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Positional Change of Optic Nerve Head Vasculature during Axial Elongation as Evidence of Lamina Cribrosa Shifting

Boramae Myopia Cohort Study Report 2

Kyoung Min Lee, MD,[1,2,*] *Ho-Kyung Choung, MD,*[1,2,*] *Martha Kim, MD,*[3] *Sohee Oh, PhD,*[4] *Seok Hwan Kim, MD*[1,2]

Purpose: To investigate the positional change of central retinal vasculature and vascular trunk to deduce the change in the lamina cribrosa (LC) during axial elongation.

Design: Prospective cohort study.

Participants: Twenty-three healthy myopic children (46 eyes).

Methods: Participants had undergone a full ophthalmologic examination and axial length measurement every 6 months for 2 years. Using spectral-domain OCT, circle scans centered around the optic disc in the glaucoma progression analysis mode, which enabled capturing of the same positions throughout the entire study period, and enhanced depth imaging of the deep optic nerve head complex were performed. Infrared imaging of the circle scans was used to measure the changes in the angles between the first and final visits. The angle between the major superior and inferior retinal arteries was measured along the circle scan twice: from the center of the circle scan and from the central retinal vascular trunk, respectively. The positional change of the retinal vascular trunk also was measured.

Main Outcome Measures: Change in vascular angle and position of vascular trunk with axial elongation and associated factors.

Results: The vascular angle measured from the center of the circle scan did not change ($P = 0.247$), whereas the angle measured from the central retinal arterial trunk decreased with axial elongation ($P < 0.001$). A generalized estimating equation analysis revealed that the factors associated with angle decrease were axial elongation ($P = 0.004$) and vascular trunk dragging ($P < 0.001$). The extent of vascular trunk dragging was associated with axial elongation ($P < 0.001$) and increased border length with marginal significance ($P = 0.053$), but the extent of dragging could not be explained fully by their combination. The major directionality of dragging was mostly to the nasal side of the optic disc, with large variations among participants.

Conclusions: During axial elongation, the retinal vasculature at the posterior pole was unchanged, whereas the position of the central vascular trunk was dragged nasally. Because the central retinal vascular trunk is embedded in the LC, its dragging indicates nasal shifting of the LC, which could explain the vulnerability of myopic eyes to glaucomatous optic neuropathy. *Ophthalmology 2018;■:1–10 © 2018 by the American Academy of Ophthalmology*

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Myopia is a well-established risk factor for development of glaucoma.[1–3] Myopic eyes often share specific anatomic optic disc features. Specifically, the optic discs occasionally are oval with parapapillary atrophy (PPA).[4,5] The oblique insertion of the optic nerve into the globe can incur the tilted disc.[6] Because these characteristics are correlated with the preferential site of damage in myopic glaucoma eyes,[7–9] optic nerve head (ONH) anatomic changes associated with axial growth could be related to a certain vulnerability to glaucomatous damage.

Glaucomatous optic nerve damage is believed to occur at the lamina cribrosa (LC).[10] The LC is connected to the sclera, which is an outer wall and thus acts as a biomechanically load-bearing structure.[11] With axial elongation, the LC and sclera are subject to tensile stress induced by eyeball expansion, and thus become deformed.[12] Therefore, anatomic change of the LC during axial elongation may explain why myopic eyes are more susceptible to glaucomatous optic nerve damage.

Central retinal vessels supply the inner part of the retina.[13] Before their appearance in the fundus, they run

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through the center of the optic tract in the retrolaminar region and pierce through the pores of the LC.[13] Within the LC, the vascular trunk is embedded in the dense connective tissue composed of multiple collagen sheets.[14] Therefore, the spatial relationship between the central retinal vasculature and the vascular trunk represents the relationship between the inner retinal structures and the outer load-bearing structures (LC and adjacent sclera) of the eye, the latter of which can change during axial elongation. In myopia, retinal vessels are reported to be located more temporally, toward the macula.[15,16] This suggests that in myopic eyes, the locations of the retinal vessels and the central retinal vascular trunk may be shifted from their original locations during the earlier developmental period. Thus, remembering that the central retinal vascular trunk is embedded in the pore of the LC, the positional change of the vascular trunk relative to the retinal vessels could be indicative of LC change relative to the inner retinal structures during axial elongation.

To the best of our knowledge, there has been no longitudinal study evaluating ONH vasculature change in myopic eyes. Thus, in the present study, we investigated ONH vasculature changes in eyes with increasing axial length. Given the change in the central retinal vascular trunk in the ONH, we deduced anatomic change in the LC with axial elongation.

Methods

This study included myopic children who had undergone regular check-ups for myopia between February 2013 and September 2014 at Seoul National University Boramae Medical Center and who subsequently had been enrolled in the Boramae Myopia Cohort Study. It was approved by the institutional review board of Seoul National University Boramae Medical Center and conformed to the tenets of the Declaration of Helsinki. All of the participants' guardians provided written informed consent before enrollment.

The Boramae Myopia Cohort Study was undertaken to identify and elucidate structural changes occurring with axial elongation in eyes with progressive myopia. With inclusion, each participant younger than 13 years of age underwent a complete ophthalmic examination including best-corrected visual acuity assessment, cycloplegic refraction test, slit-lamp biomicroscopy, tonometry, dilated funduscopic examination, keratometry for corneal curvature measurement (RKT-7700; Nidek, Hiroishi, Japan), and axial length measurement (IOLMaster version 5; Carl Zeiss Meditec, Dublin, CA). For optic disc evaluation, fundus photography (TRC-NW8; Topcon, Tokyo, Japan) and spectral-domain (SD) OCT (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany) scanning were performed. Using SD OCT, circumpapillary retinal nerve fiber layer thickness measurement was performed in the glaucoma progression analysis (GPA) mode and enhanced depth imaging (EDI) scanning was carried out to capture cross-sectional images of the deep ONH complex. Details on the scan protocol are provided below.

Myopic eyes (spherical equivalent of cycloplegic refraction test, ≤ -0.75 diopter [D]) in growing ages (7–12 years) were included. The exclusion criteria were eyes with a best-corrected visual acuity of less than 20/30, history or evidence of significant ocular disease including congenital optic disc anomaly or any kind of ocular surgery, a good-quality (i.e., quality score, >15) image could not be obtained for more than 5 sections of EDI SD OCT disc scans (when the quality score does not reach 15, the image-acquisition process automatically stops and the images of the respective sections are not obtained), and fewer than 4 visits during the study period. Both eyes were examined for the analysis.

Measurement of Angle between Retinal Vascular Arcades

Our hypothesis was that the positional change of the central retinal vasculature and vascular trunk during axial elongation represents the change of the inner retinal structures and outer load-bearing structures (LC and adjacent sclera), respectively. To capture these changes, we measured the angle between the central retinal vascular arcades from the center of the GPA mode and from the vascular trunk, respectively. The change of angle α, measured from the center of the GPA scan, visualizes the positional change of the central retinal vasculature, whereas the change of angle β, measured from the vascular trunk, represents the change of the central retinal vascular trunk.

For the measurement, confocal infrared fundus images obtained during circumpapillary retinal nerve fiber layer scans were used. First, the retinal arterial vasculature was delineated manually on the confocal images using commercial software (Photoshop; Adobe, San Jose, CA). The locations of the major superior and inferior retinal arteries on the circle scans were marked. Subsequently, the location of the central retinal vascular trunk was marked on the same infrared images. Then, the angle between them was measured twice: from the center of the circle scan (angle α) and from the central retinal vascular trunk (angle β; Fig 1).

In the GPA mode, the scan circle for the circumpapillary retinal nerve fiber layer measurement could be traced through all of the examination periods. Using this circle scan and the fovea–disc axis as references, the first and final follow-up images were aligned and transposed using commercial software (Photoshop). The differences between the final and first visit were defined as $\Delta\alpha$ and $\Delta\beta$, respectively. The positional change of the retinal vascular trunk was defined as vascular trunk dragging (d) in the 2-dimensional funduscopic plane (Fig 1). Vector analysis was used because vascular trunk dragging has both directionality and extent (Fig 1). The angle and the length were measured using Image J software version 1.51 (National Institutes of Health, Bethesda, MD).

Spectral-Domain OCT Scanning of Deep Optic Nerve Head Complex

The deep ONH complex was imaged by SD OCT using the EDI technique. Details on the EDI SD OCT protocol for ONH scanning and LC evaluation are provided in previous articles.[17,18] In brief, approximately 50 horizontal B-scan section images covering the optic disc and separated by 60 μm were obtained for each eye. For each section, 20 OCT frames were averaged, which provided the best trade-off between image quality and the cooperation of children. The value of corneal curvature was entered into the Spectralis OCT system before the scan so as to remove the magnification error. In the central horizontal EDI scan image, the diameter of Bruch's membrane opening (BMO) at the disc center and the border length (BL) were measured by the caliper tool provided by Spectralis (Fig S1, available at www.aaojournal.org). The BL was defined as the straight-line distance between the temporal BMO point and the border tissue (BT) divided by the scleral end (γ-zone PPA) when there was an externally oblique BT at the temporal margin.[19] All of the measurements were performed independently by 2 masked examiners (K.M.L. and M.K), and the average was used for the analysis.