

Peer Review File

Article information: <https://dx.doi.org/10.21037/atm-21-5695>

Reviewer A

Comment 1: The sentences are too long; can be made into smaller sentences, not using too many 'and,' for easier understanding for the readers.

Reply 1: We would like to thank for the reviewer's kindly suggestion. We have checked the manuscript thoroughly and shortened the long sentences throughout the text accordingly.

Changes in the text: Page 3, line 47; Page 6, line 95, 97, 110; Page 7, line 115, 121, 130-134; Page 8, line 137, 141; Page 9, line 176; Page 11, line 217; Page 12, line 223; Page 13, line 246, 255, 261; Page 14, line 267, 275, 280-285; Page 15, line 289; Page 16, line 311, 315; Page 17, line 338, 347, 352; Page 18, line 355-359; Page 19, line 388; Page 20, line 399; Page 21, line 428, 434, 441; Page 22, line 446; Page 23, line 469, 483; Page 24, line 499; Page 25, line 511, 513, 516-522; Page 26, line 537, 538, 541, 545, 550.

Comment 2: Line 178, word 'middle' could be replaced with 'intermediate'

Reply 2: We would like to thank for the reviewer's suggestion. We have modified our text as advised.

Changes in the text: Page 10, line 182.

Comment 3: Line 227, could read 'such as a decreased VD and CMvD,

Reply 3: We would like to thank for the reviewer's suggestion. We have amended the according sentence in our text.

Changes in the text: Page 12, line 231.

Comment 4: Line 232, word 'quicker' could be replaced with 'faster'

Reply 4: We would like to thank for the reviewer's suggestion. We have modified the sentence in our text accordingly.

Changes in the text: Page 12, line 236.

Comment 5: Line 233, could add 'than normal eyes' to finish the sentence.

Reply 5: We would like to thank for the reviewer's kindly reminder. We are sorry about the confusion caused by our ambiguous description. We have amended the according sentence in our text as advised.

Changes in the text: Page 12, line 237-238.

Comment 6: Line 306-7 I suggest "Such findings have enhanced the role of better evaluation of microvasculature for the assessment of glaucoma."

Reply 6: We would like to thank for the reviewer's suggestion. We have modified the sentence in our text as advised.

Changes in the text: Page 16, line 316-318.

Comment 7: I have little hesitance in accepting comparison of POAG v/s PACG; the gradual worsening in POAG is vastly different than acute rise in pressure in PACG, and their pathophysiology is much different. Something to think about.

Reply 7: We would like to thank for the reviewer's kindly suggestion. Though POAG differs from PACG in pathophysiology, they share some similar fundus morphological changes compared with normal eyes. We listed the microvascular alterations of both types of the primary glaucoma to make the review more comprehensive. We are sorry if certain expression caused confusion of our main focus. We have deleted the according sentence in our text.

Changes in the text: Page 11, line 213-214.

Reviewer B

Comment 1: This is an extensive review investigating vascular alteration as a pathogenesis of glaucoma.

This review includes two main topics of; overview of vascular alterations in glaucoma, and the role of retinal vascular endothelium. The authors in part suggested potential link between the two topics, which is not supported by definite scientific evidence. Therefore, combination of the two subjects makes the manuscript unclear and hard to follow.

Reply 1: We would like to thank for the reviewer's kindly suggestion. As the reviewer said, there is indeed no very definite scientific evidence between the two topics. However, there have been some studies implying the relationship between the glaucomatous vascular changes and the endothelial system.(1, 2) We have added the references and according sentences in our text to make the context more coherent and reasonable (see Page 19, line 386-391; Page 20, line 401-403). In addition, the main topic of the review is the microvascular alterations in glaucoma, and endothelial cell is the main and critical structure of microvasculature. Endothelial cell is also a potential important target in improving retinal vascular function in glaucoma.(3) Therefore, the vascular endothelium is not a separate topic independent of the microvascular alteration, and we thought the discussion of endothelium had better be included in the review. We are truly sorry about the confusion caused by our unclear description. Thanks for the reviewer's suggestion, we realized the narration of endothelium contains some redundant sections that were unrelated to our main topic. Therefore, we have deleted the irrelevant content in our text according to the reviewer's suggestion, to make the manuscript more clear and easier to follow (see Page 20-21, line 415-422).

Changes in the text: Page 19, line 386-391; Page 20, line 401-403; Page 20-21, line 415-422.

References

1. Costa VP, Harris A, Anderson D, et al. Ocular perfusion pressure in glaucoma. *Acta Ophthalmol* 2014;92(4):e252-66.
2. Kiyota N, Shiga Y, Suzuki S, et al. The Effect of Systemic Hyperoxia on Optic Nerve Head Blood Flow in Primary Open-Angle Glaucoma Patients. *Invest Ophthalmol Vis Sci* 2017;58(7):3181-8.

3. Resch H, Karl K, Weigert G, et al. Effect of dual endothelin receptor blockade on ocular blood flow in patients with glaucoma and healthy subjects. Invest Ophthalmol Vis Sci 2009;50(1):358-63.

Comment 2: In the similar context, Abstract conclusion is too long. It should be shorten it to maximum 5 sentences or less.

Reply 2: We would like to thank for the reviewer's kindly suggestion. We have revised the Abstract conclusion and shortened it into 5 sentences accordingly.

Changes in the text: Page 4, line 70-85.