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EDITORIAL

Update on acute kidney injury: some progresses and a long way to go

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Acute kidney injury (AKI) is common and associated with substantial morbidity and mortality. Despite advances in understanding its prevention and management, there has been little improvement in clinical outcomes, and gaps in knowledge remain. In this review, we highlight some select publications to illustrate this point.

Pathophysiology and prognostic consequences

AKI encompasses a heterogeneous spectrum of syndromes linked to adverse short- and long-term outcomes, including chronic kidney disease and increased mortality. The identification of recovery patterns and the standardization of the definition of recovery have been a matter of interest.

Gómez et al. analyzed 190,550 patients admitted to 16 hospitals in the US and identified severe persistent AKI—defined as stage 3 persisting for ≥ 72 h or progression from stage 2 to persistent stage 3—as a distinct and prognostically adverse phenotype [1]. Although relatively uncommon (4.2%), this type was associated with higher 90-day mortality (adjusted HR 1.49; 95% CI 1.42–1.56), increased rate of readmission, and dramatically lower renal recovery. Whether severe persistent AKI can be prevented remains, however, to be demonstrated.

Beyond clinical definitions, mechanistic work is advancing. Velho et al. performed targeted metabolomics profiling in patients undergoing cardiopulmonary bypass, cardiac surgery without bypass, or vascular surgery [2]. Distinct postoperative metabolic patterns were observed, including amino acid and protein-catabolic signatures associated with postoperative AKI. Although small ($n = 53$), this study highlights how metabolic fingerprints can illuminate pathogenic mechanisms and potentially guide therapeutic decision-making.

Oyaert et al. evaluated the role of urinary renal tubular epithelial cells detected by flow cytometry as biomarkers of early AKI [3]. Diagnostic performance was modest at 4–12 h but excellent at 24 h (AUC 0.88; 95% CI 0.83–0.92). External validation and feasibility studies are now required before translation into routine perioperative care.

Specific populations and clinical contexts

Azoulay and colleagues issued an expert consensus on thrombotic thrombocytopenic purpura, emphasizing diagnostic differentiation from other types of microangiopathic AKI and management with plasma exchange, corticosteroids, Rituximab and Caplacizumab [4].

Several previous studies concluded that obesity may be an AKI risk factor. In a 15-year single-center study, Monet et al. showed that severe AKI was common in obese patients with 13.5% requiring renal replacement therapy (RRT), which was independently associated with mortality and persistent AKI [5]. This study open-up a whole new field of research, for instance to investigate whether the association between obesity and AKI is causal and whether there is a need to tailor RRT differently in this patient cohort.

Geographic disparities also remain striking. Tangchitthavorngul et al. reported outcomes of severe AKI across India and Asia [6]. Nearly one in two patients died within 28 days, and long-term follow-up revealed high rates of adverse kidney events and impaired quality of life, highlighting global inequities in AKI management and the need for region-specific interventions.

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Table 1 Top ten research priorities arising from last year articles' selection

Topic	Top ten remaining research questions
AKI epidemiology	Incidence and outcome of AKI in subpopulations (e.g.patients with obesity)
AKI prevention	Identification of preventable risk factors for persistent severe AKI
Risk stratification	Omics profile performance in identifying patients at risk of AKI
Biomarkers	Prospective validation of RTEC performance versus other biomarkers Identification and validation of biomarkers of persistent AKI
Global inequities	Description of global AKI epidemiology including patient-important outcomes
Hemadsorption	Impact of hemoadsorption on patient-centered outcomes
Amino-Acids infusion	Role of amino-acid infusion in different surgical populations on patient-important endpoints
Blood pressure management	Benefits of MAP target individualization in different patient cohorts, including surgical and non-surgical patients
Acidosis management	Role of bicarbonate in patients with metabolic acidosis and identification of threshold to initiate therapy
RAS Inhibitors	Identification of optimal timing for initiation of RAS inhibitors after ICU-acquired AKI

AKI acute kidney injury, *RTEC* renal tubular epithelial cells, *MAP* mean arterial pressure, *RAS* renin–angiotensin system, *ICU* intensive care unit

Management and future research

Prevention of AKI and its dire consequences is mandatory, especially in urgent or elective surgery. A recent review in the journal summarizes various strategies that have been proposed, along with the uncertainty surrounding their benefits [7]. In this regard, four important trials deserve to be highlighted.

In a multicenter randomized clinical trial (RCT), Legrand et al. tested whether withholding renin–angiotensin system (RAS) inhibitors before non-cardiac surgery reduced the risk of hypotension or AKI [8]. They showed that continuation was not associated with higher risk of perioperative hypotension or postoperative complications, suggesting that routine discontinuation of RAS inhibitors (as commonly done) may be unnecessary.

Pérez-Fernández et al. conducted an intriguing study on high-risk cardiac surgery patients requiring cardiopulmonary bypass (CBP) [9]. In this bicentric RCT, the authors investigated whether connecting the CBP to a nonselective acrylonitrile–sodium methallyl sulfonate/polyethylenimine hemadsorption membrane improved short-term outcomes, including risk of AKI. While day-7 AKI incidence decreased, need for RRT, mortality and length of stay were unchanged, raising concerns regarding potential confounders such as AKI misclassification associated with hemofiltration accompanying hemadsorption.

Landoni et al. also focused on patients undergoing cardiac surgery requiring CBP and demonstrated that high-dose perioperative amino acid infusion (2 g/kg) reduced AKI risk (RR 0.85; 95% CI 0.77–0.97), but again without difference in RRT use, mortality or renal recovery [10].

Finally, Saugel et al. recently published an RCT assessing the benefits of individualized blood pressure management during major abdominal surgery [10]. Target mean arterial pressure (MAP) in the individualized group was aimed to be as close as possible to the MAP before induction. Although the trial successfully increased MAP in patients randomized to the individualized group, no benefits were observed in terms of major postoperative complications, including AKI.

Decision support and hemodynamic targets

The Kidney Action Team Trial evaluated the role of individualized electronic recommendations for hospitalized patients with AKI [11]. Among 4,003 patients, the intervention did not significantly reduce the composite outcome of worsening AKI, dialysis, or death (19.8% vs 18.4%). Despite good adherence, no improvement in hard outcomes was observed, suggesting that isolated electronic prompts may be insufficient to modify complex renal outcomes in hospitalized patients.

Hemodynamic management in septic shock continues to attract debate. A post-hoc analysis of the SEPSISPAM trial examined whether baseline characteristics modified the effect of high (80–85 mm Hg) versus low (65–70 mm Hg) MAP targets on mortality and renal outcomes [12]. No clinically meaningful heterogeneity of treatment effect was detected, supporting the view that targeting higher MAP universally does not prevent AKI and may even expose some patients to harm.

Beyond prevention, a recent emulated trial assessed whether bicarbonate infusion might benefit patients with metabolic acidosis [13]. Although a reduction in the risk of mortality was observed (risk ratio: 0.89; 95% CI: 0.84–0.95), the inherent biases related to the retrospective, observational nature of the data warrant caution in interpretation. The recently published BICAR-ICU2 multicenter open-label RCT does not

confirm this prognostic impact [14]. In this study, bicarbonate infusion was not associated with a reduction in day-90 mortality (62.1% vs. 61.7%; primary endpoint), despite a clinically significant decrease in RRT use (absolute difference: − 15.5%; 95% CI: − 8 to − 23%).

Conclusion

Despite numerous recent studies, few definitive answers have emerged, and major challenges remain in preventing, treating, and mitigating the consequences of AKI. Recent recommendations from the ADQI expert group regarding trial design may help to guide the progress through better population selection, enrichment strategies, and selection of appropriate study endpoints [15]. Future research should also focus on refining the management of AKI survivors and reducing the lasting impact (Table 1).

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