Author’s response to reviews

Title: Reoperation Following Vitrectomy for Diabetic Vitreous Hemorrhage With versus Without Preoperative Intravitreal Bevacizumab

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Response letter

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Dear Editor,

We much appreciate the editor’s and reviewer’s positive and constructive comments and suggestions regarding our manuscript entitled “Reoperation Following Vitrectomy for Diabetic Vitreous Hemorrhage With versus Without Preoperative Intravitreal Bevacizumab” (BOPH-D-18-00514).

We have studied the reviewers’ comments carefully and have made revisions according to the comments.
1. It is unclear why the first stratification factor is the presence of TRD and not the IVB, which is the aim of the authors according to the title.
Reply: Our initial idea was that the first-level classification was classified by disease and the second-level classification was organized by the treatment plan. Thank you very much for your reminder. We have ranked the first level classification according to whether or not to perform IVB treatment to highlight the key points. And the corrected section is located on Fig.1 in the revision.

2. I think the paper would benefit from organization of the results into primary and secondary analysis or a reduction of the results reported to deliver a more succinct message.
Reply: Thanks to your suggestion, we have organized the results into primary outcome and secondary outcome to provide more concise information. And the corrected part is located on page 7-8 in the revision.

3. The Abstract should clarify that "B scan" refers to ultrasonography, not to OCT.
Reply: Thank you for your careful review. We have made corrections according to your comments. And the corrected section is located on page 2 in the revision, which is marked in highlight.

4. Please, clarify if patients included were type I diabetes mellitus, II or both.
Reply: Thank you for your careful review. We have made corrections according to your comments. And the corrected section is located on page 4 in the revision, which is marked in highlight.

5. I would strongly suggest that the authors would use less tables and more Kaplan-Meyer graphs to summarize most of the results. The narrative description of the results, with six groups and comparisons between them, makes it difficult to follow the line of reasoning.
Reply: Thank you very much for your suggestion. We have omitted the two tables of postoperative visual acuity, reduced the groups and added the more Kaplan-Meyer graphs. And the corrected section is located on Fig.1, on page 5 and Fig. 3 in the revision.

6. The fact that almost the same number of patients was excluded because of a follow-up less than 180 days as those finally included (293 vs 362, respectively) is a potential source of bias and should be explained further. At a minimum, the baseline features of those with incomplete follow-up should be compared to those included to explore potential reasons for missingness.
Reply: Thank you for your reminder. A higher rate of loss of follow-up is indeed a potential bias factor. In China, most patients will often lose their follow-up because of recovery, or because of age, transportation, medical expenses, etc., which is one of the reasons for the high rate of reoperation in this study. We added Table 1 to compare the baseline features of those with complete and incomplete follow-up and explained the potential reasons for missingness at the end of the article. And the corrected section is located on Table.1 and on page 12 in the revision.

7. Authors should try to provide an explanation of the criteria used to select one surgical approach or another, so that readers can understand the framework in which comparisons are made.
Reply: The routine use of preoperative intravitreal bevacizumab for the diabetic vitreous hemorrhage in our hospital began in early 2014. The IVB+PPV group was drawn from consecutive patients undergoing pre-IVB plus PPV for diabetic VH from 2014 to 2016, and the PPV group was chosen from a similar number of a pathology matched cohort undergoing surgery from 2010 to 2013. We have made corrections according to your comments. And the corrected section is located on page 4-5 in the
8. Tables could show data overall and by each of the 6 groups, with comparisons of relevant baseline features across subgroups to identify potential confounders. They should also include SD, not range (as specified by the authors in Methods) and would benefit from showing percentages of a given category (for example, females) instead of showing n in each category, which is not so clear. In Table 1, I miss the duration of symptoms and/or time from the diagnosis of VH; would they be available?
   Reply: Thank you for your careful review. We have made corrections according to your comments. And the corrected section is located on Table 1 in the revision.

9. In addition, the use of odds/hazard ratio where appropriate, with 95% CI and p-values, could allow more easy comparisons between groups.
   Reply: Thank you for your careful review. We have added Table. 3 to illustrate the associations of preoperative IVB with reoperation of vitrectomy for diabetic vitreous hemorrhage, which included odds ratio with 95% CI and p-values.

10. Authors could add one or two representative images of cases pre and post-treatment.
    Reply: Thank you for your reminder. We have added Figure 4 and Figure 5 to illustrate the effect of preoperative and anti-VEGF treatment of diabetic vitreous hemorrhage with or without retinal detachment.

11. From the perspective of the analysis, one or two eyes of the same patient could be included (approximately 80 patients contributed with both eyes to the study). This needs to be addressed by statistical methods that adequately handle this (McNemar tests, GEE or, if not possible, random selection of a single eye from each patient). GEE would have the advantage of multivariable adjustment, which would be an advantage in the setting of an observational study. Using propensity scores would also be an alternative, but limited sample size within subgroups may make this approach unfeasible.
    Reply: Thank you very much for your comments. We used the statistical method of GEE to re-calculate the baseline and reoperation rates. And the corrected section is located on page 6 in the revision.

12. The Kaplan-Meyer Fig 4 conveys the information stated in the title, but only for those without TRD. I would suggest a similar analyses overall and for those with and without (as it shown) TRD, which would include the hazard ratios, 95% CI and p-values. In addition, the sample size remaining in each 6-month period (for example) would improve the Figures.
    Reply: Thank you very much for your suggestion. We have added Fig. 3 to illustrate the associations of preoperative IVB with reoperation of vitrectomy for diabetic vitreous hemorrhage with and without TRD, which included hazard ratio with 95% CI and p-values.

13. The authors may consider reducing the Discussion section.
    Reply: Thank you very much for your suggestion. We have reduced the parts we think are not closely related to the theme.

We tried our best to improve writing and made some changes in the manuscript. These changes will not influence the content and framework of the paper. We appreciate for Editors’ and Reviewers’ warm work earnestly and hope that the correction will meet with approval.

We appreciate your consideration of our manuscript, and we look forward to receiving comments from
the reviewers.
Thank you again and best regards.

Sincerely,

Zongduan Zhang