Effect of Myopia on the Progression of Primary Open-Angle Glaucoma

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Purpose. To evaluate the effect of myopia on the progression of primary open-angle glaucoma.

Methods. In this retrospective cohort study, eyes were classified into nonmyopic (NMG, >0 diopters [D]), mild to moderate (MMG, 0 to −6 D), and highly myopic glaucoma (HMG, <−6 D) groups according to the level of spherical equivalent. Glaucoma progression was determined either by optic disc/retinal nerve fiber layer (RNFL) photographs or by serial visual field (VF) data. Cox's proportional hazard models were used to detect associations between potential risk factors and glaucoma progression.

Results. Among 369 eyes from 369 glaucoma patients (average follow-up, 4.4 years), 54 of 178 eyes (30.3%) in the NMG, 49 of 151 eyes (32.5%) in the MMG, and 8 of 40 eyes (20.0%) in the HMG showed progression. When VF was used as a progression criterion, thinner baseline RNFL (hazard ratio [HR]: 0.942, $P < 0.001$) was predictive of progression. When optic disc/RNFL photographs were used, worse baseline visual field mean deviation (VF MD) and thinner RNFL were associated. The HMG category was a preventive factor for optic disc/RNFL photographic progression (HR: 0.323, $P = 0.031$).

Conclusions. No levels of myopia were associated with glaucoma progression in our study. High myopia was a protective factor for optic disc/RNFL progression. These results may be interpreted as a lower progression detection rate because of the difficulty in detecting changes in the optic disc/RNFL in HMG, or as a consequence of some of highly myopic eyes that may not be true cases of glaucoma.

Keywords: glaucoma, progression, myopia

Generally, myopia is a condition of the eye that makes it difficult to see objects that are far away without optical correction. Although myopia can be induced by lens or corneal curvature or by other factors, axially elongated eyes represent a major portion of all myopia cases. Axial elongation can affect the intraocular structure, such as the optic disc or macula, which are target sites for glaucomatous damage. Many studies have reported that myopia is a risk factor for glaucoma development.[1–3] Large-scale population-based studies have also reported that myopia is a risk factor for glaucoma development.[4–8]

Whether myopia is a risk factor for glaucoma progression is still a subject of debate.[9–12] As already mentioned, some studies have reported that myopia is a risk factor for glaucoma progression.[13,14] However, another study on young Chinese myopic eyes with a glaucomatous optic disc that were followed for 7 years did not report progression in their optic discs, regardless of glaucoma treatment.[15] Moreover, two recent papers from Japan have reported that myopia is a preventive factor for glaucoma progression.[16,17] Thus, the association between glaucoma progression and myopia remains unresolved. Considering that myopia is a common condition and that its incidence is increasing in young people, a better understanding of the relationship between myopia and glaucoma progression is an important issue that will require more intensive investigations.[18,19] Hence, to explore the effect of myopia on glaucoma progression, we have here analyzed longitudinal cohort data of medically treated primary open-angle glaucoma patients.

Additionally, high myopia is thought to have a somewhat different pathology than mild to moderate myopia. Highly myopic eyes show more aggressive pathological changes in the posterior pole of the eye and tend to deteriorate, whereas myopic changes in cases of mild to moderate myopia usually remain stable after adolescence.[20,21] Because the posterior pole includes the optic disc and macula, which are target sites for glaucomatous damage, high myopia and glaucoma might be linked.[1,3,22] Some studies have reported different retinal nerve fiber layer (RNFL) involvement patterns in highly myopic glaucomatous eyes compared to nonhighly myopic glaucomatous eyes, suggesting that the pattern of glaucoma progression may be different in myopic cases of differing severity.[23] Hence, we categorized our participants into three subgroups based on the degree of refractive error as follows: nonmyopic, mildly to moderately myopic, and highly myopic. We also evaluated the risk factors for glaucoma progression in each subgroup. One possible reason for conflicting data regarding glaucoma progression and myopia may be the small number of myopic patients who were analyzed in previous longitudinal studies. In our present study, we intended to investigate this potential association with a relatively large number of participants.

Methods

Subjects

We performed a retrospective review of the medical records of all subjects who were evaluated by a single glaucoma specialist (KRS) at the glaucoma clinic of the Asan Medical Center (Seoul, Korea) from March 2008 to April 2014. Subjects who met the inclusion criteria were consecutively enrolled. At the initial test, each participant received a comprehensive ophthalmological examination, including a review of the medical history, measurement of best-corrected visual acuity, slit-lamp biomicroscopy, Goldmann applanation tonometry, gonioscopy, central corneal thickness (CCT) measurement (DGH-550 instrument; DGH Technology, Inc., Exton, PA, USA), dilated fundoscopic examination using a 90- or 78-diopter (D) lens, stereoscopic optic disc photography, RNFL photography, a visual field (VF) test, and spectral-domain optical coherence tomography (SD-OCT). To be included in the study, participants had to meet the following criteria at their initial assessment: best-corrected visual acuity of 20/40 or better, the presence of a normal anterior chamber, an open angle on slit-lamp and gonioscopic examinations, glaucomatous optic nerve damage (the presence of focal thinning of the neuroretinal rim or notching and an RNFL defect) and glaucomatous VF defect. These findings were confirmed and agreed upon by two glaucoma specialists (KRS and JYL). Glaucomatous VF defects were defined as those with a cluster of three points with probabilities of <5% on the pattern deviation map in at least one hemifield, including at least one point with a probability of <1%; or a cluster of two points with a probability of <1% and a glaucoma hemifield test (GHT) result outside normal limits; or a pattern standard deviation (PSD) outside 95% of normal limits. We excluded participants with any other ophthalmic or neurological condition that could result in a VF defect or those who had a history of diabetes mellitus. Pseudophakic or aphakic eyes were also excluded. If both eyes of the same patient were found to be eligible, one eye was randomly selected for analysis.

All of the subjects with glaucoma in our present study 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 a 2-week period. To be included in the analyses, all subjects were followed up for at least 3 years. All participants underwent medical therapy during the follow-up period. If the subject underwent intraocular surgery or laser therapy during the follow-up period, only data obtained before such operations were included. The Institutional Review Board of the Asan Medical Center approved this study, and the study design followed the principles of the Declaration of Helsinki.

VF Assessment

Visual field tests were performed using a Humphrey field analyzer (Swedish Interactive Threshold Algorithm [SITA] 24-2; Carl Zeiss Meditec, Dublin, CA, USA). 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 come back approximately 1 month after baseline exam to check the response of the medication and underwent the third VF test at that time. Hence a total of three VF tests were performed within the first 6 weeks. The very first VF test data were excluded to obviate any learning effect. Therefore, the second and third VF results, which were obtained within 1 month, were incorporated into analysis as baseline exams. For inclusion in the study cohort, at least five reliable VF tests (except for the very first VF) that were taken at separate visits were required. Visual field progression was determined using commercial software (Humphrey Field Analyzer Guided Progression Analysis [GPA]; Carl Zeiss Meditec) and was defined as 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.[24]

Optic Disc and RNFL Assessment

The progression of optic disc and RNFL defects was determined by an evaluation of a whole series of stereoscopic optic disc and red-free RNFL photographs. Serial stereoscopic photographs were displayed on a liquid crystal display (LCD) monitor. Two glaucoma experts (KRS and JHN) independently assessed all photographs to estimate glaucoma progression. The most recent photograph was compared to the baseline photograph for 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 revealed by an increase in the extent of neuroretinal rim thinning, the appearance of new disc hemorrhage, enhancement of disc excavation, and/or any widening or deepening or new appearance of an 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 resulting from lightly pigmented fundus, the progression determination was obtained by optic disc assessment. If the opinions of the two graders differed, that eye was excluded from subsequent analysis.

SD-OCT Assessment

Spectral-domain OCT images were obtained using a Cirrus HD OCT system (Carl Zeiss Meditec). The image acquisition procedure has been described in detail elsewhere.[25–27] Our Cirrus HD OCT system is regularly calibrated by a technician employed by the manufacturer. Circumpapillary RNFL (cRNFL) thicknesses were measured using the optic disc cube mode, and ganglion cell inner plexiform complex (GCIPL) thicknesses were measured using the macular cube mode. Pupil dilation was performed when necessary. All accepted images exhibited a centered optic disc or fovea, were well focused with even and adequate illumination, exhibited no eye motion within the measurement circle, and had a signal strength of at least 7.

Statistical Analysis

The eyes of the study participants were divided into the following three groups according to the level of spherical equivalent: a nonmyopic group (>0 D, NMG), a mild to moderate myopic group (0 to –6 D, MMG), and a highly myopic group (<–6 D, HMG). Baseline and follow-up data were compared among these three groups by ANOVA test. Glaucomatous progression was defined based on two criteria, optic disc/RNFL progression and VF progression. We fitted univariate and multivariate Cox proportional hazard models to detect associations between potential risk factors, including the category of refractive error, baseline untreated intraocular pressure (IOP) and mean follow-up IOP, CCT, baseline average cRNFL and GCIPL thicknesses, baseline visual field mean deviation (VF MD), and glaucoma progression time based on two different criteria. Furthermore, we conducted subgroup

analysis for the three groups. Both univariate and multivariate analyses were performed separately for each group. Variables with a P value less than or equal to 0.20 in the univariate analyses were included as candidate variables for the multivariate regression analysis. A backward elimination process was used to develop the final multivariate model. Data are presented as adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). The Schoenfeld residuals test was used to verify the proportional hazards assumption; no violations were detected during this analysis. All statistical analyses were performed using SPSS version 15.0 (SPSS, Inc., Chicago, IL, USA).

Results

Twenty-nine eyes (7.3%) from 398 eyes that met other inclusion criteria were excluded due to disagreement between two graders regarding progression assessment. Hence, a total of 369 eyes from 369 subjects were included in our final study cohort. The mean follow-up period (± standard deviation [SD]) was 4.4 ± 1.0 years, and the mean number of analyzed optic disc/RNFL photographs and VF was 7.81 ± 1.42 and 7.70 ± 1.44 per eye, respectively. Among the 369 subjects, 192 were men, 177 were women, and all were Koreans. Among the 369 eyes, we categorized 178 eyes as NMG, 151 eyes as MMG, and 40 eyes as HMG. Clinical characteristics were described and compared among the three groups (Table 1). The age at baseline was significantly different among the three groups: oldest in the NMG group and youngest in the HMG group (65.0 ± 11.4, 49.6 ± 13.7 years, $P < 0.001$). The baseline RNFL was thinner in the HMG group than in the NMG group (76.0 ± 12.7, 80.1 ± 12.1 μm, $P = 0.043$, Table 1).

Among the 369 eyes, progression was observed in 91 eyes (24.7%) by optic disc/RNFL photographic assessment, 46 eyes (12.5%) by VF analysis, and 111 eyes (30.1%) by either optic disc/RNFL or VF examination. Among 178 eyes in the NMG group, 45 eyes (25.3%) showed progression by optic disc/RNFL photographic assessment, 24 eyes (13.5%) by VF analysis, and 54 eyes (30.3%) by either optic disc/RNFL or VF exams. Among the 151 eyes in the MMG group, 42 eyes (27.8%) showed progression by optic disc/RNFL photographic assessment, 18 eyes (11.8%) by VF analysis, and 49 eyes (32.5%) by either optic disc/RNFL or VF exams. Among the 40 eyes in the HMG group, 4 eyes (10.0%) showed progression by optic disc/RNFL photographic assessment, 4 eyes (10.0%) by VF analysis, and 8 eyes (20.0%) by either optic disc/RNFL or VF exams. Glaucoma filtering surgery was performed in 7, 8, and 2 eyes in the NMG, MMG, and HMG groups, respectively, during the follow-up period. Selective laser trabeculoplasty was performed in 7, 13, and 3 eyes in the NMG, MMG, and HMG groups, respectively, during the follow-up period.

The univariate and multivariate HRs for each putative risk factor, including the three categories of refractive error in all study participants according to the Cox proportional hazard model, are listed in Table 2. Two types of criteria for glaucoma progression, optic disc/RNFL and VF assessments, were assessed independently. When VF was used as a progression criterion, thinner baseline RNFL (HR; 0.942, $P < 0.001$) was found to be significant. When the NMG category was used as a reference, neither the MMG ($P = 0.553$) nor the HMG ($P = 0.794$) category was a significant risk factor for progression. When optic disc/RNFL photographic assessment was used as a progression criterion, worse baseline VF MD (HR; 0.949, $P = 0.007$) and thinner RNFL (HR; 0.971, $P = 0.004$) were associated with progression. The HMG category (HR; 0.323, $P = 0.031$) was a preventive factor for optic disc/RNFL photographic progression.

Table 1. Clinical Characteristics of the Three Study Groups Based on Spherical Equivalent

	NMG, $n = 178$	MMG, $n = 151$	HMG, $n = 40$	P Value
Age	65.0 ± 11.4	60.4 ± 12.5	49.6 ± 13.7	<0.002* <0.001† <0.001‡
Sex, male/female	86/92	83/68	23/17	0.195
SE	0.71 ± 1.04	−1.77 ± 1.45	−9.21 ± 3.57	<0.001* <0.001† <0.001‡
CCT	531.0 ± 50.7	534.1 ± 37.7	549.1 ± 31.9	1.00* 0.140† 0.290‡
Baseline IOP	15.6 ± 4.1	16.2 ± 4.5	17.3 ± 3.7	0.509* 0.063† 0.456‡
Mean follow-up IOP	14.4 ± 2.5	14.5 ± 2.7	15.7 ± 2.0	1.00* 0.007† 0.022‡
DH occurrence, no/yes	166/12	144/7	39/1	0.770* 0.235† 0.166‡
Baseline VF MD	−3.89 ± 4.69	−5.24 ± 5.98	−5.07 ± 4.59	0.061* 0.617† 1.00‡
Baseline RNFL thickness	80.1 ± 12.1	76.7 ± 12.8	76.0 ± 12.7	0.189* 0.043† 1.00‡
Baseline GCIPL thickness	73.7 ± 9.1	71.9 ± 10.3	69.9 ± 10.3	0.271* 0.077† 0.741‡

SE, spherical equivalent; DH, disc hemorrhage.
* NMG versus MMG.
† NMG versus HMG.
‡ MMG versus HMG.

In our subgroup analysis, a higher baseline IOP (HR; 1.089, $P = 0.001$) and thinner baseline RNFL (HR; 0.926, $P < 0.001$) were found to be associated with VF progression in the NMG group. When using optic disc/RNFL photographic assessment as a progression criterion, thinner baseline GCIPL thickness (HR; 0.939, $P < 0.001$) was associated with progression (Table 3). In the MMG cases, worse baseline VF MD (HR; 0.899, $P < 0.001$) was associated with VF progression, and thinner baseline RNFL (HR; 0.955, $P < 0.001$) was associated with optic disc/RNFL progression (Table 4). In the HMG group, thinner baseline GCIPL (HR; 0.845, $P = 0.003$) was associated with VF progression, whereas worse baseline VF MD (HR; 0.718, $P = 0.008$) was found to be associated with optic disc/RNFL progression (Table 5).

Discussion

Myopia is extremely prevalent in Asian countries, especially in the young.[18,28,29] Our present study found that approximately 52% of all analyzed glaucomatous eyes were myopic, including 10.8% of the total eyes that were highly myopic (lower than –6 D). Thus, myopia presents as a frequent condition in Asian glaucomatous eyes. Considering this finding, a determination of whether myopia is a risk factor for glaucoma progression or not is of paramount importance for the management and care of affected individuals.

Table 2. Univariate and Multivariate Cox Proportional Hazard Model With Backward Elimination for Predicting Glaucoma Progression Using VF and Optic Disc/RNFL Photographic Assessments, Respectively

	VF				Optic Disc/RNFL			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Age	1.008 (0.984–1.032)	0.516			1.005 (0.989–1.022)	0.521		
Sex, male = 1	1.012 (0.563–1.817)	0.969			0.865 (0.573–1.304)	0.488		
CCT	1.005 (0.995–1.016)	0.343			1.000 (0.994–1.005)	0.878		
Baseline IOP	1.057 (0.998–1.121)	0.060			1.009 (0.962–1.058)	0.726		
Mean follow-up IOP	1.078 (0.961–1.209)	0.202			0.979 (0.902–1.063)	0.620		
Baseline VF MD	0.910 (0.877–0.945)	<0.001			0.916 (0.890–0.942)	<0.001	0.949 (0.914–0.986)	0.007
Baseline RNFL thickness	0.942 (0.921–0.965)	<0.001	0.942 (0.921–0.965)	<0.001	0.958 (0.943–0.973)	<0.001	0.971 (0.952–0.991)	0.004
Baseline GCIPL thickness	0.936 (0.910–0.963)	<0.001			0.952 (0.934–0.971)	<0.001		
*NMG	Reference							
*MMG	0.830 (0.470–1.539)	0.553			1.019 (0.669–1.553)	0.929		
*HMG	0.868 (0.300–2.512)	0.794			0.393 (0.141–1.092)	0.073	0.323 (0.116–0.903)	0.031

* Refractive error was analyzed as a categorical variable (NMG, MMG, and HMG), and HR was calculated as a relative HR when using NMG as a reference.

Table 3. Univariate and Multivariate Cox Proportional Hazard Models With Backward Elimination for Predicting Glaucoma Progression in the NMG Patients

	VF				Optic Disc/RNFL			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Age	1.005 (0.966–1.045)	0.805			0.998 (0.972–1.024)	0.867		
Sex, male = 1	0.901 (0.393–2.065)	0.805			1.042 (0.580–1.870)	0.891		
RE	0.824 (0.492–1.379)	0.460			1.019 (0.788–1.318)	0.884		
CCT	1.003 (0.991–1.014)	0.670			1.003 (0.994–1.012)	0.475		
Baseline IOP	1.102 (1.037–1.172)	0.002	1.089 (1.034–1.148)	0.001	1.001 (0.934–1.072)	0.977		
Mean follow-up IOP	1.135 (0.962–1.340)	0.134			0.957 (0.850–1.077)	0.468		
Baseline VF MD	0.927 (0.877–0.981)	0.021			0.917 (0.879–0.958)	<0.001		
Baseline RNFL thickness	0.928 (0.897–0.961)	<0.001	0.926 (0.893–0.960)	<0.001	0.957 (0.936–0.978)	<0.001		
Baseline GCIPL thickness	0.925 (0.885–0.967)	0.001			0.938 (0.910–0.967)	<0.001	0.939 (0.910–0.968)	<0.001

RE, refractive error.

Table 4. Univariate and Multivariate Cox Proportional Hazard Models With Backward Elimination for Predicting Glaucoma Progression in the MMG Patients

	VF				Optic Disc/RNFL			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Age	0.994 (0.958–1.031)	0.740			1.011 (0.950–1.037)	0.418		
Sex, male = 1	0.813 (0.322–2.050)	0.660			0.767 (0.419–1.405)	0.391		
RE	0.875 (0.669–1.145)	0.332			1.090 (0.892–1.332)	0.398		
CCT	1.016 (0.997–1.036)	0.095			0.999 (0.989–1.009)	0.827		
Baseline IOP	1.022 (0.924–1.131)	0.672			1.033 (0.962–1.109)	0.375		
Mean follow-up IOP	1.057 (0.888–1.259)	0.534			1.044 (0.929–1.174)	0.467		
Baseline VF MD	0.899 (0.850–0.950)	<0.001	0.899 (0.850–0.950)	<0.001	0.920 (0.884–0.957)	<0.001		
Baseline RNFL thickness	0.956 (0.925–0.993)	0.018			0.955 (0.934–0.977)	<0.001	0.955 (0.934–0.977)	<0.001
Baseline GCIPL thickness	0.963 (0.920–1.007)	0.098			0.949 (0.921–0.978)	0.001		

Table 5. Univariate and Multivariate Cox Proportional Hazard Models With Backward Elimination for Predicting Glaucoma Progression in the HMG Patients

	VF				Optic Disc/RNFL			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Age	1.081 (0.989–1.181)	0.087			0.937 (0.858–1.024)	0.153		
Sex, male = 1	0.019 (0.000–66.746)	0.343			0.680 (0.093–4.700)	0.680		
RE	0.848 (0.704–1.023)	0.086			1.432 (0.706–2.902)	0.319		
CCT	0.971 (0.900–1.049)	0.458			0.966 (0.933–1.000)	0.049		
Baseline IOP	0.858 (0.628–1.174)	0.340			0.983 (0.743–1.299)	0.902		
Mean follow-up IOP	0.940 (0.551–1.602)	0.820			0.690 (0.346–1.378)	0.293		
Baseline VF MD	0.842 (0.714–0.993)	0.042			0.789 (0.656–0.949)	0.012	0.718 (0.563–0.917)	0.008
Baseline RNFL thickness	0.903 (0.812–1.003)	0.058			0.942 (0.865–1.026)	0.169		
Baseline GCIPL thickness	0.845 (0.755–0.946)	0.003	0.845 (0.755–0.946)	0.003	0.973 (0.893–1.059)	0.522		

According to longitudinal follow-up results for our current glaucoma cohort, myopia was not associated with glaucoma progression. We categorized our glaucoma patients into three groups based on the spherical equivalent. Neither the MMG nor the HMG categorization was a significant covariate for progression. Because glaucomatous damage is assessed based on structural changes in the optic disc/RNFL or functional changes in the VF, and as these structural and functional changes may not occur simultaneously in some eyes,[30] we independently used both optic disc/RNFL photographic assessments and VF exams as progression criteria. The refractive error category was found not to be a risk factor for either criterion. Interestingly, high myopia was observed to be a significant preventive factor for progression when using optic disc/RNFL photographic assessment as a criterion. This correlation may be explained by the increased difficulty in detecting progression by optic disc/RNFL photographs in highly myopic glaucomatous eyes.

Highly myopic eyes have a tendency to show a tilted optic disc with large peripapilllary atrophy, which makes it difficult to assess glaucomatous neuroretinal rim changes.[31] A lightly pigmented fundus also obscures the detection of changes in the RNFL. Hence, when adopting optic disc or RNFL photographic change as a criterion for glaucoma progression, prevalence of glaucoma progression may appear to be low because the detection rate is low. Another possible explanation is that glaucomatous structural progression per se is lower in highly myopic eyes. A myopic optic disc/RNFL change may mimic the glaucomatous optic disc/RNFL appearance. Therefore, myopic eyes that show a glaucomatous optic disc appearance may not be true glaucoma cases.[32] Hence, these eyes would not show glaucomatous progression. In other words, the HMG group may be mixed, with eyes that mimic glaucomatous optic disc and true glaucomatous eyes; this heterogeneity may lead to the lower prevalence of structural progression in HMG. This is speculation, however, and thus warrants further investigation. Additionally, the HMG group was the youngest among three groups, which may affect the outcome. However, our observation that the category of refractive error was not a significant risk factor when using the VF criterion may suggest that no level of myopia is associated with glaucoma progression in our study.

Because refractive errors are based on a numerical scale, they could be analyzed as a continuous variable rather than by the categorization into groups in our current analysis. However, we assumed that the MMG and the HMG cases may have different characteristics in which the use of the refractive error as a continuous variable may bias the result. Hence, we included the categorical covariate as a refractive error in our present analysis. However, we also performed analysis that included the refractive error as a continuous variable, and we again found that this parameter was not a significant factor for progression using either optic disc/RNFL or VF assessment as the progression criterion (data not shown).

We characterized the risk factors for glaucoma progression in each of the three groups separately with the assumption that the characteristics of glaucoma may differ among different refractive error groups. Kimura et al.[23] compared highly myopic and nonhighly myopic glaucomatous eyes for RNFL defect location and reported that high myopia is significantly associated with the nearest RNFL defect involving the papillomacular bundle. Considering that typical glaucomatous RNFL changes start at inferotemporal locations in the optic disc, this pattern of central involvement in highly myopic glaucoma is different from the usual glaucomatous pattern. Consequently, we explored whether risk factors for progression would differ among nonmyopic, mild to moderate, and highly myopic eyes. Our findings demonstrated that the risk factors for glaucoma progression are not significantly different among these subgroups. The baseline glaucoma severity, which was assessed by VF MD or OCT RNFL/GCIPL thickness, was found in our current analyses to be associated with glaucoma progression in all three study groups. Optic disc hemorrhage has been reported to be a strong risk factor for glaucoma progression by many publications.[33–35] However, since we included the occurrence of disc hemorrhage as a criterion for optic disc/RNFL progression according to the collaborative normal-tension glaucoma study criterion,[36] we did not include the occurrence of disc hemorrhage in risk factor analysis. Whether optic disc hemorrhage is a sign of glaucoma progression or a risk factor for this progression remains a subject of debate.[37,38]

Our current study has several limitations to note. We included and categorized our participants according to the refractive error. Axial length measurement may be a more direct assessment of the degree of myopia, as myopia can be induced by lens changes or other events. However, axial length is strongly associated with refractive error, and eyes with visually significant lens changes were excluded from our analysis, so those effects might not be great. Since this study was a retrospective one, there is a possibility that subjects were treated with different degrees of aggressiveness with respect to their target pressures. Thus, this should be considered in the interpretation of our results. However, as reported in previous studies, most Korean glaucoma patients have a low baseline IOP.[39,40] Consistently, approximately 80% of our current study cases had a baseline IOP of less than 21 mm Hg. And most of our patients had well-controlled IOP during the follow-up period. Relatively shorter follow-up period should be acknowledged as another limitation.

In conclusion, our results showed that no level of myopia was associated with glaucoma progression using either the VF or optic disc/RNFL criterion. High myopia was a preventive factor for glaucoma progression when using optic disc/RNFL criteria. This may be interpreted as a lower progression detection rate when using structural criteria that occurs because of a difficulty in detecting changes in the optic disc/RNFL in highly myopic eyes, or may mean that some highly myopic glaucomatous eyes are not true cases of glaucoma.

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