Author’s response to reviews

Title: Postoperative Tight Glycemic Control Reduces Postoperative Infection In Patients Undergoing Surgery: A Meta-Analysis

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Author’s response to reviews:

Dear Ernesto Maddaloni, M.D.:

Thank you very much for your valuable recommendations. We have sincerely considered your and the reviewers’ comments. We have revised our manuscript. Thanks again for your professional suggestions! Sincerely hope our revised version will be satisfactory for publication in BMC Endocrine Disorders. Great thanks to you and the referee for the time and effort you expend on this paper.

Best wishes.

Yours sincerely,

Dr. zhen-feng
Technical Comments:

Editor Comments:

As highlighted by the reviewers, there is still a major concern about the statistical power of the study. The study has not enough power to investigate mortality as the main outcome and underpowered studies cannot be published in BMC Endocrine Disorders. As suggested, if the main outcome is not mortality, the eligibility criteria should be changed including the main outcome (infections?) and a new search in the literature should be performed.

Answer: Thank you very much for your valuable recommendations. We have changed the main outcome to infections and the eligibility criteria have be changed to “the study documented any endpoints including infection or mortality” (line 17 and line 25-26 , page 6, Materials and Methods part). So a new search in the literature was be performed (Figure 1), however, only one new article was added to the included studies (Lazar HL, McDonnell MM, Chipkin S, Fitzgerald C, Bliss C, Cabral H. Effects of aggressive versus moderate glycemic control on clinical outcomes in diabetic coronary artery bypass graft patients. Ann Surg 2011; Sep;254(3):458-63). Furthermore, data was analysis again and the correspond results were achieved (Results part).

Reviewer reports:

Dear Professor Mario Luca Morieri:

Thank you very much for your valuable recommendations. We have sincerely considered your comments. Great thanks to you and the referee for the time and effort you expend on this paper.

Question 1: However as highlighted by your reply to Dr. Cavallari comments on statistical power, this study seems to report an under-powered analysis with negative result that might represent false negative findings on the main outcome.

Indeed the main outcome of this paper is the analysis on mortality (eligibility criteria --> English study, treatment with postoperative TGC; and assessed mortality endpoint).
At the same time Authors says that the study is 80% powered to detect a RR of 0.48, while instead they anticipate to have a RR of 0.66 (6.9 to 4.7 % reduction with TGC). Authors actually got a RR for TGC that indeed is not too far from the anticipated result, with a RR 0.769, 95% CI 0.464 to 1.275 (in particular if you look at the 95% C.I.). For this reason this study may shows a false negative results on the main outcome and only some positive association on secondary outcomes.

If mortality is not the main outcome, then the question is, is there any other studies focused on other outcomes e.g. on infection and hypoglycemia risk, that were not included in this meta-analysis only because did not report mortality rate?

If not, I would strongly suggest to report in the results first the results on mortality and then other outcomes. Anyway power analyses should be specified in the manuscript and Authors should disclose the they were powered only to identify a very large effect on mortality of TCG (RR 0.48).

Answer: There is a major concern about the statistical power of the study. The study has not enough power to investigate mortality as the main outcome. So we have changed the main outcome to infections and the eligibility criteria have be changed to “the study documented any endpoints including infection or mortality” (line 17 and line 25-26, page 6, Materials and Methods part). So a new search in the literature was be performed(Figure 1), however, only one new article was added to the included studies (Lazar HL, McDonnell MM, Chipkin S, Fitzgerald C, Bliss C, Cabral H. Effects of aggressive versus moderate glycemic control on clinical outcomes in diabetic coronary artery bypass graft patients. Ann Surg 2011; Sep;254(3):458-63). Furthermore, data was analysis again and the correspond results were achieved (Results part).

Question 2: additional language corrections are needed due to spelling and grammar mistake (e.g. line 3 page 9; line 9 page 4; table 2 events ...).

Answer: We are sorry to make you confused. We have changed (line 3 page 9) “We observed a significant higher in the number of patients experiencing postoperative hypoglycemia (30.8% vs. 17.2%; RR 2.254, 95% CI 1.550 to 3.276, p < 0.001; Figure. 4) and severe hypoglycemia) in the TGC group as compared to the CGC group.” to “We observed more patients experiencing postoperative hypoglycemia (32.1% vs. 17.0%; RR 2.749, 95% CI 1.750 to 4.321, p < 0.001;
Figure. 4) and severe hypoglycemia in the TGC group as compared to the CGC group.” (line 10, page 6, Materials and Methods part)

We have deleted the word of patients in (line 9 page 4) “Several studies in cardiac and general surgery patients have shown a clear association between perioperative hyperglycemia and adverse clinical outcomes including delayed wound healing, surgical site infections, and prolonged hospital stay”. (line 9-12, page 5, Background part)

We have changed “Serves hypoglycemia” to “severe hypoglycemia” in Table 2.