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Recognising acute kidney injury

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While it is often possible to identify the sick patient who is clinically dehydrated, hypotensive or septic, a diagnosis of acute renal failure (ARF) or acute kidney injury (AKI) would often not be considered until the results of the urea and electrolytes were obtained. It was felt that seemingly small changes in serum urea and creatinine were unlikely to be associated with any significant changes in outcome, so there was less urgency in making a diagnosis and instituting aggressive therapy. Within the last decade, however, it has been demonstrated that these seemingly small changes in serum creatinine are associated with significant increases in risk for the patient.

Furthermore, it has become increasingly apparent that the previous perception that patients who had ARF would usually recover completely is wrong. There is mounting evidence that patients who have suffered AKI are at far greater risk of progressing to chronic kidney disease (CKD). For this reason, greater emphasis is now placed on the rapid identification and amelioration of risks for AKI, with aggressive treatment of the underlying cause.[1]

Definitions and staging

A collaborative network of international experts representing nephrology and intensive care societies established the Acute Dialysis Quality Initiative (ADQI), and devised the RIFLE definition and staging system for AKI.[2] In this classification AKI is categorised according to the criteria of **R**isk, **I**njury, **F**ailure, **L**oss and **E**nd-stage disease for kidneys.

- *Risk*: glomerular filtration rate (GFR) decrease greater than 25%, serum creatinine increase 1.5 times or urine production less than 0.5 ml/kg/hr for six hours.
- *Injury*: GFR decrease above 50%, doubling of creatinine or urine production less than 0.5 ml/kg/hr for 12 hours.
- *Failure*: GFR decrease above 75%, tripling of creatinine or creatinine greater than 355 µmol/l (or urine output below 0.3 ml/kg/hr for 24 hr).
- *Loss*: persistent AKI or complete loss of kidney function for more than four weeks.
- *End-stage renal disease*: complete loss of kidney function for more than three months.

Subsequently, many of the original members of the ADQI group collaborated to form the Acute Kidney Injury Network (AKIN).[3] This group modified the RIFLE staging system to reflect the clinical significance of relatively small rises in serum creatinine. More recently, the international guideline group, Kidney Disease: Improving Global Outcomes (KDIGO), has produced a definition and staging system that harmonises the previous definitions and staging systems by both ADQI and AKIN. In this system, stage 1 (or 'Risk' stage) AKI is defined as:

- serum creatinine increase by at least 26 µmol/l within 48 hours *or*
- serum creatinine rise 1.5 fold or more from the reference value (this should be the lowest value recorded within three months of the event), which is known *or*
- the change in renal function is presumed to have occurred within one week *or*
- urine output less than 0.5 ml/kg/hr for more than six consecutive hours.

Causes of acute kidney injury

AKI is common among hospitalised patients.[4,5] It affects at least 3–7% of patients admitted to hospital and approximately 25–30% of patients in the intensive care unit (ICU). Although the terminology for the acute decline of renal function has changed, the mechanisms underlying the deterioration have not. The old separation of prerenal, renal and postrenal causes remains relevant.

Prerenal

Prerenal causes of AKI, which decrease effective blood flow to the kidneys, include low blood volume, low blood pressure and heart failure, as well as local changes to the blood vessels supplying the kidney – the latter include renal artery stenosis and renal vein thrombosis.

Renal

Renal or intrinsic AKI can be due to damage to the glomeruli, renal tubules or interstitium. Common causes of each are glomerulonephritis, so-called acute tubular necrosis and acute interstitial nephritis.

Postrenal

Postrenal AKI is a consequence of urinary tract obstruction that may be related to benign prostatic hyperplasia, kidney stones, obstructed urinary catheter, bladder stone, or bladder, ureteral or renal malignancy. This term may also be applied to the intrarenal obstruction associated with abnormal protein deposition in the tubules, for example as occurs with myeloma.

Practical application of definitions of acute kidney injury

What do the above definitions and classifications mean in practice? A recent National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report[6] identified many deficiencies in the care of patients at risk of and suffering from AKI (the report's recommendations are shown in Table 1).

In assessing risk, it is important to realise that most AKI is associated with ischaemia, sepsis or nephrotoxic insults. Studies have identified the risk factors most pertinent for the development of AKI:

- age over 75 years
- CKD (eGFR (electronic glomerular filtration rate) <60 ml/min/1.73 m^2)
- cardiac failure
- atherosclerotic peripheral vascular disease
- liver disease
- diabetes mellitus
- nephrotoxic medications, especially angiotensin-converting enzyme inhibitors, non-steroidal anti-inflammatory drugs and certain antibiotics.

Patients with these risk factors should be actively assessed for AKI, including a review of the physiological parameters routinely

reviewed at the bedside using Early Warning Score systems such as the National Early Warning Scoring System (NEWS). Good assessment at an early stage with institution of active measures can prevent the progression of AKI. This should result in aggressive management of underlying potential precipitating factors including:

- reduced fluid intake
- increased fluid losses
- urinary tract infection (UTI) or obstruction
- recent nephrotoxic drug ingestion
- sepsis.

Investigations

The recognition of AKI is rarely made from clinical examination alone, although it is fairly easy to predict in elderly patients presenting with sepsis and dehydration. Investigations are very important, ranging from simple bedside tests to the more resource-intensive.

Reagent strip urinalysis

Reagent strip urinalysis is a useful investigation, provided that the results are interpreted carefully and simple abnormalities are not assumed to indicate UTI. Protein values of 3+ and 4+ suggest intrinsic glomerular disease. When positive for blood, such values suggest the presence of red blood cells (>5/high power field). The observation of large numbers of red cells in the presence of proteinuria suggests a glomerular aetiology for AKI. Haematuria may also indicate tumours, infection, calculi or severe renal ischaemia. High numbers of white cells are indicative of infection, glomerulonephritis and interstitial nephritis.

Serum and urinary biochemical estimations remain the most important investigation to reveal AKI. The classic laboratory findings are shown in Table 2 but, as demonstrated above, a change in the serum creatinine is among the most important criteria for the diagnosis of AKI.

Ultrasound

A critical investigation for the presence of an obstructive uropathy is ultrasound, although in the early stages of obstruction, or in the dehydrated patient, typical hydronephrosis/hydroureter may not be seen even when obstruction is present.

Table 1. Recommendations from the NCEPOD report.[6]

- All emergency admissions should have a risk assessment for AKI.
- All emergency admissions should have electrolytes checked on admission and appropriately thereafter.
- Predictable, avoidable AKI should not occur.
- All acute admissions should receive adequate senior review (consultant review within 12 hours).
- There should be sufficient critical care and renal beds to allow rapid step-up care.
- Undergraduate medical training should include the recognition of the acutely ill patient and the prevention, diagnosis and management of AKI.
- Postgraduate training in all specialties should include training in the detection, prevention and management of AKI.

AKI = acute kidney injury; NCEPOD = National Confidential Enquiry into Patient Outcome and Death.

Table 2. Classic laboratory findings in acute kidney injury (AKI).

AKI type	U_{Osm}	U_{Na}	Fe_{Na}(%)	Urea/Cr Providing urea >10
Prerenal	<500	<10	<1	>100
Renal	<350	<20	>2	<40
Postrenal	<350	>40	>4	40–100

U = urinary; Cr = creatinine; U_{Na} = urinary sodium; Fe_{Na} = fractional excretion of sodium

Key points

Even small changes in serum creatinine are associated with poorer outcomes

Risk factors for acute kidney injury (AKI) should be recognised and modified rapidly

Adequate physiological surveillance must be in place for all patients with AKI

The underlying condition should be treated to maximise the chance of improving the AKI

Investigations of a patient with AKI should include urinalysis and renal ultrasound (when obstruction is a possibility)

KEYWORDS: acute kidney injury, AKI risk, AKI investigations

Treatment

Treatment of AKI is aimed at the underlying cause, but a mainstay is adequacy of fluid replacement. It is important that fluid resuscitation provides adequate filling of the intravascular volume, although over-replacement is also associated with an adverse outcome. Treatment of infection, removal of nephrotoxins, relief of obstruction and specific treatment of the renal insult (eg immunosuppression for vasculitides) may all be pertinent. Adequacy of treatment in the early stages of AKI means that most patients will not require active renal intervention in the form of renal replacement therapy (RRT). Often there is more than one precipitating factor; therefore clinicians must adopt a holistic approach to the assessment and management of AKI.

Outcomes

Patients who develop AKI which requires RRT in an ICU have a very high risk of mortality (50–90%), increasing with failure of each additional organ system. Studies have shown however that an increase of serum creatinine of about 50 µmol/l is associated with a 6.5-fold increased risk of mortality and with a prolonged hospital stay for the survivors. Other factors that affect outcome are:

- older age
- multiorgan failure (ie with all AKI, the more organs that fail, the worse the prognosis)
- oliguria
- hypotension
- vasopressor support
- number of transfusions
- non-cavitary surgery.

This early identification and aggressive management of AKI should be a high priority so that the patients' condition can be improved without the use of RRT if at all possible.

Developments

Recognition of AKI depends on measurement of the serum creatinine, as noted above, but an increase in this marker is often a relatively late manifestation of AKI. To improve present systems, many hospitals are introducing electronic alerts that ensure clinicians are rapidly informed by the laboratory staff of changes in the serum biochemistry, so that active intervention for the patient is not delayed.

Furthermore, the development of assays for more sensitive biomarkers has been proposed.[7] One such marker, neutrophil gelatinase-associated lipocalin (NGAL), has been demonstrated to be increased in the serum of patients suffering from `renal stress', including AKI, before more conventional markers, including serum creatinine change.[8] Such early recognition could allow earlier intervention and thus improved outcomes from AKI.

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