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Letter to the Editor

LETTER TO THE EDITOR

No difference in mortality after three different kidney replacement therapy initiation strategies in acute kidney injury

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A meta-analysis examined the benefit of the accelerated kidney replacement therapy (KRT) strategy compared with the watchful waiting KRT initiation strategy in an acute kidney injury (AKI) population [1] enrolled from the most recent Artificial Kidney Initiation in Kidney Injury 2 (AKIKI 2) trial [2]. The pairwise meta-analysis categorised the more-delay strategy group in the AKIKI 2 trial into the watchful waiting KRT initiation group. However, the inclusion criteria (blood urea nitrogen 112–140 mg/dl or oliguria/anuria for 72 h) in the AKIKI 2 trial were the KRT initiation criteria for the delay group in the AKIKI trial [3]. For this reason, analysing the more-delay strategies separately may be more appropriate. We regrouped the different KRT initiation strategies into three KRT initiation strategy categories in accordance with the various KRT initiation criteria in randomised controlled trials (RCTs): early/accelerated KRT initiation, standard KRT initiation and more-delay KRT (Fig. 1). We then conducted a network meta-analysis (NMA) to explore the prognostic effect of these KRT initiation strategies. The primary outcomes were 28-, 60- and 90-day mortality and KRT dependency. Detailed descriptions of the search strategy and statistical method are provided in the supplementary material (Supplementary Fig. 1, Supplementary Table 1).

A total of 12 RCTs with 5203 participants were identified in the present NMA [2–13]. The characteristics of the 12 studies are summarised in Supplementary Tables 2 and 3. The network plot is presented in Supplementary Fig. 2A–D. Regarding 28-, 60- and 90-day mortality, neither the early nor the more-delay KRT strategy was associated with a higher or lower risk of mortality compared with the standard KRT strategies (Fig. 2A–C), with the heterogeneity being low ($I^2 = 0\%$), moderate ($I^2 = 69.6\%$) and low ($I^2 = 31\%$), respectively. No significant difference was found in KRT dependency among the three KRT initiation strategies, with the heterogeneity being moderate ($I^2 = 40.7\%$; Fig. 2D). In accordance with the Confidence in Network Meta-Analysis framework [14], we also evaluated our confidence in the evidence in the current NMA. In the evaluation, we assumed that the clinically important odds ratio (OR) was 0.8. Thus, when evaluating 90-day mortality, some concern regarding the imprecise domain was discovered for the more-delay KRT initiation strategy compared with the standard KRT initiation strategy [the confidence interval (CI) of the NMA pooling effect extended into clinical effects; OR 1.42 (95% CI 0.83–2.42)].

By summarising the exclusion criteria in the enrolled RCTs, we found that patients with chronic kidney disease (CKD) or malignancy and patients with AKI owing to specific aetiologies were often excluded in RCTs (Supplementary Table 5). In the IDEAL study, the early KRT initiation strategy did not result in better outcomes in patients with CKD [15]. Regarding KRT initiation strategies in CKD patients who have experienced AKI, 10 of the 12 enrolled studies excluded patients with CKD, especially those with advanced CKD (estimated glomerular filtration rate <20–30 ml/min/1.73 m^2; Supplementary Table 5). Therefore it should be emphasised that the current available evidence cannot support any particular KRT initiation strategy in patients with advanced CKD who have experienced AKI.

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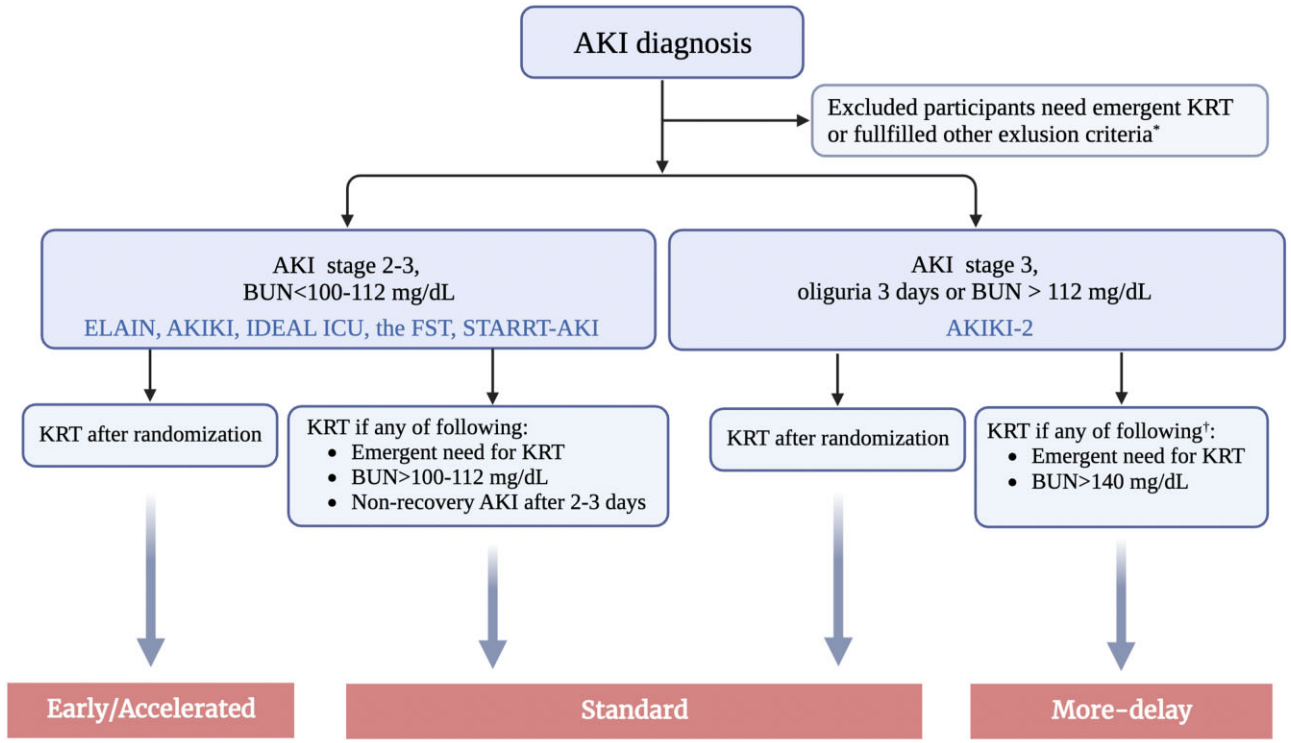

Figure 1: Three different KRT initiation strategies in published RCTs. *Most of the enrolled studies excluded participants with advanced CKD, malignancy or cirrhosis. †Duration of anuria or non-recovery AKI was not the KRT initiation indication in the AKIKI 2 trial.

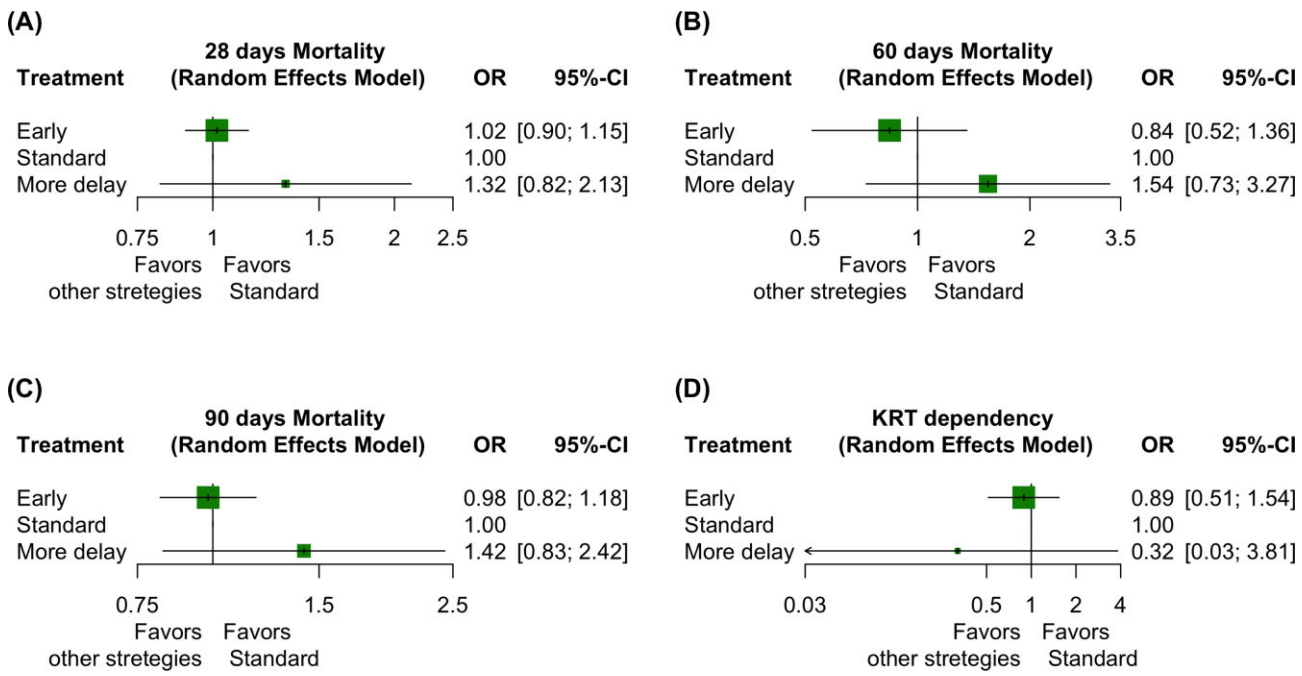

Figure 2: Forest plot of comparisons between three KRT initiation strategies: **(A)** 28-days mortality, **(B)** 60-days mortality, **(C)** 90-days mortality and **(D)** KRT dependency.

In brief, by regrouping the KRT initiation strategies, our alternative approach has a result that is in line with a recently published meta-analysis [1] that no KRT initiation is superior to another regarding mortality. Nevertheless, we would like to note two important uncertainties regarding KRT initiation strategies: uncertainty regarding the safety of the more-delay KRT initiation strategy and uncertainty regarding the optimal KRT initiation strategy for patients with advanced CKD and AKI.

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

AUTHORS' CONTRIBUTIONS

J.-J.C. and G.K. were responsible for the methodology and writing the manuscript. J.-J.C., G.K. and T.-H.L. were responsible for the formal analysis and data extraction. J.-J.C. was responsible for writing the original draft. C.-H.C. was responsible for reviewing and editing the manuscript and project administration. All authors read and approved the final manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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