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Longitudinal Changes of Optic Nerve Head and Peripapillary Structure during Childhood Myopia Progression on OCT

Boramae Myopia Cohort Study Report 1

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Purpose: To delineate longitudinal changes in the optic nerve head (ONH) and peripapillary structure during myopia progression in childhood using spectral-domain (SD) OCT and to explore the factors associated with myopic ONH and peripapillary changes.

Design: Prospective cohort study.

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

Methods: The participants underwent fundus photography, SD OCT, and axial length (AXL) measurements every 6 months for 2 years. Based on the morphologic changes of the ONH and β-zone parapapillary atrophy (PPA), eyes were classified as group A (ONH unchanged without β-zone PPA; 11 eyes), group B (ONH changed without β-zone PPA at baseline; 10 eyes), group C (ONH changed with β-zone PPA at baseline; 15 eyes), and group D (ONH unchanged with β-zone PPA; 10 eyes). The configuration of the border tissue (BT) at the temporal margin of the ONH was assessed, and the ONH parameters, including Bruch's membrane opening distance (BMOD), border length (BL), and BT angle (BTA), were measured on horizontal SD OCT scans.

Main Outcome Measures: Changes in ONH parameters and associated factors.

Results: Group B showed the greatest AXL increase per year (group B $>$ group C $>$ group A $=$ group D; $P < 0.001$). During the follow-up periods, the BT configuration initially was changed from internally oblique to externally oblique (group B) and was stretched, resulting in optic disc ovality and γ-zone PPA development (group C). In group C, BL was increased significantly nasally and BTA was decreased significantly, whereas BMOD remained stable ($P < 0.001$, $P < 0.001$, and $P = 0.100$, respectively). In the multivariate analysis using the generalized linear mixed-effect model, the changes of BL and BTA were associated with axial elongation ($P = 0.028$ and $P = 0.010$, respectively).

Conclusions: Development of myopic optic disc and γ-zone PPA during myopia progression was delineated using SD OCT images. During the ONH and peripapillary changes, the BL was increased nasally and the BTA was decreased, whereas the BMOD remained relatively stable. The association of axial elongation with ONH and peripapillary tissue changes may facilitate understanding of the relationship between myopia and glaucoma. *Ophthalmology 2018;■:1–9 © 2018 by the American Academy of Ophthalmology*

Myopia is the most common eye disorder in the world. Its prevalence among 18-year-old subjects in East Asia ranges between 80% and 90%.[1–3] Because axial elongation in myopic eyes is accompanied by scleral remodeling of the optic nerve head (ONH) and peripapillary area where glaucomatous changes occur, the myopic optic disc has attracted great interest over the past several decades.[4–7] Recently, Kim et al,[8] using fundus photography, found and confirmed progressive disc tilting and the development or enlargement of parapapillary atrophy (PPA) during the myopic shift in childhood. These results indicate that myopic optic disc and peripapillary changes are acquired features that are associated with axial elongation.

Numerous studies have been conducted to elucidate the significance of myopic optic disc or myopic ONH (characterized by optic disc tilt,[9–11] torsion,[12–15] γ-zone PPA,[16,17] and lamina cribrosa tilt[18]) to glaucoma development, progression, or both. However, studies on myopic ONH or peripapillary changes in the earlier stages of childhood are relatively few.[8,19,20] Furthermore, there is as yet no longitudinal prospective study on ONH change during myopia progression. Fortunately, the development and application of spectral-domain (SD) OCT with in vivo imaging has led to significant improvements in our understanding of the structural characteristics of the ONH.[21] Therefore, the purpose of the present study was to use SD OCT to identify longitudinal changes to the ONH and

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peripapillary tissues during childhood myopia progression and to explore the factors associated with myopic ONH and peripapillary changes in childhood.

Methods

Participants

This prospective, longitudinal, observational study (the Boramae Myopia Cohort Study) adhered to the tenets of the Declaration of Helsinki and was approved by the institutional review board of the Seoul National University Boramae Medical Center. All of the participants were informed about the study, and signed informed consent was obtained from their guardians.

Participants younger than 13 years who underwent a regular checkup for myopia were enrolled consecutively between February 2013 and September 2014. All exhibited a best-corrected visual acuity of 20/30 or better in each eye and myopic refractive errors −0.75 diopters or less, and none had any history or showed any evidence of significant ocular disease or ocular surgery. The exclusion criteria were as follows: poor-quality images for more than 5 sections of 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. All of the participants underwent complete ophthalmic examinations including best-corrected visual acuity measurement, intraocular pressure measurement by Goldmann applanation tonometry, slit-lamp examination, cycloplegic refraction, keratometry (RKT-7700; Nidek, Hiroishi, Japan), measurement of axial length (AXL; IOLMaster version 5 [Carl Zeiss Medictec, Dublin, CA]), fundus photography (TRC-NW8; Topcon, Tokyo, Japan), and OCT (Heidelberg Engineering, Heidelberg, Germany). The examinations were performed every 6 months over the course of 24 months (total examinations, 5). Both eyes were used for the analysis.

Assessment of Fundus Photographs

Serial fundus photographs were assessed independently by 2 observers (M.K. and K.M.L.). Each observer, who was masked to both the participant information and the chronological order of the photographs, classified each eye into 4 groups with respect to changes in ONH shape and the presence of β-zone PPA: group A, ONH unchanged without β-zone PPA (11 eyes); group B, ONH changed without β-zone PPA at baseline (10 eyes); group C, ONH changed with β-zone PPA at baseline (15 eyes); and group D, ONH unchanged with β-zone PPA (10 eyes). The β-zone PPA was defined as an area of visible sclera adjacent to the disc margin and without retinal pigment epithelium.[22,23] Optic nerve head change was defined as any change of disc shape or of disc margin location relative to the adjacent retinal vessels.[8] In cases of disagreement resulting from very subtle changes of the disc margin on fundus photography, a third observer (S.H.K.) was consulted to achieve consensus.

The disc photographs were evaluated in random order by 1 observer (M.K.) blinded to the participants' information. The largest disc diameter, the smallest disc diameter, and the maximum β-zone PPA width were measured using ImageJ software (available at http://rsb.info.nih.gov/ij/index.html). The ovality index was defined as the ratio between the largest and smallest disc diameters, and the PPA ratio was defined as the ratio between the maximum β-zone PPA width and the largest disc diameter. The angle between the vertical meridian and the long axis of the disc was defined as the torsion degree. The vertical meridian was identified as a vertical line 90° from a horizontal line connecting the fovea to the center of the optic disc.[24] A positive torsion degree indicated inferotemporal torsion, and a negative torsion degree indicated superonasal torsion.

Assessment of OCT Images

The ONH including the peripapillary area was imaged using Spectralis OCT. This area, as centered on the optic disc, was scanned continuously at intervals of 60 μm to obtain approximately 50 horizontal B-scan section images. For each section, 20 frames were averaged, which provided the best trade-off between image quality and patient cooperation. To remove magnification error, the value of corneal curvature was entered into the Spectralis OCT system before the scan.

For the purposes of this study, 3 horizontal B-scans were obtained, from the center, mid-superior, and mid-inferior horizontal meridians, which were spaced equally within the vertical diameter of the optic disc. From those images, we marked both ends of the Bruch's membrane opening (BMO) and connected the 2 points to draw the BMO reference plane. The distance between the 2 BMO points was defined as the BMO distance (BMOD). If there was border tissue (BT) at the temporal optic disc margin, the straight-line distance between the temporal BMO point and the BT and scleral end where the Bruch's membrane was absent (γ-zone PPA) was measured and defined as the border length (BL). The BMOD and BL measurements were performed by Spectralis OCT's built-in caliper tool. The angle between the BMO reference plane and the BT was defined as the BT angle (BTA). The images were captured in ImageJ, and the BTA was measured using the ImageJ protractor (Fig 1). The BMOD was measured in all eyes (groups A−D), whereas the BL and BTA were measured in groups C and D. All of the measurements were performed independently by 2 masked examiners (M.K. and K.M.L) and were averaged.

The distance between the fovea and the temporal margin of the BMO was measured at the baseline and the final visit, respectively.[25] A horizontal macular OCT section covering 30° of the fovea was obtained to capture the fovea and the optic disc simultaneously. Nine OCT frames were averaged to obtain 1 horizontal scan. In the glaucoma progression analysis mode, cyclotorsion was corrected, thereby aligning the positions of the fovea and the disc throughout the follow-up examinations. In the scan running through the fovea, we measured the distance of the fovea from the temporal margin of the BMO with Spectralis OCT's built-in caliper tool. In all cases, the distance was measured perpendicularly to the z-axis as if through the funduscopic plane.

Statistical Analysis

Interobserver ONH parameter (including BL, BTA, and BMOD) reproducibility was assessed by calculation of the respective intraclass correlation coefficients. Differences in continuous variables among the 4 groups were compared using the 1-way analysis of variance test and the post hoc Least Significant Difference test. Univariate and multivariate generalized linear mixed-effect models were used to determine the factors associated with ONH change during myopia progression. A generalized estimating equation was used to analyze fovea-to-BMO margin distance change. Statistical tests were performed with commercially available software (Stata version 14.0; StataCorp, College Station, TX) and the R statistical package version 3.3.3 (available at http://www.R-project.org; accessed July 10, 2017). A P value less than 0.05 was considered to represent statistical significance.