

LETTER

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Accounting for single center effects in systematic reviews cannot be overlooked

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See related research by Zou et al. <https://ccforum.biomedcentral.com/articles/10.1186/s13054-017-1707-0>

We read with interest the recently published systematic review and meta-analysis on timing of renal replacement therapy (RRT) in cardiac surgery patients [1]. However, we are worried with the presented results and the possible impact on clinical practice of this study.

The author's have included two studies that were not related to the inclusion criteria. Lange et al.'s study [2] was merely descriptive and assessed risk factors for worse outcomes, with no mention of early or late initiation of RRT. Li et al.'s study [3] compared different doses of RRT and reported no differences in mean time (h) to initiation of RRT. Furthermore, the authors included a study in the analysis that was not related to cardiac surgery [4].

In our opinion, these downsides are a threat to the internal validity of the systematic review and preclude any meaningful interpretation of results. Even more so, the author's have not reported a subgroup analysis to

investigate single-center effects, which are known to bias results from meta-analysis [5]. To address this, we have performed a random-effects meta-analysis excluding studies that were not related to the systematic review's original inclusion criteria and with a subgroup analysis to investigate single center effects (Fig. 1). When considering only multicenter trials, the point estimate is pulled to the null and the results are neutral. This is unsurprising since recent systematic reviews comprising mixed populations of critically ill patients have not shown any beneficial effect when pooling results across randomized clinical trials at low risk of bias.

Therefore, we believe the results of this meta-analysis should be cautiously interpreted before widespread adoption of early RRT as a standard practice, pending the results of adequately designed higher-quality randomized clinical trials.

Authors' response

Gaosi Xu

We are grateful to Professor Besen for his comments. First of all, we agree it is preferable for a meta-analysis to include original multi-centered randomized controlled trials; however, well-designed studies such as these are unfortunately lacking in cardiac surgery. Second, it can be seen in Fig. 1 that the heterogeneity of the multi-centered trials included is moderate (67.7%), and that only three trials are studied. Third, in Li et al.'s study [3], one of the purposes of the research was to investigate timing to RRT initiation, and the indication for RRT was urine output < 240 mL/12 h regardless of other symptoms. Li et al.'s study compared different doses of RRT as well as timing to RRT initiation, and the high-dose group received early RRT [3]. In other

words, the study indicated that an early higher continuous veno-venous hemofiltration dose was associated with better in-hospital and long-term survival [3]. As for the study by Kleinknecht et al. [4], we think that this can be included in our meta-analysis as patients who suffered from acute kidney injury in post-cardiac surgery are included. Fourth, we performed a meta-regression in our meta-analysis [1] but did not find the sources of heterogeneity, so no other subgroup analysis was done. Last but not least, the results of the analysis of early versus late RRT initiation (Additional file 1) and subgroup analysis of the timing to early RRT initiation (Additional file 2) are consistent with our original results even after exclusion of these three studies [2–4]. The results are therefore that early RRT initiation decreases 28-day mortality, especially when started within 24 h, in patients with severe acute kidney injury after cardiac surgery.

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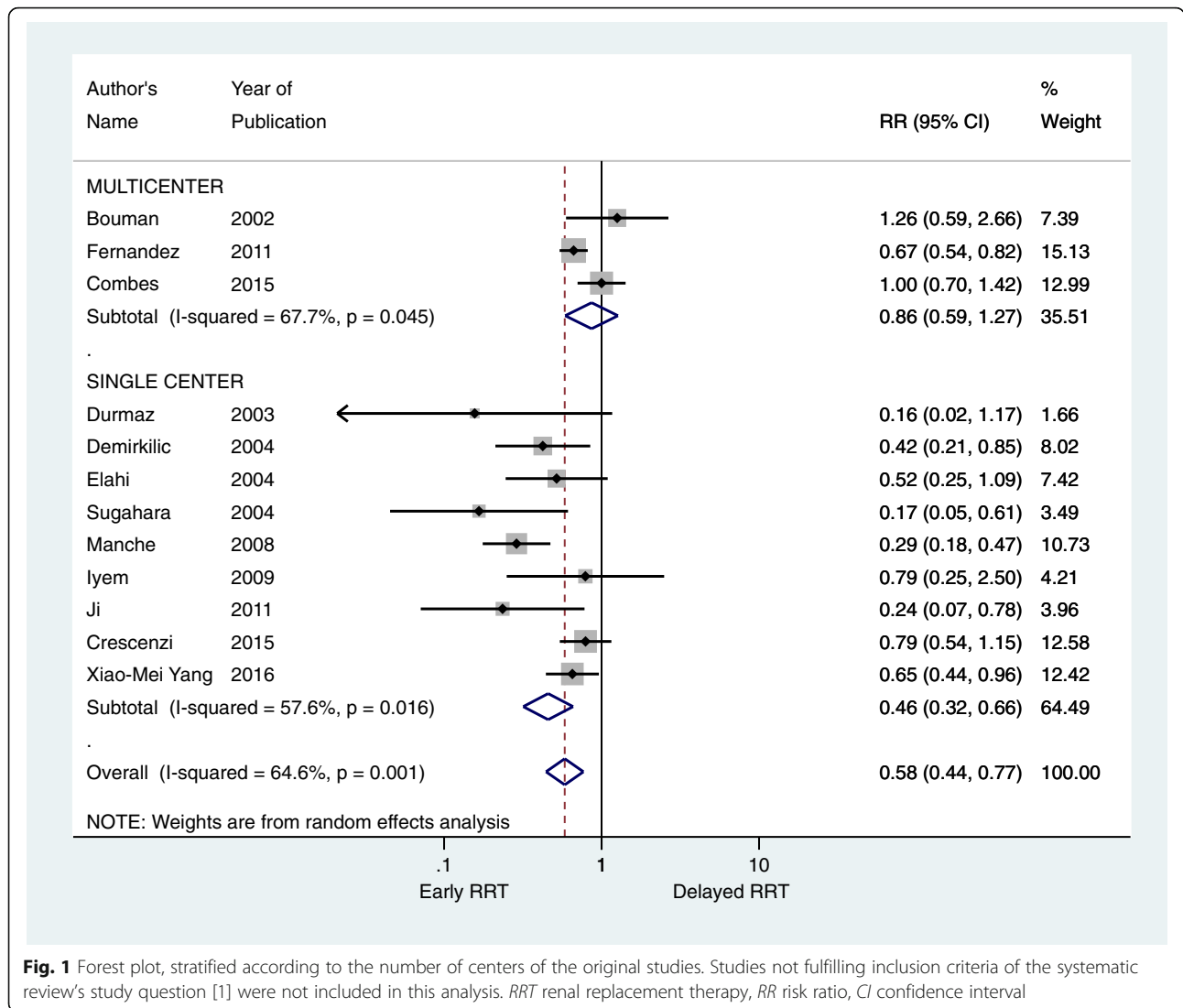


Fig. 1 Forest plot, stratified according to the number of centers of the original studies. Studies not fulfilling inclusion criteria of the systematic review's study question [1] were not included in this analysis. RRT renal replacement therapy, RR risk ratio, CI confidence interval

Additional files

Additional file 1: Forest plots showed early RRT initiation group decreased 28-day mortality in patients with AKI after cardiac surgery. (PDF 37 kb)

Additional file 2: The subgroup analysis showed early RRT initiation within 24 hours was associated with low mortality in patients with AKI after cardiac surgery. (PDF 45 kb)

Abbreviations

RRT: Renal replacement therapy

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Availability of data and materials

The data that support the findings of this study were extracted from the originally published systematic review and original articles from the references list.

Authors' contributions

BAMPB wrote the manuscript and conducted the statistical analysis presented in Fig. 1. MP and APNJ contributed with intellectual input and writing of the manuscript. All authors read and approved the final manuscript.

Authors' information

All authors are currently attending physicians also involved with research and teaching activities.

Ethics approval and consent to participate

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