Renal failure and its treatment

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Abstract

Acute kidney injury (AKI) is a common complication of acute illness. It is associated with significant morbidity and mortality as well as a high cost to healthcare systems. There are a broad range of causes of AKI which should be considered in a systematic fashion to avoid missing multiple potential causative factors. These include pre-renal causes from hypovolaemia, intrinsic renal causes such as glomerular diseases and post-renal obstructive causes. In the intensive care unit, two-thirds of AKI cases result from renal hypoperfusion, sepsis, contrast and nephrotoxic agents; up to 5% will require renal replacement therapy. Modalities of renal replacement therapy include intermittent haemodialysis, peritoneal dialysis and continuous haemofiltration. Continuous haemofiltration is usually favoured in the intensive care setting as it has greater haemodynamic stability and greater capacity to extract fluid from patients with fluid overload. Anticoagulation is recommended with haemodialysis and haemofiltration and systemic heparin, regional citrate or zero anticoagulation are the usual options.

Keywords Acute renal failure; haemodialysis; haemofiltration; renal

Royal College of Anaesthetists CPD Matrix: 1A01, 2C04

Learning objectives

After reading this article, you should be able to:

- classify renal failure
- discuss the causes of renal failure and the prevalence and outcome of renal failure
- classify the treatment of renal failure including the different modalities of renal replacement therapy

Acute kidney injury

Current definition and classification

Acute kidney injury (AKI) is a clinical syndrome characterized by a sudden decline in glomerular filtration rate (GFR) sufficient to decrease elimination of nitrogenous waste products and uraemic toxins. Kidney Disease: Improving Global Outcomes (KDIGO) defines AKI as any of the following: increase in serum creatinine by ($\geq$26.5 μmol/l within 48 h; increase in serum creatinine to $\geq$1.5 times baseline, which is known or presumed to have occurred within the prior 7 days, or urine volume $<$ 0.5 ml/kg/h for 6 h. AKI is staged for severity according to the criteria listed in Table 1.

Aetiology

There are a broad range of causes of developing AKI. Differential diagnosis must be considered in a systematic fashion to avoid missing multiple factors that may be contributing to the condition. Traditionally, AKI is divided into pre-renal, renal and post-renal causes. Pre-renal causes include hypovolaemia or a decreased effective arterial volume. Intrinsic renal causes can be considered under different anatomic components of the kidney (vascular supply; glomerular, tubular and interstitial disease). Post-renal obstructive renal failure is usually diagnosed by urinary tract dilation on renal ultrasound. In the hospital setting, pre-renal and acute tubular necrosis (ATN) account for the majority of AKI cases. These are also often superimposed on pre-existing chronic kidney disease (CKD). In the intensive care unit, two-thirds of cases of AKI are a result of the combination of impaired renal perfusion, sepsis and nephrotoxic agents.

Prevalence and outcome

Uncomplicated ATN typically recovers in 2–3 weeks. This could, however, be complicated by superimposed renal insults. Episodes of hypotension induced by haemodialysis may lead to additional ischaemic lesions and delay renal functional recovery, especially in patients who have multiple co-morbidities. It is becoming increasingly recognized that even lesser degrees of kidney injury have important implications for health as AKI represents a heterogenous clinical syndrome with multiple causes rather than one disease.

The incidence of AKI in unselected hospitalized patients has been estimated to be 18%, and AKI accounts for 1–4% of all hospital admissions. AKI has the highest incidence among those aged 65 and older. Patients with eGFR $<$30 ml/min/1.73 m^2 have a 30- to 40-fold higher risk of developing AKI. AKI is associated with high costs and adverse clinical outcomes, including increased mortality, length of stay and development or progression of CKD. The cost of AKI to the NHS in England in 2014 was estimated to be £1.02 billion. The number of cases of AKI increased from over 600,000 in 2001 to over 3 million in 2011, although mortality has significantly decreased from 21.9% to 9.1% in 2001. The mortality of AKI ranges from 8.1% in patients with AKI stage 1–33% in AKI stage 3.

The incidences of CKD and end-stage renal disease (ESRD) after AKI were 25.6 and 8.6 per 100 person-years, respectively. The annual absolute risk for developing ESRD after an episode of AKI ranges from 0.6% to 1.2% in those with mild AKI compared to 9% in those with pre-existing CKD. Patients should be followed up at 3 months after AKI for resolution, new-onset or worsening of pre-existing CKD.

AKI in the intensive care unit

AKI is an independent risk factor for death and up to 40% of ICU patients develop AKI. Up to 5% of ICU patients require renal replacement therapy. Factors that exacerbate acute kidney injury

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Staging of AKI (KDIGO composite staging)

Acute Kidney Injury Network (AKIN) and RIFLE classifications of acute kidney injury

AKIN staging		RIFLE	
Serum creatinine	**Urine output**	**Class**	**Serum creatinine or GFR**
Stage 1: Increase of x1.5 from baseline or ≥26.5 μmol/l	<0.5 ml/kg/h for > 6h	Risk	Increase in serum creatinine x1.5 or GFR decrease >25%
Stage 2: Increase of x2 from baseline	<0.5 ml/kg/h for >12 h	Injury	Serum creatinine x2 or GFR decreased >50%
Stage 3: Increase of x3 from baseline, or ≥354 μmol/l with an acute increase of at least 44 μmol/l or on RRT	<0.3 ml/kg/h for 24 h or anuria for 12 h	Failure	Serum creatinine x3, or serum creatinine ≥354 μmol/l with an acute rise >44 μmol/l or GFR decreased >75%
		Loss	Persistent acute renal failure = complete loss of kidney function for longer than 4 weeks
		End-stage kidney disease	ESRD >3 months

Table 1

include hypovolaemia in the perioperative period, repeated exposure to contrast and nephrotoxic agents, and inflammatory states. Mortality is attributed to infection, haemorrhage or persistent shock despite optimal care.

Acute management of AKI

Primary prevention and early diagnosis of AKI are essential in improving outcomes and preventing residual effects of kidney damage. All patients should have a risk assessment to identify and reverse risk factors. Major risk factors for AKI include those with older age (>75 years), diabetes, hypertension, sepsis, malignancy, surgical patients, pre-existing cardiac disease.

A key factor in preventing AKI is haemodynamic stabilization with optimization of cardiac output and blood pressure to ensure adequate renal perfusion. Adequate volume expansion is essential in decreasing risk of AKI in the perioperative period in the initial phase, but this needs to be balanced with preventing the undesirable side effects of fluid accumulation and overload. It can be particularly challenging to manage patients with severe congestive cardiac failure or diastolic dysfunction, where renal perfusion is inadequate despite normal volume status. Excessive fluid replacement is tolerated poorly in this patient group and may precipitate pulmonary oedema.

The International Guidelines for Sepsis Management by the Surviving Sepsis campaign recommends initial fluid resuscitation with crystalloids for a minimum of 30 ml/kg and adding albumin in patients who continue to require substantial amounts of crystalloid to maintain adequate mean arterial pressure (MAP). Fluid challenge should be continued for as long as haemodynamic parameters continue to improve. Late and aggressive fluid resuscitation in critically ill patients have been associated with worse renal outcomes and increased mortality. The Fluid and Catheter Treatment Trial (FACTT) indicates that after initial resuscitation, a conservative approach to fluid administration is associated with faster weaning from mechanical ventilation and decreased ICU length of stay without any deterioration of kidney function or worse outcomes in patients with acute lung injury. The Vasopressin and Septic Shock Trial (VASST) study showed that the best survival outcomes are with a positive fluid balance of approximately 3 litres within 12 hours. Therefore, a liberal fluid approach appears to be beneficial in the first hours of shock, whilst a conservative approach following resolution of shock is preferred.

KDIGO AKI guidelines recommend isotonic crystalloids instead of colloids for intravascular expansion in patients at risk of AKI. In critically ill patients receiving mechanical ventilation, respiratory changes in left ventricular stroke volume can predict fluid responsiveness. In hypovolaemic patients, positive-pressure ventilation may induce a fall in venous return and lead to an increase in cardiac output.

Prevention of drug and nephrotoxin-induced acute kidney injury

Risk factors for developing nephrotoxicity include age older than 60 years, pre-existing CKD, volume depletion, diabetes, heart failure and sepsis. Drug monitoring of nephrotoxins is crucial in at-risk patients. Preventative measures include correctly estimating the GFR before initiation of therapy, adjusting the dosage of potential nephrotoxins, and monitoring renal function during therapy.

Contrast-induced nephropathy (CIN)

AKI secondary to contrast nephropathy (defined as increase in creatinine of >44 μmol/l) typically occurs in patients with underlying renal impairment and is rarely seen in patients with normal renal function. It may occur with intravenous and intra-arterial contrast, but not with oral contrast. The incidence of CIN is 20% in patients with creatinine levels of more than 176 μmol/l and 50% when levels are more than 440 μmol/l. Other risk factors include diabetic nephropathy, advanced age (older than

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