Master of Science

근시 녹내장 환자에서
시신경유두주위위축의 점진적 변화

Progressive Change in Peripapillary Atrophy
in Myopic Glaucomatous Eyes

The Graduate School
of the University of Ulsan
Department of Medicine
Minkyung Song

Progressive Change in Peripapillary Atrophy in Myopic Glaucomatous Eyes

Supervisior : Kyung Rim Sung

A Dissertation

Submitted to
The Graduate School of the University of Ulsan
In partial Fulfillment of the Requirements
for the degree of

Master of Science

by

Minkyung Song

Department of Medicine
Ulsan, Korea
February 2018

Progressive Change in Peripapillary Atrophy in Myopic Glaucomatous Eyes

This certifies that the dissertation
of Minkyung Song is approved.

Jae Yong Kim
Committee Chair Dr.

Kyung Rim Sung
Committee Member Dr.

Joo Yong Lee
Committee Member Dr.

Department of Medicine
Ulsan, Korea
February 2018

Abstract

Aim: To evaluate the progressive change in peripapillary atrophy (PPA) according to its shape and explore the relationship between PPA progression and glaucoma worsening in myopic eyes.

Methods: A total of 159 eyes of 159 myopic (axial length (AXL) ≥24mm) glaucoma patients (mean follow-up, 4.4 years, 35 eyes with minimal PPA, 40 concentric-type PPA eyes (≥ 270° around the optic disc), and 84 eccentric-type PPA eyes (< 270°)) were included. Sequential stereoscopic color optic disc photographs were evaluated to qualitatively determine PPA progression. Factors associated with PPA progression were explored by Cox proportional hazard modeling in each PPA group.

Results: Concentric PPA patients were older than eccentric PPA patients (54.1 ± 11.7 vs. 44.1 ± 11.7 years, $P < 0.001$), and AXL was longer in the eccentric group than in the other groups (25.54 ± 1.68 vs. 25.28 ± 1.53 vs. 26.41 ± 1.29 mm; $P < 0.001$). 26 eyes (65%) in the concentric group and 36 eyes (42.9%) in the eccentric group showed PPA progression. Older age (hazard ratio (HR; 1.059, $P = 0.008$), lower baseline visual field mean deviation (HR; 0.857, $P = 0.009$), and greater baseline PPA area (HR 1.000, $P = 0.012$) were associated with PPA progression in the concentric type. Glaucoma progression (HR 0.271, $P = 0.002$) and longer AXL (HR 1.521, $P = 0.002$) were associated with PPA progression in the eccentric type.

Conclusions: Relationship between glaucoma worsening and PPA progression was significantly stronger in myopic glaucomatous eyes with eccentric type PPA.

Keywords: glaucoma, myopia, peripapillary atrophy

Index

Tables and Figures

Introduction

Myopia is closely linked to glaucoma development.[1-4] If we accept the theory that the lamina cribrosa is the primary site of glaucomatous damage, it follows that myopic eyes would be more vulnerable to glaucomatous damage, because axially myopic eyes have weaker and thinner sclera and, thus, lamina cribrosa tissue within the optic nerve head (ONH). A recent study showed that eyes with a longer axial length (AXL) had a thinner lamina cribrosa.[5]

One of the key features of myopic ONH is peripapillary atrophy (PPA). Kim et al[6] longitudinally surveilled the optic disc in myopic children and observed a relationship between an increment in the optic disc tilt and PPA. Hence, in some myopic eyes, it seems that one side of peripapillary sclera becomes stretched and the ONH tilts in such a way that the stretched area develops PPA. For this reason, it may be more reasonable to call this peripapillary area "border tissue" instead of "atrophy", although PPA is the widely-accepted name for this region. If the temporal sclera is stretched, the optic disc appears to be horizontally tilted; if the inferior sclera is stretched, it seems to be vertically tilted; and if 360° of the sclera is relatively evenly stretched, the optic disc maintains a round shape with a halo-shaped PPA. PPA can be caused by other reasons such as aging and reduced choroidal perfusion around ONH.[7,8]

The relationship between PPA and glaucoma has been an interesting issue. A temporal relationship has been reported between PPA and glaucomatous neuroretinal rim change and the corresponding visual field (VF) damage.[9] A correlation between PPA progression and glaucoma progression was shown in one study but another study failed to identify a temporal association between neuroretinal rim change and PPA progression.[10,11] Therefore, the relationship between PPA changes and glaucoma progression seems controversial. Accordingly, in this study, we longitudinally evaluated the progressive change in PPA in myopic glaucomatous eyes. In addition, we explored the relationship between PPA and glaucomatous progression according to different PPA shapes.

Methods

The medical records of all patients evaluated by a single glaucoma specialist (K.R.S.) at the glaucoma clinic of the Asan Medical Center, Seoul, Korea between January 2009 and June 2016 were retrospectively reviewed. Initial testing involved 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, VF testing, central corneal thickness measurement (DGH-550 instrument; DGH Technology, Inc., Exton, PA), and AXL measurement (IOL Master, Carl Zeiss Meditec, Inc., Dublin, CA). RNFL thickness was measured using a spectral-domain optical coherence tomography (SD-OCT; Spectralis OCT; Heidelberg Engineering, Inc., Dossenheim, Germany).

The inclusion criteria at initial assessment were BCVA of 20/40 or better, AXL equal or longer than 24 mm, normal anterior chamber, and open angle on slit-lamp biomicroscopic and gonioscopic examinations. Patients with glaucomatous optic disc changes, as confirmed by 2 glaucoma specialists (K.R.S. and J.W.S.), 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, 1 eye was randomly selected for analysis. All patients with glaucoma were followed-up at 6-month intervals using stereoscopic optic disc photography, RNFL photography, VF testing, and SD-OCT scanning. To be included, patients had to have undergone follow-up examinations for at least 3 years. All patients underwent medical therapy during the follow-up period. If any patients underwent intraocular surgery or laser therapy during the follow-up period, only data obtained before such operations were included.

The VF tests were performed using 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. Data from the first VF test were excluded to obviate any learning effect. Patients who underwent ≥ 5 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 glaucoma hemifield test results outside the normal limits or a pattern standard deviation outside the 95% range for normal limits. 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

Red-free RNFL photographs centered on the optic disc were obtained using a nonmydriatic retinal camera. The optic disc tilt was measured on these photographs by a well-trained single examiner (J.M.P.) using the National Institutes of Health image analysis software ImageJ (version 1.48; developed by Wayne Rasband, National Institutes of Health, Bethesda, MD). The optic disc tilt was defined according to previously-described criteria.[12-14] The optic disc tilt was identified 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.[15]

Assessment of Peripapillary Atrophy

Optic disc and PPA areas were measured from optic disc/RNFL photographs by a single examiner (M.S.) using ImageJ software. The border of optic disc and the β-zone PPA (area of visible sclera and larger choroidal vessels) was drawn using a mouse-driven cursor to trace the disc and PPA margins directly onto the image. Then, the pixel areas of the total optic disc area and PPA were measured. The PPA area to disc area ratio (PDR) was obtained as the PPA pixel area divided by the total optic disc pixel area.[16] Subjects were classified in the minimal group when no apparent PPA was observed or the PPA area was minimal (lower than 8000 pixels calculated by ImageJ). Eyes were classified in the concentric group when the PPA

occupied more than or equal to 270° around the optic disc. When the PPA occupied less than 270°, the eyes were classified in the eccentric group. Representative examples are shown in Figure 1 (A, minimal; B, concentric; C, eccentric).

The qualitative evaluation of sequential stereoscopic color optic disc photographs was performed separately with respect to PPA change. Two specialists (K.R.S. and J.K.) evaluated each subject's standard color stereoscopic optic disc/RNFL photographs at baseline and the last visit. A conspicuous increase in vessel visibility and atrophy was considered to indicate PPA progression. PPA progression was confirmed with the two experts' agreement. If the opinions of the 2 graders differed, a third examiner (J.W.S.) made the final decision.

Assessment of Glaucoma Progression

Glaucoma progression was determined by either optic disc/RNFL photographs or serial VF data. Serial stereoscopic optic disc/RNFL photographs were displayed on a liquid-crystal display (LCD) monitor. Two other glaucoma experts (J.K. and J.Y.L.) independently assessed all photographs to estimate glaucoma progression. The most recent photograph was compared with the baseline photograph of each patient. The experts were not aware of each other's assessments and were blinded to all clinical data including OCT, VF information, and the assessment of PPA progression. If the evaluation of the RNFL photographs was difficult 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 2 graders differed, a third examiner (K.R.S.) made the final decision.

VF progression was determined using commercial software (Humphrey Field Analyzer Guided Progression Analysis; Carl Zeiss Meditec).[17]

Statistical Analysis

Baseline and follow-up clinical characteristics were compared among the 3 PPA groups using the one-way ANOVA for normally-distributed data and the Kruskal-Wallis test for nonparametric data. Agreement between PPA and glaucoma progression was determined by Kappa statistics in all 3 PPA groups.[18]

Factors associated with PPA progression were explored by univariate and multivariate Cox proportional hazard modeling in each PPA group as well as in all participants. Variables with a *P* value less than or equal to 0.20 in the univariate analyses were included as candidate variables in the multivariate regression analysis. A backwards 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 22.0 (SPSS Inc., Chicago, IL).

Results

A total of 159 eyes of 159 patients with myopic glaucoma were included in the final analysis: 35 eyes had minimal PPA, 40 had concentric-type PPA, and 84 had eccentric-type PPA. The baseline characteristics of the 3 groups are shown in Table 1. Concentric PPA patients were significantly older than eccentric PPA patients (54.1 ± 11.7 vs. 44.1 ± 11.7 years, $P < 0.001$), but there were no other differences in age among the other group comparisons. The AXL of the eccentric group was significantly longer than those of the other groups (25.54 ± 1.68 vs. 25.28 ± 1.53 vs. 26.41 ± 1.29 mm; $P < 0.001$) but no difference was found between the minimal and concentric PPA groups ($P = 0.39$). Baseline IOP, glaucoma severity determined by RNFL thickness, and VF MD were not different among three groups.

The clinical courses of three groups were compared in Table 2. In the assessment of optic disc photographs, the 2 experts agreed on PPA progression in 140 eyes (88.1%). The mean follow-up IOP, reduction in IOP from baseline, and last VF MD were not different among the 3 groups. Only 1 eye in the minimal group showed PPA progression, unlike 26 eyes (65%) in the concentric group and 36 eyes (42.9%) in the eccentric group. However, the prevalence of glaucoma progression was not different among the 3 groups.

Because only 1 eye showed PPA progression in the minimal group, Kappa analysis and Cox proportional hazard modeling were limited to the concentric and eccentric groups. A Venn diagram illustrates the agreement between the progressions of glaucoma and PPA in the concentric and eccentric groups (Figure 2). The Kappa values were 0.278 and 0.469 in the concentric and eccentric groups, respectively.

When we assessed the parameters associated with PPA progression in all participants, the PPA type showed a significant association with PPA, with the concentric type having the greatest risk in the multivariate Cox proportional hazard model (HR vs. the minimal PPA group, 13.413, $P = 0.013$). Additionally, glaucoma progression (HR 3.299, $P < 0.001$) and baseline PPA area (HR 1.03, $P < 0.001$) were related to PPA progression (Table 3).

In subgroup analysis, older age (HR 1.059, $P = 0.008$), lower baseline MD (HR 0.857, $P = 0.009$), and greater baseline PPA area (HR 1.000, $P = 0.012$) were significantly associated

with PPA progression in the concentric type (Table 4).

However, in the eccentric type, both glaucoma progression (HR 0.271, $P = 0.002$) and AXL (HR 1.521, $P = 0.002$) were associated with PPA progression (Table 5).

Representative case examples showing PPA progression (concentric type (A) and eccentric type (B)) are shown in Figure 3.

Discussion

Myopia is a risk factor for glaucoma development.[1-4] However, discrepancies were seen in the outcomes of previous studies, with myopia found to be a risk factor for glaucoma progression in some studies but not others.[19-24] One possible explanation for the differences in the results may be variations in myopic glaucoma prognosis among individuals. Recent studies reported that glaucomatous progression was related to the type of PPA.[25,26] The shape of optic disc and PPA may differ among myopic eyes according to axial elongation. Thus, glaucomatous progressive changes may differ according to optic disc shape and PPA. When evaluating PPA in our eligible participants, we found that a substantial proportion of myopic glaucomatous eyes had no or minimal PPA; we arbitrarily considered these eyes to be minimal-type PPA. Consequently, we distinguished the 3 types of PPA and intended to evaluate the change in PPA in various shapes of myopic glaucomatous eyes and its relationship with glaucoma worsening via a longitudinal assessment.

Our current data clearly revealed differences in the characteristics of the 3 groups. The eccentric PPA group showed a longer AXL and higher optic disc tilt ratio than the other groups. Tay et al[10] found that an increased optic disc tilt was associated with higher myopia. These findings may suggest that more myopic eyes showed an eccentric shape of PPA. In addition, the patients were younger in the eccentric group, which is in line with the current result.[27] However, IOP values and glaucoma severity were not different among the 3 groups.

Overall, 39% of the eyes (63 out of 159) in our current study series showed PPA progression, which corresponds to the results of a previous study.[8] Uchida et al[8] reported that 37% of their patients showed PPA progression during a follow-up of 4 years. However, the incidence of PPA progression was different among the 3 groups in our results, with the PPA of the concentric group showing the highest rate of progression (65.0%), followed by the eccentric group (42.9%) and minimal group (2.9%). Therefore, the PPA shape appears to influence PPA progression. PPA progression was definitely higher for the concentric type and the mean change in the PDR was also greatest in the concentric group. As a next step, therefore, we explored which factor was related to PPA progression during the follow-up

period. Cox proportional hazard regression analysis of all participants obtained similar findings. The adjusted HR for PPA progression was 13.28 for concentric PPA with the minimal PPA group as reference and 8.16 for eccentric PPA. Moreover, both univariate and multivariate analyses determined that the presence of glaucoma progression, optic disc tilt ratio, and extent of baseline PPA were significant factors in PPA progression. Interestingly, only 1 eye showed PPA progression in the minimal PPA group. Hence, subgroup analysis was performed with both the concentric and eccentric groups. In the subgroup analysis of the Cox proportional hazard modeling, older age, worse VF MD, and greater PPA at baseline were associated with PPA progression in the concentric group. Glaucoma progression was marginally associated with PPA progression in univariate analysis, but not in multivariate. However, in the eccentric group, both longer AXL and glaucoma progression were strongly associated with PPA progression. Hence, both the glaucomatous change and axial myopia were related to the PPA change in the eccentric type. Kappa statistics also revealed that the agreement between glaucoma and PPA progression was stronger in the eccentric group than in the concentric group.

Our current study has several limitations. First, our follow-up period was relatively short (mean, 4.4 years). Second, because we analyzed patients of a single ethnic group (Koreans), caution needs to be exercised with the generalization of our results. Lastly, we judged the qualitative progressive PPA change in a subjective manner, but we added quantitative PPA enlargement to overcome this subjectivity.

In conclusion, a substantial proportion of patients with PPA in myopic glaucomatous eyes show progressive change in their PPA, with the factors associated with PPA progression differing according to PPA shape. PPA progression is most frequently found in concentric-type PPA, and older age and baseline wider PPA are significant factors in this group. However, in eccentric-type PPA, which is observed in younger patients, PPA progression is associated with longer AXL and progressive glaucoma.

Conclusion

Relationship between glaucoma worsening and PPA progression was significantly stronger in myopic glaucomatous eyes with eccentric type PPA.

References

1. Wang Q, Klein BE, Klein R, Moss SE. Refractive status in the Beaver Dam Eye Study. Invest Ophthal mol Vis Sci 1994;35:4344-4347.
2. Katz J, Tielsch JM, Sommer A. Prevalence and risk factors for refractive errors in an adult inner city population. Invest Ophthal mol Vis Sci 1997;38:334-340.
3. Wensor M, McCarty CA, Taylor HR. Prevalence and risk factors of myopia in Victoria, Australia. Arch Ophthalmol (Chicago, Ill : 1960) 1999 ;117:658-663.
4. Attebo K, Ivers RQ, Mitchell P. Refractive errors in an older population: the Blue Mountains Eye Study. Ophthalmology 1999;106:1066-1072.
5. Yun S-C, Hahn IK, Sung KR, Yoon JY, Jeong D, Chung HS. Lamina cribrosa depth according to the level of axial length in normal and glaucomatous eyes. Graefe's Archive for Clinical and Experimental Ophthalmology 2015;253:2247-2253.
6. Kim T-W, Kim M, Weinreb RN, Woo SJ, Park KH, Hwang J-M. Optic disc change with incipient myopia of childhood. Ophthalmology 2012;119:21-26. e3.
7. Lee EJ, Kim TW, Lee SH, Kim JA. Underlying Microstructure of Parapapillary Deep-Layer Capillary Dropout Identified by Optical Coherence Tomography Angiography. Invest Ophthalmol Vis Sci. 2017;58:1621-1627.
8. Iwase A, Sawaguchi S, Sakai H, Tanaka K, Tsutsumi T, Araie M. Optic disc, rim and peripapillary chorioretinal atrophy in normal Japanese eyes: the Kumejima Study. Jpn J Ophthalmol. 2017;61:223-229.
9. Jonas J, Naumann G. Parapapillary chorioretinal atrophy in normal and glaucoma eyes. II. Correlations. Investigative ophthalmology & visual science 1989;30:919-926.
10. Uchida H, Ugurlu S, Caprioli J. Increasing peripapillary atrophy is associated with progressive glaucoma. Ophthalmology 1998;105:1541-1545.
11. See JL, Nicolela MT, Chauhan BC. Rates of neuroretinal rim and peripapillary atrophy area change: a comparative study of glaucoma patients and normal controls. Ophthalmology 2009;116:840-847.

12. Tay E, Seah SK, Chan S-P, et al. Optic disk ovality as an index of tilt and its relationship to myopia and perimetry. Am J Ophthalmol 2005;139:247-252.
13. 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.
14. Lee JE, Sung KR, Park JM, et al. Optic disc and peripapillary retinal nerve fiber layer characteristics associated with glaucomatous optic disc in young myopia. Graefes Arch Clin Exp Ophthalmol 2017;255:591-598.
15. 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 Ophthal mol Vis Sci 2015 ;56:2958-2967.
16. Lee EJ, Kim T-W, Weinreb RN, Park KH, Kim SH, Kim DM. β-Zone parapapillary atrophy and the rate of retinal nerve fiber layer thinning in glaucoma. Investigative ophthalmology & visual science 2011;52:4422-4427.
17. Heijl A, Leske MC, Bengtsson B, et al, EMGT Group. Measuring visual field progression in the Early Manifest Glaucoma Trial. Acta Ophthalmol Scand 2003;81:286-293.
18. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159-174.
19. Sung KR, Lee S, Park SB, et al. Twenty-four hour ocular perfusion pressure fluctuation and risk of normal-tension glaucoma progression. Invest Ophthal mol Vis Sci 2009;50:5266-5274.
20. Doshi A, Kreidl KO, Lombardi L, Sakamoto DK, Singh K. Nonprogressive glaucomatous cupping and visual field abnormalities in young Chinese males. Ophthalmology 2007;114:472-479.
21. 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.
22. Araie M, Shirato S, Yamazaki Y, Matsumoto C, Kitazawa Y, Ohashi Y. Risk factors for progression of normal-tension glaucoma under beta-blocker monotherapy. Acta ophthalmologica 2012;90:e337-343.

23. Lee JE, Sung KR, Lee JY, Park JM. Implications of Optic Disc Tilt in the Progression of Primary Open-Angle Glaucoma. Invest Ophthal mol Vis Sci 2015;56:6925-6931.
24. Lee JY, Sung KR, Han S, Na JH. Effect of myopia on the progression of primary open-angle glaucoma. Invest Ophthal mol Vis Sci 2015;56:1775-1781.
25. Yamada H, Akagi T, Nakanishi H, et al. Microstructure of Peripapillary Atrophy and Subsequent Visual Field Progression in Treated Primary Open-Angle Glaucoma. Ophthalmology 2016;123:542-551.
26. Kim YW, Lee EJ, Kim T-W, Kim M, Kim H. Microstructure of β-zone parapapillary atrophy and rate of retinal nerve fiber layer thinning in primary open-angle glaucoma. Ophthalmology 2014;121:1341-1349.
27. Shim SH, Sung KR, Kim JM, et al. The Prevalence of Open-Angle Glaucoma by Age in Myopia: The Korea National Health and Nutrition Examination Survey. Curr Eye Res 2017;42:65-71.

Table 1. Comparisons of the Baseline Clinical Characteristics Among the 3 Groups Defined by PPA Shape

PPA type	Minimal PPA (group I)	Concentric PPA (group II)	Eccentric PPA (group III)	*P* value
Numbers	35	40	84	
Age (years)	48.5 ± 13.6	54.1 ± 11.7	44.1 ± 11.7	<0.001† 0.145 (I vs. II)* <0.001 (II > III)* 0.235 (I vs. III)*
Sex (M/F)	21/14	30/10	44/40	0.211‡
Baseline IOP (mmHg)	17.3 ± 4.8	16.7 ± 3.2	16.1 ± 3.2	0.668§
Baseline average RNFL thickness (μm)	72.71 ± 16.30	74.22 ± 14.61	74.24 ± 12.59	0.851†
Axial length (mm)	25.54 ± 1.68	25.28 ± 1.53	26.41 ± 1.29	<0.001§ 0.387 (I vs. II)** <0.001 (II< III)** <0.001 (I < III)**
Baseline VF MD (dB)	–5.11 ± 6.18	–4.02 ± 4.35	–3.96 ± 4.00	0.883§
Optic disc tilt ratio	1.17 ± 0.13	1.15 ± 0.10	1.33 ± 0.16	<0.001§ 0.489 (I vs. II)** <0.001 (II< III)** <0.001 (I < III)**
Baseline PPA (pixels)	3087.5 ± 3209.9	21700.9 ± 18803.8	20143.5 ± 9606.7	<0.001§ <0.001 (I < II)** 0.229 (II vs. III)** <0.001 (I < III)**
Baseline PDR	0.09 ± 0.10	0.60 ± 0.45	0.74 ± 0.42	<0.001§ <0.001 (I < II)** 0.011 (II < III)** <0.001 (I < III)**

PPA = peripapillary atrophy; IOP = intraocular pressure; RNFL = retinal nerve fiber layer; VF = visual field; MD = mean deviation; PDR = PPA and disc area ratio

†One way ANOVA.

‡Linear-by-linear association.

§Kruskal-Wallis test.

*Bonferroni post hoc test.

**Mann-Whitney post hoc test.

Table 2. Comparisons of the Clinical Course Among the 3 Groups Defined by PPA Shape

PPA type	Minimal PPA (group I, 35)	Concentric PPA (group II, 40)	Eccentric PPA (group III, 84)	*P* value
Follow up days (day)	1425.3 ± 465.8	1439.5 ± 469.3	1352.6 ± 421.6	0.287[†]
Mean follow-up IOP (mmHg)	14.4 ± 2.5	14.6 ± 2.2	14.3 ± 2.0	0.772[‡]
Mean reduction in IOP from baseline	12.9 ± 18.8	10.9 ± 14.1	9.7 ± 13.4	0.553[‡]
Last VF MD (dB)	–5.86 ± 6.74	–6.10 ± 6.05	–4.92 ± 4.73	0.492[§]
Mean change in VF MD (dB)	0.7 ± 1.6	2.0 ± 3.1	1.0 ± 2.2	0.030[§] 0.025 (I < II)* 0.054 (II vs. III)* 0.555 (I vs. III)*
PPA progression (n/%)	1/2.9%	26/65.0%	36/42.9%	<0.001 (chi) 0.034 (II > III) <0.001 (I <II) <0.001 (I<III)
Glaucoma progression (n/%)	15/42.9%	22/52.5%	38/45.2%	0.504 (chi)
Mean change in PDR	0.000 ± 0.000	0.048 ± 0.109	0.041 ± 0.093	0.037[§] <0.001 (I < II)* 0.726 (II vs. III)* <0.001(I vs. III)*

PPA = peripapillary atrophy; IOP = intraocular pressure; VF = visual field; MD = mean deviation; PDR = PPA and disc area ratio

[†]Kruskal-Wallis test.

[‡]Linear-by-linear association.

[§]One way ANOVA.

*Mann-Whitney post hoc test.

Table 3. Univariate and Multivariate Cox Regression Hazard Ratios for PPA Progression in All Eyes

	Univariate			Multivariate		
	HR	95% CI	*P* value	Adjusted HR	95% CI	*P* value
Age	1.007	0.99–1.03	0.467			
PPA type (minimal)			0.004			0.024
PPA type (concentric)	27.16	3.68–200.45	0.001	13.413	1.74–103.26	0.013
PPA type (eccentric)	20.67	2.83–150.87	0.003	8.92	1.17–68.03	0.035
Baseline IOP	0.968	0.90–1.04	0.349			
Mean follow-up IOP	0.97	0.87–1.09	0.599			
Glaucoma progression	3.22	1.88–5.26	<0.001	3.299	1.96–5.78 1.91–5.70	<0.001
Initial average thickness	1.01	0.99–1.03	0.264			
Axial length	1.07	0.91–1.26	0.431			
VF MD	1.02	0.94-1.12	0.277			
Tilt ratio	3.57	0.88–14.55	0.075	4.18	0.911–19.13	0.066
First-visit PPA	1.04	1.03–1.05	<0.001	1.03	1.02–1.05	<0.001
First PDR	2.63	1.72–4.06	<0.001			

PPA = peripapillary atrophy; IOP = intraocular pressure; VF = visual field; MD = mean deviation; PDR = PPA and disc area ratio

Table 4. Univariate and Multivariate Cox Regression Hazard Ratios for PPA Progression in Eyes with Concentric PPA

	Univariate			Multivariate		
	HR	95% CI	*P* value	Adjusted HR	95% CI	*P* value
Age	1.029	0.99–1.07	0.107	1.059	1.015–1.102	0.008
Baseline IOP	0.852	0.740–0.981	0.026			
Mean IOP reduction	0.976	0.951–1.001	0.061			
Glaucoma progression	0.449	0.196–1.028	0.058			
Initial average thickness	1.023	0.992–1.054	0.145			
Axial length	0.772	0.521–1.144	0.198			
VF MD	0.917	0.844–0.997	0.042	0.857	0.764–0.962	0.009
Tilt ratio	0.353	0.0060–21.424	0.353			
First-visit PPA	1.000	1.000–1.000	0.002	1.000	1.000–1.000	0.012

PPA = peripapillary atrophy; IOP = intraocular pressure; VF = visual field; MD = mean deviation;

Table 5. Univariate and Multivariate Cox Regression Hazard Ratios for PPA Progression in Eyes with Eccentric PPA

	Univariate			Multivariate		
	HR	95% CI	*P* value	Adjusted HR	95% CI	*P* value
Age	1.000	0.973–1.029	0.983			
Baseline IOP	1.011	0.921–1.110	0.817			
Mean IOP reduction	1.011	0.985–1.037	0.427			
Glaucoma progression	0.285	0.137–1.595	0.001	0.271	0.12–0.612	0.002
Initial average thickness	1.005	0.981–1.031	0.670			
Axial length	1.614	1.222–2.132	0.001	1.521	0.16–1.994	0.002
VF MD	1.048	0.965–1.139	0.264			
Tilt ratio	7.138	1.251–40.717	0.027			
First-visit PPA	1.000	1.000–1.000	0.253			

PPA = peripapillary atrophy; IOP = intraocular pressure; VF = visual field; MD = mean deviation;

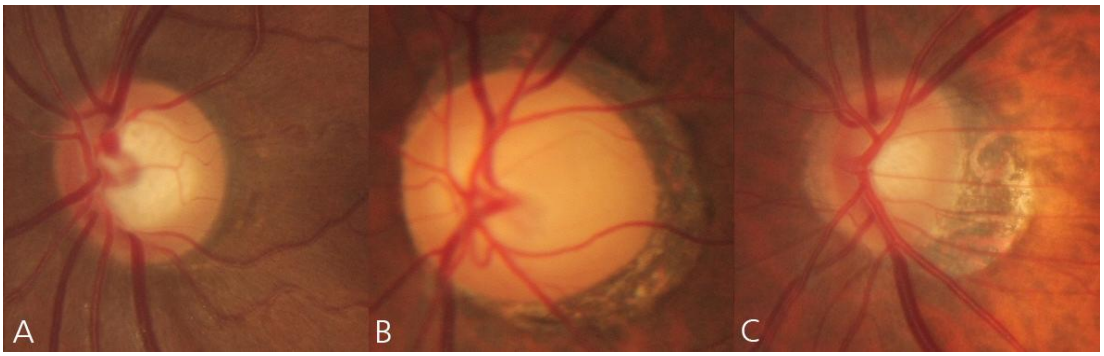

Figure 1. Eyes were classified in the concentric group when the PPA was more than or equal to 270° around the optic disc. When the PPA was less than 270°, eyes were classified in the eccentric group. Eyes with no or minimal PPA were categorized in the minimal group. Representative examples are shown (A, minimal; B, concentric; and C, eccentric groups).

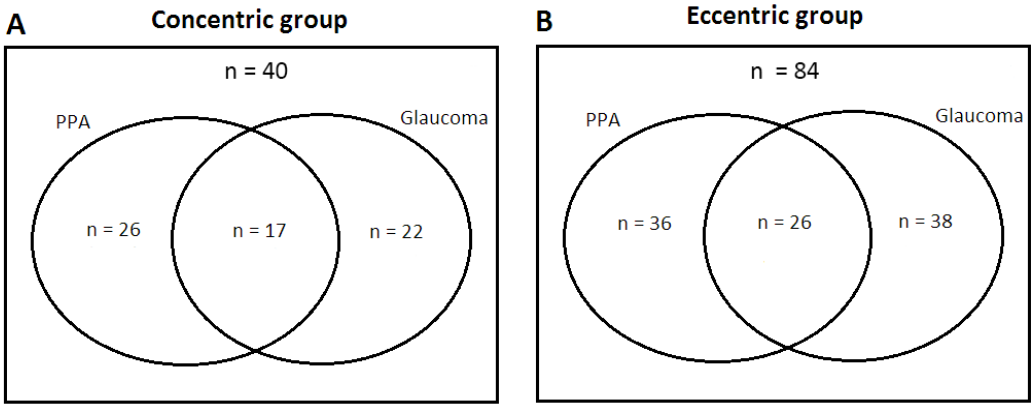

Figure 2. Agreement between PPA progression and glaucoma progression was determined in the concentric (A) and eccentric (B) groups.

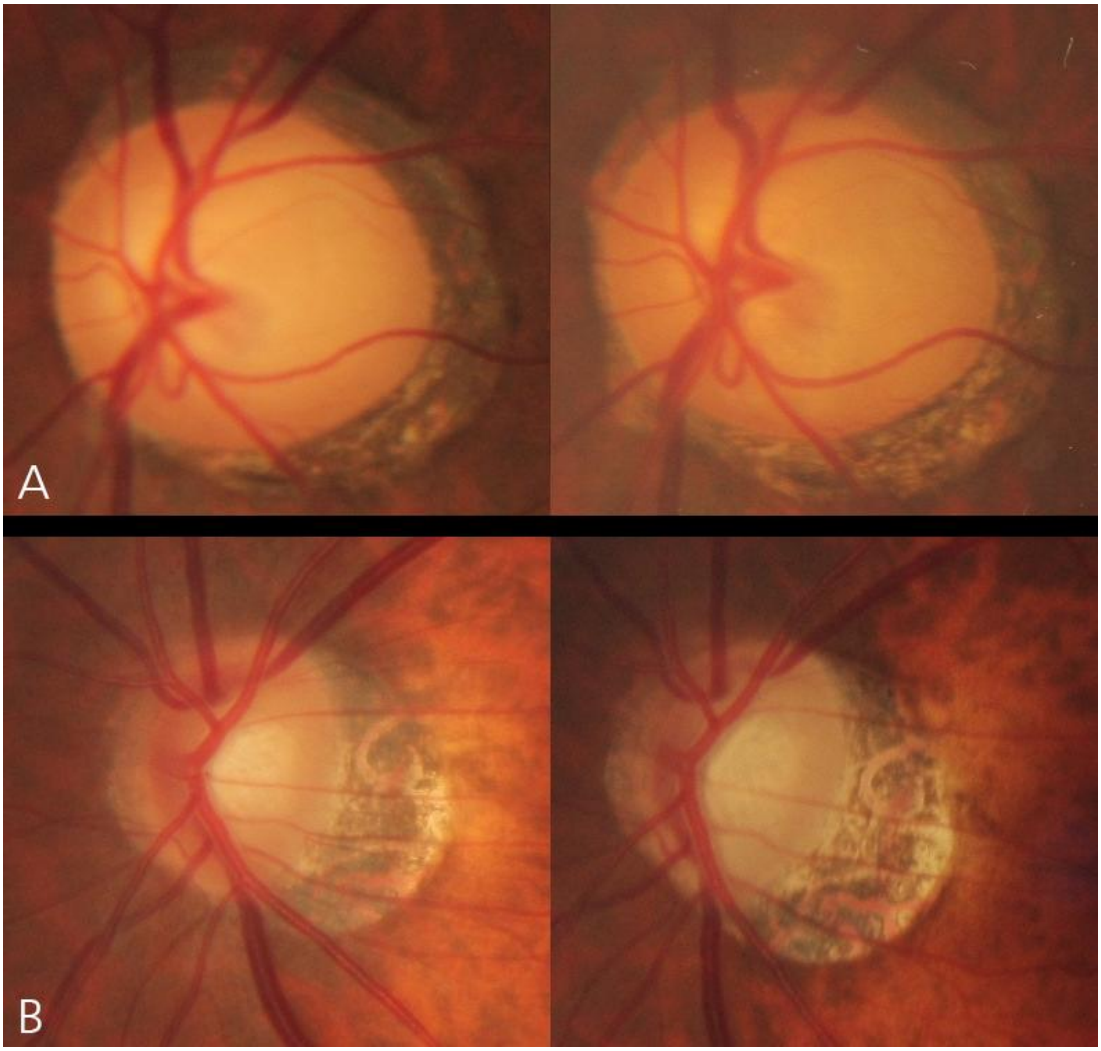

Figure 3. Representative case examples with PPA progression (concentric type (A) and eccentric type (B)) are shown. The gray dots represented PPA of the baseline (left side).

국문요약

목적: 근시인 녹내장 환자에서 시신경유두주위위축의 모양에 따른 점진적 변화를 평가하고, 시신경유두주위위축의 진행과 녹내장 진행의 관계에 대해서 알아보고자 하였다.

방법: 159 명 159 안의 근시(안축장 길이 24mm 초과)인 녹내장 환자를 포함하였다. 이들의 평균 관찰기관은 4.4 년이였으며, 35 안은 최소 (minimal) 시신경유두주위위축, 40 안은 동심성 (concentric) 시신경유두주위위축 (시신경유두주위 270 도 이상), 84 안은 편심성 (eccentric) 시신경유두주위위축 (시신경유두주위 270 도 미만)으로 분류되었다. 시신경유두주위위축의 질적인 변화를 보기 위해서 연속적인 입체 시신경 유두 사진을 통해 평가하였다. 각 시신경유두주위위축 그룹별로 콕스비례위험모델을 통해 시신경유두주위위축의 진행과 관련된 인자를 평가하하였다.

결과: 동심성 그룹은 편심성 그룹보다 나이가 많았으며 (54.1 ± 11.7 vs. 44.1 ± 11.7 년, P < 0.001), 편심성 그룹에서 다른 그룹들 보다 안축장이 길었다 (25.54 ± 1.68 vs. 25.28 ± 1.53 vs. 26.41 ± 1.29 mm; P < 0.001). 동심성 그룹 26 안 (65%), 편심성 그룹 36 안 (42.9%)이 시신경유두주위위축의 진행을 보였다. 동심성 그룹에서는 고령일수록 (위험률; 1.059, P = 0.008), 초기 시야검사의 평균편차가 작을수록 (위험률; 0.857, P = 0.009), 초기 시신경유두주위위축 면적이 클수록 (위험률; 1.000, P = 0.012) 시신경유두주위위축의 진행과 연관성을 보였다. 편심성그룹 에서는 녹내장의 진행여부 (위험률; 0.271, P = 0.002), 안축장이 길수록 (위험률; 1.521, P = 0.002) 시신경유두주위위축의 진행과 연관성을 보였다.

결론: 근시인 녹내장 환자에서 시신경유두주위의 모양이 편심성을 보이는경우, 녹내장의 진행과 시신경유두주위위축의 진행이 강한 상관관계를 보임을 확인하였다.

중심 단어: 근시, 녹내장, 시신경유두주위위축