Intensive Care Med
DOI 10.1007/s00134-017-4751-y

WHAT'S NEW IN INTENSIVE CARE

The AKI glossary

Antoine Schneider[1] and Marlies Ostermann[2*]

Introduction

Critical Care Nephrology has emerged as an important area of Intensive Care Medicine. This has coincided with the introduction of new terminology, changing definitions and new tests and technologies that may be confusing for those who are less familiar with the field of acute kidney injury (AKI). In this paper, we present a short glossary of terms that commonly appear in the literature. Our goal is not to provide a comprehensive review of AKI but rather a short guide for the beginner and the perplexed.

Acute kidney injury

The term "acute kidney injury (AKI)" was introduced in 2004 to replace commonly used but not well defined terms like "acute renal failure', "acute kidney dysfunction" or "acute renal impairment" [1]. The definition evolved from the Risk- Injury -Failure-Loss-End stage (RIFLE) criteria in 2004 to the AKI Network classification in 2007 to the most recent Kidney Disease Improving Global Outcomes (KDIGO) consensus classification in 2012 [1–3]. According to the KDIGO criteria, AKI is diagnosed if serum creatinine increases by ≥26.5 µmol/l in ≤48 h, or rises to ≥1.5-fold from baseline which is known or presumed to have occurred in the preceding 7 days. There are three stages based on the changes in serum creatinine or urine output:

AKI stage 1 Rise in serum creatinine by ≥26.5 µmol/l in ≤48 h, or rise 1.5–1.9 times from baseline in 7 days, or urine output <0.5 ml/kg/h for 6–12 h.

AKI stage 2 Rise in serum creatinine 2.0–2.9 times from baseline or urine output <0.5 ml/kg/h for ≥12 h.

AKI stage 3 Rise in serum creatinine 3 times from baseline or to ≥353.6 µmol/l, or initiation of renal replacement therapy (RRT) irrespective of serum creatinine, or urine output <0.3 ml/kg/h for ≥24 h, or anuria for ≥12 h. In patients <18 years decrease in estimated glomerular filtration rate (eGFR) to <35 mL/min/1.73 m^2.

Acute kidney disease

AKI is defined as occurring over a 7-day period or less, and chronic kidney disease (CKD) starts when kidney disease has been present for >90 days [3]. The term "acute kidney disease (AKD)" describes acute impairment of renal function up to day 90, including AKI [3, 4]. There is no consensus on the definition of renal recovery after AKI or AKD. To date, recovery encompasses any improvement in renal function to complete return to baseline function.

Diagnosis

Serum creatinine and urine output

The diagnosis of AKI is based on a rise in serum creatinine or fall in urine output [3]. Creatinine is a metabolite of creatine, a molecule that is synthesized from glycine and arginine in liver, pancreas and kidneys and serves as a reserve of high-energy phosphates in skeletal muscle. It is excreted unchanged into urine and has an inverse exponential relationship with the glomerular filtration rate (GFR) but can be affected by muscle mass, fluid status and liver function.

Urine output is a cheap and easy test to evaluate renal function. It is a sensitive marker of AKI and has been given equal weighting as serum creatinine in existing AKI classifications [1, 2, 5]. It is expressed in ml/kg/h but there is no consensus as to whether to use actual or ideal

*Correspondence: Marlies.Ostermann@gstt.nhs.uk
[2] Department of Critical Care and Nephrology, King's College London, Guy's and St Thomas Hospital, Foundation Hospital, London SE1 7EH, UK
Full author information is available at the end of the article

Springer

body weight. Importantly, short-lived oliguria might be entirely physiologic.

Creatinine clearance

GFR can be determined by measuring creatinine clearance using a simple formula ($U_{creatinine}$ × volume)/(time × $P_{creatinine}$) [6].

It requires the collection of urine for 2, 6, 12 or 24 h and measurement of creatinine concentration in both blood and urine. Creatinine clearance tends to overestimate GFR at low levels of renal function, cannot be calculated in anuric patients and relies on serum creatinine concentrations being stable [6].

eGFR

Several equations have been proposed to estimate GFR based on serum creatinine concentrations [7]. They can be useful to determine stable premorbid kidney function but are unreliable in critically ill patients. The main reason is that creatinine based equations are influenced by fluid overload and creatinine production both of which vary during critical illness [7].

Urinalysis

Urine dipstick testing for blood, protein, leucocytes, nitrites and glucose is recommended for all patients with AKI. It may indicate the presence of a primary renal disease or urinary tract infection but results should always be interpreted alongside the clinical picture [8].

Urinary electrolytes

Measuring urinary electrolytes and fractional excretion (FE) of urea, uric acid or sodium

$$\frac{(\mathrm{FENa} = U_{natrium} \times P_{creatinine})}{U_{creatinine} \times P_{natrium}}$$

may provide information about the underlying aetiology of AKI but has not been consistently shown to have a clear correlation with clinical and histopathological findings [9].

New AKI biomarkers

New markers of renal function or tubular damage have been evaluated, with variable success, as tools to diagnose AKI earlier than traditional tests and prognosticate outcomes [10, 11]. Only cystatin C, neutrophil gelatinase-associated lipocalin (NGAL) and markers of cell cycle arrest (Insulin-like growth factor binding protein-7 and tissue metalloproteinase-2) are commercially available at present.

Treatment

Renal replacement therapy

Different RRT modalities are provided in the ICU, including traditional intermittent hemodialysis (IHD), hybrid therapies such as "sustained low efficiency dialysis" (SLED), "extended daily dialysis" (EDD) and "prolonged intermittent renal replacement therapy" (PIRRT), continuous renal replacement therapy (CRRT) and peritoneal dialysis (PD) (Table 1). IHD, hybrid therapy or CRRT require vascular access via a double lumen catheter. The nomenclature related to access, circuit and membrane characteristics has recently been redefined [12, 13]. To provide PD, insertion of a peritoneal dialysis catheter is necessary.

Hemodialysis

Hemodialysis is based on diffusion whereby blood flows through hollow fibers which are immersed in a sterile dialysate solution with flow in the opposite direction. Bi-directional solute exchanges occur across the membrane depending on molecular size, concentration gradients, membrane cut-off and exchange duration. To enable fluid removal, ultrafiltration is added.

Hemofiltration

Hemofiltration is based on convection whereby a pressure gradient is generated across the membrane and solutes are removed along with fluid through the pores of the membrane. To compensate for unwanted losses of fluid and electrolytes, a sterile solution (replacement solution) is administered either before (pre-dilution) or after the filter (post-dilution) or both. Hemodialysis and hemofiltration can be provided intermittently or continuously, alone or in combination [i.e. continuous veno-venous hemodialysis (CVVHD), continuous veno-venous hemofiltration (CVVH), continuous veno-venous hemodiafiltration (CVVHDF)].

Dose of RRT

In IHD and CRRT, the total volume of blood cleared of waste products in 24 h depends mainly on the duration of RRT, surface area of the membrane, incidence of filter clotting or clogging, duration of down-time, degree of re-circulation and prescribed filter fraction. Anticoagulation is usually required to prevent premature filter clotting.

Aki interactions

Cardiorenal syndrome

The term cardiorenal syndrome defines disorders of the heart and kidneys whereby acute or chronic dysfunction

Table 1 Glossary: RRT modalities for AKI and relevant technical terms

Parameter	Definition
RRT modalities	
Intermittent therapies	Blood purification techniques which are provided intermittently for 4–16 h per day or alternate days
Intermittent haemodialysis (IHD)	IHD is typically provided for 3–5 h on a daily or alternate day basis. The advantages of IHD are high efficiency, rapid clearance of small molecules (potassium, creatinine) and lower costs than CRRT. Disadvantages include metabolic fluctuations, fluid shifts and risk of haemodynamic instability in case of rapid fluid removal
Slow low efficiency dialysis (SLED) Prolonged intermittent RRT (PIRRT) Extended daily dialysis (EDD)	Hybrid therapies that provide RRT for longer than standard IHD, i.e. usually for 8–12 h. IHD and hybrid therapies have a role in situations where mobilization and rehabilitation are priority, provided metabolic fluctuations and fluid shifts can be tolerated
Continuous renal replacement therapy (CRRT)	CRRT is intended to be provided for 24 h per day. The advantages include less fluid shifts, better haemodynamic tolerance in case of fluid removal and less metabolic fluctuations compared to IHD
Continous veno-venous Hemodialysis (CVVHD)	CRRT technique in which the dominant method of solute removal is diffusion
Continous veno-venous Hemofiltration (CVVH)	CRRT technique in which the dominant method of solute removal is convection
Continous veno-venous Hemodiafiltration (CVVHDF)	CRRT technique where dialysis and hemofiltration are combined. Both, a dialysate and pre- or post dilution replacement solutions are used
Slow continuous Ultrafiltration (SCUF)	Continuous technique aimed to remove fluid only. The necessary filters and catheters are smaller and blood flow is slower compared to standard CRRT
Peritoneal Dialysis (PD)	PD is a blood purification technique where a sterile glucose-containing solution is infused into the peritoneal cavity through a permanent peritoneal dialysis catheter, and the peritoneum serves as the membrane across which solutes and water are exchanged from the blood. Clearance and degree of fluid removal depend on the osmolarity of the solution, dwell time and thickness of the peritoneum. Acute PD is the preferred technique in infants. It is also commonly used for AKI in developing countries
Technical terms	
Vascular access	Access to systemic blood flow is established through double lumen catheters inserted into a central vein (jugular, femoral or subclavian vein)
Double lumen catheters (cuffed or non-cuffed)	Double lumen catheters are specifically designed lines which are inserted in central veins. Their diameter is usually 11-14 French. Blood is drawn through one lumen (often called "arterial lumen") and returned via the other lumen (often called "venous lumen") Standard dual lumen catheters for temporary RRT do not have a cuff. In contrast, dual lumen catheters for longer-term RRT have a cuff to seal the entry point and reduce the infection risk. They can be used for longer periods (months to years)
Fluids	
Replacement solution	Sterile solution which is infused pre or post filter to compensate for fluid and electrolytes lost during hemofiltration. The composition of replacement fluids can vary according to protocols and manufacturers
Dialysate	Sterile solution which flows through the filter (outside the fibres) and against which the plasma equilibrates through the membrane
RRT filter	
Cut-off	The cut-off of a filter represents the molecular weight of the smallest solutes retained by the membrane. As membrane pores are not uniform, the given cut-off value corresponds to the molecular weight of a solute with a Sieving coefficient of 0.1
High cut-off membranes	Membranes with a cut-off value close to the molecular weight of albumin. Such membranes have demonstrated high in vitro capacity for clearance of middle-molecular weight substances
Membrane ultrafiltration coefficient (KUF, flux)	KUF represents the water permeability of the filter membrane per units of pressure and surface. A high flux membrane is usually defined as a KUF > 25 ml/h/mmHg [13]
Surface area	Filter surface area is proportional to the number of fibres, their length, mean internal radius and the number of pores and their mean internal radius. Typical adult filter surface area for CRRT ranges between 1.2 and 2 m^2 [13]
Anticoagulation	Blood purification techniques involve an extra-corporeal circuit (except for PD). Anticoagulation is usually required to prevent activation of the coagulation cascade and premature clotting. The options include systemic anticoagulants (i.e. heparin, epoprostenol, argatroban) or regional techniques (citrate)

Table 1 continued

Parameter	Definition
RRT dose	RRT dose defines the volume of blood cleared of waste products and toxins by RRT per unit of time. CRRT dose corresponds to the sum of the hourly rates of pre-dilution, post-dilution and dialysate (=the effluent rate) and is expressed in ml/kg/h. Current guidelines recommend to deliver an average dose of 20–25 ml/kg/h and to adjust the dose on a daily basis [3]. In IHD, dose is based on urea clearance using the Kt/V formula
Kt/V	Kt/V is used to describe dialysis dose in IHD. K refers to urea clearance across the filter (i.e. filter performance), t is the time when the dialytic treatment is applied and V is the patient's distribution volume of urea. The latter is usually difficult to evaluate in critically ill patients which limits the value of this parameter in the ICU
Downtime	Time during which CRRT is not applied. The reasons for downtime range from elective discontinuation for diagnostic or therapeutic purposes to premature clotting
Circuit	
In-flow ("access" or "arterial") pressure	Hydrostatic pressure measured in the blood circuit before the blood pump. It is a negative pressure. Very negative in-flow pressure is indicative of difficult aspiration of blood into the catheter which may be due to intravascular hypovolemia, low cardiac output state or a kinked/clamped line
Outflow ("return" or "venous") pressure	Pressure measured in the blood circuit after the filter. It is a positive pressure. High outflow pressure is caused by difficult return of the blood to the patient. Common causes are access problems, including a thrombosed or kinked catheter. Low venous pressure may indicate that the extracorporeal circuit has become disconnected
Transmembrane pressure (TMP)	TMP describes the pressure gradient across the membrane. It is a positive pressure that increases with reducing filter permeability. It varies along the filter and is also influenced by blood oncotic pressure. It cannot be measured directly but is estimated by the CRRT machine based on pre-filter and effluent pressures
Recirculation	Circulation of recently dialysed blood from the outflow line back into the inflow line of the catheter. Recirculation dilutes the undialysed blood from the systemic circulation and thereby reduces total solute clearance. Shorter femoral catheters (15 cm) have a higher risk of recirculation than longer ones (24 cm)
Effluent	Liquid collected from the outer part of the hemofilter consisting of used dialysate and ultrafiltrate. It is discarded as waste
Clogging	Clogging is the process by which proteins and red blood cells progressively deposit on the filter membrane which results in reduced permeability and efficacy. It is associated with an increase in TMP and decreased Sieving coefficient
Clotting	Clotting of the RRT circuit can occur in any part of the circuit (filter, venous chamber, catheter etc.) and translates into increased upstream circuit pressures (i.e. it is associated with increased pre-filter pressure)
Filtration fraction (FF)	FF is the ratio between ultrafiltration rate and plasma flow rate. The higher the FF, the higher the haematocrit at the end of the filter and the higher the risk of clotting. Ideally, it should be kept under 25%

ICU intensive care unit, *RRT* renal replacement therapy

in one organ may induce acute or chronic dysfunction of the other [14].

Hepatorenal syndrome

Hepatorenal syndrome describes potentially reversible AKI in individuals with cirrhosis or fulminant liver failure in the absence of other identifiable causes. It is characterized by functional impairment of the kidneys due to vasoconstriction of the renal arteries in the setting of splanchnic vasodilation [15].

Author details
[1] Adult Intensive Care Unit, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland. [2] Department of Critical Care and Nephrology, King's College London, Guy's and St Thomas Hospital, Foundation Hospital, London SE1 7EH, UK.

Compliance with ethical standards

Conflicts of interest
MO received speaker honoraria and research funding from Fresenius Medical Care, and consulting honoraria from Baxter Gambro. AS received speaker honoraria from Fresenius Medical Care, Baxter Healthcare Corp and consulting honoraria from B.Braun Melsungen AG.

Received: 10 January 2017 Accepted: 27 February 2017
Published online: 01 April 2017

References

1. Bellomo R, Ronco C, Kellum JA et al (2004) Acute renal failure—definition, outcome measures, animal models, fluid therapy and information technology needs: the second international consensus conference of the acute dialysis quality initiative (ADQI) group. Crit Care 8:R204–R212

2. Mehta RL, Kellum JA, Shah SV et al (2007) Acute kidney injury network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 11:R31
3. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group (2012) KDIGO clinical practice guideline for acute kidney injury. Kidney Int 2:1–138
4. Chawla LS, Bellomo R, Bihorac A et al (2017) Acute kidney disease and renal recovery: guideline report of the acute disease quality initiative (ADQI) 16 Workgroup. Nat Rev Nephrol 13(4):241–257
5. Prowle JR, Liu YL, Licari E et al (2011) Oliguria as predictive biomarker of acute kidney injury in critically ill patients. Crit Care 15:R172
6. Stevens LA, Coresh J, Greene T et al (2006) Assessing kidney function—measured and estimated glomerular filtration rate. N Engl J Med 354:2473–2483
7. Carlier M, Dumoulin A, Janssen A et al (2015) Comparison of different equations to assess glomerular filtration in critically ill patients. Intensive Care Med 41:427–435
8. Schneider AG, Bellomo R (2013) Urinalysis and pre-renal acute kidney injury: time to move on. Crit Care 17:141
9. Bagshaw SM, Bennett M, Devarajan P et al (2013) Urine biochemistry in septic and non-septic acute kidney injury: a prospective observational study. J Crit Care 28(4):371–378
10. Malhotra R, Siew ED (2016) Biomarkers for the early detection and prognosis of acute kidney injury. Clin J Am Soc Nephrol 8:CJN-01300216. **[Epub ahead of print]**
11. Ostermann M, Joannidis M (2015) Biomarkers for AKI improve clinical practice: no. Intensive Care Med 41(4):618–622
12. Villa G, Neri M, Bellomo R et al (2016) Nomenclature for renal replacement therapy and blood purification techniques in critically ill patients: practical applications. Crit Care 20:283
13. Neri M, Villa G, Garzotto F et al (2016) Nomenclature for renal replacement therapy in acute kidney injury: basic principles. Crit Care 20:318
14. Di Lullo L, Bellasi A, Russo D et al (2017) Cardiorenal acute kidney injury: epidemiology, presentation, causes, pathophysiology and treatment. Int J Cardiol 227:143–150
15. Wong F (2012) Recent advances in our understanding of hepatorenal syndrome. Nat Rev Gastroenterol Hepatol 9(7):382–391