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Authors' Response

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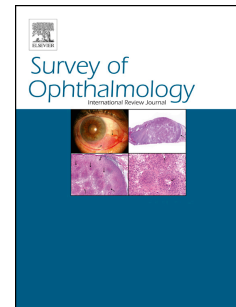
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Reply to correspondence by Calugaru and Calugaru to the article entitled “Ischemic retinal vein occlusion: characterizing the more severe spectrum of retinal vein occlusion” by Khayat et al.

Authors: Meiaad Khayat, Michael Williams, Noemi Lois.

We would like to thank Calugaru and Calugaru for their interest in our article entitled “Ischemic retinal vein occlusion: characterizing the more severe spectrum of retinal vein occlusion”.

Calugaru and Calugaru stated in their letter that we had not provided in our review diagnostic criteria for the ischemic type of acute central retinal vein occlusion (CRVO) when marked and extensive intraretinal hemorrhages prevented a clear angiographic evaluation of the retinal capillary non-perfusion zones. They proposed the use of at least four of the following five criteria:¹ (1) visual acuity (VA) \leq 20/400 Snellen equivalent; (2) ability to see \leq V/4e isopter based on the Goldmann perimeter; (3) presence of relative afferent pupillary defect; (4) extensive ocular fundus changes (striking amount of hemorrhages, venous tortuosity, cotton-wool spots [>5], and disk and macular edema); and (5) intraocular pressure (IOP) reduction in the affected eye of \geq 4 mmHg compared with the fellow eye. They had used these criteria in a study of 57 patients with CRVO (ischemic=21; non-ischemic=36), seven of whom had extensive retinal haemorrhages preventing adequate interpretation of their fundus fluorescein angiograms (FFA).² In the summary section of our manuscript,³ however, and based on identified literature, we stated that a visual acuity of $<6/60$ (20/200 Snellen equivalent) and a relative afferent pupillary defect of ≥ 0.9 log units using neutral density filters were highly suggestive of ischemic CRVO and these criteria can be used in any patient with this disease. We also stated that the presence of extensive retinal hemorrhages in four quadrants on fundus examination, on itself, was a very suspicious sign of ischemic

CRVO.³ We think Goldman perimetry is only very rarely used and available in clinical practice now and, thus, we do not consider it a current diagnostic tool for the evaluation of patients with RVO. However, we also discussed the usefulness of this test for the diagnosis of ischemic CRVO in the Clinical Findings and Ancillary Studies section (6.3.1.2. Visual fields)³ of our manuscript. We are not aware of other studies that had identified a reduction in IOP in the affected eye of ≥ 4 mmHg when compared with the fellow eye as indicative of ischemic CRVO. We are sorry for having overlooked their study,² which indeed would have met the eligibility criteria set in our review and we thank them for having pointed it out to us in their letter.

Calugaru and Calugaru agreed with our recommendation of identifying areas of retinal ischemia by using ultra wide field FFA. Indeed, the current technology that obtains these images (Optos PLC, Dunfermline, UK) allows visualisation of nearly the entire retinal vascular tree; such images are possible using only 1.5 mls of fluorescein. Calugaru and Calugaru noted in their letter, as we did too and pointed it out in Figure-3 of our manuscript and in the Clinical Findings and Ancillary Studies section (6.3.2.3. Optical coherence tomography angiography),³ that Optical Coherence Tomography Angiography (OCT-A) is a very helpful imaging modality in the assessment of patients with RVO and should be undertaken to evaluate the status of the perifoveal capillaries. Calugaru and Calugaru stated that OCT-A is a sensitive indicator of ischemia. We understand the Authors are referring to macular ischaemia herein and we agree with them on this.

As mentioned above, we are sorry for having inadvertently omitted their study from our review, where they presented their results using bevacizumab in a group of 57 patients with CRVO/ HRVO.² The authors stated that the efficacy of the treatment depends primarily on the promptness of the therapy after CRVO onset, which they considered a key driver predicting visual and functional outcomes. All patients included in their study, however, had

an onset of less than 1 month (this was one of the inclusion criteria set). Thus, although their outstanding results suggest that early treatment may lead to a superior recovery, only an RCT in which patients with RVO and no new vessels were to be randomised to either early versus later (e.g. within 1 month of onset versus >1 but < 3 months from onset) intervention would truly determine whether early treatment achieves better outcomes in CRVO/HRVO. The Authors found that at month 36 patients with non-ischemic CRVO/HRVO gained 17.15 ETDRS letters and those with ischemic CRVO/HRVO 26.81 ETDRS letters and stated that Bevacizumab was more effective in patients with ischemic occlusions than in those with the non-ischaemic counterpart. It is unclear, though, whether corrections for baseline vision were included in the statistical analysis of the data; this could potentially have an impact on their results. In any case, the results of Calugaru and Calugaru are in agreement with those presented in our review on the benefits provided by the use of anti-VEGF therapies in patients with CRVO.

References

1. Călugăru D, Călugăru M. Ischemic retinal vein occlusion: characterizing the more severe spectrum of retinal vein occlusion. *Survey of Ophthalmology*. 2019
2. Călugăru D, Călugăru M. Intravitreal bevacizumab in acute central/hemicentral retinal vein occlusions: three-year results of a prospective clinical study. *J Ocul Pharmacol Ther*. 2015;31(2):78-86
3. Khayat M, Williams M, Lois N. Ischemic retinal vein occlusion: characterizing the more severe spectrum of retinal vein occlusion. *Surv Ophthalmol*. 2018;63(6):816-50