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Optic Disc Rotation as a Clue for Predicting Visual Field Progression in Myopic Normal-Tension Glaucoma

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Purpose: To investigate factors associated with visual field (VF) progression in myopic normal-tension glaucoma (NTG) and to determine the relationship between optic disc rotation and VF progression.

Design: Retrospective, observational study.

Subjects: Ninety-two patients with myopic NTG, with VF loss confined to a single hemifield, who were followed up over a 2-year period.

Methods: Systemic and ocular findings such as optic disc tilt and optic disc rotation were evaluated. The eyes with optic disc rotation accompanying a corresponding VF defect were defined as those with correspondence. Visual field progression was defined by Early Manifest Glaucoma Trial criteria. The Cox proportional hazards model was used to determine the risk factors for VF progression.

Main Outcome Measures: Progression of VF.

Results: The mean age of subjects was 37.83±10.89 years, mean spherical equivalent refractive error was −5.51±3.37 diopters, and mean axial length was 26.18±1.79 mm. Mean follow-up duration was 55.78±30.12 months. Among 92 eyes, 37 showed VF progression. A multivariate Cox proportional hazard model revealed that percentage reduction in intraocular pressure (IOP) from baseline (hazard ratio [HR], 0.965; $P = 0.013$), optic disc hemorrhage (HR, 2.623; $P = 0.019$), and optic disc rotation−VF defect correspondence (HR, 0.441; $P = 0.016$) were associated with VF progression in myopic NTG eyes.

Conclusions: In addition to the percentage reduction in IOP from baseline and optic disc hemorrhage, optic disc rotation−VF defect correspondence may be an important prognostic factor for patients with myopic NTG. *Ophthalmology 2016;■:1−10 © 2016 by the American Academy of Ophthalmology.*

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Elevated intraocular pressure (IOP) is considered a major risk factor in the pathogenesis of glaucoma, but other possible factors have been suggested, including age, family history of glaucoma, ethnicity, thin central cornea, pseudoexfoliation, and myopia.[1−4] Among these factors, myopia has been recently recognized to be of considerable concern. Many population-based studies identified an increased prevalence of glaucoma in patients with moderate or high myopia and longer axial length and suggested that myopia is a risk factor for the development of glaucoma.[5−13] However, the underlying mechanism of glaucomatous damage in patients with myopia remains unclear and is being debated.

Morphologic features of the myopic optic disc recently have become candidates to explain glaucoma pathogenesis. β-Zone parapapillary atrophy (PPA) was reported to be associated with the location and progression of visual field (VF) defects in patients with myopic primary open-angle glaucoma.[14,15] Choi et al[16] reported that measurements of the vertical disc tilt provided valuable information about the superior and inferior regional susceptibilities to glaucomatous damage, and Lee et al[17] demonstrated the protective role of the myopic optic disc tilt on glaucoma progression. We found several reports of a close relationship between the direction of optic disc rotation and the location of VF defects in myopic glaucomatous eyes.[18−20] It has been suggested that superior rotation of the optic disc results in superior retinal nerve fiber layer (RNFL) damage that presents with inferior VF defects and vice versa. We recently demonstrated that there are differences in the characteristics between eyes with superior and inferior rotation of the optic disc, and we suggested that the inferior RNFL might be more vulnerable to mechanical stress during the development of optic disc rotation.[21]

Although the VF defect as a consequence of myopic optic nerve head (ONH) changes has been well documented by cross-sectional studies, the way in which morphologic changes of the ONH can affect VF progression has been investigated in less detail.[14,15,17] Thus, this study was designed to investigate the factors associated with VF progression in myopic normal-tension glaucoma (NTG) and to determine the relationship between optic disc rotation, which is one of the important myopic ONH changes, and VF progression.

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Methods

Subjects

This retrospective study was approved by the Institutional Review Board of Chonnam National University Hospital and followed the tenets of the Declaration of Helsinki. The medical records of patients who were diagnosed with myopic NTG in the glaucoma clinic at Chonnam National University Hospital from October 2006 to October 2013 were reviewed for entry. At baseline examination, the diagnosis of NTG was based on the presence of glaucomatous optic neuropathy, corresponding abnormal 30-2 Swedish Interactive Thresholding Algorithm standard automated perimetry examinations (Humphrey Field Analyzer; Carl Zeiss Meditec Inc., Dublin, CA), open anterior chamber angles on gonioscopy, no identifiable secondary cause of glaucoma, and all known untreated IOPs $\leq$21 mmHg measured by Goldmann applanation tonometry. Glaucomatous optic nerve damage was defined as a vertical cup-to-disc ratio $\geq$0.7, asymmetry in the vertical cup-to-disc ratio between both eyes of more than 0.2, the presence of focal neural rim notching, or generalized loss of the neural rim on disc photography and red-free RNFL photography (Canon, Tokyo, Japan). To be included in the study, all subjects with myopic NTG had to meet the following criteria: $\geq$18 years old, best-corrected visual acuity better than 20/40, spherical equivalent (SE) refractive error ≤ -1.0 diopters (D), and astigmatism within $\pm$2.0 D. To investigate the effect of spatial correspondence between optic disc rotation and VF defect on VF progression, all subjects required 1 normal visual hemifield, and the glaucomatous VF damage had to be confined to a single hemifield. Each patient had to have been followed regularly for more than 2 years after the initial visit at 3- to 6-month intervals and to have 5 or more reliable VF examinations. Patients with a history of intraocular or refractive surgery, pathologic myopia (patch chorioretinal atrophy, lacquer crack lesions, intrachoroidal cavitations, choroidal neovascularization), other evidence of retinal pathology, opaque media such as cataract, previous or current use of systemic or topical steroids, or any history of neurologic disease leading to VF abnormality were excluded. Patients with an optic disc suspicious of congenital disc anomaly were excluded. Patients with a horizontally oval disc and situs inversus of the retinal vessels, suggestive of tilted disc syndrome, also were excluded from the analysis. Eligibility was determined by 2 glaucoma specialists (M.S.S. and S.W.P.), who evaluated the optic disc appearance on stereoscopic disc photographs, RNFL defects on red-free fundus photographs, and results of VF examinations. Evaluators were masked to all other patient and ocular data, and an eye was excluded from study analyses if a consensus could not be reached. When both eyes satisfied the inclusion criteria, only 1 randomly selected eye from each participant was included in the study.

All patients with NTG received topical IOP-lowering medications. The target was reduction by 20% of baseline IOP. When this was not accomplished, further treatment decisions were made by the treating physician.

Visual Field Examination and Determination of Progression

A reliable VF was required to have a fixation loss <20% and a false-negative and false-positive rate $\leq$15%. An apparently normal hemifield required having no test location worse than $P < 0.01$ on the pattern deviation plot. A glaucomatous hemifield required having a cluster of $\geq$3 contiguous test locations at $P < 0.05$ on the pattern deviation plot, with $\geq$1 test location at $P < 0.01$. The results of the first test were excluded to remove the learning effect from the analysis. The second VF examination was performed within 1 month from the first visit. The average values from the first 2 reliable fields were used for baseline mean deviation (MD), pattern standard deviation (SD), mean of the entire numeric total deviation (TD) values, and mean of the abnormal hemifield TD values.

Follow-up VF tests usually were performed at 6- to 12-month intervals. Early Manifest Glaucoma Trial criteria were used to confirm VF progression during follow-up.[22] The average of the 2 baseline field measurements was compared with those of subsequent tests using glaucoma change probability maps (Humphrey Field Analyzer) based on pattern deviation. Progression of glaucoma is considered to have occurred if there is statistically significant deterioration ($P < 0.05$) in at least 3 locations on pattern deviation change probability maps; these locations do not have to be contiguous. This significant deterioration must then be confirmed on 2 consecutive tests. To calculate the VF progression rate, the time course of the MD and mean of the entire and hemifield TD values were evaluated. Specifically, to evaluate the progression rate of the glaucomatous hemifield on the basis of the TD values, the 74 test points were separated into 2 zones: the superior and inferior hemifield. Then, the mean thresholds of the entire inferior hemifield zone were calculated in eyes with inferior VF defects, and the mean thresholds of the entire superior hemifield zone were calculated in eyes with superior VF defects. The change in mean threshold from the baseline mean threshold of each hemifield was used to calculate the progression rate.

Clinical Data and Potential Factors

Baseline factors evaluated were age at diagnosis, sex, SE refractive error, axial length, central corneal thickness, baseline IOP before treatment, family history of glaucoma, and various systemic factors, including diabetes mellitus, hypertension, cold hands/feet, and migraine. Goldmann applanation tonometry was used for all IOP measurements. Central corneal thickness and axial length were measured more than 3 times by ultrasound pachymetry (UP-1000; Nidek Co., Ltd., Tokyo, Japan) and A-scan ultrasonography (model US-800; Nidek Co., Ltd.), respectively, at the initial visit, and an average was calculated. Mean follow-up IOP, IOP fluctuation, percentage reduction in IOP from baseline during the follow-up period before detection of VF progression, and occurrence of disc hemorrhage were evaluated during follow-up. Mean follow-up IOP was calculated by averaging all IOP measurements during the follow-up period before detection of the VF progression, and IOP fluctuation was defined as the SD of this value. Disc hemorrhage was defined as a splinter-like or flame-shaped hemorrhage within the RNFL or neuroretinal rim.

Measurements of Optic Disc Tilt, Rotation, and Area

Digital retinal photographs centered on the optic disc and macula were obtained using standard settings on a nonmydriatic retinal camera. Each photograph was exported to a desktop computer as a TIFF image file. By using public-domain Java-based image processing software developed by the National Institutes of Health (ImageJ, version 1.4.1; Wayne Rasband; National Institutes of Health, Rockville, MD), the optic disc tilt, rotation, and optic disc area were measured by 2 independent examiners. Averaged data were used in the final analysis. The measurement of optic disc tilt has been described previously.[17,19–21] Briefly, optic disc tilt was measured as the tilt ratio, defined as the ratio between the longest and shortest diameters of the optic disc. Optic disc rotation was defined as the deviation of the long axis of the optic disc from the reference line, 90° from a horizontal line connecting the fovea and