근시개방각녹내장에서 부분적 시야 진행의 예후인자 분석

Predictive Factor Analysis of Sectoral Visual Field Progression in Myopic Primary Open Angle Glaucoma

문혜인, 성경림

Haein Moon, MD, Kyung Rim Sung, MD

울산대학교 의과대학 아산병원 안과학교실

Department of Ophthalmology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Purpose: To analyze predictive factors and the progression rate of sectoral visual field progression in myopic primary open angle glaucoma.

Methods: In this retrospective chart review study, eyes were categorized into mild to moderate myopic group (MMG, 0 to -6 diopter [D]) and high myopic group (HMG, < -6D) according to an axial length (26.0 mm) and/or spherical equivalent. The disc tilt ratio, disc torsion angle, torsion angle degree, initial intraocular pressure (IOP), mean IOP, disc hemorrhage, average retinal nerve fiber layer thickness and central corneal thickness were compared and analyzed. Mean deviation (MD) in each sector determined by glaucoma hemifield test location of the visual field was calculated and the progression rates of MD in each sector were obtained with linear regression analysis. Predictive factor for MD progression was determined by using linear regression analysis

Results: A total of 83 eyes were included. There were significant differences in baseline age (52.6 ± 12.1 , 45.5 ± 13.4 years, $p = 0.013$) and disc tilt ratio (1.2 ± 0.1 , 1.3 ± 0.2 , $p < 0.001$) between 2 groups. In linear regression analysis for predictive factors, initial IOP, mean reduction of IOP during follow-up (%), and baseline age were generally associated with progression in MMG. In HMG, IOP and disc hemorrhage were significant predictive factor for progression in superior visual field.

Conclusions: Factors associated with visual field progression were different between mild to moderate and high myopic POAG.

Key words: Myopia, Glaucoma, Visual field

Introduction

High myopia is generally defined as an extremely elongated eye ball which allows seeing only very near sighted object. Of course there are many theoretical causes of myopia, an axial elongation is generally accepted cause of myopia. Axial elongation is the result of scleral remodelling and this

process also cause other structural change, especially on optic disc and macula which are target sites for glaucomatous damage, such as disc torsion and tilt, peripapillary atrophy, large optic disc and disc cupping.¹⁻⁶ Myopia is also related to many ocular disease, for example retinal detachment, cataract, macular degeneration and primary open angle glaucoma (POAG). Among those disease entities, POAG has become to be interested recently. Many studies have reported that myopia is a risk factor for POAG development and many POAG patients also have myopia.⁷⁻¹¹ Traditionally, old age has been considered a risk factor for POAG development, but prevalence of young glaucoma patient is increasing especially in East Asian countries and considerable portion of POAG patients are myopic. Hence, the association between POAG and myopia is of clinical importance.¹²⁻¹⁴

Received: 2018. 4. 10.

Revised: 2018. 5. 10.

Accepted: 2018. 5. 28.

Corresponding Author: Kyung Rim Sung, MD

Department of Ophthalmology, Asan Medical Center, University of Ulsan College of Medicine, #88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea

Tel: +82-2-3010-3680, Fax: +82-2-470-6440

E-mail: sungeye@gmail.com

There are some debates whether high myopia is a risk factor for glaucoma progression or not. Some reports showed high myopia is a risk factor for progression.¹⁵⁻¹⁷ However, other studies did not find the evidence to support this speculation.¹⁸⁻²¹ Recently published Japanese articles, myopia is not a predictive factor but a protective factor of progression not in POAG.^{18,22} As such, we hypothesized conflicting results might be induced from heterogeneity of myopic population. In other words, some of them would progress faster and others would remain stable. Conflicting results may be stem from the proportion of these two groups. And subsequently, there might be some difference between the non-progressive glaucomatous eyes and progressive glaucomatous eyes within high myopic glaucoma group. If we admit that we may not have long enough time to follow the glaucoma patient and to conclude the specific patient has progressed or stable, there might be some difference between the slowly progressing and fast progressing glaucomatous eyes within high myopic glaucoma group at least. There are some studies to find these differences between progressive group and nonprogressive group in myopic POAG and disc tilt ratio and torsion direction are suggested as predictive factors of progression.^{23,24} However, there is also opposite result of these factors.²⁵

To explore this issue, we categorized myopic glaucomatous eyes into two groups according to the level of myopia and compared characteristics between two groups. We compared several aspects, i.e., demographics, clinical features and ocular characteristics. In addition to basic ocular parameters, we included myopia related optic disc change such as optic disc tilt and torsion determined by spectral domain optical coherence tomography (SD-OCT) imaging. If we find the factors associated with progression in high myopic glaucomatous eyes, it would be beneficial to treat high myopic glaucomatous eyes by predicting the prognosis and controlling the risk factors.

Materials and Methods

Subjects

We performed a retrospective review of the medical re-

cords of all subjects who were evaluated by a single glaucoma specialist at the glaucoma clinic of the Asan Medical Center from March 2008 to May 2015. Subjects who met the inclusion criteria were consecutively enrolled. At the initial test, each participant received a comprehensive ophthalmological examination, including a review of their medical history, measurement of best-corrected visual acuity (BCVA), 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, retinal nerve fiber layer (RNFL) photography, a visual field test (VF), axial length (AL) measurement (IOL Master, Carl Zeiss Meditec Inc., Dublin, CA, USA), and SD-OCT imaging (Spectralis, Heidelberg Engineering, Dossenheim, Germany). To be included in the study, participants had to meet the following criteria at their initial assessment: BCVA of 20/40 or better, the presence of a normal anterior chamber, and an open-angle on slit-lamp and gonioscopic examinations, $AL \geq 26.0$ mm, spherical equivalent (SE) < 0 D, glaucomatous optic nerve damage (the presence of focal thinning of the neuroretinal rim or notching and an RNFL defects) and glaucomatous VF defect; these findings were confirmed and agreed upon by two glaucoma specialists. 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 outside 95% of normal limits. We excluded participants with any other ophthalmic or neurological condition that could result in a VF defect, or 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 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

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 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

VF 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 total 3 VF tests were performed within the first 6 weeks. The very first VF test data was excluded to obviate any learning effect. Therefore, the second and third VF results which were performed 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.

Optic Disc Torsion and Tilt Assessment

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 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.^{3,5} 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. When the tilt ratio was > 1.3, the

optic disc was classified as tilted disc.^{25,26} Optic disc torsion was defined as the deviation of the long axis of the optic disc from the vertical meridian according to previously described criteria.^{3,5} 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.^{25,26} When the torsion degree was > 10°, the optic disc was classified as torsional disc. The each cut-off-value of torsion and tilt was determined according to the result of area under receiver operating characteristics curve, AUROC using SPSS version 19.0 (SPSS, Chicago, IL, USA) analysis program.

Calculation of Visual Field Progression Rate and Assessment of Progression

Visual field was divided into each sector according to GHT area. In total deviation map, sectoral mean deviation (MD) was calculated as the sum of each point values decibel (dB) divided with the number of points in each GHT sector (Fig. 1).²⁷ Because GHT provides five corresponding and mirrored areas in the superior and inferior visual fields,

Figure 1. Glaucoma hemifield test (GHT) area.

there are total 10 sectors per each VF test. Progression rate in each sector in each subject during follow-up period was calculated with linear regression analysis.²⁶

VF 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 MD data. If the sectoral mean deviation rate calculated with linear regression was lower than -1, we defined that as progression.

Statistical Analysis

The independent *t*-test was used to compare the demographic and clinical characteristics after the normality of the data was checked. The Pearson chi square test for independence and Fischer's exact test were used to compare categorical data. Continuous variables were expressed as the mean $\pm$ standard deviation. Variables included age, gender, tilt ratio, torsion direction, absolute torsional degree, AL, baseline VF MD, CCT, SE, baseline untreated intraocular pressure (IOP), mean follow-up IOP, mean reduction of follow-up IOP (IOP reduction [%] from baseline visit was calculated at each visit and mean value of all visits were calculated), SD-OCT-measured average RNFL thickness, disc hemorrhage, and follow-up duration. We categorized all participants into two groups, moderate myopic group (MMG) group and high myopic group (HMG) group. Subjects were also categorized into 2 groups according to progression and the variables were also compared. The expectant regression coefficient (Exp [B]) for the association between factors and each sectoral MD rate were determined by using logistic regression analysis. Univariable analyses were separately performed for each variable. Variables with $p < 0.2$ on the univariable analysis were included in the multivariable Cox proportional hazards model. A backward elimination process was used to develop the final multivariable model, and adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated

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

Result

A total of 83 myopic glaucomatous eyes were included in the final analysis. Among the subjects, 53 were men (63.9%), and all were Koreans. The mean age was 48.8 ± 13.3 years and the follow-up period was 40.4 ± 20.4 months. The mean optic disc tilt ratio was 1.2 ± 0.2 , the absolute torsional degree was 6.51 ± 5.14 degree, and 31 eyes (36.1%)

Table 1. Demographics and clinical characteristics of subjects (n = 83)

Gender (male:female)	53 (63.9%):30 (36.1%)
Age	48.8 ± 13.3
Tilt ratio	1.2 ± 0.2
Tilt group, n (%) [*]	30 (36.1)
Absolute torsional degree	6.51 ± 5.14
Positive torsional direction, n (%)	31 (37.3)
Torsion group, n (%) [†]	20 (24.1%)
Spherical equivalent (D)	-5.5 ± 3.4
Baseline IOP	17.5 ± 4.8
Mean F/U IOP	14.3 ± 2.3
Mean reduction of IOP (%)	15.6 ± 11.0
Central corneal thickness	533.4 ± 37.6
Average RNFL thickness	69.4 ± 10.7
Axial length	26.5 ± 1.9
Disc hemorrhage, n (%)	11 (13.3)
Initial MD (dB)	-5.86 ± 4.7
Follow-up duration (months)	40.4 ± 20.4

IOP = intraocular pressure; F/U = follow up; RNFL = retinal nerve fiber layer; MD = mean deviation.

^{*}Tilt group: tilt ratio ≥ 1.3 ; [†]Torsion group: absolute torsion degree ≥ 10 degree.

Table 2. Comparison of demographics and clinical characteristics between MMG group and HMG group

	MMG (n = 39)	HMG (n = 44)	p-value
Gender (male:female)*	23:16	30:14	0.384
Age†	52.6 ± 12.1	45.5 ± 13.4	0.013
Tilt ratio‡	1.2 ± 0.1	1.3 ± 0.2	0.000
Absolute torsional degree‡	6.2 ± 4.8	6.8 ± 5.5	0.590
Positive torsion group, n§	13	18	0.476
Spherical equivalent (D)†	-3.3 ± 1.6	-7.5 ± 3.4	0.000
Baseline IOP‡	17.6 ± 3.7	17.4 ± 5.6	0.215
Mean F/U IOP†	14.7 ± 2.3	14.0 ± 2.2	0.162
Mean reduction of IOP (%)‡	15.0 ± 8.7	16.2 ± 12.7	0.913
Central corneal thickness‡	535.9 ± 36.8	531.2 ± 38.6	0.596
Average RNFL thickness†	69.6 ± 9.8	69.1 ± 11.6	0.832
Axial length†	24.7 ± 0.6	27.6 ± 1.4	0.000
Disc hemorrhage, n§	3	8	0.204
Initial MD (dB)‡	-6.12 ± 5.33	-5.27 ± 4.29	0.743
Follow-up duration (months)†	39.4 ± 18.6	41.2 ± 22.1	0.700

MMG = moderate myopic group; HMG = high myopic group; IOP = intraocular pressure; F/U = follow up; RNFL = retinal nerve fiber layer; MD = mean deviation.

*Pearson chi square test for independence; †Independent-sample t-test; ‡Mann-Whitney test; §Fischer's exact test.

Table 3. Multivariable logistic regression analysis for prediction of progression of each superior GHT sector in MMG

GHT sector	Variable	Multivariable logistic regression analysis	
		β coefficient (95% CI)	p-value
Superior 1 sector	Age	-0.081 (-0.147, -0.015)	0.02
	Initial IOP	-2.976 (-5.520, -0.433)	0.025
	Mean follow-up IOP	3.567 (0.340, 6.794)	0.032
	Mean reduction of follow-up IOP	0.747 (0.158, 1.336)	0.016
Superior 2 sector	Initial IOP	-2.745 (-4.415, -1.075)	0.003
	Mean follow-up IOP	3.035 (0.916, 5.154)	0.008
	Mean reduction of follow-up IOP	0.631 (-0.161, -0.011)	0.004
Superior 3 sector	Age	-0.086 (-0.161, -0.011)	0.028
	Initial IOP	-3.162 (-5.613, -0.710)	0.015
	Mean follow-up IOP	3.686 (0.587, 6.785)	0.023
	Mean reduction of follow-up IOP	0.726 (0.162, 1.290)	0.016
Superior 4 sector	Age	-0.064 (-0.116, -0.013)	0.017
	Initial IOP	-3.450 (-5.430, -1.471)	0.002
	Mean follow-up IOP	3.830 (1.319, 6.341)	0.005
	Mean reduction of follow-up IOP	0.775 (0.317, 1.233)	0.003
Superior 5 sector	Age	-2.507 (-4.956, -0.058)	0.045
	Mean follow-up IOP	0.575 (0.006, 1.144)	0.048

GHT = glaucoma hemifield test; MMG = moderate myopic group; CI = confidence interval; IOP = intraocular pressure.

Table 4. Multivariable logistic regression analysis for prediction of progression of each inferior GHT sector in MMG

GHT sector	Variable	Multivariable logistic regression analysis	
		β coefficient (95% CI)	p-value
Inferior 1 sector	Age	-0.149 (-0.221, -0.076)	0.001
	Average RNFL thickness	-0.151 (-0.235, -0.066)	0.002
	Initial IOP	-2.665 (-4.509, -0.821)	0.008
	Mean follow-up IOP	3.502 (1.169, 5.835)	0.006
	Mean reduction of follow-up IOP	0.726 (0.300, 1.151)	0.003
	AL	-1.640 (-2.925, -0.356)	0.016
Inferior 2 sector	Age	-0.047 (-0.078, -0.016)	0.006
	Initial IOP	-1.891 (-2.887, -0.895)	0.001
	Mean follow-up IOP	2.367 (1.107, 3.627)	0.001
	Mean reduction of follow-up IOP	0.392 (0.162, 0.622)	0.003
	Baseline sectoral MD	0.135 (0.073, 0.197)	0.000
Inferior 3 sector	Age	-0.192 (-0.270, -0.115)	0.000
	Average RNFL thickness	-0.154 (-0.237, -0.072)	0.002
	Disc tilt ratio	-11.536 (-21.334, -1.739)	0.025
	Initial IOP	-4.282 (-5.929, -2.634)	0.000
	Mean follow-up IOP	5.382 (3.295, 7.469)	0.000
	Mean reduction of follow-up IOP	0.983 (0.603, 1.363)	0.000
Inferior 4 sector	AL	-1.782 (-2.952, -0.611)	0.006
	Age	-0.061 (-0.101, -0.021)	0.006
	Initial IOP	-1.792 (-3.095, -0.489)	0.011
	Mean follow-up IOP	2.271 (0.631, 3.911)	0.010
	Mean reduction of follow-up IOP	0.370 (0.069, 0.671)	0.020
Inferior 5 sector	Baseline sectoral MD	0.141 (0.048, 0.233)	0.006
	Age	-0.028 (-0.051, -0.005)	0.021
	Initial IOP	-1.289 (-2.074, -0.504)	0.004
	Mean follow-up IOP	1.510 (0.516, 2.504)	0.006
	Mean reduction of follow-up IOP	0.292 (0.105, 0.478)	0.005
	Baseline sectoral MD	-0.064 (-0.119, -0.010)	0.024

GHT = glaucoma hemifield test; MMG = moderate myopic group; CI = confidence interval; RNFL = retinal nerve fiber layer; IOP = intraocular pressure; AL = axial length.

had positive torsion direction (Table 1). Of the 83 eyes analyzed, 44 eyes were categorized into HMG group and they were younger and had more tilted disc than MMG group (Table 2).

In multivariable logistic regression analysis, age, initial IOP, and mean reduction of follow-up IOP were generally significantly related progression factors in superior GHT in MMG (Table 3). In inferior GHT in MMG, age, initial IOP, mean reduction of follow-up IOP, and mean follow-up IOP

were significant factors of progression in all sectors, and in several sectors, AL, average RNFL thickness, and baseline sectoral MD were found to be progression factor. Disc tilt was related to progression in inferior 3 sector (Table 4). In HMG, initial IOP and disc hemorrhage were found to be significantly predictive of progression in superior sector, and the only AL was significant factor in inferior sector (Table 5).

We also analyzed subjects sub-grouped into progression

Table 5. Multivariable logistic regression analysis for prediction of progression of each GHT sector in HMG

GHT sector	Variable	Multivariable logistic regression analysis	
		β coefficient (95% CI)	p-value
Superior 1 sector	Disc hemorrhage	-1.555 (-2.399, -0.711)	0.001
	Initial IOP	-0.172 (-0.332, -0.012)	0.036
Superior 2 sector	Disc hemorrhage	-1.538 (-2.882, -0.194)	0.026
Superior 3 sector	Initial IOP	-0.284 (-0.491, -0.077)	0.009
	AL	0.447 (0.110, 0.783)	0.011
Superior 5 sector	Disc hemorrhage	-2.109 (-3.955, -0.263)	0.027
	AL	0.595 (0.028, 1.163)	0.040
Inferior 2 sector	AL	-0.187 (-0.350, -0.024)	0.026

GHT = glaucoma hemifield test; HMG = high myopic group; CI = confidence interval; IOP = intraocular pressure; AL = axial length.

Table 6. Comparison of demographics and clinical characteristics between progression group and non progression group (n = 83)

	Progression group (n = 36)	Non progression group (n = 47)	p-value
Gender (male:female)*	25:11	28:19	0.354
Age†	50.5 ± 14.8	47.6 ± 11.9	0.319
Tilt ratio‡	1.22 ± 0.17	1.26 ± 0.18	0.211
Tilt group, n*	10	20	0.165
Absolute torsional degree‡	6.33 ± 5.43	6.65 ± 4.95	0.330
Torsion group, n	10	10	0.492
Positive torsional direction, n (%)*	13	18	0.838
Spherical equivalent (D)‡	-5.61 ± 3.11	-5.44 ± 3.60	0.682
Baseline IOP‡	18.4 ± 5.6	16.7 ± 3.9	0.114
Mean F/U IOP†	14.7 ± 2.4	14.1 ± 2.2	0.177
Mean reduction of IOP (%)‡	17.3 ± 11.6	14.4 ± 10.4	0.144
Central corneal thickness†	534.0 ± 35.2	532.9 ± 39.6	0.898
Average RNFL thickness†	67.7 ± 10.1	70.7 ± 11.1	0.213
Axial length†	26.5 ± 1.8	26.6 ± 1.9	0.884
Disc hemorrhage, n§	7	4	0.196
Baseline MD (dB)‡	-7.46 ± 5.48	-4.29 ± 3.70	0.006
MD rate†	-0.81 ± 0.98	+0.11 ± 0.41	0.000
Total rate‡	-0.83 ± 1.08	+0.22 ± 0.38	0.000
Follow-up duration (months)†	31.2 ± 19.1	47.4 ± 18.7	0.000

IOP = intraocular pressure; F/U = follow up; RNFL = retinal nerve fiber layer; MD = mean deviation.

*Pearson chi square test for independence; †Independent-sample t-test; ‡Mann-Whitney test; §Fischer's exact test.

group and non-progression group. Between the two groups, baseline MD, MD rate, total rate, and follow-up duration were significantly different (Table 6). Subgroup analysis was performed according to progression area. Superior sector progression and inferior sector progression were found in 25 eyes and 21 eyes respectively. baseline MD, MD rate,

and follow-up duration were significantly different in each subgroup compared to non progression group (Table 7, 8). Between superior sector and inferior sector progression group, only baseline total MD was significantly different (Table 9).

Disc hemorrhage (HR = 3.917, $p = 0.002$), disc tilt (HR =

Table 7. Comparison of demographics and clinical characteristics between superior sector progression group and non progression group (n = 72)

	Superior sector progression group (n = 25)	Non progression group (n = 47)	p-value
Gender (male:female)*	18:7	28:19	0.296
Age†	50.2 ± 16.8	47.5 ± 11.9	0.483
Tilt ratio‡	1.22 ± 0.17	1.26 ± 0.18	0.306
Tilt group, n*	7	20	0.225
Absolute torsional degree‡	5.79 ± 5.23	6.65 ± 4.95	0.158
Torsion group, n*	6	10	0.791
Positive torsional direction, n (%)*	9	18	0.848
Spherical equivalent (D)†	-5.21 ± 2.91	-5.44 ± 3.60	0.788
Baseline IOP‡	19.1 ± 6.4	16.7 ± 3.9	0.059
Mean F/U IOP†	15.0 ± 2.56	14.1 ± 2.20	0.093
Mean reduction of IOP (%)‡	18.2 ± 12.9	14.4 ± 10.4	0.093
Central corneal thickness†	535.3 ± 36.1	532.9 ± 39.6	0.811
Average RNFL thickness†	70.64 ± 9.41	70.66 ± 11.08	0.994
Axial length†	26.2 ± 1.5	26.6 ± 1.9	0.474
Disc hemorrhage, n§	6	4	0.085
Baseline MD (dB)‡	-8.84 ± 6.18	-5.29 ± 6.04	0.005
Superior MD rate†	-1.54 ± 1.69	0.24 ± 0.48	0.000
Follow-up duration (months)†	31.7 ± 18.7	47.4 ± 18.7	0.001

IOP = intraocular pressure; F/U = follow up; RNFL = retinal nerve fiber layer; MD = mean deviation.

*Pearson chi square test for independence; †Independent-sample *t*-test; ‡Mann-Whitney test; §Fischer's exact test.**Table 8.** Comparison of demographics and clinical characteristics between inferior sector progression group and non progression group (n = 68)

	Inferior sector progression group (n = 21)	Non progression group (n = 47)	p-value
Gender (male:female)*	14:7	28:19	0.578
Age†	52.2 ± 14.1	47.5 ± 11.9	0.166
Tilt ratio‡	1.19 ± 0.14	1.26 ± 0.18	0.091
Tilt group, n§	20	4	0.098
Absolute torsional degree‡	6.38 ± 5.40	6.65 ± 4.95	0.478
Torsion group, n*	6	10	0.512
Positive torsional direction, n (%)*	9	18	0.723
Spherical equivalent (D)†	-5.74 ± 3.26	-5.44 ± 3.60	0.742
Baseline IOP‡	18.1 ± 4.2	16.7 ± 3.9	0.163
Mean F/U IOP‡	15.1 ± 2.6	14.1 ± 2.2	0.112
Mean reduction of IOP (%)‡	15.2 ± 7.6	14.4 ± 10.4	0.550
Central corneal thickness‡	531.7 ± 35.7	532.9 ± 39.6	0.914
Average RNFL thickness†	66.33 ± 11.05	70.66 ± 11.08	0.141
Axial length†	26.7 ± 2.0	26.6 ± 1.9	0.890
Disc hemorrhage, n§	3	4	0.668
Baseline MD (dB)‡	-8.29 ± 6.24	-3.65 ± 3.86	0.001
Inferior MD rate†	-1.01 ± 1.4	0.20 ± 0.37	0.000
Follow-up duration (months)†	29.4 ± 18.4	47.4 ± 18.7	0.000

IOP = intraocular pressure; F/U = follow up; RNFL = retinal nerve fiber layer; MD = mean deviation.

*Pearson chi square test for independence; †Independent-sample *t*-test; ‡Mann-Whitney test; §Fischer's exact test.

Table 9. Comparison of demographics and clinical characteristics between superior sector progression group and inferior sector progression group (n = 36)

	Superior sector progression group (n = 25)	Inferior sector progression group (n = 21)	p-value
Gender (male:female)*	18:7	14:7	0.695
Age†	50.2 ± 16.8	52.2 ± 14.1	0.676
Tilt ratio‡	1.22 ± 0.17	1.19 ± 0.15	0.421
Tilt group, n§	7	4	0.514
Absolute torsional degree‡	5.79 ± 5.23	6.38 ± 5.40	0.683
Torsion group, n*	6	6	0.725
Positive torsional direction, n (%)*	9	9	0.764
Spherical equivalent (D)†	-5.21 ± 2.91	-5.74 ± 3.26	0.563
Baseline IOP‡	19.1 ± 6.4	18.1 ± 4.2	0.773
Mean F/U IOP‡	15.0 ± 2.6	15.1 ± 2.6	0.974
Mean reduction of IOP (%)†	18.2 ± 12.9	15.2 ± 7.6	0.356
Central corneal thickness†	535.3 ± 36.1	531.7 ± 35.7	0.756
Average RNFL thickness†	70.64 ± 9.41	66.33 ± 11.05	0.160
Axial length†	26.2 ± 1.5	26.7 ± 2.0	0.464
Disc hemorrhage, n§	6	3	0.478
Baseline total MD (dB)†	-5.81 ± 4.77	-10.02 ± 5.58	0.008
MD rate†	-0.97 ± 1.11	-0.97 ± 1.11	0.997
Total MD rate†	-1.10 ± 1.19	-0.89 ± 1.20	0.552
Follow-up duration (months)†	31.7 ± 18.7	29.4 ± 18.4	0.677

IOP = intraocular pressure; F/U = follow up; RNFL = retinal nerve fiber layer; MD = mean deviation.

*Pearson chi square test for independence; †Independent-sample *t*-test; ‡Mann-Whitney test; §Fischer's exact test.**Table 10.** Multivariable Cox proportional hazard model data for prediction of progression

Group	Variable	multivariable Cox proportional hazard ratio analysis	
		HR (95% CI)	p-value
Progression	Disc hemorrhage	3.917 (1.625–9.445)	0.002
	Tilt group	0.460 (0.217–0.979)	0.044
	Initial visual field MD	0.922 (0.868–0.980)	0.009
Superior sectoral VF progression	Disc hemorrhage	6.908 (2.356–20.250)	0.000
	Tilt ratio	0.032 (0.002–0.503)	0.014
	Superior baseline MD	0.924 (0.866–0.987)	0.018
	Mean follow-up IOP	1.255 (1.020–1.544)	0.032
Inferior sectoral VF progression	Disc hemorrhage	5.363 (1.319–21.801)	0.019
	Tilt group	0.222 (0.068–0.721)	0.012
	Inferior baseline MD	0.865 (0.802–0.934)	0.000

HR = hazard ratio; CI = confidence interval; MD = mean deviation; VF = visual field test; IOP = intraocular pressure.

0.460, $p = 0.044$) and initial visual field MD (HR = 0.922, $p = 0.009$) were found to be significantly predictive of progression by the multivariable Cox proportional hazards

model. Disc hemorrhage, disc tilt and each sectoral baseline MD were found to be significantly predictive of progression and mean follow-up IOP (HR = 1.255, $p = 0.032$) was addi-

tionally significant factor in superior sectoral VF progression group (Table 10).

Discussion

Myopia is highly prevalent disease in Asian and a number of normal tension glaucoma (NTG) patient also have myopia. The relationship between myopia and glaucoma is a rising issue for myopic POAG and NTG patient management in these countries.^{12-14,20} Recently, many studies investigating that myopic structural change has effect on development and progression of glaucoma were conducted. One of them is focusing on the theory that disc tilt and torsion would be a predictive factor for progression of myopic POAG.²⁸⁻³⁰ Disc tilt and torsion is one of them that considered as predictive factor for progression of glaucoma and being studied.²⁸⁻³⁰ Sung et al.²³ had demonstrated that disc hemorrhage, reduction of IOP, and disc tilt were associated with progression of VF in myopic NTG eyes and disc torsion was not associated with progression of VF in them. In that study, Myopic eyes with progression had a smaller optic disc tilt ratio and the non-tilted eyes had a greater probability of progression than the tilted group in the Kaplan-Meier survival analysis. In our study, the result also demonstrated that disc tilt had a low risk for progression (HR = 0.460, $p = 0.044$) and even for the sectoral VF progression with Cox proportional hazard model (Table 10).

Intraocular pressure and disc hemorrhage were predictive factors for progression in this study as proved previous many studies (Table 10).³¹⁻³⁴ Disc hemorrhage is especially associated deteriorating superior sectoral MD rate in HMG with multivariable logistic regression analysis (Table 5). We also analyzed location of disc hemorrhage and most disc hemorrhage was located in lower half of disc (data is not shown), the superior sectoral VF MD progression corresponded that result anatomically. On the other hand, in MMG, disc hemorrhage was not associated with sectoral VF MD progression. Possible theory for explanation of this observation is more prominent axial elongation with structural change in high myopic eye. With axial elongation, choroid and sclera is flexible tissue and could be elongated

along with axial elongation, but vessels is not well stretched and flexible, vessels would be stressed and be vulnerable structurally. Further investigation for this issue should be needed.

Our study had several limitations. First, we excluded profoundly progressed myopic POAG eyes. Because the purpose of this study was to evaluate associated factors for progression, eyes with late stage were not appropriate to analyze progression and had a difficulty to analyze. Hence, we can't sure that there is no other factor that has effect on progression but is not proved in this study. Second, eyes with pathologically structural change due to very high myopia were excluded because of the difficulty to evaluate the disc tilt and torsion. The weakness of the exclusion is elimination of a possibility of actual relationship between pathologic structural change with glaucoma showing more obvious effect of myopia. Therefore, in highly myopic POAG eyes with pathologic change, this result has limited to apply. Third, some of our patients were imaged with Cirrus HD OCT and others with Spectralis OCT. However, measurements by two different devices did not demonstrate significant differences (data is not shown), we combined those two measures to evaluate the RNFL thickness. Fourth, our participants were all myopic and myopia is more prevalent in younger POAG patient, therefore, subjects in this study were relatively young (mean age, 48.8 years) compared with those of the general glaucoma population, and hence our results should be interpreted with caution in this regard.

However, as far as our present knowledge goes, this is the first study to analyze sectoral VF MD progression and predictive factors for sectoral VF progression. The analysis also included previous mentioned anatomical change of myopic POAG eyes.

In conclusion, myopic POAG is heterogenous group and therefore, there would be many confounding factors in analysis of progression factor. Myopic eyes with tilted optic disc demonstrated a smaller optic disc tilt may be protective against glaucoma progression in some sectors. Disc hemorrhage and IOP were still significant progression factors in myopic POAG eyes as in non-myopic POAG eyes.

References

1. Goldschmidt E. Ocular morbidity in myopia. *Acta Ophthalmol Suppl* 1988;185:86-7.
2. McBrien NA, Gentle A. Role of the sclera in the development and pathological complications of myopia. *Prog Retin Eye Res* 2003;22:307-38.
3. Tay E, Seah SK, Chan SP, et al. Optic disk ovality as an index of tilt and its relationship to myopia and perimetry. *Am J Ophthalmol* 2005;139:247-52.
4. Tokoro T. On the definition of pathologic myopia in group studies. *Acta Ophthalmol Suppl* 1988;185:107-8.
5. 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;133:679-85.
6. Kim TW, Kim M, Weinreb RN, et al. Optic disc change with incipient myopia of childhood. *Ophthalmology* 2012;119:21-6.e1-3.
7. Marcus MW, de Vries MM, Junoy Montolio FG, Jansonius NM. Myopia as a risk factor for open-angle glaucoma: a systematic review and meta-analysis. *Ophthalmology* 2011;118:1989-94.e2.
8. Mitchell P, Hourihan F, Sandbach J, Wang JJ. The relationship between glaucoma and myopia: the Blue Mountains Eye Study. *Ophthalmology* 1999;106:2010-5.
9. Suzuki Y, Iwase A, Araie M, et al. Risk factors for open-angle glaucoma in a Japanese population: the Tajimi Study. *Ophthalmology* 2006;113:1613-7.
10. Wu SY, Nemesure B, Leske MC. Refractive errors in a black adult population: the Barbados Eye Study. *Invest Ophthalmol Vis Sci* 1999;40:2179-84.
11. Xu L, Wang Y, Wang S, et al. High myopia and glaucoma susceptibility the Beijing Eye Study. *Ophthalmology* 2007;114:216-20.
12. Lam CS, Goldschmidt E, Edwards MH. Prevalence of myopia in local and international schools in Hong Kong. *Optom Vis Sci* 2004;81:317-22.
13. Lee SJ, Urm SH, Yu BC, et al. The prevalence of high myopia in 19 year-old men in Busan, Ulsan and Gyeong-sangnam-do. *J Prev Med Public Health* 2011;44:56-64.
14. Wong TY, Foster PJ, Hee J, et al. Prevalence and risk factors for refractive errors in adult Chinese in Singapore. *Invest Ophthalmol Vis Sci* 2000;41:2486-94.
15. 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.
16. Perdicchi A, Iester M, Scuderi G, et al. Visual field damage and progression in glaucomatous myopic eyes. *Eur J Ophthalmol* 2007;17:534-7.
17. Lee YA, Shih YF, Lin LL, et al. Association between high myopia and progression of visual field loss in primary open-angle glaucoma. *J Formos Med Assoc* 2008;107:952-7.
18. Araie M, Shirato S, Yamazaki Y, et al. Risk factors for progression of normal-tension glaucoma under β -blocker monotherapy. *Acta ophthalmol* 2012;90:e337-43.
19. Doshi A, Kreidl KO, Lombardi L, et al. Nonprogressive glaucomatous cupping and visual field abnormalities in young Chinese males. *Ophthalmology* 2007;114:472-9.
20. Lee JY, Sung KR, Han S, Na JH. Effect of myopia on the progression of primary open-angle glaucoma. *Invest Ophthalmol Vis Sci* 2015;56:1775-81.
21. Sohn SW, Song JS, Kee C. Influence of the extent of myopia on the progression of normal-tension glaucoma. *Am J Ophthalmol* 2010;149:831-8.
22. 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;22:250-4.
23. Sung MS, Kang YS, Heo H, Park SW. Optic disc rotation as a clue for predicting visual field progression in myopic normal-tension glaucoma. *Ophthalmology* 2016;123:1484-93.
24. Han JC, Lee EJ, Kim SH, Kee C. Visual field progression pattern associated with optic disc tilt morphology in myopic open-angle glaucoma. *Am J Ophthalmol* 2016;169:33-45.
25. 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;56:6925-31.
26. Heijl A, Leske MC, Bengtsson B, et al. Measuring visual field progression in the Early Manifest Glaucoma Trial. *Acta Ophthalmol Scand* 2003;81:286-93.
27. Åsman P, Heijl A. Glaucoma hemifield test: automated visual field evaluation. *Arch Ophthalmol* 1992;110:812-9.
28. 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;56:2958-67.
29. 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;119:1844-51.
30. Lee KS, Lee JR, Kook MS. Optic disc torsion presenting as unilateral glaucomatous-appearing visual field defect in young myopic Korean eyes. *Ophthalmology*

- 2014;121:1013-9.
31. Budenz DL, Anderson DR, Feuer WJ, et al. Detection and prognostic significance of optic disc hemorrhages during the ocular hypertension treatment study. *Ophthalmology* 2006;113:2137-43.
 32. Kim KE, Jeoung JW, Kim DM, et al. Long-term follow-up in preperimetric open-angle glaucoma: progression rates and associated factors. Reply: To PMID 25448320. *Am J Ophthalmol* 2015;159:816-7.
 33. Jeoung JW, Park KH, Kim JM, et al. Optic disc hemorrhage may be associated with retinal nerve fiber loss in otherwise normal eyes. *Ophthalmology* 2008;115:2132-40.
 34. Kim SH, Park KH. The relationship between recurrent optic disc hemorrhage and glaucoma progression. *Ophthalmology* 2006;113:598-602.