Author Response: Retinal Capillary Flow and Diabetic Retinopathy

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We thank Quigley[1] for his comments on our article entitled "Decreased Retinal Capillary Flow Is Not a Mediator of the Protective Myopia-Diabetic Retinopathy Relationship."[2] His explanation regarding the attenuation of intraluminal arteriolar pressure with increasing axial length (AL) offers an intriguing alternative as to how decreased capillary pressure in axial myopia may be protective of the onset and progression of diabetic retinopathy (DR) even when capillary flow remains unchanged.

While there is controversy over the role of retinal blood flow changes in diabetes, there is unequivocal evidence supporting an increase in retinal blood flow in concordance with increasing DR severity levels.[3,4] The converse has been shown for axial myopia, where retinal blood flow is reduced compared to healthy emmetropic eyes.[5,6] Therefore, we hypothesized in our original article that the reduction in capillary flow in axial myopic eyes with diabetes (relative to diabetic eyes without myopia) would result in decreased capillary pressure exerted, leading to lesser chances of leakage and rupture of compromised capillaries in diabetes (Starling and Laplace's Laws).[7,8] As the article in question has demonstrated, this hypothesis was not supported by our results.

Nonetheless, as noted by Quigley,[1] we were unable to assess capillary pressure directly; hence, we were unable to determine if intraluminal capillary pressure was decreased in myopic eyes with diabetes even in the absence of obvious reductions in capillary flow, especially in the range of AL captured in our study. That was the main reason why we stated that the increased blood flow with greater DR severity, and not increased capillary pressure, was unlikely to be a major factor driving the protective myopia-DR relationship. However, we would also like to draw the readers' attention to another study that we published on the associations of oxygen saturation (SO_2) with AL and retinal function (assessed using multifocal electroretinogram [mfERG]).[9] In that article, we reported strong linear associations between longer AL, reduced O_2 uptake, and decreased retinal function. Path analysis modeling further showed that the reduced O_2 uptake with increasing AL could be attributed to the indirect effects of decreased retinal function. Since hypoxia has been established as one of the risk factors associated with the development and progression of DR,[10–12] we speculated that a decreased O_2 requirement in eyes with longer AL may help offset some of the effects of hypoxia in the diabetic retina and, hence, protect against DR

In conclusion, the mechanisms underlying the protective myopia-DR relationship are likely to be multifactorial, as shown by our work as well as that of Quigley.[1] Therefore, longitudinal studies and experimental research to elucidate the effects of retinal metabolism (SO_2, capillary pressure) on the onset and progression of DR in subjects with diabetes are warranted.

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