Reviewer's report
Title: Intravitreal injection of anti-vascular endothelial growth factor agents versus photodynamic therapy for polypoidal choroidal vasculopathy: A meta-analysis
Version: 1 Date: 31 December 2014
Reviewer: Augustinus Laude

Reviewer's report:
The authors have done a nice review of the studies related to the treatment outcomes of PCV patients using either PDT or anti-VEGF injections. The methodology used is sound and the paper is well-written.

Major revisions
1. Reviewer 1: One of the major limitations of this findings is that most of the studies identified were retrospective in nature and this point has been mentioned. However, I was surprised that there were no considerations given to the frequency of retreatments either for the PDT group or more importantly, the antiVEGF group. The frequency and intervals between treatments can have a profound impact on the clinical outcomes, including the VA and macula thickening. So, the authors need to discuss how they address this major confounder between the study groups.

Our response: Thank you for the review and careful reading of our manuscript. We entirely agree. We listed the frequency of retreatments for both the PDT and anti-VEGF groups in Table 2. The authors discussed this major confounder between the study groups in the revised manuscript. (page 9; paragraph 1, line 232-235).

2. Reviewer 1: Another major issue is how the definition of PCV cases were made in these studies. The diagnosis of PCV is not universally agreed upon and many imaging modalities are used for diagnosis incl. but not limited to ICG angiography and OCT. So, the description of how the diagnosis of the PCV
cases should be made clear in order to inform the reader about the confidence of the case definitions.
Our response: Thank you for raising this important question. As advised, we had added the definition of PCV in the table 2.

Minor Revisions
1. Reviewer 1: I think line 60 should be revised. I am not sure if the cited paper is meant to be generalized to all forms of PCV. We know for example that solitary PCV may be associated with a benign course and good prognosis.
Our response: Thank you As advised, we had changed this sentence to “Different forms of PCV had different prognosis. The natural course of PCV with clustered polypoidal choroidal lesions is always related to a poor prognosis”.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: I declare that I have no competing interests

Reviewer's report
Title: Intravitreal injection of anti-vascular endothelial growth factor agents versus photodynamic therapy for polypoidal choroidal vasculopathy: A meta-analysis
Version: 1 Date: 31 December 2014
Reviewer: Fiona O J Luk

Reviewer's report:
Major Compulsory Revisions
1. Reviewer 2: The title of the paper and the aim in the abstract should be more consistent. The title should be changed to 'PDT vs Anti-VEGF agents for polypoidal choroidal vasculopathy'.
Our response: Thank you for your careful review and valuable suggestion. We had changed the title to “photodynamic therapy versus anti-vascular endothelial growth factor agents for polypoidal choroidal vasculopathy: A meta-analysis"

Our response: Thank you As advised, we had changed this sentence to “Different forms of PCV had different prognosis. The natural course of PCV with clustered polypoidal choroidal lesions is always related to a poor prognosis”.

3. Reviewer 2: Line 69: typo error. Anti-VEGF agents were tested against PDT, not PCV.
Our response: The authors apologize for the spelling error which has been corrected in the revised manuscript. (page 3; paragraph 3, line 69).
4. Reviewer 2: Line 76: "For example" should be deleted.
Our response: Thank you. Following your suggestion, we had deleted the "For example" in the revised manuscript.

5. Reviewer 2: Line 112: Please define improved, stable and deteriorated VA
Our response: Thank you for raising this important question. We had defined improved, stable and deteriorated VA in the revised manuscript (page 4; paragraph 4, line 112-114).

6. Reviewer 2: Line 159: Three case reports were 'excluded'.
Our response: Thank you. We had changed it to “Eleven of the studies were excluded because they focused on combined therapy, three case reports were excluded, and two articles were excluded because they included non-treatment-naive patients.” (page 6; paragraph 3, line 160-161).

7. Reviewer 2: Line 191: Did all the studies use time-domain or spectral-domain OCTs? Does the author refer to 'central subfield thickness'?
Our response: Thank you for raising this important question. Among the included studies, three used time-domain OCT and three used spectral-domain OCT. We stratified another subgroup based on different types of OCT when assessing CRT in the revised manuscript. The results showed that subgroups of different types of OCT did not alter the pooled results at any follow-up time point (page 8, paragraph 1, lines 204–205) (Table 5). Yes, the authors referred to “central subfield thickness.” We defined central retinal thickness (CRT) in the revised manuscript as follows: “Central retinal thickness (CRT) was defined as the distance between the internal limiting membrane and the inner surface of the RPE, and measured manually at the fovea.” (page 7; paragraph 3, line 192-193)

8. Reviewer 2: line 237: What is meant by 'PCV levels'?
Our response: Thank you! We had changed it to “CRT is another strong prognostic measure of PCV severity.” in the revised manuscript.

Our response: We thank you for this insightful suggestion. Accordingly, we had added the related content and cited this reference in the revised manuscript. “The previous meta-analysis had also proved that combined treatment appeared to result in better visual acuity and lower retinal haemorrhage.” (page 9; paragraph 3, line 256-258).

10. Reviewer 2: Reference 12, 13 and 14 were cited wrongly in the text.
Our response: Thank you for the review and careful reading of our manuscript. We entirely agree. We add changed three references here correctly.
11. Reviewer 2: Table 1: please clarify the fractions under age and follow up columns.

Our response: Thank you! We had clarified the fractions under age and follow up columns in the Table 1. “PDT group/ anti-VEGF group”

12. Reviewer 2: Table 2: please consider adding a column of follow up duration for different studies as the number of treatments varied very much among different studies.

Our response: Thank you. Following your suggestion, we had added another column on follow up duration in the table 2.

13. Reviewer 2: Please correct grammatical mistakes.

Our response: Thank you. Following your suggestion, we have now corrected these errors with the help of two American Ophthalmologists who are native English speaker.

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published.

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests: I declare that I have no competing interests.

Reviewer’s report

Title: Intravitreal injection of anti-vascular endothelial growth factor agents versus photodynamic therapy for polypoidal choroidal vasculopathy: A meta-analysis

Version: 1 Date: 31 December 2014

Reviewer: Elizabeth Wong

Minor Essential Revisions


Our response: This is a spelling error. The authors apologize for the spelling error which has been corrected to “I2” in the revised manuscript (page 6; paragraph 1, line 145). Thank you!

2. Reviewer 3: Lines 185-186: When VA change was treated as a categorical variable, the percentages of improved, stable, and deteriorated VA at final visits were compared. The duration to final follow-up for each selected study were not the same and could lead to lack of consistency, and should be highlighted.

Our response: Thank you for raising this important question. We entirely agree. Most of the studies reported this outcome only at the follow-up end point, so the analyses of this outcome were based on final-visit data. This is a limitation of the meta-analysis, which we described as follows in the revised manuscript: “A fifth limitation is that the analyses of the VA change, which was treated as a categorical variable, regression rates of polyps, and adverse events were based
on data pooled from trials of different durations due to a lack of reported data in all follow-up phases. It was a compromise proposal to choose the data of follow-up end point.” (page 10; paragraph 4, line 291-295)

3. Reviewer 3: Table 1: Header for Age and Follow-up do not explain what each pair of data meant, unlike Sex, which indicated that the pair of numbers was for male/female.

Our response: We thank you for calling our attention to this important issue. As also pointed out in the reply to “11. Reviewer 2”, we had clarified the fractions under age and follow up columns in the Table 1. “PDT group/ anti-VEGF group”

4. Reviewer 3: Table 2: Header should include (mean ± SD) for Lesion GLD, similar to Number of Treatments.

Our response: Thank you. We had added the mean ± SD for Lesion GLD in the Table 2.

5. Reviewer 3: Was there an attempt to obtain the individual patient data from the study investigators / authors? It would have been better if the literature search included unpublished trials as well.

Our response: Thank you for raising this important question. To avoid publication bias, we conducted not only an electronic search, but also a manual search in order to identify all potentially relevant articles, including both published and unpublished studies. Unfortunately, it is possible that we may have failed to include some papers, especially those published in other languages. This is a limitation of our meta-analysis (page 11, paragraph 1, lines 295–299). However, the publication bias analysis showed that there was little potential publication bias among the included trials.

6. Reviewer 3: Line 89-98: It was mentioned that there were 2 reviewers who did the data extraction. Did the same reviewers do the screening for selection of studies, which was narrowed down to the 6 studies, independently?

Our response: Thank you for your query. Yes, the same reviewers do the screening for selection of studies, which was narrowed down to the 6 studies, independently.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests