Acute kidney injury and the critically ill

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Abstract

Acute renal failure is commonly encountered in the intensive care unit. It is associated with considerable morbidity and mortality. There are many possible aetiologies in the critically ill, including nephrotoxic agents, hypovolaemia and sepsis. While many classification systems for acute renal failure exist, the RIFLE (Risk, Injury, Failure, Loss, End-stage) criteria and the Acute Kidney Injury Network (AKIN) criteria are the most commonly utilized. Many supportive therapies are employed to minimize the degree of renal injury once recognized, such as fluid resuscitation and maintenance of an adequate mean arterial pressure (with the use of inotropes in persistent hypotension despite fluid and treatment of the underlying aetiology). However, if renal failure becomes established, then renal replacement therapy (RRT) may be needed to maintain homoeostasis. While there are no clear guidelines with respect to the ideal mode or timing of RRT, we will discuss pros and cons of the various bedside options.

Keywords Acute kidney injury; critical care; intensive care medicine; renal failure

Royal College of Anaesthetists CPD Matrix: 2C00; 3I00

Learning objectives

After reading this article, you should be able to:

- describe the classification of AKI using the RIFLE and AKIN criteria, as well as their limitations
- list the limitations of current biomarkers in the detection of early AKI, and describe the novel biomarkers being investigated
- describe the various forms of renal replacement therapy available, including their advantages and disadvantages
- discuss of the issues surrounding intensity, duration, and timing of RRT in the critically ill
- explain other supportive therapies used to minimize renal injury and prevent further damage
- describe the outcome following RRT for AKI, particularly mortality and need for further on going dialysis

Acute kidney injury (AKI) is a deterioration in renal function associated with the accumulation of nitrogenous solutes. The incidence of AKI is increasing both among hospitalized patients and in the critically ill. Recent studies using new definitions have reported incidences of 35–40% in critically ill and 10–18% in hospitalized patients. Furthermore, 5% of patients in intensive care units (ICUs) will develop AKI requiring renal replacement therapy (RRT).[1] AKI in critically ill patients is associated with considerable morbidity and mortality, approximately 40–50% at 6 months. Reported 90-day mortality among critically ill patients requiring RRT is between 50% and 60%.

Classification of kidney injury

AKI has been defined by different classification systems, based on changes in serum creatinine and/or urine output within varying time intervals. There are different grades of severity, associated with an incremental risk of worse outcome. The RIFLE system, describing a continuum of kidney injury (AKI) including acute renal failure (ARF) (Table 1), is based on estimated glomerular filtration rate (GFR) and urine output.[2] It comprises three levels of renal dysfunction (Risk, Injury, Failure) as well as two clinical outcomes, (namely Loss of kidney function and End-stage kidney disease). The AKIN criteria (Table 1), a modification of the RIFLE criteria were later developed by Mehta et al.[3] as a potential improvement, but are not as sensitive as the RIFLE criteria.[3] The main difference with the RIFLE criteria is that the use of GFR was disregarded, a baseline creatinine is not needed and hypovolaemia and renal tract obstruction must be excluded. The most recent definition and classification of AKI is the KDIGO classification, which harmonizes the RIFLE classification system and AKIN criteria (Table 1).[4] According to these consensus guidelines, AKI is defined by an increase in the serum creatinine level of 0.3 mg/dL (26.5 μmol/L) or more within 48 hours; a serum creatinine level that has increased by at least 1.5 times the baseline value within the previous 7 days; or a urine volume of less than 0.5 mL per kilogram of body weight per hour for 6 hours. It is important to note that none of these definitions or classifications encompasses the pathogenesis of AKI.

Aetiology of AKI in the critically ill

The causes of ARF are classically divided into pre-renal, renal and post-renal (Table 2). It is important to note that the aetiology of AKI in the critically ill is frequently multi-factorial with several distinct insults occurring simultaneously (i.e. a hypovolemic patient with sepsis and the concurrent use of nephrotoxic antibiotic therapy). Most common causes of AKI in critically ill in descending order are listed in Table 3.[1]

Risk factors for AKI in critically ill

Risk factors for developing AKI in critically ill can be divided into non-modifiable risk factors like age, genetic factors, obesity, diabetes and pre-existent renal disease. Modifiable risk factors are hypovolaemia, hyperuricemia, shock, sepsis, hypoalbuminemia, rhabdomyolysis, surgery and nephrotoxic agents.

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Three classifications systems for kidney injury in the critically ill (RIFLE, top table; AKIN, middle table; KDIGO, lower table)

	GFR criteria	Urine output criteria
Risk	Increased creatinine × 1.5 or GFR decrease >25%	UO <0.5 mL/kg/hour × 6 hours
Injury	Increased creatinine × 2 or GFR decrease >50%	UO <0.5 mL/kg/hour × 12 hours
Failure	Increased creatinine × 3 GFR decrease >75% OR creatinine >4 mg/dL	UO <0.3 mL/kg/hour × 24 hours or anuria × 12 hours
Loss	Persistent ARF = complete loss of kidney function over 4 weeks	
End-stage kidney disease	ESKD (more than 3 months)	

From Bellomo et al.[2]

	Serum creatinine criteria	Urine output criteria
Stage 1	Increase in serum creatinine of ≥0.3 mg/dL (≥26.4 μmol/l) or increase ≥150%–200% (1.5- to 2-fold) from baseline	UO <0.5 mL/kg/hour × 6 hours
Stage 2	Increase in serum creatinine >200%–300% (>2- to 3-fold) from baseline	UO <0.5 mL/kg/hour × 12 hours
Stage 3	Increase in serum creatinine ≥300% (>3-fold) from baseline (or serum creatinine ≥4.0 mg/dL [≥354 μmol/L] with an acute increase of ≥0.5 mg/dL [44 μmol/L]) or initiation of RRT	UO <0.3 mL/kg/hour × 24 hours or anuria × 12 hours

From Mehta et al.[3]

	Serum creatinine criteria	Urine output criteria
Stage 1	Increase in serum creatinine of ≥0.3 mg/dL (≥26.4 μmol/L) within 48 hours OR increase ≥150%–200% (1.5- to 2-fold) from baseline, which is known or presumed to have occurred within the prior 7 days	UO <0.5 mL/kg/hour × 6 hours
Stage 2	Increase in serum creatinine >200%–300% (>2- to 3-fold) from baseline	UO <0.5 mL/kg/hour × 12 hours
Stage 3	Increase in serum creatinine ≥300% (>3-fold) from baseline OR serum creatinine ≥4.0 mg/dL [≥ 354 μmol/L] OR initiation of RRT OR In patients o18 years, decrease in eGFR to <35 mL/min per 1.73 m^2	UO <0.3 mL/kg/hour × 24 hours or anuria × 12 hours

From KDIGO group[4]

Table 1

Causes of acute kidney injury in the critically ill

	Examples
Pre-renal (50–70% of cases in ICU)	Cardiac failure, intravascular depletion, hypotension, bleeding, sepsis, burns
Renal (10–30% of cases in ICU)	Acute tubular necrosis (ATN), nephrotoxins (endogenous- myoglobin, haemoglobin and exogenous- contrast, lithium, aminoglycosides etc), allergic interstitial nephritis (i.e. secondary to cephalosporins), hepatorenal syndrome, glomerulonephritis, vasculitis
Post-renal (1–15% of cases in ICU)	Ureteric calculus, blocked urinary catheter

Table 2

Investigation in suspected AKI

Investigation begins with clinical assessment of the patient and exclusion of easily correctable causes such as blocked indwelling urinary catheters (IDC). Signs of a cause should be sought (i.e. a rash, suggesting allergic interstitial nephritis), an examination of the medication chart for potential causative agents (e.g.

Common causes of acute kidney injury in the critically ill[1]

Sepsis	48%
Major surgery	34%
Cardiogenic shock	27%
Hypovolaemia	26%
Nephrotoxic agents	19%
Hepatorenal syndrome	5.7%

Table 3