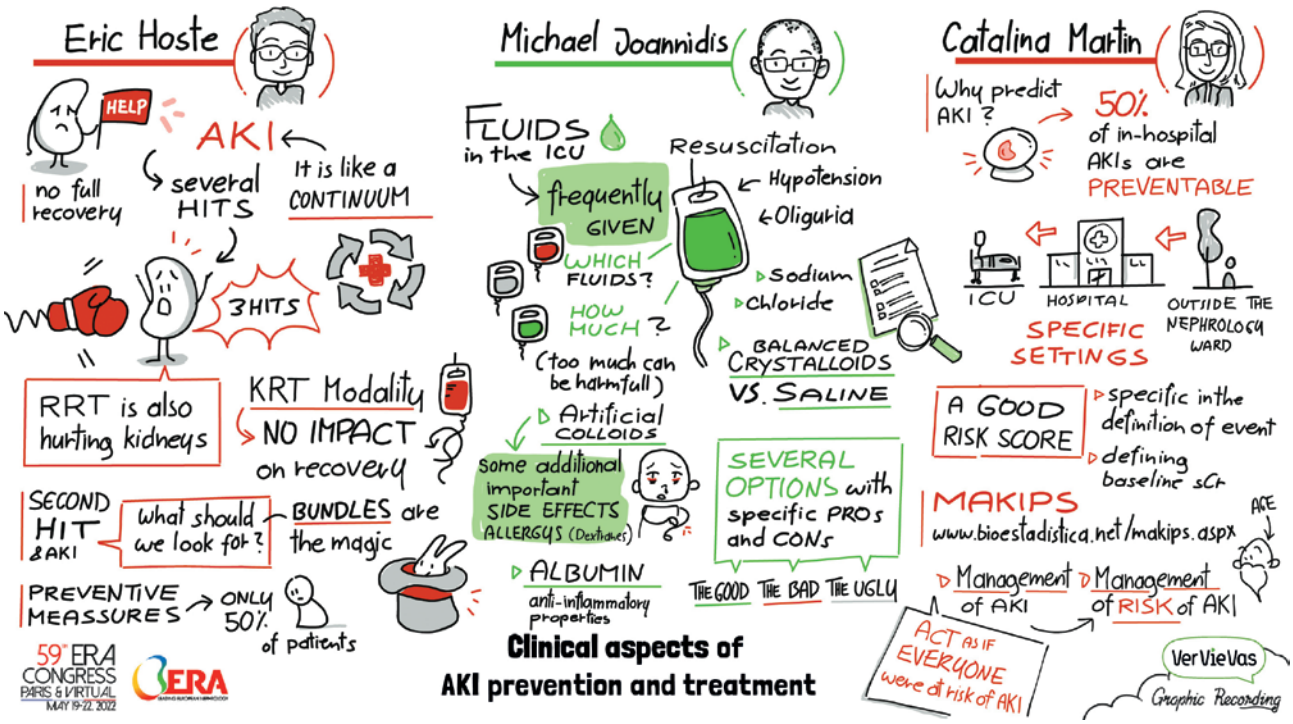
Symposium 8.3
Clinical aspects of AKI prevention and treatment



The second hit hypothesis – What should we look for?

Eric Hoste, Belgium

The KDIGO guidelines define acute kidney injury (AKI) based on the RIFLE criteria as an abrupt decrease in kidney function occurring over seven days or less and manifesting with an increase in serum creatinine accompanied by a decrease in urine output. The presence of AKI stage 1 or greater ≥7 days after the initiating event indicates a condition named acute kidney disease (AKD). The trajectory of AKD can take many forms depending on the severity of the initial AKI episode. One of the possibilities is the so-called "second hit" episode of AKI, when the initial deterioration lasting for at least 48 hours is followed by a period of sustained reversal, before the second episode of AKI ensues, leading to AKD. In some circumstances, as in COVID-19, in patients with acute myocardial infarction and cardiogenic shock, or those with multiple infectious complications, the primary injury can even be followed by more than one exacerbation. The common issue in all these cases is that a higher degree of kidney injury in single hits is associated with worse overall outcomes. Furthermore, renal replacement therapy (RRT), even adds to the risk of developing a decline in urine output, especially when more intensive protocols and

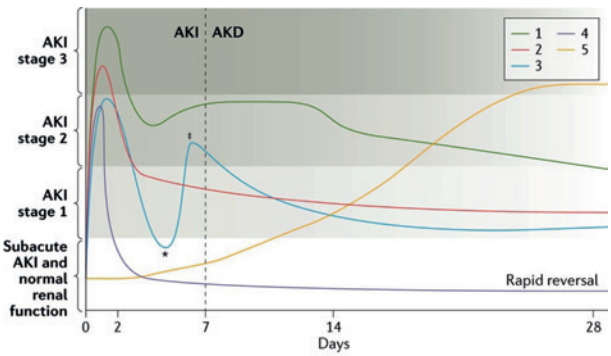


Figure 1.
Evolution of AKI into AKD – represented with a blue line is an episode of persistent AKI followed by a period of sustained reversal and then a second AKI episode (from ref. 1)

early initiation are implemented. A recently published analysis of randomized clinical trials involving critically ill patients with AKI treated with continuous, intermittent, or hybrid RRT hypothesized that RRT-related hypotensive episodes might also affect renal outcomes. However, the studies included presented such high heterogeneity in terms of outcome definitions and measurement that the conduction of the projected meta-analysis ended up being impossible. Nevertheless, a very interesting observation was made that there was no significant difference in the achieved hemodynamic stability and kidney survival related to different RRT modalities.

There are several possible approaches to preventing the second-hit AKI. The post-surgery "care bundles" recommended by the KDIGO include avoidance of nephrotoxic and radiocontrast agents, discontinuation of ACE inhibitors and ARBs for the first 48h after surgery, close hemodynamic monitoring, and optimization of volume status. These measures proved efficient in reducing AKI frequency and severity in high-risk patients after cardiac surgery. Further analysis of the treatment effects of individual bundle components identified hemodynamic optimization as the most powerful preventive measure. Regrettably, despite their simplicity, it appears that in clinical practice these preventive measures are seldom thoroughly followed. It is therefore essential to actively institute measures to hamper the second-hit AKI episodes, specifically focusing on the modifiable factors such as hemodynamic status, increased intra-abdominal pressure, and RRT.

Fluids in ICU – Which is the right one?

Michael Joannidis, Austria

Intravenous fluid therapy is among the most common interventions in critically ill patients. Fluids are administered for resuscitation, replacement, maintenance, and/or organ protection. The most frequent indications for resuscitation are hypotension and oliguria. The main considerations when planning intravenous fluid therapy should be the type and amount of solutions.

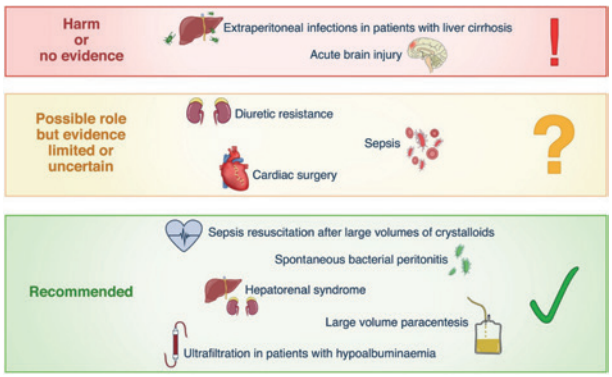


Figure 2.
Albumin therapy in critical care (from ref. 15)

Normal saline is the most often used crystalloid solution. Even though it is commonly called a „physiological solution", NaCl 0.9% has higher sodium and chloride levels than plasma, contains neither bicarbonates nor lactates, and can even induce metabolic acidosis and renal hypoperfusion. Nevertheless, in clinical practice, there has been no report of any marked long-term harm in critically ill patients receiving normal saline. Various balanced crystalloid solutions have been developed to overcome the disadvantages of normal saline, such as Ringer's lactate, Plasma-Lyte, and ELO-MEL Isoton. Nevertheless, even though they all have sodium and chloride levels closer to those of the plasma, the results of their application are conflicting. Some studies report only a moderate advantage of balanced solutions compared to normal saline in restoring hydration status and electrolyte balance. The Saline Against Lactated Ringer's or Plasma-Lyte in the Emergency Department (SALT-ED) study concluded that the amount of fluid, rather than composition, was associated with favorable outcomes. Another study, however, stated a lower rate of the composite outcome of death from any cause, new RRT, or persistent renal dysfunction with the use of balanced solutions compared to normal saline. One of the largest trials comparing the effects of a balanced multielectrolyte solution and saline, which included over five thousand ICU patients, found no evidence that the risk of death or AKI was lower with the balanced solution, and serum creatinine levels over time exhibited a virtually identical pattern in both groups. Also, in this cohort, the rate of fluid administration seemingly made no difference.

Colloid solutions are another therapeutic option in critically ill patients. It is commonly believed that their administration would reduce the overall need for fluid as compared with the administration of crystalloids. In fact, this impact is only moderate, whereas their use is associated with potential adverse effects. Nevertheless, albumin administration in patients with cirrhosis and ascites may help prevent AKI and it does improve fluid removal by preventing intradialytic hypotension during RRT.

Identifying patients at high risk of in-hospital AKI

Catalina Martin, Spain

AKI is an important risk factor for new-onset CKD and is strongly associated with an increased risk of death in hospitalized patients. Therefore, early recognition of this common, but highly preventable condition, is of fundamental importance to improve the outcomes.

A good risk score should be simple, accurate, easily interpreted, and inexpensive. A good AKI risk score should be highly specific, externally validated, well-calibrated, digitizable, and able to discriminate between community- and hospital-acquired AKI, and between CKD and AKI. Despite a myriad of available risk scores for AKI associated with conditions requiring intensive care, there are very few such scores for non-critical patients and only one for community-acquired AKI.

Currently, there are four available models to predict hospital-acquired AKI in non-critically ill patients: by Bedford et al, by Martin-Cleary et al, by Segarra et al., and the Acute Kidney Injury Prediction Score (APS). All are based on historical serum creatinine, but they also incorporate 7 to 22 other variables to predict the development of AKI. For example, the Madrid Acute Kidney Injury Prediction Score (MAKPIS) by Martin-Cleary et al. contains 23 variables, obtainable automatically from electronic clinical records at admission, such as age, comorbidities, surgical interventions, and laboratory parameters (white blood cells, serum sodium, potassium, calcium, glucose, urea, and uric acid). The tool is freely available at http://www.bioestadistica.net/MAKIPS.aspx.

Until now there is no data on the impact of clinical implementation of the available AKI prediction scores. AKI management still relies on supportive therapy to optimize renal perfusion, preventive measures to minimize nephrotoxicity, and causal treatment when applicable. In the majority of cases, appropriate follow-up is still lacking. Therefore, future work should focus on timely AKI prediction based on baseline serum creatinine and age as the crucial parameters, as well as on the evaluation of AKI risk scores' significance in clinical practice.

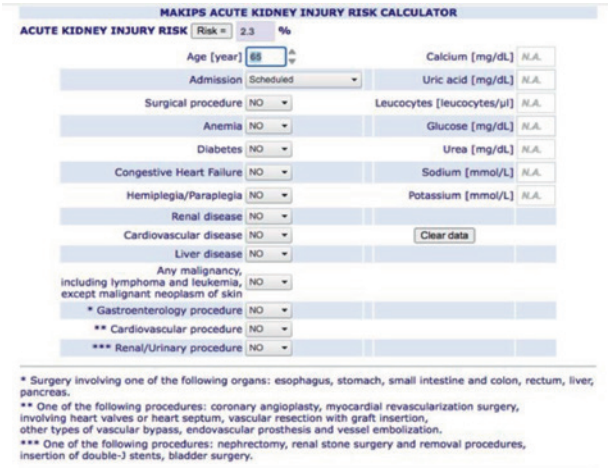


Figure 3.
The MAKIPS acute kidney injury risk calculator

Further readings

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All the speakers reviewed and approved the content.