Reviewer's report

Title: Early initiation of renal replacement therapy in critically ill patients: a meta-analysis of randomized clinical trials

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Reviewer: Demetrio Pittarello

Reviewer's report:

It is a well-structured work that highlights the early initiation of RRT vs the RRT standard.

Several previous systematic reviews have compared early vs standard RRT in different clinical settings (cardiac surgery, ICU) and by inclusion of studies with different designs (cohort studies and RCTs).

Early initiation of RRT may provide better control of fluid and electrolyte balance, superior acid-base homeostasis, increased removal of uremic waste, and prevention of subsequent complications attributable to AKI. Furthermore, early RRT could potentially limit the kidney-specific and remote organ injuries that result from fluid overload, electrolyte imbalance, and systemic inflammation. However, early RRT may also increase the risk of hemodynamic instability, anticoagulation-induced bleeding, blood-stream infection, and inflammatory or oxidative stress due to the bioincompatibility of the dialyzer membranes. Standard initiation of RRT may allow more time for hemodynamic optimization prior to RRT and may prevent the need for RRT and its associated complications.

Studies analyzed were conducted over a wide range of time, during which the management of AKI patients has changed a lot. In the past decade the KDIGO Clinical Practice Guideline contributed to standardize AKI treatment. This mean that more recent studies published after 2010 failed to show a significant survival benefit from early RRT treatment, while a reduction in mortality was shown by older studies. In other words, although many studies have investigated the optimal timing for initiation of RRT, the results remain controversial. Initiation of RRT, to some extent, depends on SCr level and urine output, namely, the Kidney Disease: Improving Global Outcomes (KDIGO) criteria. So I think that the question remains the definition of early criteria, that varied among the included studies, and this may have led to differences in the requirements for RRT and their therapeutic impact. This is the reason why, despite the conclusions obtained, is necessary to perform large, multicentered RCTs to confirm the results of this meta-analysis. Beyond these considerations I consider valid and important the study that provides a further contribution to the attempt to answer the question.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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Yes

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