Author's response to reviews

Title: Neovascular Glaucoma: A Retrospective Review From a Tertiary Center in China

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Author's response to reviews: see over
Dear editors:

Thanks for your work and suggestions that are very important on our manuscript writing and research work. We have studied the valuable comments from reviewers carefully, and tried our best to revise the manuscript. The point to point responds to the reviewer’s comments are listed below.

Best wishes!
Dr. Wang

Responds to the reviewer’s comments:

**Reviewer: Paolo Brusini**

**Comment 1: The definition of neovascular glaucoma, which seems to be rather vague and somewhat debatable.**

Reply: Methods, page 4, line 3-5 “The diagnosis of NVG was based on an IOP>21 mmHg on applanation tonometry associated with neovascularization of the iris and/or angle of the anterior chamber[9].” The definition was referred to Ref # 9. Strictly speaking, patients with signs of neovascular in iris and a slight ocular hypertension was not true NVG. Maybe the word “rubeosis iridis” described this situation was more appropriate. However, it could be the early stage of NVG. Moreover, this definition would not affect the success rate analysis, because for this part of patients the glaucoma surgeries were not needed and this part accounted for few proportions.

**Comment 2: discuss the high success rate of trabeculectomy and lower complication rate of GDD**

Reply: Discussion, page 10 (line 21-22), page 11 (line 1-3) “Considering the poor follow-up situation (i.e. patients with mild complications mostly like lost follow-up) and some data unavailable in this retrospective study, the extreme low complication rate could not compare with previous high complication rate reports from Asian directly [6, 29]. While, these findings still could indicate which complications were common in NVG operations and which surgeries induced more.” Discussion, page 11, line 11-14. “The choice of managements were partially affected by patients’ insurance status and personal affordability that would induce some bias. Although the economic situation should be taken into consideration, the adequate treatment was still the pursuit of medical goals. Hence we might take enormous care in choosing patients for trabeculectomy (i.e. mild NVG), due to the poor prognosis as previous reported [5].”

The other possible reason is the small sample of trabeculectomy group (only 7 cases)

**Comment 3: about the management of NVG depended not only on surgeon preference but also on insurance cover as well as capacity to pay.**

Reply: As far as the insurance and management is concerned, we need to say that is the system in China and the bias will be present in every hospital based study.
Comment 4: Background, page 3: a short description and definition of neovascular glaucoma should be included.
Reply: Background, page 3, line 9-11 “It develops secondarily to ocular ischemia, which leads to neovascular fibrous tissues occupy the iris and trabecular meshwork, resulting in obstruction of aqueous flow and an elevation of intraocular pressure (IOP) eventually[3, 4].”

Comment 5: Background, page 3, line 11: “negative” can be added before “prognostic factors”.
Reply: In fact, some surveys found that some factors are positive prognostic factors, i.e. hyphema.
Ref#6

Comment 6: Methods, page 5, line 6: the use of mitomycin C for trabeculectomy in neovascular glaucoma after anti-VEGF intravitreal injection should be mandatory and not determined by the individual surgeon.
Reply: Methods, page 5 line 8-9. After confirming with surgeons, it has been revised as “The decision to use mitomycin C with GDD was made by the individual surgeon, while all trabeculectomy cases were used mitomycin C.”

Comment 7: Methods, page 5, line 9: “in previous studies” can be added after “described”.
Reply: Accepted and has been revised.

Comment 8: Methods, page 5, line 10: when using TSCPC, the laser power should be set to avoid (as opposed to achieving) a “pop”, which is a sign of an excessively high laser energy treatment.
Reply: After confirming with surgeons, it has been revised as “avoid” and the energy should be lowered down when achieved a “pop”.

Comment 9: Results, page 6, line 13: the prevalence of neovascular glaucoma amongst glaucoma patients appears to be rather high. This may be due to the definition used in this study, as reported above.
Reply: Discussion, Page 8, line 15-16 “This is similar to the proportion in the survey mentioned earlier, the 6.7% of 1232 Chinese subjects diagnosed as glaucoma in a population based survey in Singapore[16].” According to this, our prevalence was similar to them and not very high. And just as explanation before (reply comment 1), this part of patients accounted few proportion.

Comment 10: Results, page 6, line 21: “pseduophakic” should read “pseudophakic”.
Reply: Accepted and has been revised.

Comment 11: References, page 12, Ref # 15: the first letter of “king khaled” should be capitalized.
Reply: Accepted and has been revised.
Reviewer: Luca M Rossetti

Comment 1: The prevalence of NVG was 5.8%, consistent with the one reported for Asian population and this despite the fact that it’s coming from a tertiary practice. This point deserves discussion.
Reply: Discussion, page 8 (line 18-21), page 9 line (1-2). “One possible reason is that the prevalence of glaucoma and NVG is low, which leads to small number of glaucoma (45) and NVG (3) in 1232 adult Chinese Singaporeans. In this condition without enough large sample size, even one case would have powerful influence on the proportion. The other possible reason is the different survey region and population composition that causes the tiny discrepancy, although all are Chinese people in Asia.”

Comment 2: Treatment modalities depended on different variables other than clinical conditions (e.g. reimbursement, copayment, etc.); this may lead to a biases estimate of success rates of the procedures. Needs discussion.
Reply: Discussion, page 11, line 11-14. “The choice of managements were partially affected by patients’ insurance status and personal affordability that would induce some bias. Although the economic situation should be taken into consideration, the adequate treatment was still the pursuit of medical goals. Hence we might take enormous care in choosing patients for trabeculectomy (i.e. mild NVG), due to the poor prognosis as previously reported [5].”
As far as the insurance and management is concerned, we need to say that is the system in China and the bias will be present in every hospital based study.

Comment 3: How many patients received an anti-VEGF injection?
Reply: 9 patients received an anti-VEGF injection in our survey.

Comment 4: About 40% of NVG cases were loss to f-up. Did they differ accordingly to main prognostic factors from cases followed at the Center?
Reply: There are no so much difference between them in prognostic factors according to the available data. There are many reasons responsible for it. The most possible reason is that some people are not from Zhejiang province and they maybe come back to their hometown to seek medical help; The other reason is that some people maybe go to another ophthalmology center to visit the reputed oculists in glaucoma.

Comment 5: The primary cause for NVG could not be determined in about 20% of cases. Please explain why (i.e. data not available?)
Reply: Discussion, page 9, line 9-10 “Due to the limitation of retrospective study, some data were not available and there were still 19% cases that the definite causes were unknown.”
Although all patients with NVG treated in our hospital were investigated to determine the cause, there were still a very few patients who refused to do some examination especially the invasive ones (i.e. Digital subtraction angiography).