Invited Commentary

Retinal Sensitivity in Areas of Retinal Nonperfusion

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The study by Hamilton-Perais and colleagues[1] leveraged both ultra-widefield fluorescein angiography and static automated perimetric threshold to study the association of retinal sensitivity deficits with retinal capillary nonperfusion in people with diabetic retinopathy. Developing and validating end points is a priority to design clinical trials on interventions for retinal capillary nonperfusion. The strength of this study is that the retinal sensitivity deficit was elicited across a much larger area of the retina (100°) compared with previous studies that have limited these correlation studies to the fovea or macula over 1 year.[2-5]

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The findings are intriguing and raise important methodological considerations regarding the interpretation of the observations. First, the study does not report the absolute values of the point-to-point sensitivity, which is important to consider in addition to relative values, especially when the test was performed on a relatively new device (MonCvONE perimeter, software version 2023J [Metrovision]) that, to my knowledge, has not been tested previously on people with diabetic retinopathy.[6] The retinal sensitivity deficit is defined as the difference between normative age-matched data vs the absolute value obtained at a point in the test. However, the test-retest values of mean as well as point-to-point retinal sensitivity deficits are not reported, which would seem to be necessary to have further confidence in the interpretation of the results.

Second, the authors do not appear to explain clearly why greater than 5 dBs was defined as abnormal retinal sensitivity deficits. In Figure 1, the relative perfusion deficit is greater than 8 dB. A clinically meaningful difference needs to be elicited to understand the clinical implications of this study.[6]

Third, I concur with the authors that it is essential to report accurately both normal and abnormal retinal sensitivity deficits in both perfused and nonperfused areas over time. However, the rate of change in sensitivity deficit of −0.03 dB/year (95% CI, −0.24 to 0.17) in the perfused compared with the nonperfused group may have been different, but clinically, the magnitude of the difference did not seem meaningful.

In addition, the mean global changes of retinal sensitivity deficit of −1.7 dB at 1 year and −2.8 dB at 2 years are based on values obtained from 27 and 10 participants, respectively, so the point estimate findings undoubtedly have wide confidence intervals that reflect the likely true global change. Of these, only 12 and 2 participants, respectively, had at least severe nonproliferative diabetic retinopathy, a surrogate for larger areas of retinal capillary nonperfusion. It is difficult, if not impossible, to know how these few participants relate to the hundreds of thousands of individuals with this level of diabetic retinopathy around the world. Of note, the retinal ischemic index in this study cohort was relatively low, with most being below 20%, indicating that the total retinal capillary nonperfusion in more than half the study cohort at baseline was too small to provide answers to this research question. Studies correlating visual function with retinal nonperfusion likely should include eyes with at least Diabetic Retinopathy Severity Score (DRSS) level 47 to arrive at clinically meaningful conclusions.

In conclusion, the hypotheses generated by the findings of Hamilton-Perais and colleagues[1] warrant replication and expansion to eyes with more severe DRSS levels and an adequate number of individuals that also address expected loss to follow-up after estimating a clinically meaningful difference in retinal sensitivity deficits.

ARTICLE INFORMATION

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REFERENCES

1. Hamilton-Perais JA, Wright DM, Lim A, et al. Retinal sensitivity and retinal perfusion in diabetic retinopathy. *JAMA Ophthalmol*. Published online October 30, 2025. doi:10.1001/jamaophthalmol.2025.3980

2. Tsai WS, Thottarath S, Gurudas S, et al. The natural history of retinal sensitivity loss in diabetic macular ischemia over one year evaluated by microperimetry. *J Clin Med*. 2024;13(8):2219. doi:10.3390/jcm13082219

3. Thottarath S, Tsai WS, Gurudas S, et al. Macular capillary nonperfusion in eyes with stable laser-treated proliferative diabetic retinopathy. *JAMA Ophthalmol*. 2025;143(1):45-52. doi:10.1001/jamaophthalmol.2024.5105

4. Tsai ASH, Jordan-Yu JM, Gan ATL, et al. Diabetic macular ischemia: influence of optical coherence tomography angiography parameters on changes in functional outcomes over one year. *Invest Ophthalmol Vis Sci*. 2021;62(1):9. doi:10.1167/iovs.62.1.9

5. Tsai WS, Thottarath S, Gurudas S, Pearce E, Giani A, Sivaprasad S. Topographic correlation of microperimetry with structural characteristics in diabetic macular ischemia. *Am J Ophthalmol*. 2024;257:25-33. doi:10.1016/j.ajo.2023.09.007

6. Thottarath S, Tsai WS, Gurudas S, et al. Intersession repeatability of visual function and OCTA metrics in eyes with diabetic macular ischaemia. *Eye (Lond)*. 2025;39(5):906-912. doi:10.1038/s41433-024-03505-3