Implications of Optic Disc Tilt in the Progression of Primary Open-Angle Glaucoma

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Submitted: August 6, 2015
Accepted: September 16, 2015

Citation: Lee JE, Sung KR, Lee JY, Park JM. Implications of optic disc tilt in the progression of primary open-angle glaucoma. *Invest Ophthalmol Vis Sci.* 2015;56:6925–6931. DOI:10.1167/iovs.15-17892

Purpose. To evaluate the effect of optic disc tilt on the progression of glaucoma in myopic glaucomatous eyes.

Methods. The disc tilt ratio was estimated on disc photographs. Glaucomatous progression was determined either by stereoscopic optic disc/retinal nerve fiber layer photographs or serial visual field data. All participants were categorized into two groups according to tilt ratio (nontilted [<1.3] or tilted [≥1.3]). Kaplan-Meier life-table analysis was used to compare the survival experiences (time to confirmed glaucomatous progression) between groups. The hazard ratios (HRs) for the associations between potential risk factors and progression were determined by using Cox proportional hazards modeling.

Results. A total of 85 eyes in 85 myopic glaucoma patients (axial length > 24 mm; mean follow-up, 4.1 years) were included. Among them, 42 eyes (49.4%) demonstrated progression and 43 eyes (50.6%) were stable on follow-up. The mean disc tilt ratio was significantly smaller, and the prevalence of disc hemorrhage higher, in the progression than the stable group ($P = 0.032$, $P = < 0.001$, respectively). The cumulative probability of progression was 24.7% in the tilted group and 68.7% in the nontilted group ($P = 0.005$). Disc hemorrhage (HR = 3.317; $P = 0.001$) and the tilt ratio (HR = 0.110; $P = 0.046$) were predictive of progression.

Conclusions. Myopic eyes with tilted disc demonstrated a smaller probability of glaucomatous progression. Optic disc tilt may be protective against glaucoma progression, or tilted myopic glaucomatous eyes may have less progressive characteristic by nature.

Keywords: glaucoma, myopia, progression, optic disc tilt

Glaucoma is a progressive optic neuropathy that accompanies the functional loss of vision. Myopia has been classified as a risk factor for the development of glaucoma in numerous studies to date.[1–5] However, it remains controversial whether the presence of myopia worsens the severity of glaucoma. In other words, some studies have shown that glaucoma patients with myopia progressed faster, and other publications report that myopia is not associated with glaucoma progression.[6–12] Some studies[13–15] even demonstrate that myopia is a protective factor against glaucoma progression.

Regarding these conflicting results, one possible explanation is that myopic glaucoma is a mixture of disorders with different clinical characteristics. Conflicting results may stem from the proportion of these different groups included in each study. This hypothesis is somewhat plausible because "myopia" is a general term used to define the condition that one cannot see far-sighted objects without optical correction. The reason why it has been speculated that myopia may be related to glaucoma is that the axial elongation of the eyeball causes structural changes in the optic disc and/or peripapillary retina, which are the target tissues for this condition. However, the eyeballs do not experience the same changes in the optic disc and/or peripapillary retina according to the elongation of eyeball, and thus myopia does not have the same features in terms of the optic disc and peripapillary retina. In other words, myopic glaucoma demonstrates different configurations in the optic disc and peripapillary retina. These differing anatomic characteristics between myopic glaucomatous optic discs and peripapillary retina may be associated with different clinical courses during long-term follow-up.

We reviewed our myopic glaucoma patients who had a long axial length and had been followed up longitudinally, and we compared the clinical characteristics of the myopic eyes that demonstrated progressive glaucomatous changes with myopic eyes that remained stable during follow-up. We paid particular attention to the relationship between optic disc tilt and torsion, which are frequently observed in myopic optic discs and glaucoma progression.

Methods

Subjects

The medical records of all patients who were evaluated by a single specialist (KRS) at the glaucoma clinic of Asan Medical Center, Seoul, Korea, between March 2008 and May 2015 were retrospectively evaluated. Initial testing included a comprehensive ophthalmologic examination, which included medical history review, measurement of best-corrected visual acuity (BCVA), slit-lamp biomicroscopy, multiple intraocular pressure (IOP) measurements using Goldmann applanation tonometry, gonioscopy, dilated fundoscopic examination using a 90- or 78-diopter (D) lens, stereoscopic optic disc photography, retinal nerve fiber layer (RNFL) photography, visual field (VF) testing,

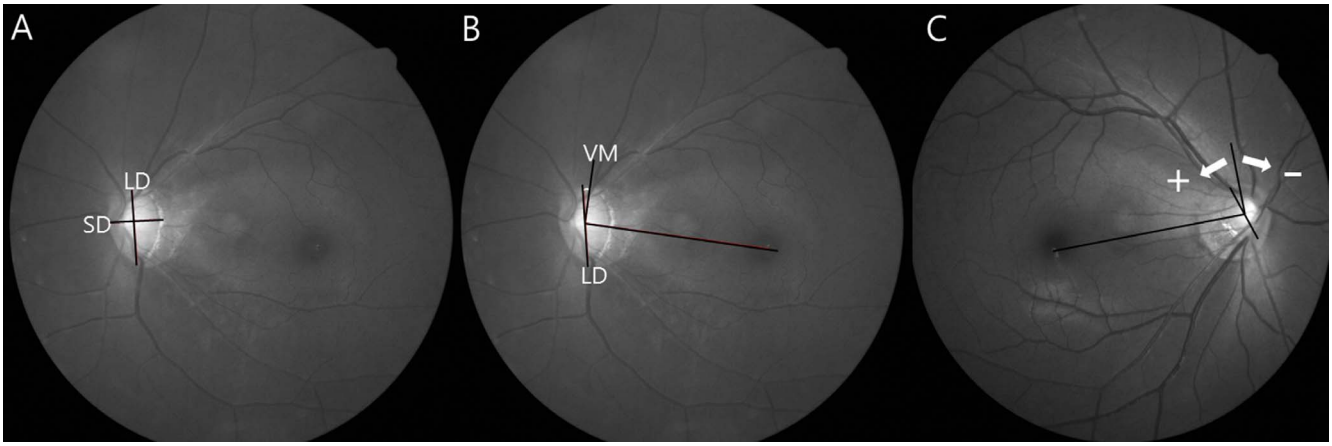

FIGURE 1. Optic disc tilt was defined as the ratio between the LD and SD of the optic disc (**A**). Optic disc torsion was defined as the deviation of the long axis of the optic disc from the VM (**B**, **C**). The VM was identified as a vertical line 90° from a horizontal line connecting the fovea to the center of the optic disc. The angular degree between the horizontal line and VM of the optic disc was named the torsional degree (**B**). A positive torsion value indicated inferotemporal torsion and a negative torsion value indicated superonasal torsion (**C**). LD, longest diameter; SD, shortest diameter; VM, vertical meridian.

central corneal thickness (CCT) measurement (DGH-550 instrument; DGH Technology, Inc., Exton, PA, USA), and axial length (AXL) measurement (IOL Master; Carl Zeiss Meditec, Dublin, CA, USA). The RNFL thickness measurement was performed by using spectral-domain optical coherence tomography (SD-OCT) (either the Cirrus HD OCT system [Carl Zeiss Meditec] or Spectralis OCT [Heidelberg Engineering, Dossenheim, Germany]).

Inclusion criteria at initial assessment included BCVA of 20/40 or better, AXL > 24 mm, normal anterior chamber, and an open angle on slit-lamp and gonioscopic examinations. Patients with glaucomatous optic disc changes, such as diffuse or focal neural rim thinning, disc hemorrhage, or RNFL defects, as confirmed by two glaucoma specialists (KRS, JYL), were included. Patients with any other ophthalmic or neurologic condition that could result in a VF defect, history of diabetes mellitus, or severe myopic fundus precluding adequate examinations were excluded. Pseudophakic and aphakic eyes were also excluded. If both eyes in the same patient were found to be eligible, one eye was randomly selected for analysis. All patients with glaucoma were followed up at 6-month intervals with stereoscopic optic disc photography, RNFL photography, VF testing, and SD-OCT scanning. All tests were performed at the same visit or within 2 weeks. To be included, patients received follow-up examinations for at least 3 years. All patients underwent medical therapy during the follow-up period. If the patient underwent intraocular surgery or laser therapy during the follow-up period, only data obtained before such operations were included.

The VF tests were performed with a Humphrey field analyzer (Swedish Interactive Threshold Algorithm [SITA] 24-2; Carl Zeiss Meditec). Only reliable VF test results (false-positive errors < 15%, false-negative errors < 15%, and fixation loss < 20%) were included in the analysis. The VF test was repeated within 2 weeks of the baseline measurement for confirmation. Patients were expected to return approximately 1 month after the baseline examination to assess their responses to medication and undergo a third VF test. Hence, all patients underwent three VF tests within the first 6 weeks. Data from the first VF test were excluded to obviate any learning effects, and the results of the second and third VF tests, which were performed within 1 month of each other, were considered the baseline examinations. Patients who underwent at least five reliable VF tests, excluding the first VF test, at separate visits were included. All participants had to have glaucomatous optic disc and glaucomatous VF defects, as defined by the glaucoma hemifield test results outside the normal limits or a pattern standard deviation outside the 95% range for normal limits. In addition, these eyes had to have a cluster of three points with probabilities < 5% on the pattern deviation map in at least one hemifield, including at least one point with a probability < 1% or a cluster of two points with a probability < 1%. Glaucomatous VF defects had to be confirmed on at least two VF examinations. The study was approved by the institutional review board of Asan Medical Center, and the study design followed the principles of the Declaration of Helsinki.

Assessment of Optic Disc Tilt and Torsion

Red-free RNFL photographs centered on the optic disc were obtained by using a nonmydriatic retinal camera. Optic disc tilt and torsion were measured on these photographs by glaucoma experts (KRS, JEL) using the National Institutes of Health image analysis software (ImageJ 1.48v, developed by Wayne Rasband; (http://imagej.nih.gov/ij/; provided in the public domain by the National Institutes of Health, Bethesda, MD, USA). Optic disc tilt and torsion were defined according to previously described criteria.[16,17] Optic disc tilt was identified by using the ovality index. Hence, the tilt ratio was defined as the ratio between the longest and shortest diameters of the optic disc (Fig. 1A). When the tilt ratio was >1.3, the optic disc was classified as tilted disc.[18] Optic disc torsion was defined as the deviation of the long axis of the optic disc from the vertical meridian (Figs. 1B, 1C). The vertical meridian was identified as a vertical line 90° from a horizontal line connecting the fovea to the center of the optic disc. The angular degree between the horizontal line and vertical meridian of the optic disc was named the torsional degree. A positive torsion value indicated inferotemporal torsion, and a negative torsion value indicated superonasal torsion (Figs. 1B, 1C).

Assessment of Progression

Glaucomatous damage involves both structural and functional changes, which may not appear at the same time. Therefore, in this study, we determined glaucoma progression by either a structural or a functional measure. Structural progression was

Table 1. Demographics and Clinical Characteristics of All Subjects ($n = 85$)

Sex, male:female	54:31
Age, y	48.3 ± 13.1
Tilt ratio	1.3 ± 0.2
Absolute torsional degree,°	12.8 ± 10.2
Spherical equivalent, D	−5.5 ± 3.4
Baseline IOP, mm Hg	16.9 ± 3.5
Mean follow-up IOP, mm Hg	14.6 ± 2.2
Mean reduction of IOP, %	12.1 ± 12.7
Central corneal thickness, μm	533.4 ± 37.3
Average RNFL thickness, μm	69.3 ± 10.6
Axial length, mm	26.5 ± 1.9
Disc hemorrhage, *n* (%)	10 (11.8)
Initial VF MD, dB	−5.8 ± 4.8
Positive torsional direction, *n* (%)	37 (43.5)

determined by evaluating a whole series of stereoscopic optic-disc and red-free RNFL photographs. Serial stereoscopic photographs were displayed on a liquid-crystal display monitor. Three glaucoma experts (KRS, JYL, JEL) independently assessed all photographs to estimate glaucoma progression. The most recent photograph was compared to the baseline photograph of each patient. The experts were not aware of each other's assessments and were blind to all clinical, OCT, and VF information. Each grader reviewed all photographs of each eye before making an assessment and was asked to determine glaucomatous optic disc or RNFL progression, as demonstrated by the increase in the extent of neuroretinal rim thinning, enhancement of disc excavation, and/or any widening, deepening, or newly appeared RNFL defect. Each grader classified each glaucomatous eye as either stable or progressing. If the RNFL photographs were difficult to evaluate because of diffuse atrophy or invisible RNFL that resulted in a lightly pigmented fundus, progression was determined by optic disc assessment. If the opinions of the three graders differed, consensus was reached after discussion, and if the consensus was not reached, that eye was excluded from the subsequent analyses.

Functional progression was defined by VF assessment. Visual field progression was determined with commercial software (Humphrey Field Analyzer Guided Progression Analysis; Carl Zeiss Meditec) and was defined as the significant deterioration from the baseline pattern deviation at three or more of the same test points that were evaluated on three consecutive examinations, or as a significantly negative slope ($P < 0.05$) in a linear regression analysis using VF mean deviation (MD) data.[18]

Statistical Analysis

The independent *t*-test was used to compare the demographic and clinical characteristics between the progression group and stable group after the normality of the data was checked. The χ^2 test was used to compare categorical data. Continuous variables were expressed as the mean ± standard deviation. Variables included age, tilt ratio, torsion direction, absolute torsional degree, AXL, baseline VF MD, CCT, spherical equivalent, baseline untreated IOP, mean follow-up IOP, mean reduction of follow-up IOPs (IOP reduction [%] from baseline visit was calculated at each visit and mean value of all visits were calculated), and SD-OCT–measured RNFL thickness. We categorized all participants into two groups, using a tilt ratio of 1.3 as the cutoff value based on a previous report (nontilted group [tilt ratio < 1.3] or tilted group [≥1.3]).[19] The variables were also compared between the tilted disc group and nontilted disc group. Kaplan-Meier life-table analysis and the log-rank test were used to compare the survival experiences (time to confirmed glaucomatous progression) between the tilted and nontilted disc groups.

The hazard ratios (HRs) for the associations between potential risk factors and glaucomatous progression were determined by using Cox proportional hazards modeling. Univariate analyses were separately performed for each variable. Variables with $P < 0.2$ on the univariate analysis were included in the multivariate Cox proportional hazards model. A backward elimination process was used to develop the final multivariate model, and adjusted HRs with 95% confidence intervals (CIs) were calculated (all statistical analyses were performed with SPSS version 18.0 [SPSS, Inc., Chicago, IL, USA]).

Results

A total of 85 myopic glaucomatous eyes were included in the final analysis. Among the 85 enrolled patients, 54 were men, 31 were women, and all were Koreans. The mean age (±standard deviation) was 48.3 ± 13.1 years and the follow-up period was 4.1 ± 1.1 years. The mean optic disc tilt ratio was 1.3 ± 0.2, and the absolute torsional degree was 12.8° ± 10.2° (Table 1).

Of the 85 eyes analyzed, 42 eyes demonstrated progression on the optic disc/RNFL photographs or serial VFs during the follow-up period and 43 eyes remained stable. Among those 42 eyes studied, 38 eyes showed progression by optic disc/RNFL

Table 2. Comparison of Progression Group and Stable Group

	Stable Group, $n = 43$	Progression Group, $n = 42$	*P* Value
Age, y	48.3 ± 11.8	49.3 ± 14.5	0.726
Tilt ratio	1.3 ± 0.2	1.2 ± 0.2	0.032
Absolute torsional degree,°	11.5 ± 11.0	14.0 ± 9.4	0.270
Spherical equivalent, D	−5.3 ± 3.5	−5.6 ± 3.3	0.673
Baseline IOP, mm Hg	16.4 ± 3.8	17.4 ± 3.2	0.198
Mean follow-up IOP, mm Hg	14.1 ± 2.1	15.1 ± 2.3	0.058
Mean reduction of IOP, %	12.1 ± 12.7	12.1 ± 13.0	0.977
Central corneal thickness, μm	531.3 ± 37.0	535.8 ± 38.0	0.600
Average RNFL thickness, μm	69.4 ± 10.6	69.2 ± 10.7	0.905
Axial length, mm	26.7 ± 2.0	26.3 ± 1.8	0.465
Disc hemorrhage, *n* (%)	0 (0)	10 (26.3)	<0.001
Initial VF MD, dB	−5.4 ± 4.2	−6.1 ± 5.4	0.476
Positive torsional direction, *n* (%)	16 (37.2)	21 (50.0)	0.234

Table 3. Univariate and Multivariate Cox Proportional Hazards Model Data for Prediction of Progression

	Univariate Analysis			Multivariate Analysis		
Variable	**HR**	**95% CI**	***P* Value**	**HR**	**95% CI**	***P* Value**
Age, y	0.996	0.973–1.021	0.770			
Tilt ratio	0.074	0.008–0.690	0.022	0.110	0.013–0.966	0.046
Absolute torsional degree, deg	1.015	0.990–1.042	0.243			
Spherical equivalent, D	1.006	0.919–1.101	0.893			
Baseline IOP, mm Hg	1.026	0.951–1.107	0.512			
Mean follow-up IOP, mm Hg	1.074	0.940–1.228	0.293			
Mean reduction of IOP, %	1.002	0.981–1.024	0.835			
Central corneal thickness, μm	0.999	0.990–1.007	0.738			
Average RNFL thickness, μm	1.003	0.974–1.033	0.832			
Axial length, mm	0.879	0.717–1.078	0.217			
Disc hemorrhage, *n*, %	6.806	3.082–15.031	<0.001	3.317	1.600–6.875	0.001
Initial VF MD, dB	0.982	0.923–1.045	0.566			
Positive torsional direction, *n*, %	1.462	0.797–2.682	0.220			

photographic assessment, 26 eyes by VF analysis, and 22 eyes by both methods. The tilt ratio was significantly lower (1.2 vs. 1.3, respectively; $P = 0.032$) and the prevalence of disc hemorrhage was higher in the progression group than the stable group (10 vs. 0, respectively; $P < 0.001$). No other variables, including age, IOP parameters, and initial VF severity, differed between the progression and stable groups (Table 2).

Tilt ratio and disc hemorrhage were found to be significantly predictive of progression by the univariate Cox proportional hazards model. Since tilt ratio and disc hemorrhage showed *P* value less than 0.2, both of them were included in the multivariate analysis. By multivariate analysis, disc hemorrhage (HR = 3.317; $P = 0.001$) and the tilt ratio (HR = 0.110; $P = 0.046$) were still significantly associated with glaucomatous progression (Table 3).

When comparing the tilted (28 eyes) and nontilted groups (57 eyes), 8 eyes (28.5%) and 34 eyes (59.6%) in each group demonstrated progression, respectively. The nontilted disc group demonstrated a greater cumulative probability of progression when assessed with Kaplan-Meier analysis (Fig. 2). The cumulative probability of progression was 24.7% in the tilted disc group (dotted line) and 68.7% in the nontilted disc group (solid line) at 62 months ($P = 0.005$). Absolute torsional degree, spherical equivalent, mean follow-up IOP, and AXL were significantly different between the tilted and nontilted disc groups. Age, baseline IOP, mean reduction of follow-up IOPs, CCT, average RNFL thickness, presence of disc hemorrhage, initial VF MD, and the positive torsional direction rate were similar between the groups (Table 4).

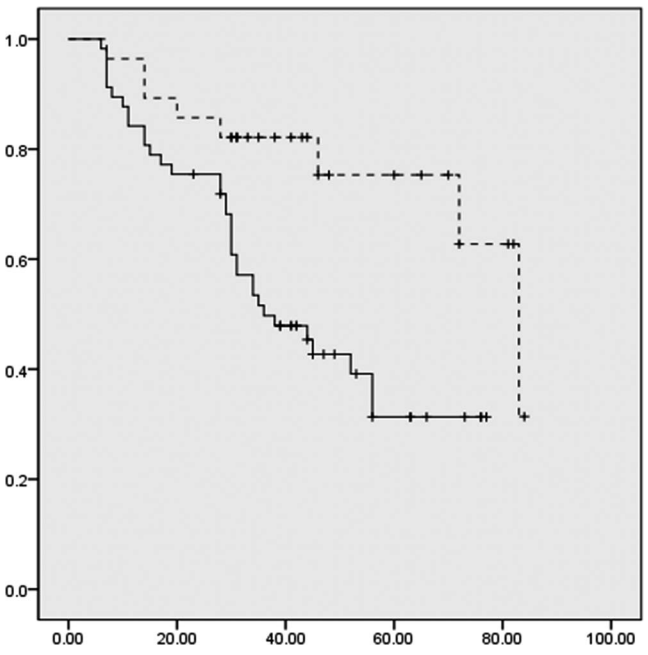

Figure 2. The nontilted disc group demonstrated a greater cumulative probability of progression when assessed with Kaplan-Meier analysis. The cumulative probability of progression was 24.7% in the tilted disc group (*dotted line*) and 68.7% in the nontilted disc group (*solid line*) at 62 months ($P = 0.005$).

Ten representative case examples are shown in Figures 3 and 4. Figure 3 shows five eyes with the smallest tilt ratios among total participants (tilt ratio, VF MD at baseline, and VF MD last follow-up): Figures 3A: 1.03, –6.62 dB, –9.43 dB; 3B: 1.04, –3.18 dB, –17.5 dB; 3C: 1.04, –16.8 dB, –19.1 dB; 3D: 1.05, –16.7 dB, –21.7 dB; and 3E: 1.07, –3.19 dB, –6.11 dB. All five eyes in Figure 3 demonstrated progression during the follow-up period. Figure 4 shows five eyes with the greatest tilt ratios among total participants (Figs. 4A: 1.85, –3.63 dB, –3.66 dB; 4B: 1.79, –8.43 dB, –8.38 dB; 4C: 1.78, –8.90 dB, –8.79 dB; 4D: 1.54, –1.11 dB, –3.08 dB; and 4E: 1.53, –9.35 dB, –8.79 dB). Among five eyes in Figure 4, only one eye (Fig. 4D) showed progression during the follow-up period. The upper and lower images were taken at baseline and the last follow-up examination, respectively.

Discussion

Most glaucoma patients in Korea and Japan demonstrate a statistically normal IOP range.[20,21] Recent studies[15,22] performed in those countries revealed that more than half of such normal tension glaucoma (NTG) patients are myopic. Hence, the relationship between glaucoma and myopia is an interesting issue for glaucoma patient management in such countries. Furthermore, the prevalence of optic disc tilt or torsion is reportedly high in Korean NTG patients.[22] Therefore, optic disc changes, such as tilt or torsion according to axial elongation, may have some association with the glaucomatous changes that develop in myopic glaucoma patients.

Among 85 myopic glaucomatous eyes, 42 eyes (49.4%) demonstrated progression on optic disc/RNFL photographic assessments or serial VFs during the follow-up period. When we compared the progression and stable groups, the most prominent difference was the degree of optic disc tilt. Myopic eyes with progression demonstrated a smaller optic disc tilt

Table 4. Comparison of Tilted Disc Group and Nontilted Disc Group

	Nontilted Disc Group, $n = 57$	Tilted Disc Group, $n = 28$	*P* Value
Age, y	50.0 ± 12.8	46.4 ± 13.6	0.227
Tilt ratio	1.1 ± 0.1	1.5 ± 0.2	<0.001
Absolute torsional degree, deg	15.1 ± 10.8	8.1 ± 7.1	0.001
Spherical equivalent, D	−4.8 ± 2.9	−6.8 ± 4.0	0.009
Baseline IOP, mm Hg	17.4 ± 3.8	16.0 ± 2.6	0.084
Mean follow-up IOP, mm Hg	15.0 ± 2.2	13.8 ± 2.1	0.023
Mean reduction of IOP, %	11.7 ± 13.7	12.8 ± 10.8	0.711
Central corneal thickness, μm	536.6 ± 33.5	526.3 ± 44.6	0.265
Average RNFL thickness, μm	68.8 ± 11.9	70.3 ± 7.5	0.507
Axial length, mm	25.8 ± 1.6	27.7 ± 1.8	<0.001
Disc hemorrhage, *n* (%)	7 (12.3)	3 (10.7)	1.000
Initial VF MD, dB	−5.8 ± 5.2	−5.8 ± 3.9	1.000
Positive torsional direction, *n* (%)	22 (38.6)	15 (53.6)	0.191

ratio. This was also reflected on the Cox proportional hazards model. The optic disc tilt ratio was associated with progression by both univariate and multivariate analyses. When we categorized all participants into two groups, using a tilt ratio of 1.3 as the cutoff value, the nontilted group demonstrated a greater probability of progression than the tilted group in the Kaplan-Meier survival analysis ($P = 0.005$). Hence, it seems that the myopic eyes with greater optic disc tilt demonstrated a more stable clinical course during the follow-up period in our cohort. This is not a completely new finding however. In a previous study, Doshi et al.[11] have followed up young to middle-aged Chinese glaucomatous eyes for up to 7 years and report that those eyes are stable regardless of IOP-lowering therapy. These authors also report that their condition is related to myopia and tilted discs.

Our current observation that eyes with a greater myopic optic disc tilt are associated with a more stable clinical course may be explained from two different viewpoints. One of these possibilities is that tilted myopic glaucomatous optic discs do not have progressive glaucomatous characteristics by nature. Myopic eyes reportedly have an optic disc that tilts during myopization and, more specifically, axial elongation of the eyeball.[23] While the optic disc is tilting, the lamina cribrosa (LC) may experience some level of deformation. Recently, Lee et al.[19] have demonstrated that the shape of the LC surface changes as the axis of the optic disc tilts. Such insults delivered to the LC during axial elongation may accelerate damage to the RNFL. Because those myopic changes tend to stabilize as the myopic patient becomes an adult, damage to the LC via optic disc tilt may not further progress when one becomes an adult. This explanation can be summarized as glaucomatous changes or glaucoma-like changes in the tilted optic disc, which may be associated with myopic changes that occur during childhood or adolescence.[11,23,24] If this is true, two questions remain. First, why nontilted myopic optic discs did not demonstrate tilting during axial elongation and why nontilted myopic optic discs are more prone to progressive glaucomatous change? This might be explained by the vulnerability or deformability of the LC in such nontilted myopic optic discs. The LC is a sieve-like elastic structure composed of multiple collagenous sheets. In younger patients, the LC is more elastic and deformable. Theoretically, if the LC is weak and easily deformable, those optic discs may experience the deformation of LC (i.e., compression or posterior displacement of the LC [increase in

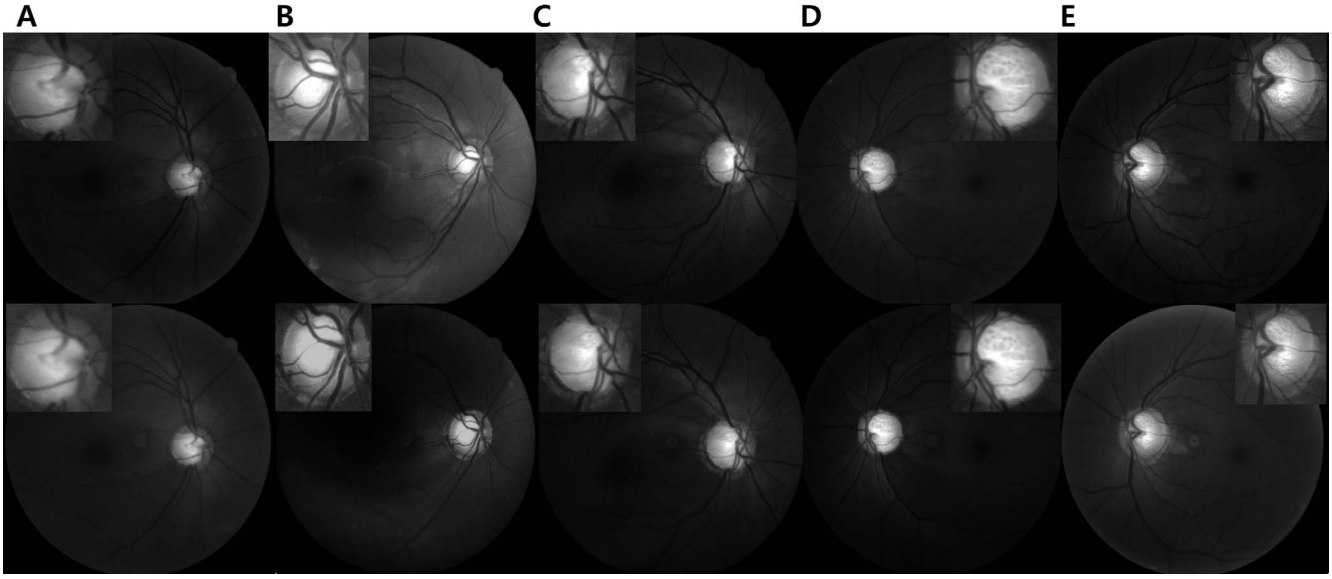

Figure 3. Clinical examples of five eyes with the smallest tilt ratios among total participants are shown. The *upper* and *lower* images were taken at baseline and the last follow-up examination, respectively. Tilt ratio, visual field mean deviation at baseline, and last follow-up were as follows: (**A**) 1.03, −6.62 dB, −9.43 dB; (**B**) 1.04, −3.18 dB, −17.5 dB; (**C**) 1.04, −16.8 dB, −19.1 dB; (**D**) 1.05, −16.7 dB, −21.7 dB; (**E**) 1.07, −3.19 dB, −6.11 dB, respectively. All five eyes in Figure 3 demonstrated progression during the follow-up period.

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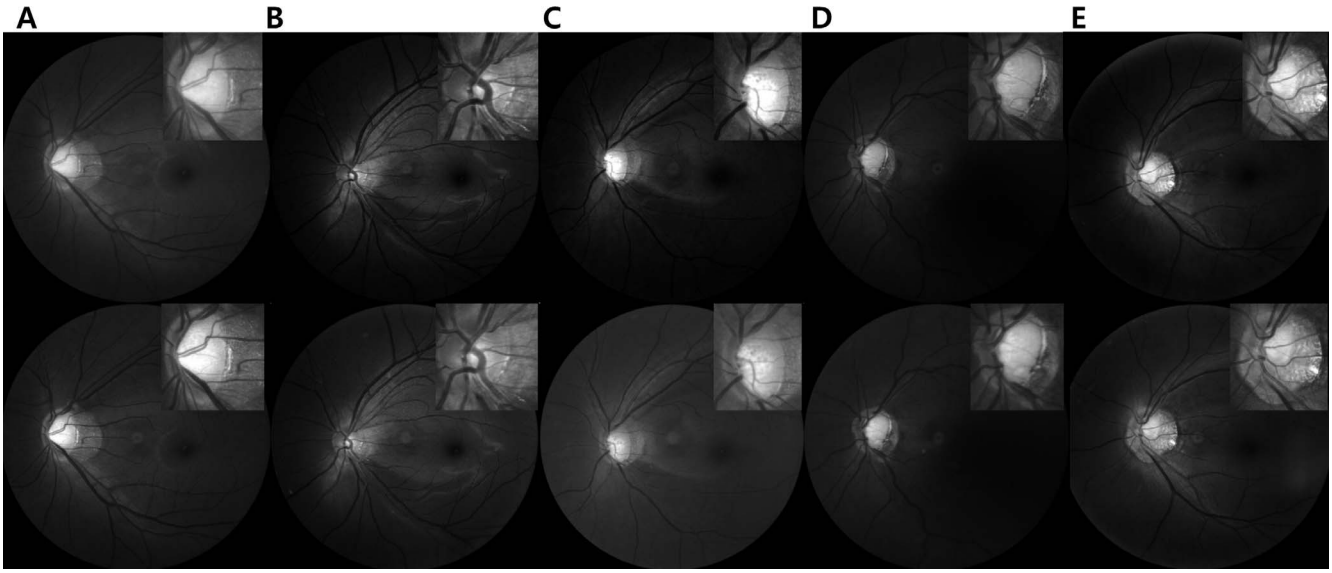

FIGURE 4. Clinical examples of five eyes with the greatest tilt ratios among total participants are shown. The *upper* and *lower* images were taken at baseline and the last follow-up examination, respectively. Tilt ratio, visual field mean deviation at baseline, and last follow-up were as follows: (**A**) 1.85, –3.63 dB, –3.66 dB; (**B**) 1.79, –8.43 dB, –8.38 dB; (**C**) 1.78, –8.90 dB, –8.79 dB; (**D**) 1.54, –1.11 dB, –3.08 dB; (**E**) 1.53, –9.35 dB, –8.79 dB, respectively. Among five eyes in Figure 4, only one eye (**D**) showed progression during the follow-up period.

cupping]) rather than tilting the optic disc during axial elongation. Axial myopia is characterized by the thinning of the sclera, and optic disc tilt is also caused by mechanical stress on the peripapillary sclera. According to the location of scleral thinning, the optic disc and macula reportedly have different configurations.[25,26] Eyes with scleral thinning (including the macula) tend to have a titled optic disc, and eyes with scleral thinning (including the optic disc) tend to have a megalodisc.[25,26] It may be reasonable to think that the weakest point of the whole posterior segment in each eye undergoes thinning more easily during axial elongation. However, there seems to be no clear evidence for why the area of scleral thinning differs among myopic eyes. In eyes with progressive glaucomatous changes in the optic disc, the LC may be the weakest point in the posterior pole and, hence, mechanical stress could primarily affect the LC and not other areas such as the peripapillary sclera or macula. To provide a feasible explanation in the future, the pathophysiology of a myopic optic disc tilt may need to be explored.

Another explanation for why greater myopic optic disc tilt is associated with a more stable clinical course in eyes with glaucoma is that optic disc tilt itself may protect against progressive glaucomatous damage. The LC and peripapillary sclera are load-bearing tissues in biomechanical terms, and IOP acts as a stress.[27,28] In the tilted optic disc, the LC is displaced in a skewed position and the peripapillary sclera (the area of peripapillary atrophy) partially replaces the area where the LC originally exsisted.[23] Hence, mechanical stress, which is supposed to transfer wholly to the LC, may be dispersed into the skewed LC and peripapillary sclera (i.e., the area of peripapillary atrophy). Therefore, the LC in the optic disc would have less stress than when it was in the original position. However, this is pure speculation and needs to be investigated in future studies.

Optic disc torsion may be another change related to deformations in the posterior pole due to scleral thinning.[22,24,25] When we compared our tilted and nontilted optic disc groups, the degree of torsion was significantly different between them.

As expected and confirmed by other studies,[29,30] eyes with tilted optic disc were more myopic and had a longer AXL in our study. The baseline IOP was slightly lower in our tilted group, but this did not reach a statistically significant lower level ($P = 0.084$), and the follow-up IOP was lower in the titled group. Although, difference of baseline IOP did not reach a statistically significant level, since baseline IOP is one of the most important factors associated with the progression of glaucoma, this issue warrants further investigation with more participants.

Our study had several limitations of note. There are several methods that can be used to measure optic disc tilt, but to avoid confusion we used the ovality index because this is the most frequently cited method.[16,17] Second, some of our patients were imaged with Cirrus HD OCT and others with Spectralis OCT. Since measurements by two different devices did not demonstrate significant differences (data not shown), and RNFL thickness was not our main interest in this study, we combined those two measures to determine the RNFL thickness. Third, our participants were all myopic and myopia is more prevalent in younger generation; therefore, our subjects were relatively young (mean age, 48.3 years) compared with those of the general glaucoma population, and hence our results should be interpreted with caution in this regard.

In conclusion, myopic eyes with tilted optic disc demonstrated a smaller probability of glaucomatous progression. Optic disc tilt may be protective against glaucoma progression, or tilted myopic glaucomatous eyes may have less progressive characteristic by nature.

Acknowledgments

Supported by Grant 2013-500 from the Asan Institute for Life Sciences, Asan Medical Center, Seoul, Korea, and the Basic Science Research Program through the National Research Foundation of Korea (NRF), which is funded by the Ministry of Education, Science, and Technology (No. NRF-2014R1A1A3A04051089). The authors alone are responsible for the content and writing of the paper.

Disclosure: **J.E. Lee**, None; **K.R. Sung**, None; **J.Y. Lee**, None; **J.M. Park**, None

References

1. Marcus MW, de Vries MM, Junoy Montolio FG, et al. Myopia as a risk factor for open-angle glaucoma: a systematic review and meta-analysis. *Ophthalmology*. 2011;118:1989–1994.
2. Chon B, Qiu M, Lin SC. Myopia and glaucoma in the South Korean population. *Invest Ophthalmol Vis Sci*. 2013;54:6570–6577.
3. Mitchell P, Hourihan F, Sandbach J, et al. The relationship between glaucoma and myopia: the Blue Mountains Eye Study. *Ophthalmology*. 1999;106:2010–2015.
4. Suzuki Y, Iwase A, Araie M, et al. Risk factors for open-angle glaucoma in a Japanese population: the Tajimi Study. *Ophthalmology*. 2007;114:216–220.
5. Xu L, Wang Y, Wang S. High myopia and glaucoma susceptibility the Beijing Eye Study. *Ophthalmology*. 2007;114:216–220.
6. Heijl A, Leske MC, Bengtsson B, et al. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. *Arch Ophthalmol*. 2002;120:1268–1279.
7. Kim YJ, Yun SC, Na JH, et al. Glaucoma progression in eyes with a history of refractive corneal surgery. *Invest Ophthalmol Vis Sci*. 2012;53:4485–4489.
8. Sohn SW, Song JS, Kee C. Influence of the extent of myopia on the progression of normal-tension glaucoma. *Am J Ophthalmol*. 2010;149:831–838.
9. Chihara E, Liu X, Dong J, et al. Severe myopia as a risk factor for progressive visual field loss in primary open-angle glaucoma. *Ophthalmologica*. 1997;211:66–71.
10. Perdicchi A, Iester M, Scuderi G, et al. Visual field damage and progression in glaucomatous myopic eyes. *Eur J Ophthalmol*. 2007;17:534–537.
11. Doshi A, Kreidl KO, Lombardi L, et al. Nonprogressive glaucomatous cupping and visual field abnormalities in young Chinese males. *Ophthalmology*. 2007;114:472–479.
12. Sung KR, Lee S, Park SB, et al. Twenty-four hour ocular perfusion pressure fluctuation and risk of normal-tension glaucoma progression. *Invest Ophthalmol Vis Sci*. 2009;50:5266–5274.
13. Sakata R, Aihara M, Murata H, et al. Contributing factors for progression of visual field loss in normal-tension glaucoma patients with medical treatment. *J Glaucoma*. 2013;22:250–254.
14. Araie M, Shirato S, Yamazaki Y, et al. Risk factors for progression of normal-tension glaucoma under β-blocker monotherapy. *Acta Ophthalmol*. 2012;90:337–343.
15. Lee JY, Sung KR, Han S, Na JH. Effect of myopia on the progression of primary open-angle glaucoma. *Invest Ophthalmol Vis Sci*. 2015;56:1775–1781.
16. Vongphanit J, Mitchell P, Wang JJ. Population prevalence of tilted optic disks and the relationship of this sign to refractive error. *Am J Ophthalmol*. 2002;133:679–685.
17. Tay E, Seah SK, Chan SP. Optic disk ovality as an index of tilt and its relationship to myopia and perimetry. *Am J Ophthalmol*. 2005;139:247–252.
18. Heijl A, Leske MC, Bengtsson B, Bengtsson B, Hussein M; Early Manifest Glaucoma Trial Group. Measuring visual field progression in the Early Manifest Glaucoma Trial. *Acta Ophthalmol Scand*. 2003;81:286–293.
19. Lee KM, Lee EJ, Kim TW. Lamina cribrosa configuration in tilted optic discs with different tilt axes: a new hypothesis regarding optic disc tilt and torsion. *Invest Ophthalmol Vis Sci*. 2015;56:2958–2967.
20. Kim CS, Seong GJ, Lee NH, Song KC; Namil Study Group, Korean Glaucoma Society. Prevalence of primary open-angle glaucoma in central South Korea the Namil study. *Ophthalmology*. 2011;118:1024–1030.
21. Iwase A, Suzuki Y, Araie M, et al. The prevalence of primary open-angle glaucoma in Japanese: the Tajimi Study. *Ophthalmology*. 2004;111:1641–1648.
22. Park HY, Lee KI, Lee K, Shin HY, Park CK. Torsion of the optic nerve head is a prominent feature of normal-tension glaucoma. *Invest Ophthalmol Vis Sci*. 2014;56:156–163.
23. Kim TW, Kim M, Weinreb RN, Woo SJ, Park KH, Hwang JM. Optic disc change with incipient myopia of childhood. *Ophthalmology*. 2012;119:21–26.
24. Park HY, Lee K, Park CK. Optic disc torsion direction predicts the location of glaucomatous damage in normal-tension glaucoma patients with myopia. *Ophthalmology*. 2012;119:1844–1851.
25. Park HY, Jung Y, Park CK. Posterior staphyloma is related to optic disc morphology and the location of visual field defect in normal tension glaucoma patients with myopia. *Eye*. 2015;29:333–341.
26. Moriyama M, Ohno-Matsui K, Hayashi K, et al. Topographic analyses of shape of eyes with pathologic myopia by high-resolution three-dimensional magnetic resonance imaging. *Ophthalmology*. 2011;118:1626–1637.
27. Burgoyne CF, Downs JC, Bellezza AJ, Suh JK, Hart RT. The optic nerve head as a biomechanical structure: a new paradigm for understanding the role of IOP-related stress and strain in the pathophysiology of glaucomatous optic nerve head damage. *Prog Retin Eye Res*. 2005;24:39–73.
28. Norman RE, Flanagan JG, Sigal IA, Rausch SM, Tertinegg I, Ethier CR. Finite element modeling of the human sclera: influence on optic nerve head biomechanics and connections with glaucoma. *Exp Eye Res*. 2011;93:4–12.
29. Hosseini H, Nassiri N, Azarbod P, et al. Measurement of the optic disc vertical tilt angle with spectral-domain optical coherence tomography and influencing factors. *Am J Ophthalmol*. 2013;156:737–744.
30. Hwang YH, Yoo C, Kim YY. Characteristics of peripapillary retinal nerve fiber layer thickness in eyes with myopic optic disc tilt and rotation. *J Glaucoma*. 2012;21:394–400.

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