Peripapillary Nerve Fiber Elevation in Young Healthy Eyes

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PURPOSE. Eyes with a peripapillary nerve fiber elevation (pNFE) are those with a discrepancy between the optic disc margin in a color fundus photograph and the Bruch’s membrane opening in an optical coherent tomographic (OCT) cross-sectional image. The purpose of this study was to determine the prevalence of pNFE in young healthy eyes, and to compare the axial length and optic disc tilt between pNFE and non-pNFE groups.

METHODS. This was a prospective, observational, cross-sectional study of 117 right eyes. All participants (mean age 25.8 ± 4.0 years) underwent a comprehensive ophthalmologic examination. The pNFE was determined from the color fundus photographs, scanning laser ophthalmoscopic images, and optic disc cross-sectional OCT images. The degree of optic disc tilt was determined by the sine curve technique. Mann-Whitney U tests were used to determine the significance of the differences in the axial length and optic disc tilt between the pNFE and non-pNFE groups.

RESULTS. Fifty-nine eyes were placed in the pNFE group and 58 eyes in the non-pNFE group. The axial length of the pNFE group (26.0 ± 1.4 mm) was significantly longer than that of the non-pNFE group (24.9 ± 1.2 mm; P < 0.001). The optic disc tilt of the pNFE group (42.1 ± 16.5 pixels) was significantly greater than that of the non-pNFE group (33.2 ± 16.8 pixels; P = 0.003).

CONCLUSIONS. The presence of pNFE is not rare in young healthy eyes. The eyes with pNFE have longer axial lengths and greater optic disc tilt. The pNFE should be considered when the disc margin is assessed.

Keywords: peripapillary nerve fiber elevation, optic disc, glaucoma

The outer margin of the optic disc is considered to be the inner margin of the scleral ring, which is also called Elschnig’s scleral ring. It is observed as a white-colored circle by ophthalmoscopy. This designation has been widely accepted and is described in textbooks and guidelines.1-3 This is based on the idea that the margin of the scleral ring coincides with the edge of the choroid, Bruch’s membrane, and RPE. For example, a cup/disc ratio (C/D ratio) calculated using the optic disc margin by this definition is used for many epidemiologic studies on glaucoma.4-15

Recent advances of optical coherence tomography (OCT) has enabled clinicians to record three-dimensional (3D) in situ images of the optic disc.16,17 This then allows an automatic 3D segmentation of the optic disc, segmentation of the RNFL, and measurements of the area of the optic disc and other structures. For these automatic measurements, it is essential to identify the optic disc margin correctly. In most of the programs embedded in the commercially available OCT instruments, the margin of Bruch’s membrane/RPE layer is used as the margin of the optic disc. However, recent studies have shown that the border of scleral ring, the edge of the choroid, Bruch’s membrane, and RPE layer do not necessarily end at the same point.18-21 Chauhan et al.22-23 showed that there were some cases in which the scleral ring did not coincide with the edge of Bruch’s membrane, and these morphologic landmarks did not agree with the ophthalmoscopic margin of the optic disc. This is very important because the location of the optic disc margin is an important landmark that is used to diagnosis glaucoma and its progression.

We found that an elevation of the RNFL was frequently observed in the nasal peripapillary area of the optic disc where the scleral ring did not coincide with the ophthalmoscopic optic disc margin by OCT analysis in healthy young eyes. Specifically, a white-colored elevated tissue that is located mostly on the nasal side of the optic disc margin ophthalmoscopically is quite similar to the optic disc rim. Scanning laser ophthalmoscopy (SLO) showed that the inner margin of the elevation is clear and outer margin of the elevation is not clear. In the OCT cross-sectional images, the RNFL is elevated above the optic nerve rim with the same reflectivity as the ganglion cell/inner plexiform layer (GC/IPL, Fig. 1). In addition, there is a disagreement between the nasal border of the optic disc margin in the color fundus photographs and Bruch’s membrane opening in the cross-sectional OCT images. We defined this as a peripapillary nerve fiber elevation (pNFE).

The purpose of this study was to determine the prevalence of eyes with a pNFE and to investigate the relationship of the pNFE and the presence of a conus, the axial length, and optic disc tilt in young healthy adults.

METHODS

All of the procedures used conformed to the tenets of the Declaration of Helsinki. A written informed consent was...
obtained from all of the subjects after an explanation of the procedures to be used. The study was approved by the Ethics Committee of Kagoshima University Hospital, and it was registered with the University Hospital Medical Network (UMIN)-clinical trials registry (CTR). The registration title was, “Morphological analysis of the optic disc and the retinal nerve fiber in myopic eyes” and the registration number was UMIN000007154. A detailed protocol is available (in the public domain) by the National Institutes of Health, using the ImageJ software (http://imagej.nih.gov/ij/; provided in the public domain by the National Institutes of Health, Bethesda, MD, USA). The ‘x’ and ‘y’ coordinates of the B-scan images were converted to a new set of ‘x’ and ‘y’ coordinates with the center of the wave as the origin. Finally, the converted data were fit to a sine wave equation (\( y = a \times \sin(b \times x - c) \)) with the curve fitting program of ImageJ. The amplitude of the sine curve ‘a’ was defined as the degree of the optic disc tilt.

Assessment of pNFE, Conus, and Optic Disc Tilt

The presence of pNFE was determined by examining the color fundus photographs, SLO images, and optic disc cross-sectional images. The definition of a pNFE was a white-colored tissue similar to the optic disc rim by ophthalmoscopy, tissue on the optic disc rim with a clear inner margin but not clear outer margin by SLO, an elevated tissue continuous with the optic disc with the same reflectivity as the GC/IPL (Fig. 1). Eyes with all of these characteristics were placed in the pNFE group and those without these characteristics were placed in the non-pNFE group. The presence of the conus was determined by the presence of a parapapillary crescent in the color fundus photographs. The assessments of the pNFE and the conus were made by two raters independently. If raters disagreed, the eye was excluded from the study. Nine eyes were excluded because of a disagreement on the presence of a pNFE between the two masked raters. Two eyes were excluded because of a disagreement on the presence of a conus between the two masked raters, and these two eyes were included in the nine eyes excluded because of the disagreement on the presence of a pNFE.

The degree of optic disc tilt was determined as described in detail in our recent publication. Briefly, the optic disc tilt was quantified using a sine curve method of the Topcon 3D OCT-1000 Mark II RNFL 3.4-mm circle scan, B scan images. The course of the RPE was marked on the B-scan images manually. The coordinates of each pixel were determined automatically using the ImageJ software (http://imagej.nih.gov/ij/; provided in the public domain by the National Institutes of Health, Vienna, Austria). The ‘x’ and ‘y’ coordinates of the B-scan images were converted to a new set of ‘x’ and ‘y’ coordinates with the center of the wave as the origin. Finally, the converted data were fit to a sine wave equation (\( y = a \times \sin(b \times x - c) \)) with the curve fitting program of ImageJ. The amplitude of the sine curve ‘a’ was defined as the degree of the optic disc tilt.

Statistical Analyses

All statistical analyses were performed with the SPSS statistics 21 for Windows (SPSS, Inc., IBM, Somers, NY, USA) and the statistical programming language R (version 3.0.2; The R Foundation for Statistical Computing, Vienna, Austria). The intra-rater agreements of the pNFE and the conus were assessed with the kappa coefficient. Mann-Whitney U tests were used for the analyses.
were used to determine the significance of the differences of the axial lengths and optic disc tilt between the pNFE and non-pNFE groups. To determine the independent factors of the pNFE, the optimal linear models were selected among all possible combinations of the predictors based on the second order bias corrected Akaike Information Criterion index.26,27

RESULTS

The demographic information of the subjects is presented in the Table. Fifty-nine eyes were placed in the pNFE group and 58 eyes in the non-pNFE group. The interrater agreement in the pNFE and the conus were high with the kappa of 0.86 and 0.96, respectively. The axial length of the eyes in the pNFE group was significantly longer than in the non-pNFE group (P <0.001; Fig. 2A). The optic disc tilt of the pNFE group was significantly greater than that of the non-pNFE group (P = 0.003; Fig. 2B). The prevalence of a conus was significantly higher in the pNFE group (91.5%) than in the non-pNFE group (46.6%).

Multiple logistic regression analysis showed that the independent factors associated with a pNFE were the existence of a conus (odds ratio [OR] 8.86; 95% confidence interval [CI] 2.99–26.24, P < 0.001) and longer axial length for a 1-mm increase (OR 1.54 for a 1-mm increase; 95% CI 1.09–2.17, P = 0.014).

DISCUSSION

Our results showed that eyes with a pNFE were not rare in young healthy eyes. The characteristics found suggest the clinical importance of this configuration and can explain the possible formation of a pNFE.

The first important characteristic of an eye with a pNFE is its frequent association with myopic changes. These include longer axial lengths, greater optic disc tilt, and higher association with a conus. An examination of the C/D ratio has been accepted as a gold standard method to determine the presence of glaucoma, and it has been used in many clinical studies.4–15 However, its accuracy and value have not been well investigated. For example, in the three optic discs shown in Figures 3A through 3C, the horizontal C/D ratio was 0.55, 0.28, and 0.37, respectively, based on the ophthalmoscopic images and 0.40, 0.53, and 0.42, respectively, based on the OCT images in which the edge of Bruch’s membrane was used as the margin of the optic disc. So the C/D ratio can be measured to be smaller by ophthalmoscopic analysis than by OCT imaging in eyes with pNFE. Although it is unclear which C/D ratio data would be most suitable for representing the status of glaucoma, we must remember that the frequent presence of a pNFE would make differences in the evaluation especially in myopic eyes. Further investigation is necessary.

![Figure 2](image_url) **Figure 2.** Box plot of the axial length (A) and optic disc tilt (B) in the pNFE group and non-pNFE group.

To know the process for the formation of a pNFE, it is necessary to perform a longitudinal cohort study. However, this would take a considerable length of time to complete this study. Instead, the results of the present study suggest the following explanations. The first explanation is that the entire retina is dragged posteriorly as the axial length elongates leading to the tucking of the nasal retina in the nasal optic disc. In eyes with a pNFE, a conus was usually present on the side opposite the elevation. The cross-sectional OCT image of a pNFE and optic disc showed that the nasal retina appeared to be wrapped around the optic disc. The GCL/IPL appeared to be engulfed (Fig. 3). These findings would be consistent with the first hypothesis that the entire retina was dragged posteriorly as the axial length elongated. Indeed, the nonfoveal retina and choroid are both thinner, and the degree of thinning is proportional to the elongation of the axial length.28,29 This would indicate that the retina and choroid are unusually stretched in these eyes. However, there must be some variations in this structure and forming process.

The second possibility is that the tilting of the optic disc may cause an unusual distortion of the periopic disc. Because

![Figure 3](image_url) **Figure 3.** Three representative cases of peripapillary nerve fiber elevation (pNFE): (A) 38 years male with axial length 25.3 mm and refractive error of −6.5 D. (B) 24 years male with axial length 24.7 mm and refractive error of −1.5 D. (C) 29 years male with axial length 25.8 mm and refractive error of −4.0 D. There is a disagreement between nasal border of optic disc margin in the color fundus photographs (red lines) and Bruch’s membrane opening in the cross sectional image (yellow lines).
pNFE is essentially the configuration of the globe of the eye adjacent to the optic disc head, it is possible that the unusual tilting of the optic disc would primarily be the first pathological change leading to the pNFE. As described, univariate analysis showed that the presence of a conus, longer axial length, and greater tilting of optic disc were independent factors associated with the presence of the pNFE. However, the multiple regression analysis also showed that the independent factors for the pNFE were the existence of the conus and longer axial length alone. Thus, the tilting of the optic disc is not an independent factor correlated with the presence of a pNFE, and the second hypothesis most likely can be rejected.

There are several limitations in this study. First, this was a cross-sectional correlation study, and conclusions of the chronologic changes of the pNFE cannot be made. Second, this was a study of a young Japanese population. A recent epidemiologic study showed that the Japanese were the most myopic population worldwide. A pNFE was common in young healthy eyes, this might be a specific characteristic of the Japanese population. Thus, the present findings may not be applicable to other ethnic groups. These limitations should be remembered in interpreting and generalizing the present results.

In conclusion, we reported the unique configuration of the pNFE. This structure is not rare in young healthy eyes. The presence of a pNFE is often associated with myopic changes, such as the presence of a conus, longer axial length, and greater optic disc tilt. Because this structure can affect the evaluation of C/D ratio, the pNFE should be considered when the disc margin assessments are made especially in myopic eyes.

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References


