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RECENT ADVANCES IN ICU

Acute kidney injury

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The introduction by the KDIGO group (Kidney Disease: Improving Global Outcomes) of an accepted definition of acute kidney injury (AKI) has highlighted that AKI is commonly encountered in the critically ill and influences outcomes [1, 2]. Hence, in recent years, much attention has focussed on not only prevention of AKI but also optimising treatment.

Prevention of AKI

The KDIGO guidelines propose supportive measures for patients at high risk for AKI, although data proving effectiveness for these approaches remain scarce. In 2017, the PrevAKI trial demonstrated that biomarker guided implementation of a bundle based on the KDIGO approach (i.e. discontinuation of nephrotoxins, optimization of volume status and perfusion pressure, consideration of functional haemodynamic monitoring, close monitoring of serum creatinine and urine output, avoidance of hyperglycemia, and consideration of alternatives to radio contrast agents) reduced the incidence of AKI [3]. Subsequently, the two-phase PrevAKI2 trial performed a survey which demonstrated that implementation of the KDIGO bundle in surgical high-risk patients was rarely performed routinely. This was followed by the randomised interventional trial which reproduced the results of PrevAKI with a significant reduction in moderate and severe AKI in patients receiving the KDIGO bundle [1]. On investigating the effects of each intervention within the care bundle, haemodynamic optimisation was at least as important as discontinuing nephrotoxins, whilst avoidance of hyperglycemia or contrast agents appeared to have no significant effect [4].

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Conservative management of AKI

Fluid administration remains one of the primary measures to prevent AKI, but avoidance of volume overload is also important [5]. Although fluid restriction may initially seem to be counterintuitive, the REVERSE-AKI feasibility trial addressed this and randomised 100 patients judged not to be hypovolaemic with AKI stage one or higher but not requiring renal replacement therapy (RRT) to receive restrictive fluid management targeting a cumulative negative fluid balance but at least < 300 ml/day [6]. Fluid input was restricted with diuretic use to achieve the desired target for 72 h, allowed was fluid bolus therapy if clinically required. The intervention resulted in a 72 h cumulative balance of around − 1100 ml compared to neutral in the standard arm. This negative fluid balance further increased to − 2200 ml at intensive care unit (ICU) discharge/day 7. Importantly, 13% received RRT in the intervention compared to 30% in the control group and serious adverse events were also lower. This demonstrates the feasibility of such an approach which could reduce the need for RRT in patients with AKI. However, two recent randomised clinical trials (RCTs), the CLASSIC and the CLOVER trial [7, 8], investigating a restrictive versus a standard fluid regimen in septic patients did not show any effect on AKI, though this was not a primary endpoint and RRT not reported. Therefore, whether a restrictive fluid management is advantageous for all forms of AKI or just specific subphenotypes remains to be determined [9] (Fig. 1).

Timing of RRT

Optimal timing of initiation of RRT has been investigated in several RCTs and a reduction in RRT using a "watch and wait" strategy has been observed. Although how long to delay RRT safely remained unanswered. The multicentre AKIKI2 trial compared a delayed versus a more delayed RRT strategy. Patients with AKI stage 3, oliguric for > 72 h, and/or a blood urea > 40 mmol/l were randomised to receive

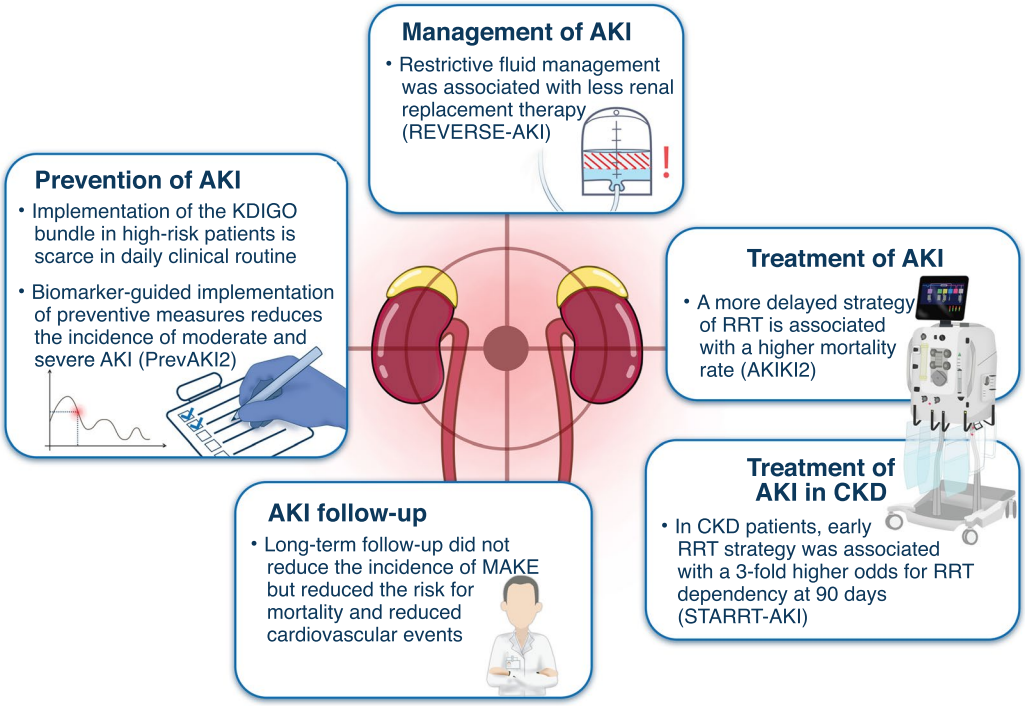

Fig. 1 Towards better management of AKI. *CKD* chronic kidney disease, *KDIGO* kidney disease: improving global outcomes, *MAKE* major adverse kidney events, *RRT* renal replacement therapy

immediate treatment or delay until absolute RRT criteria were reached. [10]. In the more delayed group, 20% fewer received RRT (98% versus 79%, $p < 0.00001$), but the hazard for death at 60 days increased significantly (HR 1.65, 95% CI 1.09–2.50, $p = 0.018$), indicating a more delayed strategy be avoided.

Chronic kidney disease (CDK) is a major risk for the AKI development. A secondary analysis of the STARRT-AKI study [11] including 1121 patients with a known pre-randomisation measure of kidney function demonstrated CKD in 39% [12]. When compared to patients without CKD, there was a higher rate of cardiovascular comorbidities, diabetes, mortality, and 90 day RRT dependency. Furthermore, in patients with CKD randomised to the early treatment arm, a threefold higher odds for RRT dependency at day 90 (aOR 3.18; 95% CI 1.41–7.91) was observed. Interestingly, in the first AKIKI trial, CKD patients receiving early RRT showed an increased mortality [13] which could not be reproduced by STARRT-AKI trial. Given that CKD patients have a reduced renal reserve, a higher rate of RRT dependency after AKI is to be expected. However, it remains to be investigated how exposure to RRT may potentially result in maladaptive repair following AKI.

Post-AKI follow-up

The potential benefits of longer-term follow-up for our patients have been observed in ICU survivors and a similar approach has been considered in survivors from AKI. A Canadian study matched 164 patients from an AKI follow-up clinic with 656 patients who received standard of care with a follow-up of more than 2 years [14]. No reduction in major adverse kidney events could be observed, but a lower risk of all-cause mortality (HR 0.71, 95% CI 0.55–0.91) and a reduction in cardiovascular events were demonstrated. Although encouraging, further research is needed to determine which, if any, specific intervention(s) translate into improved outcomes. Additional studies focussing on the optimal timing of follow-up as well as implementation of such processes should be encouraged. This study reinforces the message that our patients who survive will fare even better if a similar degree of care is taken after discharge as is given during their ICU stay.

Outlook

Despite a degree of nihilism from some that given the syndromic nature of AKI, no “cure” exists we are making small but significant steps. Biomarkers aid our diagnosis

and shed insights into the longevity of an AKI episode. We have more knowledge with regard to fluid prescription, haemodynamic monitoring where appropriate, and where RRT is considered, we have a better idea as to when not to start. Some may be persuaded that other tools may help identify AKI early, including artificial intelligence (AI). The role of AI will undoubtedly influence the practice of medicine significantly in the future and recent meta-analyses of currently published models showed promising performance for early prediction of postoperative AKI [15]. However, a word of caution. External validation for many models is lacking and often shows a reduced accuracy when performed. Also few, if any, have been shown to have clinical effects when used, either improving clinical decision-making or not. There is also the concern that physicians may await instruction from an AI system rather than use their clinical skills to take action promptly.

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Declarations

Conflicts of interest
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Not applicable.

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