Correspondence

Characteristics of Neovascularization in Early Stages of Proliferative Diabetic Retinopathy by Optical Coherence Tomography Angiography

EDITOR:

WE READ WITH INTEREST THE ARTICLE TITLED "CHARACteristics of Neovascularization in Early Stages of Proliferative Diabetic Retinopathy by Optical Coherence Tomography Angiography" by Pan and associates.[1]

The duration of diabetes has not been mentioned, and we were curious to know if either the duration or the level of blood sugar control had any correlation with the type of neovascularization elsewhere (NVE) noted.

It has been mentioned that the type of neovascularization could prognosticate the surgical outcomes and decide the type of surgery; however, we would like to ask the authors if they would not consider panretinal photocoagulation in either of the NVE types. Also, do the authors feel the results of photocoagulation could be impacted by the NVE types? We propose that a masked study could have proved better to prognosticate by assessing the level of difficulty faced by the surgeon in a particular type of NVE. Moreover, a single patient may have all 3 types of NVEs.

Though the authors have mentioned that the study sample was small, specifying the confidence interval along with the percentages and significance levels could help to extrapolate it to the population at large.

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REFERENCE

1. Pan J, Chen D, Yang X, et al. Characteristics of neovascularization in early stages of proliferative diabetic retinopathy by optical coherence tomography angiography. *Am J Ophthalmol* 2018;192:146–156.

REPLY

WE HAVE DESCRIBED 3 SUBTYPES OF NEOVASCULARIZATION elsewhere (NVE) that originate from different vessels in proliferative diabetic retinopathy (PDR) in our study.[1] Type 1 NVEs originate from the venous side and are located at the margin of capillary nonperfusion (CNP). Type 2 NVEs originate from the capillary plexus and are located in the CNP. Type 3 NVEs originate from the sea-fan-like intraretinal microvascular abnormalities (IRMAs) and are located in the CNP.

Type 1 NVEs have a partially detached posterior hyaloid face and are observed as a "tabletop"; types 2 and 3 NVEs have numerous dense roots and are adhered firmly to the posterior hyaloid's face with short attachments to the retina. Moreover, affiliated nonperfusion areas (NPAs) observed in our study performed as type 1 < type 3 < type 2. Another important fact is that a single eye may have all 3 types of NVEs and that the distribution and patterns of NVE can be entirely different between eyes in a single patient. Based on these observations, we speculate that NVE patterns are closely associated with local situations such as local hypoxia and vitreous status, rather than with the level of blood sugar control. Nevertheless, further studies and larger numbers of patients are needed to clarify the relationship between NVE patterns and the levels of blood sugar control.

Considering that new vessels change morphologically and histologically, both by panretinal photocoagulation (PRP) and by anti-VEGF therapy,[2,3] we enrolled patients who were naïve to treatment to uncover the characteristics of neovascularization in early PDR. Further research is needed to discover the characteristics of neovascularization after therapy in PDR. In fact, we are planning a study of the characteristics of neovascularization after PRP. We obtained some interesting findings: fine new vessel regression; some new vessels maturing rather than regressing; and type 2 NVEs more easily regress than do types 1 and 3 NVEs after PRP. A masked study would have been preferable with respect to prognostication by assessing the level of difficulty faced by the surgeon for a particular type of NVE. However, it is important to note that we enrolled patients in early stages of PDR, and they would be treated by PRP or by anti-VEGF. Most of these patients would not necessarily be treated by pars plana vitrectomy in the short term. Moreover, if PDR progressed and reached surgical indications, it would be difficult to identify the NVE patterns because of the shielding caused by vitreous hemorrhage or by the NVE complex shadow.

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CONFLICT OF INTEREST DISCLOSURES: SEE THE ORIGINAL article for any disclosures of the authors.

REFERENCES

1. Pan J, Chen D, Yang X, et al. Characteristics of neovascularization in early stages of proliferative diabetic retinopathy by optical coherence tomography angiography. *Am J Ophthalmol* 2018;192:146–156.
2. Ishibazawa A, Nagaoka T, Yokota H, et al. Characteristics of retinal neovascularization in proliferative diabetic retinopathy imaged by optical coherence tomography angiography. *Invest Ophthalmol Vis Sci* 2016;57(14):6247–6255.
3. Kohno R, Hata Y, Mochizuki Y, et al. Histopathology of neovascular tissue from eyes with proliferative diabetic retinopathy after intravitreal bevacizumab injection. *Am J Ophthalmol* 2010;150(2):223–229.

Elastin Content and Distribution in Endothelial Keratoplasty Tissue Determines Direction of Scrolling

EDITOR:

WE WELCOME THE RECENT PUBLICATION BY MOHAMMED and associates,[1] which demonstrates the surgical implications of the corneal elastic system in scrolling in endothelial keratoplasty. We have pioneered the characterization of the corneal elastic system in normal human[2] and keratoconic[3] corneas and in knock-out mouse models of Marfan syndrome.[4] The current article adds to our knowledge by showing the presence and depth distribution of elastin in the posterior cornea, which provides further confirmation that the corneal elastic system (predominantly elastin and fibrillin) is an integral part of the cornea.

We have previously shown the nanoscopic 3-dimensional distribution and arrangement of elastic fibers in the human cornea using an electron microscopy elastic stain for amorphous elastin and fibrillin[2] and the high-resolution technique of serial block face scanning electron microscopy. We also showed that the concentration of elastic fibers, as a function of depth, was highest in the 8 μm region of the stroma immediately above the Descemet membrane and fell significantly distal to this region. Transmission electron microscopy morphologic observations in the same study also revealed that true elastic fibers containing fibrillin sheaths and amorphous elastin cores were restricted to the corneal peripheral region, limbus, and trabecular meshwork (TM) while thinner, predominantly fibrillin-1 fibers, previously described by Hanlon and associates,[5] were only present in low densities in the central posterior cornea. Since our previous studies, we have now characterized the human elastic fiber system using a range of antibodies including elastin and fibrillin-1,[6] and we have clarified the association and distribution of elastin- and fibrillin-1-containing fibers within the corneal elastic fiber system.

We note that in this study by Mohammed and associates[1] a band of homogenous elastin immunofluorescence was identified above the Descemet membrane. We would be interested to know if the authors examined the elastin concentration between the posterior peripheral and central regions; if so, were any differences detected?

We initially proposed the potential implications of the elastic fiber system in glaucoma[2] and we have now revealed that the posterior elastic fibers in the corneal stroma are indeed linked with the TM.[6] The results in the current article fit nicely with our results, as the authors show that these fibers contain a high concentration of elastin that is continuous with the TM. Interestingly, it is known that full-thickness keratoplasty has been shown to cause high incidence of glaucoma when compared to partial-thickness deep anterior keratoplasty. A surgery that preserves the peripheral posterior component of the corneal elastic system would seem to be crucial.

Once again, we welcome this article for highlighting the elastic properties of the cornea, which has clear surgical implications, including the formation of big bubble in keratoplasty and scrolling.

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