Reviewer's report

Title: Dexmedetomidine Prevents Acute Kidney Injury After Cardiac Surgery: A Meta-analysis of Randomized Controlled Trials

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Reviewer: Alessandro Belletti

Reviewer's report:

In their manuscript, dr. Chen and colleagues investigated the effect of dexmedetomidine, an alpha-2 adrenergic agonist with sedative properties, on incidence of acute kidney injury after cardiac surgery. They performed a meta-analysis of 10 RCTs which showed a significant reduction in incidence of postoperative AKI in the dexmedetomidine-treated group, as compared with control group. The study is overall well conducted, and deals with a topic which has a relevant impact on everyday clinical practice and patients' outcome.

I have some comments and suggestions which I hope may help to improve Authors' work:

1. The Authors reported to have assessed quality of included trials according to Cochrane Risk of Bias tool. However, the items suggested by the Cochrane Handbook are slightly different from those reported by the Authors. In particular, Cochrane Handbook recommend to distinguish between blinding of participants and personnel, and blinding of outcome assessors; attrition bias (dropout and intention-to-treat) is grouped together; selective outcome reporting and possible other biases are also assessed. More importantly, a final judgement on overall risk of bias should be provided. In my opinion, the Authors should perform this assessment. After that, a sensitivity analysis including only low risk of bias trials should be performed.

2. The primary endpoint of the study was incidence of AKI defined by RIFLE, AKIN or KDIGO criteria. Does this mean that studies reporting AKI defined according to other criteria were excluded? If yes, this should be specified.

3. The Authors reported to have analyzed data using random-effects model for the potential clinical inconsistency. However, they do not describe any method for assessing possible inconsistency. I think that methods for assessing heterogeneity (e.g. I^2) should be described. If analysis suggest possible heterogeneity, the Authors should try to identify
possible sources of inconsistency (e.g. different baseline characteristics? Different study drug dosing scheme?)

4. The analysis of continuous outcome should be better described. Did all the trials reported mean and standard deviations? I understand that included trials reported either mean and SD or median (IQR) or median (range), and mean/SD were then estimated by the Authors according to the method by Hozo et al. (Hozo et al, BMC Medical Research Methodology 2005, 5:13. doi:10.1186/1471-2288-5-13). However, Hozo method only allow to estimate mean and SD from median and range. I believe that Authors may have actually used the updated Wan et al method (Wan et al, BMC Medical Research Methodology 2014, 14:135. doi:10.1186/1471-2288-14-135)

5. The Authors reported to have analyzed data with Stata; however, manuscript figures seems to me to have been generated with Review Manager

6. In addition to the study flow-chart, I think that Authors should provide a complete list of 88 excluded studies together with references and reason for exclusion, ideally as Supplementary Appendix.

7. Was need for renal replacement therapy reported only in the trial by Djaiani et al? If not, I think that analyzing the effect of dexmedetomidine on need for RRT might be a very interesting analysis.

8. There are some subgroup analyses which might be interesting to performed, with particular reference to Authors' conclusions: the Authors could assess whether a subgroup effects exist in pre/intraoperative versus postoperative dexmedetomidine administration, loading dose vs no loading dose use, and low vs high dose continuous infusion. Additional analyses could be CABG only surgery, and studies using placebo as control.

9. Additional sensitivity analyses for the primary outcome which could be performed include removing each trial at a time and reanalyzing the remaining dataset (to assess whether results are heavily influenced by a single trial), changing analysis method
(Mantel-Haenszel or Inverse Variance) or changing summary statistics (RR vs OR vs RD).

10. Two recent experts consensus article on AKI have been recently published (Joannidis et al, Intensive Care Med. 2017 Jun;43(6):730-749. doi: 10.1007/s00134-017-4832-y; and Bellomo et al, Ann Intensive Care. 2017 Dec;7(1):49. doi: 10.1186/s13613-017-0260-y), which discussed also new possible therapies/preventive measures. I think that Authors should discuss their results also in light of current evidence as summarized by these two articles.

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?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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