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Correspondence

Comment on: Optical Coherence Tomography Angiography Features in Post-COVID-19 Pneumonia Patients: A Pilot Study

To the Editor,

We read with interest the article by Cennamo and associates,[1] who used optical coherence tomography (OCT) and OCT-angiography (OCTA) to assess differences in the retinal structure and microvasculature between post-SARS-CoV-2 patients and a control group. The main outcomes evaluated were differences in the ganglion cell layer and retinal fiber layer, as well as in vessel density in both the superficial and deep capillary plexus. The authors found statistically significant changes in some of the OCTA metrics and suggest that these may correspond to consequences of infection-related thrombotic microangiopathy.

We congratulate the authors on conducting this study, as there are considerable gaps in our knowledge concerning both the pathogenesis and long-term consequences of systemic SARS-CoV-2 infection. However, we would like to raise some concerns in interpreting the findings.

First, the authors state that the ophthalmology assessments and imaging were performed after 6 months of full recovery from SARS-CoV-2 infection; however, as depicted in Table 1, the mean recovery time from the infection was 4.1 ± 1.3 months. In order to elucidate if recovery time influenced the outcomes, it would be good to clarify the influence of the range of time elapsed between the infection and retinal imaging and to compare patients with earlier versus later assessments. In addition, it would be interesting to include the baseline SpO_2 values in both groups (if available) in Table 1, as the influence of mild hypoxemia in OCTA metrics has been well described.[2,3]

Second, when assessing the vessel density between groups, several reasons may have contributed to some degree of measurement bias. The authors included three areas of measurement: i) whole image, ii) parafovea, and iii) fovea. As previously reported, given the large interindividual variation in the FAZ area, it is recommended that this be excluded from analysis, to reliably identify changes in vessel density.[4] Therefore, it would be more informative to include the "perifovea" area (ie, a perifoveal ring) instead of the "whole image". This would also decrease the chance of including peripheral areas of the image that usually have lower resolution, such as the ones evident in the top margin of Figures A1 and B1, in the analysis. As most of the observed between-group differences were in the "whole image" only, these clarifications would contribute to better understand the clinical relevance of the findings. An additional factor was the low threshold of scan quality considered by the authors (ie, ≥ 6, range 1-10). Signal strength bias is another well-reported potential confounder in OCTA metrics: a lower signal strength will underestimate the vessel density values.[4] Therefore, it would be important to use either a higher threshold for scan quality or to compensate for this by taking into account the reflectance of individual vascular voxels.[5]

Lastly, despite the statistical significance found in some of the analyzed outcomes, the data spread was significant, as informed by the relatively large standard deviation values – were there any relevant outliers? It would also be worth clarifying how the study eye was selected for each patient and if the fellow eyes were also analyzed and similar outcomes observed.

We thank our colleagues for this interesting work. Our comments raise awareness of the potential issues associated with OCTA metrics and its interpretation. We emphasize the importance of carefully considering these issues before drawing conclusions regarding the clinical relevance of OCTA findings.

The authors attest that they meet the current ICMJE criteria for authorship.

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REFERENCES

1. Cennamo G, Reibaldi M, Montorio D, D'Andrea L, Fallico M, Triassi M. Optical coherence tomography angiography features in post-COVID-19 pneumonia patients: a pilot study. *Am J Ophthalmol.* 2021;227(January):182–190. doi:10.1016/j.ajo.2021.03.015.
2. Cheng RW, Yusof F, Tsui E, et al. Relationship between retinal

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blood flow and arterial oxygen. *J Physiol*. 2016;594(3):625–640. doi:10.1113/JP271182.
3. Sousa DC, Leal I, Moreira S, et al. Retinal Vascular reactivity in type 1 diabetes patients without retinopathy using optical coherence tomography angiography. *Invest Ophthalmol Vis Sci*. 2020;61(6):49. doi:10.1167/iovs.61.6.49.
4. Hormel TT, Jia Y, Jian Y, et al. Plexus-specific retinal vascular anatomy and pathologies as seen by projection-resolved optical coherence tomographic angiography. *Prog Retin Eye Res*. 2020:100878. doi:10.1016/j.preteyeres.2020.100878.
5. Camino A, Zhang M, Liu L, Wang J, Jia Y, Huang D. Enhanced quantification of retinal perfusion by improved discrimination of blood flow from bulk motion signal in OCTA. *Transl Vis Sci Technol*. 2018;7(6):20. doi:10.1167/tvst.7.6.20.