)
- Age >75
- Sepsis
- Cardiac failure
- Liver disease
- Diabetes mellitus
- Drugs affecting renal function
- Hypovolaemia
- Atherosclerotic peripheral vascular disease

eGFR, estimated glomerular filtration rate.

Table 1

idiosyncratic, they cannot necessarily be prevented but should be borne in mind as a potential aetiology for AKI.

Patients with one or more risk factors for AKI should undergo more frequent (daily) biochemical monitoring and regular clinical review of fluid balance, volume status and medications.

Maintaining vigilance for the risk factors for AKI allows preventative intervention:

- the elderly diabetic may require temporary omission of an ACE inhibitor during an episode of infectious gastroenteritis
- the immediate postoperative patient with pre-existing CKD should avoid NSAID analgesia
- the initiation of an ACE inhibitor in the elderly patient with CKD and cardiac failure may be entirely justified provided there is close monitoring of renal function.

Fluid management

Appropriate fluid management can mitigate the risk of AKI. A decision on whether fluid is required for 'maintenance' (routine requirements) or 'replacement' (correction of abnormal losses) will guide the choice of fluid and electrolyte.

Colloid resuscitation with high-molecular-weight hydroxyl ethyl starch solutions may increase the risk of AKI in those with severe sepsis.[19]

So-called 'normal saline' (sodium chloride 0.9%) puts the patient at risk of sodium overload and hyperchloraemic metabolic acidosis if used injudiciously (2 litres will provide 308 mmol of sodium, at least three times the usual daily requirement). Structured guidance on optimal fluid prescribing, including the use of the more balanced solutions — lactated Ringer's and Hartmann's — is given elsewhere.[20]

Contrast nephropathy prophylaxis

Consider this if other risk factors for AKI, in particular pre-existing CKD, are present. If the investigation cannot be avoided, specific prophylactic measures include:

- omission of 'higher risk' drugs on the day of investigation until renal function is stable
- omission of metformin for 48 hours from the day of investigation[21]
- selection of alternative contrast agent: low osmolar agents carry a lower risk than high osmolar agents[22] and iso-osmolar agents may carry a lower risk than low osmolar agents in pre-existing CKD[23]
- prophylactic volume expansion:
  - sodium chloride 0.9% at 1 ml/kg/hour for 12 hours pre- and post-procedure[24] **or**
  - isotonic sodium bicarbonate at 3 ml/kg/hour for 1 hour pre-procedure and 1 ml/kg/hour for 6 hours post-procedure.[25]

Assess volume status carefully before, during and after these regimens to prevent fluid overload.

Monitor renal function for up to 72 hours post-procedure in high-risk patients (i.e. those in whom prophylaxis has been considered).

There is no clear evidence supporting the routine use of N-acetylcysteine in contrast nephropathy prophylaxis.[26,27]

Rhabdomyolysis

Filtered myoglobin can cause intra-tubular cast formation and also dissociates to release tubulo-toxic free iron in more acid urine. The risk of AKI is low if peak serum creatine kinase is less than 10,000 U/litre,[28–31] but those with greater muscle damage may benefit from an early diuresis[32,33] and urinary alkalinization.[34,35] One regimen involves sodium chloride 0.9% at 10–15 ml/kg/hour to achieve urinary flow rates over 100 ml/hour, with the cautious addition of sodium bicarbonate 1.4% to maintain urinary pH>6.5.[36] Look out for fluid overload and exacerbation of hypocalcaemia by alkalinization. Once AKI is established and progressing, further fluid therapy should be continued only very cautiously.

Definition

Definitions in the literature cover a wide range of disease severity, but an international consensus is developing following introduction of the Acute Kidney Injury Network (AKIN) staging system[37] (see Table 2). A previous iteration, using the RIFLE criteria,[38] is still evident in much contemporary literature and practice.

Aetiology and categorization

AKI has a wide range of causes but can be broadly categorized as shown in Figure 1.

Pre-renal azotaemia

This is an appropriate response to reduced renal perfusion, by which the kidneys attempt to retain sodium and water and, as a result, renal excretory capacity is impaired. Importantly, no renal cellular injury has occurred (hence 'azotaemia' — the accumulation of uraemic waste products — rather than 'injury'). Table 3 details the usual causes.

Intrinsic AKI

This is caused by tubulo-interstitial, glomerular or micro-vascular cellular injury.

Most intrinsic AKI is tubular in aetiology and usually takes the form of acute tubular necrosis (ATN). ATN may be caused by ischaemia, sepsis or, less commonly, nephrotoxins, such as aminoglycoside antibiotics, NSAIDs, radio-contrast media (which also cause renal vasoconstriction), myoglobin or cisplatin. Less common causes of tubulo-interstitial disease include acute allergic interstitial nephritis (e.g. secondary to diuretics, NSAIDs, penicillins and proton pump inhibitors) and cast nephropathy

