Author’s response to reviews

Title: Macular hole surgery recovery with and without face-down posturing: a meta-analysis of randomized controlled trials

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Author’s response to reviews:

Dear Dr. Guangde Tu,

We are hereby re-submitting the attached manuscript for your consideration. We thank you for providing us with the opportunity to submit a revised manuscript. We appreciate the reviewers’ favorable comments and helpful suggestions for improving our paper. We have read their comments carefully, revised the manuscript accordingly (the revised sections are marked in red in the manuscript), and provided point-by-point responses below.

We hope that the revised manuscript is now suitable for publication in your journal, and we look forward to hearing from you.

Yours sincerely,

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Response to Reviewers' Comments

Reviewer reports:

(Reviewer 1): This is a well written manuscript. I commend the authors on their extensive literature search and for selecting the most appropriate papers for analysis into the meta-analysis. The analysis of data was both complete and thoughtful.

Response: Thank you for your careful review of our manuscript and for giving us a positive evaluation.

Comment 1: On area I wish to see commentary in the discussion regards the chronicity of macular hole duration as this also is an important variable with regards to closure rates. The duration of macula hole may not have been readily available in the studies which were pooled for analysis, but this paper's discussion will be further complimented by this discussion.

Response: Thank you for your positive and insightful comment. Although macular hole (MH) duration prior to surgical intervention is an important variable affecting closure rate, there was no significant difference in MH duration between the FDP and nFDP groups in the included studies; hence, we believe that MH duration did not influence the results of our meta-analysis. We have included this information in the Discussion (Lines 269-273, Page 12).

(Reviewer 2):

Comment 1. In the Outcomes of Meta-analysis section, you have confirmed the publication bias for MH sizes smaller than 400 μm. Please also mention and explain this in the Discussion section.

Response: Thank you for your valuable suggestion. Lange et al. and Yorston et al studies reported 100% MH closure rate in the FDP and nFDP group for MH sizes smaller than 400 μm, which resulted in a reduction in the number of publications included in the bias analysis. This methodology resulted in an overemphasis on positive results and neglect of negative results, potentially accounting for the publication bias described. We have explained this in the Discussion (Line 279-283, Page 13).

Comment 2. From lines 114 to 115, "Afterwards, the the remaining potentially relevant reports were assessed for eligibility by the full text based on inclusion and exclusion criteria described below." Please delete the duplicate word 'the'.

Response: Thank you for your comment. We have corrected this mistake. (Line 114, Page 5)
Comment 3. The posturing period and the type of gas used are all different in the five studies included in the analysis. C3F8 gas was used in most of the studies, but Guillaubey et al. used SF6 in MHs of small size below 500um and C2F6 or C3F8 in MH of size larger than 500um. What are your thoughts on the possibility of different outcomes depending on the type of gas used?

Response: Thank you for your pertinent and insightful comment. SF6, C2F6, and C3F8 are all expanding gases that can maintain internal tamponade longer than air. The action time of expanding gas is more than 7 days, which is sufficient to help the macular hole to close. In addition, Guillaubey et al. also reported in their article: “As the bubbles in the present study were always nearly complete, the influence of the type of gas was probably negligible.” Hence, we believe that the use of different gases did not influence the outcomes of our meta-analysis.

Comment 4. Also, when analyzing the effect of face down position on MH of less than 400um, Guillaubey et al. maintained face down for 5 days for 8 hours and Zhang et al. for 16 hours for 3 days. In addition, Zhang et al. used the inverted ILM flap technique when performing MH of more than 400um. Therefore, when performing the meta-analysis, patients with a MH of 400 μm will be blended with patients with conventional ILM peeling and those with inverted ILM flap technique. Each of these studies has different types of gases, different pruning times, and different surgical techniques. These points might have affected the results.

Response: Thank you for your insightful comments.

With regard to the different types of gases used, as we explained in response to comment 3, SF6, C2F6, and C3F8 are all expanding gases that can maintain internal tamponade longer than air. The action time of expanding gas is more than 7 days, which is sufficient to help the macular hole to close. In addition, Guillaubey et al. also reported in their article: “As the bubbles in the present study were always nearly complete, the influence of the type of gas was probably negligible.” Hence, we believe that the use of different gases did not influence the outcomes of our meta-analysis.

With regard to different pruning times, we have discussed this aspect in detail in our manuscript (Line 259-269, Page 12): “The studies included in this meta-analysis did not provide the same FDP time following surgery. It should be noted that because many MH patients are elderly, compliance to the prone position is usually not high due to systemic factors, and, therefore, the five included studies only required patients to keep the FDP for a few hours per day. In addition, although patients are advised to remain face down every day by their surgeon, they cannot be supervised after they leave the clinical setting. Hence, there may be some patients showing low compliance who did not spend sufficient time in the FDP to meet treatment requirements, which may have affected the accuracy of the study results. As there is currently no consensus on the number of hours necessary for patients with larger MHs to remain in the FDP daily, RCT studies with large samples sizes investigating this topic are necessary in future.”

Lastly, with regard to different surgical techniques, although Zhang et al. used the inverted ILM flap technique when performing surgery on MHs larger than 400 μm, the rate of use of the
inverted ILM flap technique was not significantly different between the FDP and nFDP groups. However, 100% MH closure was achieved in patients undergoing the inverted ILM flap technique with and without face-down posturing. Therefore, although we believe that the use of different surgical techniques did not affect the results of our meta-analysis, it remains a possible source of bias. We have added this section to the revised manuscript (Line 283-289, Page 13).

Page 7, Line 159 : 19 did not included did not include

Response: Thank you for pointing out our mistake. We have made the necessary correction. (Line 159, Page 7)

Ref. 8, 20, 21, 27, 33 : The references listed here do not follow the guideline suggested. Please check the format.

Response: Thank you for your helpful suggestion. We have changed the format of the references to meet journal guidelines.