Comment on "Scleral Thickness in Simple Versus Complex Central Serous Chorioretinopathy"

WE READ THE REPORT BY IMANAGA ET AL[1] WITH GREAT interest. Their theory of the pathogenesis of pachyvein formation in central serous chorioretinopathy based on the thickened sclera is very plausible. However, to further strengthen their theory, it may be interesting and important to clarify whether the thickened sclera will or will not become normal after resolution. It may be important to determine whether the scleral thickening is primary or secondary. Did the authors measure the scleral thickness after resolution in at least some of the affected eyes? Or do they have a plan to measure it in the future?

We recently proposed our finalized theory of the pathogenesis of pachyveins.[2] After exudation in the choriocapillaris, when albumin-containing blood plasma is lost, the blood density increases in the lower reaches of the choriocapillaris and venules. From Bernoulli's equation, $1/2\ V^2 + P/\rho = C$, the increase on the blood density (ρ) itself affects the increase in blood pressure (P). Moreover, the blood density increase affects the decrease in the blood flow velocity (V). This phenomenon of blood flow velocity is observed clinically in dehydration syndrome[3] and polycythemia vera,[4] in which the blood density also increases excessively with a decrease in the capillary blood flow velocity. The decreased blood flow velocity induces the blood pressure rise in accordance with Bernoulli's theorem, which may expand the venules to form pachyveins. When the expanded veins exceed the scleral foramen, blood congestion occurs, further enhancing the pachyveins. The authors' and our theory share the role of the scleral foramen.

There is another common causative anatomic condition for both theories. The physiologic blood flows generally in the following sequence: aorta-arteries-arterioles-capillaries-venules-veins-vena cava. The capillaries are usually formed in the plexus and anastomosis but the choriocapillaris is not formed in the plexus, but, at least in the posterior pole region, in the complex of an individual segment without anastomosis: one arteriole-capillaries-one venule.[5] This characteristic anatomic condition encourages formation of the pachyveins. Pachyveins may not always develop; if they do, they have much less intensity if the choriocapillaris forms in the usual capillary structure, because the effect and extent of the exudation, that is, the increase of the blood density and decrease of blood flow velocity, may be reduced by being widely distributed within the plexus capillaries with anastomosis. This anatomic construction of the choriocapillaris can explain the phenomenon that Maruko et al[6] observed in ultra-wide-field optical coherence tomography images, that is, pachyveins were seen in the posterior pole region limited to within an angle of about 50° and not seen peripherally outside the region. This observation coincides with the particular anatomic structure of the choriocapillaris since it also is seen only at the posterior pole region and not peripherally outside of the posterior region.

From this perspective, we think it is all the more important whether the thickened sclera the authors observed is a primary or secondary phenomenon to further clarify the pathogenesis of pachyveins and pachychoroid formation.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Okihiro Nishi: Writing – original draft. **Tsutomu Yasukawa:** Writing – original draft.

OKIHIRO NISHI*
Nishi Eye Hospital (O.N.), Osaka, Japan

TSUTOMU YASUKAWA
Department of Ophthalmology and Visual Science (T.Y.), Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

Inquiries to Okihiro Nishi, Nishi Eye Hospital, Higashinari-ku, Nakamici 4-14-26, 537-0025 Osaka, Japan.
E-mail address: okihiro@nishi-ganka.or.jp

Acknowledgment: None.

Financial Disclosures: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

REFERENCES

1. Imanaga N, Terao N, Wakugawa S, et al. Scleral thickness in simple versus complex central serous chorioretinopathy. *Am J Ophthalmol.* 2024;261(5):103–111.
2. Nishi O, Nishi Y, Tatsumichi, et al. Pathogenesis of pachyvein formation in central serous chorioretinopathy: a hydrodynamic analysis. *J Clin Med.* 2024;13:4777. doi:10.3390/jcm13164777.
3. Flemming S, Gill P, Jones C, et al. The diagnostic value of capillary refill time for detecting serious illness in chil-

Accepted for publication September 25, 2024.

0002-9394/$36.00
https://doi.org/10.1016/j.ajo.2024.09.039

dren: a systematic review and metaanalysis. *PLoS One*. 2015;10:e0138155.
4. Fiermonte G, Aloe Spiriti MA, Latarliata R, et al. Polycythemia vera and cerebral blood flow: a preliminary study with transcranial Doppler. *J Intern Med*. 1993;234(6):599–660. doi:10.1111/j.1365-2796.1993. tb 01019.x.
5. Lee EJ, Ahn KS, Park KH, et al. Functional end-arterial circulation of the choroid assessed by using fat embolism and electric circuit simulation. *Sci Rep*. 2017;7:2490. doi:10.1038/s41598-017-02695-z.
6. Maruko I, Maruko R, Kawano T, et al. Comparisons of choroidal thickness and volume in eyes with central serous chorioretinopathy to that of control eyes determined by ultra-widefield optical coherence tomography. *Graefes Arch Clin Exp Ophthalmol*. 2024;262(2):2135–2143.

Reply to the Comment on Scleral Thickness in Simple Versus Complex Central Serous Chorioretinopathy

REPLY

WE THANK DR. NISHI AND DR. YASUKAWA FOR THEIR interest in our paper.[1] The authors hypothesized that dilated large choroidal veins (what they refer to as pachyveins) in central serous chorioretinopathy (CSC) are driven by increased blood density and pressure following plasma exudation in the choriocapillaris, which reduces blood flow velocity and causes venule expansion per Bernoulli's equation. They also speculated that the unique structure of the choriocapillaris in the posterior pole differs from that of typical capillaries because it lacks anastomosis and forms isolated segments, predisposing this region to dilated choroidal veins. They seemed to think that the scleral thickening observed in patients with CSC is a secondary phenomenon caused by the pachychoroid.

We evaluated changes in choroidal and scleral thickness for over 3 months after half-dose photodynamic therapy (PDT) for CSC using wide-field and anterior segment optical coherence tomography. We found that choroidal thickness significantly decreased 3 months after PDT in both the macula and periphery; however, there was no change in scleral thickness (manuscript in preparation). This finding suggests that PDT for CSC does not affect scleral thickness even if it extensively thins the choroid. Furthermore, our previous study on scleral thickness in unilateral CSC found that the choroid was significantly thicker in affected eyes than in fellow eyes, with no difference in scleral thickness.[2] This finding implies that choroidal thickening in CSC does not cause clinically significant scleral swelling. Collectively, scleral thickening in CSC seems to be a primary phenomenon, and not secondary to a thickened choroid. We believe that scleral thickening is an important predisposing factor for the pathogenesis of CSC.

However, we do not believe that the pathophysiology of CSC can be explained solely by disturbances in the drainage of vortex veins through the sclera. Takahashi and Kishi[3] reported that scleral buckling surgery for rhegmatogenous retinal detachment leads to venous congestion, resulting from vortex vein occlusion. Matsumoto et al.[4] reported that ligation of vortex veins in a monkey model induced vortex vein congestion and pachychoroid-like features, suggesting that vortex vein congestion contributes to pachychoroid pathogenesis. However, these models do not replicate certain hallmark features of CSC such as serous macular detachment and multifocal choroidal vascular hyperpermeability. Therefore, CSC development cannot be fully attributed to vortex vein congestion caused by scleral thickening alone.

CSC seems to be caused by a combination of anatomical factors, such as short axial length, scleral thickening, asymmetric vortex vein, and physiological factors, such as increased sympathetic activity and steroids affecting choroidal circulation.[5] We support the "two-hit theory"[6] and believe that scleral thickening is a primary cause of CSC development and an anatomical risk factor. Furthermore, as stated in our paper,[1] greater scleral thickening is a significant risk factor for widespread retinal pigment epithelial atrophy in eyes with CSC.

We anticipate that future studies will delve deeper into the pathogenesis of CSC and other pachychoroid diseases. Such research holds the potential to develop more effective treatment and prevention approaches, and we are excited to see progress in this field.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

NAOYA IMANAGA: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Writing – original draft, Writing – review & editing. **HIDEKI KOIZUMI:** Conceptualization, Methodology, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

NAOYA IMANAGA
HIDEKI KOIZUMI*
Department of Ophthalmology, Graduate School of Medicine, University of the Ryukyus (N.I., H.K.), Okinawa, Japan

Inquiries to Hideki Koizumi, MD, PhD, Department of Ophthalmology, Graduate School of Medicine, University of the Ryukyus, 207 Uehara, Nishihara-cho, Nakagami-gun, Okinawa 903-0215, Japan
E-mail address: hkoizumi@med.u-ryukyu.ac.jp

Funding/Support: This work was supported by JSPS KAKENHI grant number JP23K15911. Financial Disclosures: The authors indicate no financial support or conflicts of interest.

Acknowledgment: We would like to thank Editage (www.editage.com) for English language editing.

Accepted for publication November 1, 2024.

0002-9394/$36.00
https://doi.org/10.1016/j.ajo.2024.11.002

REFERENCES

1. Imanaga N, Terao N, Wakugawa S, et al. Scleral thickness in simple versus complex central serous chorioretinopathy. *Am J Ophthalmol*. 2024;261:103–111. doi:10.1016/j.ajo.2024.01.025.
2. Aichi T, Terao N, Imanaga N, et al. Scleral thickness in the fellow eyes of patients with unilateral central serous chorioretinopathy. *Retina*. 2023;43(9):1573–1578. doi:10.1097/IAE.0000000000003850.
3. Takahashi K, Kishi S. Remodeling of choroidal venous drainage after vortex vein occlusion following scleral buckling for retinal detachment. *Am J Ophthalmol*. 2000;129(2):191–198. doi:10.1016/s0002-9394(99)00425-0.
4. Matsumoto H, Mukai R, Saito K, Hoshino J, Kishi S, Akiyama H. Vortex vein congestion in the monkey eye: a possible animal model of pachychoroid. *PLoS One*. 2022;17(9):e0274137. doi:10.1371/journal.pone.0274137.
5. Koizumi H, Imanaga N, Terao N. Central serous chorioretinopathy and the sclera: what we have learned so far. *Jpn J Ophthalmol*. 2024;68(5):419–428. doi:10.1007/s10384-024-01101-2.
6. Hirooka K, Saito M, Yamashita Y, et al. Imbalanced choroidal circulation in eyes with asymmetric dilated vortex vein. *Jpn J Ophthalmol*. 2022;66(1):14–18. doi:10.1007/s10384-021-00889-7.