General management of acute kidney injury

Introduction

Acute renal failure, or acute kidney injury, is a relatively common problem that occurs in patients under the care of all medical specialties. Around 7% of hospital admissions (Kaufman et al, 1991; Nash et al, 2002) and up to 20% of critically ill patients experience acute kidney injury during the course of their illness. The severity of acute kidney injury directly contributes to mortality, and even relatively small changes in serum creatinine levels can confer a worse outcome (Lassnigg et al, 2008).

Trainees often find the management of acute kidney injury a challenge because of its perceived complexity, difficulty in assessment of volume status and the potentially wide differential diagnosis. This article provides a structured approach for the general prevention, assessment and management of acute kidney injury in hospital.

Definitions, aetiology and classification

Acute kidney injury is characterized by a rapid deterioration in renal excretory function resulting from a wide range of causes. The aetiology (*Figure 1*) is usually divided into pre-renal, intrinsic or post-renal (obstructive).

Pre-renal failure is a functional response to reduced renal perfusion in which no renal cellular injury has occurred. A failure to restore renal perfusion, e.g. through volume replacement or vasopressor therapy, will lead to ischaemic acute tubular necrosis in which cell injury is now present. Acute tubular necrosis can also arise from other insults such as sepsis and nephrotoxins.

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About 75% of all acute kidney injury cases can be attributed to the combination of pre-renal failure and acute tubular necrosis. Isolated acute kidney injury not requiring intensive care is associated with 10% mortality (Hou et al, 1983; Shusterman et al, 1987). Patients who have acute kidney injury with sepsis and multi-organ failure have been reported to have mortality rates of over 50% (Liaño et al, 1998).

There are two sets of criteria used in evaluating acute kidney injury currently. The RIFLE criteria (Bellomo et al, 2002) group acute kidney injury into five categories: risk, injury, failure, loss and end-stage kidney disease, based on changes in creatinine or urine output. The Acute Kidney Injury Network (AKIN) developed these criteria to include smaller and absolute changes in creatinine (*Table 1*) (Davenport et al, 2008). AKIN stage 1 corresponds to risk, stage 2 to injury and stage 3 to failure, while loss and end-stage kidney disease remain as outcomes. Whenever possible, patients should be staged to either of these criteria to allow uniformity of clinical assessment, as well as for audit and research purposes. The choice of staging criteria should be determined by departmental policy.

Prevention

Up to 30% of acute kidney injury cases can be prevented with early recognition and simple management of patient risk factors (Davidman et al, 1991; Vijayan and Miller, 1998; Stevens et al, 2001). Patients should be specifically assessed for certain risk factors on admission to hospital and before undergoing investigations or interventions that can precipitate acute kidney injury. Those risk factors are:

- Known chronic kidney disease
- Age > 60 years
- Sepsis
- Cardiac failure
- Liver disease
- Diabetes mellitus
- Nephrotoxic medication
- Hypovolaemia (Davenport et al, 2008).

There are two common areas where preventative strategies for acute kidney injury can be easily implemented: surgery and contrast media examinations.

Figure 1. Causes of acute kidney injury as divided by aetiology. Pre-renal acute kidney injury and acute tubular necrosis can form part of a clinical spectrum separated by the absence or presence (respectively) of tubular cell injury (see text).

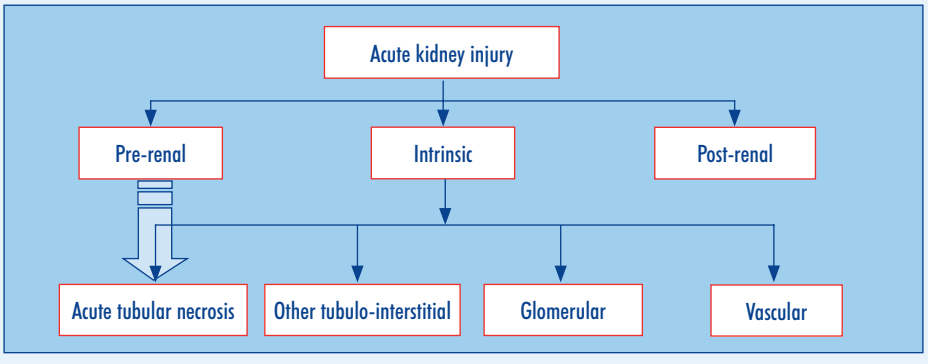

Table 1. Acute kidney injury network modified staging system

Stage	Serum creatinine criteria	Urine output criteria
1	Creatinine ≥26.4 μmol/litre or creatinine ≥150–200% from baseline	<0.5 ml/kg/hr for >6 hours
2	Creatinine >200–300% from baseline	<0.5 ml/kg/hr for >12 hours
3	Creatinine >300% from baseline or creatinine ≥354 μmol/litre with an acute rise of ≥44 μmol/litre in ≤24 hours or initiated on renal replacement therapy (irrespective of stage at time of initiation)	<0.3 ml/kg/hr for 24 hours or anuria for 12 hours

Changes in serum creatinine or urine output are defined over a 48-hour period and staging is conferred by the more severe criterion. These criteria apply only after adequate fluid resuscitation has been performed. From Davenport et al (2008)

Surgery

Postoperative acute kidney injury is a significant cause of hospital morbidity and mortality. When assessing a patient pre- and postoperatively, one should consider:

Does the patient have existing risk factors?

This should prompt more frequent biochemical and clinical monitoring.

Is the patient taking any medications that might increase risk?

Examples include non-steroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers and diuretics. The decision to discontinue these agents and for what duration depends on the clinical context.

Is the patient at risk of reduced effective circulating volume?

Risk factors include prolonged procedures, open surgery, patients who are 'nil by mouth', and causes of 'third spacing', e.g. bowel obstruction, acute pancreatitis and sepsis. Regular assessment of volume status and renal perfusion is essential. Decreased effective circulating volume should be treated promptly, with regular, frequent monitoring of therapeutic response.

The choice of fluid replacement depends on the nature of the fluids lost. The normal daily sodium requirement for an individual is approximately 70–100 mmol/day. The stress response following surgery results in water and sodium retention. Excessive use of 0.9% sodium chloride can result in sodium and water overload, and a hyperchloraemic metabolic acidosis, contributing to morbidity and mortality (Lobo et al, 2006). Use of excessive 5% dextrose can result in hyponatraemia. Particular attention should be paid to solutions containing potassium in these patients because of the increased risk of hyperkalaemia.

Contrast media examinations

Contrast examinations can lead directly to nephrotoxicity, particularly in patients with an estimated glomerular filtration rate of 60 ml/min or less, or the risk factors mentioned earlier. Patients who fall into the former category should be discussed with a nephrologist before investigation. The following steps should be taken to minimize patient risk:

1. Temporary discontinuation of nephrotoxic medications – as for surgery. Patients with an estimated glomerular filtration rate <60 ml/min should have metformin stopped on the day of the investigation and not restarted until renal function is stable
2. Consideration of iso-osmolar contrast agents
3. Prophylactic volume expansion. Two prophylactic regimens decrease the incidence of acute kidney injury. The first, described by Mueller et al (2002), involves giving 0.9% sodium chloride 1 ml/kg/hour for 12 hours pre- and post-procedure. The second involves giving isotonic sodium bicarbonate at 3 ml/kg/hour for 1 hour pre- and 1 ml/kg/hour 6 hours post-procedure (Merten et al, 2004). Before starting one of these regimens volume status should be carefully assessed to avoid fluid overload.
4. Monitoring of serum creatinine at 12, 24 and 48 hours post-procedure. Contrast-induced nephropathy should be managed in the same way as any presenting acute kidney injury; although there may be an obvious precipitant, other differentials should be considered.

The initial assessment

The cornerstone of effective management of acute kidney injury is the same as with any other presenting problem: an appropriate history, thorough clinical examination and selection of relevant investigations. Specific points to consider in a history include: evidence of sepsis, previous documented evidence of chronic kidney disease, risk factors for volume depletion, prescribed and non-prescribed medication, urinary symptoms, and evidence of esoteric disease processes, such as fevers, arthralgias or haemoptysis.

Clinical examination should particularly address patient volume status, the presence of a distended bladder and reagent strip urinalysis. Following this, basic investigations should include serum biochemistry with venous bicarbonate, full blood count, inflammatory markers and, if there is blood and/or protein on urinalysis, urine culture and microscopy for casts. Unless obstruction can be confidently excluded, urgent renal imaging is required. If an esoteric diagnosis is suspected an immune screen should be sent. This includes autoantibodies (antinuclear, anti-neutrophil cytoplasmic, and anti-glomerular basement membrane antibodies), serum complement levels and a myeloma screen.

The five questions a clinician needs to ask in the initial diagnosis of a patient with possible acute kidney injury are:

Is this really acute kidney injury?

If previous measurements of renal function are not available, 12-hourly monitoring of serum creatinine level should be considered. A rapidly rising level is much more likely to be acute kidney injury than chronic kidney disease, which will show relative short-term stability. The exception to this is pre-renal failure or acute tubular necrosis on the cusp of recovery, which may require a longer period of monitoring.

Is this pre-renal failure?

Are there risk factors for reduced renal perfusion? The therapeutic response to restoration of renal perfusion can be diagnostic; failure of renal function to improve after this either suggests progression to overt acute tubular necrosis or an alternative aetiology.

Is post-renal acute kidney injury a possibility?

This should be considered in all cases, especially if there is a history of lower urinary tract symptoms, renal stones, pelvic surgery or possible gynaecological malignancy. The gold standard test is a renal tract ultrasound. However, early obstruction may not be detectable as the pelvi-calyceal system is initially non-compliant and may not dilate. Imaging should be repeated if there is a high index of suspicion.

Is this acute tubular necrosis?

Diagnosis is usually on clinical grounds based on the presence of risk factors (e.g. nephrotoxins, renal hypoperfusion, sepsis).

Is there a more esoteric diagnosis?

Acute tubular necrosis usually recovers after 7–21 days but may be more prolonged if the initial insult is severe or there are subsequent repeated insults. More esoteric causes should be considered if there is no obvious insult, or if renal recovery is delayed beyond 21 days without evidence of further insult. Other factors on initial assessment that may prompt further investigation include blood and/or protein on urinalysis, or the systemic symptoms listed in *Table 2*.

Initial management

The five questions a clinician needs to ask in the initial management of a patient with possible acute kidney injury are:

Have I treated the underlying cause?

This should include a specific search for causes, e.g. sepsis, renal under-perfusion through volume or vasopressor therapy, or nephrotoxins. Fluid resuscitation should be performed with care (small volume boluses with close monitoring of volume status).

Table 2. Features suggesting esoteric diagnoses

Symptom	Possible diagnoses
Fever, arthralgias, rashes	Vasculitis, e.g. Wegener's granulomatosis, microscopic polyangiitis, systemic lupus, anti-glomerular basement membrane antibody disease
Haemoptysis	Vasculitis, anti-glomerular basement membrane antibody disease
Haemolysis, thrombocytopaenia	Haemolytic uraemic syndrome
Hypercalcaemia, hyperuricaemia, bone pain, lytic lesions	Multiple myeloma
Recent vascular intervention +/- rash	Cholesterol embolization syndrome
Raised serum creatinine kinase >10 000 iu/litre, prolonged severe immobility, crush injuries	Rhabdomyolysis

Is renal perfusion being maintained?

Maintenance of renal perfusion optimizes the chance of renal recovery regardless of aetiology. Volume replacement risks iatrogenic fluid overload; fluid requirements should be assessed at least daily with clinical examination and weighing.

Am I performing appropriate monitoring?

As a minimum the patient should have daily assessment of volume status including input-output charting, clinical examination and daily weights. *Table 3* outlines the clinical assessment of volume status. The frequency of routine observations should be dictated by at least daily assessment of illness severity, e.g. with Modified Early Warning Score.

Blood samples, again on a daily basis, should be taken for biochemistry (including calcium and phosphate levels), haematology, inflammatory markers and acid-base status (e.g. venous bicarbonate or arterial blood gases if suitable). If the patient is stable the frequency of blood tests can be reduced.

Vigilance for sepsis is essential – if an inflammatory response is developing, infection must be sought and treated promptly. Antibiotic choice is ideally dictated by liaison with microbiology, local protocol and subsequent organism sensitivity, with dose adjustment according to level of renal function and renal replacement therapy modality (if applicable).

A further issue that requires consideration is the catabolic state associated with renal failure. Patients are at risk of developing adverse sequelae associated with undernutrition, and early referral for monitoring by appropriately qualified dietetic staff is recommended.

Table 3. Assessment of volume status

Assessment method	Details
Lying or standing (or sitting) blood pressure	A drop of >20/10 mmHg indicates significant volume depletion in the correct context (also other causes such as autonomic neuropathy)
Assessment of jugulo-venous pressure	Presence at 2–3 cm vertically above the sternal angle suggests adequate filling. Usually a sensitive indicator of overload
Auscultation for third heart sound	An early indicator of hypervolaemia
Auscultation of lung bases	For evidence of pulmonary oedema
Urine output monitoring	Output of 0.5 mg/kg/hour is a minimum in the absence of diuretics. This is the most sensitive marker for renal perfusion
Daily weights	A reliable marker of fluid status, enabling trends to be easily documented and identified
Invasive assessment, e.g. central venous pressure monitoring	To be considered where there is risk of volume overload or if difficulty in assessment

Am I successfully preventing or managing any complications?

Medication should be reviewed and doses adjusted according to the level of renal function and renal replacement therapy modality (if applicable); failure to do so is a significant cause of morbidity (Schiff et al, 2003). Prevention of sepsis, including removal of potential sources of infection, e.g. redundant urinary catheters, changes of central and peripheral vascular access and pressure area care, is essential.

Other complications associated with acute kidney injury include hyperkalaemia, pulmonary oedema and acidosis. The essential aspects of treating these conditions are summarized in *Table 4*.

Should I contact the renal unit?

Patients with acute kidney injury stage 3 or those with indications for renal replacement therapy (*Table 5*) should receive critical care or renal unit care – the determining factor being the level of non-renal organ support that is needed (Department of Health, 2000). Additionally, early contact is needed in cases where an esoteric diagnosis is possible (Kanagasundaram and Paganini, 2005) and for patients who are likely to have ongoing renal replacement therapy needs following critical care discharge. Patients who have persistent renal impairment but do not require renal replacement therapy after hospital discharge should be managed as per local chronic kidney disease protocols.

Conclusions

Acute kidney injury is a growing problem in the UK, because of a general increase in life expectancy and co-morbidity. Although the initial management may seem daunting, a logical approach can help prevent acute kidney injury, guide successful treatment and facilitate appropriate referral if necessary. Assessment should consist of a search for risk factors and underlying causes, adequate volume repletion with regular clinical and biochemical monitoring, and appropriate management of any complications. If the acute kidney injury is not improving despite initial measures, or alter-

native aetiologies are possible, then a renal consult should be sought before emergency indications for dialysis develop. BJHM

Conflict of interest: none.

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KEY POINTS

- Acute kidney injury is a common problem increasingly faced by all specialities in medicine.
- Assessment should include a search for risk factors and underlying causes, adequate volume repletion and regular biochemical and clinical monitoring.
- Where possible, patients should be scored to defined criteria to determine risk.
- Complications of renal failure should be anticipated and treatment instituted early.
- If there is suspicion of esoteric diagnoses, or renal function fails to resolve as expected, a nephrology opinion should be sought.

Table 4. Management of complications of acute kidney injury

Hyperkalaemia	Treat as an emergency in the presence of electrocardiogram changes or if serum K+ >6.5 mmol/litre
	Cardioprotection: give either 10 ml of 10% calcium gluconate, or 5 ml of 10% calcium chloride solution over 2–5 minutes intravenously. Reversal of electrocardiogram changes occurs within 1 minute, lasting for 1 hour. The dose should be repeated at 5-minute intervals if electrocardiogram changes persist, up to a maximum of four doses
	Intracellular K+ transfer via NA+K+ATPase: give 15 iu Actrapid in 50 ml 50% dextrose via a large bore cannula over 10 minutes. Action occurs within 15–30 minutes, lasting for 2–4 hours. This can be repeated every 4 hours. Capillary blood glucose must be monitored for 6 hours after administration, and hypoglycaemia treated
	Increased cellular K+ uptake: give 200–500 ml of 1.26% or 1.4% sodium bicarbonate intravenously over 15–60 mins. This should only be used if venous bicarbonate is <16 mmol/litre with no volume overload. Rapid correction of acidaemia can precipitate a fall in ionized calcium, leading to tetany, seizures and cardiac instability. The solution must be given via a different route to calcium as they are incompatible. In cardiac arrest, use 50 ml 8.4% or 50–100 ml 4.2% sodium bicarbonate for rapid onset
Pulmonary oedema	Treatment includes: high-flow oxygen
	Intravenous furosemide: dose should be titrated to response (N.B. this should not be used to 'treat' or prevent acute kidney injury per se)
	Intravenous nitrates: this should be instituted with close monitoring and titrated to blood pressure
	Continuous positive airway pressure
Prevention of severe metabolic acidosis	See above for hyperkalaemia and use of sodium bicarbonate

Table 5. Absolute indications for dialysis

Biochemical indications	Refractory hyperkalaemia >6.5 mmol/litre
	Serum urea >30 mmol/litre
	Refractory metabolic acidosis pH <7.1
	Refractory electrolyte disturbance (hypo- or hypernatraemia, hypercalcaemia)
	Tumour lysis syndrome (with hyperuricaemia and hyperphosphataemia)
	Urea cycle defects and organic acidurias
Clinical indications	Anuria for 12 hours or urine output < 0.3 ml/kg/hour for 24 hours
	Acute kidney injury with multiple organ failure
	Refractory volume overload
	End organ damange: uraemic bleeding, neuropathy, encephalopathy, myopathy or pericarditis
	To create intravascular space for plasma and other blood product infusions
	Severe poisoning or drug overdose, severe hypo- or hyperthermia

From Davenport et al (2008)