Author’s response to reviews

Title: Beta-blockers for the primary prevention of anthracycline-induced cardiotoxicity: a meta-analysis of randomized controlled trials

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Version: 2 Date: 28 Mar 2019

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Response to Technical Comments

Comment 1: We note that you have not included an acknowledgements section. If you have no acknowledgements please put ‘Not Applicable’ in this section.

Reply 1: Thank the editor. We add it.

Change in text: Declarations section, line 22, page 22, line 1, page 23.

Comment 2: Please include the title “Declarations” above the corresponding section of your manuscript.
Reply 2: Thank the editor. We add it.

Change in text: Declarations section, line 20, page 21.

Comment 3: In accordance with BioMed Central editorial policies (http://www.biomedcentral.com/submissions/editorial-policies#standards+of+reporting), could you please ensure your manuscript reporting adheres to PRISMA guidelines (http://www.prisma-statement.org/) for reporting systematic reviews. This is so your methodology can be fully evaluated and utilised. Can you please include a completed PRISMA checklist as an additional file when submitting your revised manuscript.

Reply 3: Thank the editor. We made this meta-analysis according to PRISMA guidelines. (see Methods section). We include the PRISMA checklist as an additional file when submitting our revised manuscript.

Comment 4: At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files.

Reply 4: Thank the editor. We prepare the clean version.

Response to Tao Zhan (Reviewer 1)

Comment 1: The authors kindly revised the manuscript accordingly. I am glad to see that the article has been improved both in terms of methodology and writing.

However, some data of endpoints were pooled in spite of the fact that there was essential heterogeneity among the included studies.

Reply 1: Thank the reviewer for helping us improve our manuscript. Because of heterogeneity, we used random effect model to minimize the effects of heterogeneity on this process, which was recommended in Cochrane Handbook for Systematic Reviews of Interventions (version 5.2).
Comment 2: I especially wouldn't suggest pooling the data from studies using different experimental agents unless the authors can provide very persuasive reasons, or illustrate urgent clinical demands in the article.

Reply 2: Because the agents shared the same mechanisms to play the cardioprotective roles [1, 2], we pooled the data from studies using different experimental agents in the main analysis. In case that this introduced bias to this analysis, we made two substudies. The first substudy included the studies using carvedilol and the second one included the studies using metoprolol and nebivolol. The results of substudies were similar to that of main analysis. All the results indicated that carvedilol, metoprolol and nebivolol were beneficial to patients undergoing anthracycline chemotherapy.

Comment 3: Sensitivity analysis is indeed an effective way for testing the heterogeneity and the stability of results of data pooling, but it shouldn't be considered as a statistical approach to calibrate heterogeneity from different study design. A reasonable sensitivity analysis should exclude one study at a time and then re-conduct data pooling to see if there shows significant change after the exclusion. Even this process is only justified after discreetly making sure that the included studies are consistently designed.

Reply 3: Different authors prefer to use different methods to make the sensitivity analysis. There is no best method that is recommended in Cochrane Handbook for Systematic Reviews of Interventions (version 5.2). Some authors preferred to exclude one study at a time [3] and some authors preferred to do what we did in our meta-analysis [4]. Based on the design and results of included studies, we thought the method that we used was appropriate.

Comment 4: Included studies conducted by Liu, Elitok and Beheshti did not use placebo as the control intervention. These 3 studies simply used no additional preventive agents against potential cardiotoxicity. The authors are suggested to re-read the reports carefully to be sure about this issue.

Reply 4: We re-read the included studies. For the study conducted by Liu, placebo as the control intervention was mentioned in the Methods section. For the studies conducted by Elitok and Beheshti, placebo as the control intervention was mentioned in the Abstract and Methods sections. We are sure about this issue.
References


