FOCUS EDITORIAL

Focus on acute kidney injury and fluids

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An acute deterioration of kidney function, currently known as acute kidney injury (AKI), frequently develops in ICU patients and is always bad news. In this overview we will highlight recent findings related to its diagnosis, epidemiology, and extracorporeal treatment.

Epidemiology of AKI

The AKI-EPI study, a worldwide cross-sectional study on the occurrence of acute kidney injury (AKI) in the first week in intensive care unit (ICU), found AKI in 57 % of the 1800 included patients. AKI severity was associated with adverse patient and kidney outcome at hospital discharge [1]. Analysis of a large cohort (32,045) in a single medical center confirmed the high prevalence (74.5 %) and further illustrated that both AKI severity and duration and the criteria used to define it (creatinine, urine output, or both) had significant impact on short- and long-term outcomes [2]. Another large cohort study in 580 patients with out-of-hospital cardiac arrest found severe AKI in 43 % of the patients and the association with mortality but not with neurological outcome [3]. Last, it must be noted that first validation of the Kidney Disease Improving Global Outcomes (KDIGO) criteria was performed in a large pediatric population [4].

Assessment of renal prognosis and of renal function

Several studies demonstrated limits of usual renal dysfunction criteria and of biomarkers in assessing renal function or predicting renal prognosis. First, short episodes of oliguria in ICU patients are frequent and do not always predict subsequent AKI by creatinine criteria. Legrand et al. explored whether AKI biomarkers could predict worsening of kidney function (WKF) in 111

critically ill patients with first episode of oliguria. Interestingly, although plasma neutrophil gelatinase-associated lipocalin (NGAL) might improve the prediction of WKF, the biomarker had a similar performance to serum creatinine [5]. Furthermore, the follow-up of the furosemide stress test study found limited performance of biomarkers to predict WKF, which were largely outperformed by the furosemide stress test [6].

The gold standard for glomerular filtration rate (GFR) determination is inulin clearance, but this cannot be measured easily. Carlier and co-workers compared inulin clearance with creatinine clearance and several creatinine and/or cystatin C-based GFR equations in 68 critically ill patients with stable kidney function. As a result of tubular secretion of creatinine, measured creatinine clearance resulted in a slight overestimation of GFR while creatinine-based equations had the worst performance with overestimation of the true GFR; the overestimation increased with hospital stay [7]. This confirms previous findings showing increasing differences between discharge estimated GFR (eGFR) and creatinine clearance with increasing ICU stay in both AKI and non-AKI patients. Reduced creatinine excretion resulting from muscle loss was the main determinant of this difference [8]. Since cystatin is not influenced by muscle mass, the cystatin-based equations did not share the hospital stay-induced bias [7].

Recovery from AKI

Another relatively new research field is the association between AKI and long-term kidney outcome. A post hoc analysis of the EPaNIC trial showed significant impact of the chosen definitions for renal recovery and of the use of a surrogate to estimate baseline creatinine on the incidence of renal recovery. In addition, this analysis confirmed the limitations of serum creatinine when assessing recovery since discharge eGFR overestimated true GFR because of sarcopenia. Indeed, as many as 40 % of the patients with known baseline

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creatinine had a discharge creatinine lower than their baseline [9].

Resuscitation fluid

Recent large randomized trials have suggested an impact of the choice of fluids for resuscitation on kidney function. The extended analysis of Yunos et al.'s before/after trial confirmed that change from saline to buffered crystalloid solutions might decrease the risk of AKI [10]. However, this study also reported large fluctuations in AKI incidence across 6-month study periods suggesting unidentified confounders [10]. The neutral results of the subsequent double-blinded, cluster randomized, double-crossover trial comparing buffered crystalloid solution to saline (SPLIT trial) indicated no harm from saline, at least in patients with low illness severity, who were admitted mainly after elective surgery [11]. Thus these results should be confirmed in more severely ill, those with sepsis, and patients requiring large volumes of fluid [12].

In a follow-up of the 6S trial, Perner and colleagues reported that the long-term mortality rate did not differ in patients with severe sepsis receiving starches when compared to crystalloids (mean follow-up 22 months, range 13–36); there was a trend toward fewer days alive and out of hospital in the starches group [24 % (0–87) vs. 63 % (0–90); $P = 0.07$] [13]. Among factors that may cause the deleterious effect of starches, tissue accumulation has been found to be frequent, rapid, nearly ubiquitous, persistent, and associated with adverse events [14]. Interestingly, although this systematic review suggested tissue accumulation to be dose-related, both dermal deposits and subsequent pruritus were observed with cumulated dose as low as 0.4 mL/kg [14].

The results of trials comparing colloids, mainly starches, to crystalloids have progressively changed practices of fluid resuscitation. A large study reporting results of six cross-sectional point prevalence studies on the use of resuscitation fluids in Australia and New Zealand ICUs demonstrated a progressively decreased use of colloids over crystalloids and a progressive increase in the use of buffered crystalloid solutions over 0.9 % saline [15]. The FENICE study further confirmed that buffered crystalloid solutions have become the most used fluid by intensivists worldwide [15, 16].

Extracorporeal blood purification

Although blood purification techniques as an adjunct to sepsis treatment is a seducing idea, authors still struggle to prove its efficacy. In line with the negative results of the IVOIRE trial, Quenot et al. found no benefit of the CASCADE technique, allowing very high volume

hemofiltration, in a pilot study randomizing 60 patients [17], while Combes et al. found no benefit of high volume hemofiltration randomizing 224 patients with post-cardiac surgery shock [18]. Finally, Payen and colleagues found no benefit of polymyxin (PMX) hemoperfusion in 232 adult postoperative patients with documented peritonitis and septic shock [19].

Optimal timing of renal replacement therapy (RRT) remains unknown although the START-AKI pilot study provided interesting results. This study randomized 101 patients with AKI stage 2 according to modified criteria to receive either RRT in the 12 h following inclusion or based upon predefined classical criteria for RRT. Even though the design of this feasibility study precludes any conclusions regarding outcome, it must be noted that accelerated RRT initiation resulted in a 50 % increase in need for RRT when compared to standard indications [20].

Abbreviations

AKI: Acute kidney injury; eGFR: Estimated glomerular filtration rate; GFR: Glomerular filtration rate; ICU: Intensive care unit; KDIGO: Kidney Disease Improving Global Outcomes; NGAL: Neutrophil gelatinase-associated lipocalin; PMX: Polymyxin; RRT: Renal replacement therapy; WKF: Worsening of kidney function.

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Compliance with ethical standards

Conflicts of interest

None.

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