Risk Factors for Progression of Visual Field Defect in Young Normal-tension Glaucoma Patients

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Risk Factors for Progression of Visual Field Defect in Young Normal-tension Glaucoma Patients

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The Master's Thesis
submitted to the Department of Medicine
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree
of Master of Medical Science

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December 2011

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December 2011

ACKNOWLEDGEMENTS

First of all, I very much appreciate my thesis supervisor, Prof. Chan Yun Kim for giving me great advice and inspiration that has been helpful for taking a degree. I thank him for his supervision and encouragement to study this subject.

I also appreciate professors, Dong Goo Kim, Kyoung Yul Seo who gave me expert and warm support. I wish to thank all members of our department for their helpful assistance and supports.

Finally, I would like to thank to my parents for allowing me to being me now. And I specially thank to my love, Jungyeon, who always believes and encourages me. My expecting baby, DoDo, I love you with all my heart.

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ABSTRACT

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Prevalence of glaucoma is increasing with ageing. Young aged glaucoma patients are uncommon and age is not a modifiable factor. That is why there have been no studies about young aged open angle glaucoma (OAG). In case of young OAG patients, life expectancy is remained longer than older OAG patients. As there will be more chances of irreversible glaucomatous progression, more strict and steady examination and treatment are needed.

The purpose of this study was to investigate the risk factors for the progression of visual field defect in young (18 to 40 years old) normal-tension glaucoma (NTG) patients.

We retrospectively reviewed the records of all 1489 patients who had been diagnosed with NTG between 1998 and 2008 at two large medical centers, Severance hospital and Gangnam severance hospital of Yonsei university. Among the 1489 NTG patients, only 22 patients, 27 eyes were eligible for inclusion and exclusion criteria and were enrolled in this retrospective study. Criteria for glaucoma progression were similar to those of the Collaborative NTG Study. Univariate analysis were performed between patients with visual field progression and those with no progression. In addition, Cox proportional hazard regression and survival analysis were performed.

Twenty two patients, 27 eyes, were enrolled in this study. With 15% lowering IOP, 58% young NTG patients (<40 years old) have shown visual field

deterioration in 5 years follow up. Almost eyes have myopic refractive error, and 54% eyes were high myopia (under -6.00 diopter). beta-zone parapapillary atrophy (β-PPA) were prevalent in young aged NTG patients (85.7%). In Cox proportional hazards regression analysis, presence of β-PPA (HR=29.46; P=0.04) was associated with visual field progression.

In conclusion, Patients with high myopia and β-PPA are frequent in young NTG patients. β-PPA was associated with visual field progression in young NTG patients. Further study would be needed to elucidate the pathogenetic mechanism of NTG in young patients.

Key words : young, normal-tension glaucoma, high myopia, beta-zone parapapillary atrophy

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I. INTRODUCTION

Glaucoma is known to be elderly people's disease. Prevalence of open angle glaucoma (OAG) is increasing with ageing. Age is known to be one of the most important risk factors of developing of OAG.[1-4] Also, previous large multi-centered randomized clinical trials showed that age is one of the prognostic factors for the progression of OAG.[5-7] According to one meta-analysis article about prevalence of OAG, in 36 of total 48 papers, only over 40 years old patients were enrolled and in 46 of total 48 papers, over 30 years old patients were enrolled.[8] One Japanese epidemiologic study showed that prevalence of OAG was, 0.49% among patients aged between 6 to 14 years old, while 0.54 between 15 to 24 years old and 0.70 in 25 to 34 years old. These rates showed relatively lower prevalence than older patients.[9] As age is not modifiable factor and prevalence of OAG is relatively low in younger age, that is why there have been no studies about young aged OAG patients. Large eastern epidemiologic studies about OAG, Tajimi study in Japan, Namil study in South Korea, are focused on over 40 years old OAG patients.[10-11] Glaucoma causes irreversible visual field (VF) defect and retinal nerve fiver layer (RNFL) deterioration. Normally thickness of retinal nerve fiber layer is decreasing with

ageing. In case of young OAG patients, life expectancy is remained longer than older OAG patients. As there will be more chances of irreversible progression, more strict and steady examination and treatment are needed.

When compared with high-tension OAG, normal-tension glaucoma (NTG) occurs at an older age. Previous study reported a mean age of 66.5 years for NTG patients in contrast to a younger mean age of 51.7 years for high-tension OAG patients.[12-13] In pathogenesis of NTG, besides intraocular pressure (IOP), systemic factor like vascular insufficiency is considered important.[14-15] So, diabetes, stoke, migraine, Raynaud phenomenon, nocturnal hypotension, history of hypovolemic shock are regarded as risk factors of NTG related to vascular insufficiency.[16-20] The purpose of this study was to investigate the risk factors for the progression of visual field defect in young (18 to 40 years old) normal-tension glaucoma patients. Young NTG patients might show different characteristics from elderly patients.

II. MATERIALS AND METHODS

We retrospectively reviewed the records of all 1489 patients who had been diagnosed with NTG between 1998 and 2008 at two large medical centers, the glaucoma clinic of ophthalmology, Severance hospital and Gangnam severance hospital of Yonsei university. Among the 1489 NTG patients, only 22 patients, 27 eyes were eligible for inclusion and exclusion criteria and were enrolled in this retrospective study. The study was approved by the Yonsei University Severance Hospital institutional review board (IRB no. 4-2011-0446) and conformed to the Declaration of Helsinki.

Subjects

Normal-tension glaucoma was defined as follows :

(1) documented intraocular pressure (IOP) consistently lower than 21 mmHg without antiglaucoma medication. (2) Open drainage angles on dark room gonioscopy. (3) glaucomatous optic disc cupping and loss of neuroretinal rim (4) Visual field (VF) defect according to Collaborarive NTG study (5) Glaucoma hemifield test results in outside normal limit (6) Pattern standard deviation with a p value less than 0.05 (7) A cluster of 3 points or more in the pattern deviation plot in a single hemifield with a p value less than 0.05, one of which must have a p value less than 0.01. any one of these criteria, if repeatable, was considered to be sufficient evidence of a glaucomatous VF defect (8) Absence of secondary causes for glaucomatous optic neuropathy (e.g., previous trauma, steroid use, uveitis, etc.).

Inclusion criteria was NTG patient aged from 18 to 40 years old at diagnosis. Each patient had to have been followed up in the outpatient clinic for 3 years or more and to have a VF test at least yearly for a total of 5 or more VF tests.

Exclusion criteria were listed as follows: (1) Previous any ocular disorder (2) previous ocular surgery or trauma history (3) visual acuities of less than 20/25

(4) History of cerebrovascular accident

Ophthalmic assessment

Ophthalmic assessment included best-corrected visual acuity, IOP, slit-lamp examination, dark room gonioscopy, disc assessment, and dilated fundal examination. These assessments were obtained at baseline and then at 6 month intervals for over 3 years. Central corneal thickness (CCT) was measured at baseline. Pachymetry was determined using an A-scan ultrasonic pachymeter (USP; Pocket-II; Quantel Medical, Inc.,Bozeman, MT). The median of 3 readings was taken as the CCT. IOP was measured with Goldmann applanation tonometry. Refraction was measured via an auto-refractometry using a spherical equivalent. Dark room gonioscopy was performed using a Goldmann 2-mirror gonioscope. The vertical cup-to-disc ratio was taken as the longest vertical cup diameter divided by the longest vertical disc diameter. The vertical disc diameter and beta-zone parapapillary atrophy were evaluated on the initial color disc stereophotograph. Disc hemorrhage was examed every 12 month on the color disc stereophotographs .

Visual fields were evaluated using the central 30-2 or 24-2 (Swedish interactive threshold algorithm standard) program in the Humphrey Visual field analyzer (Carl Zeiss Ophthalmic system, Inc., Dublin, California, USA), also at intervals of 6 to 12 months. A reliable VF had to fulfill 3 criteria: fixation loss less than 15%, a false-positive rate of 10% or less, a false-negative rate of 10% or less. The first 2 reliable tests were regarded as a baseline VF test. Progressions of VF defects were judged by 2 experienced glaucoma specialists, each of whom was masked with regard to the subject’s identity and to all other variables. Visual field progression was deemed to have occurred, and the end point was when the first perimetric abnormality was detected.

The details of topical antiglaucoma medications were not evaluated in this study. For this reason, the contents of medications were not constant in the

follow-up period, and there were differences depending on the condition and compliance of each patient.

Chart review and additional interview

Systemic and ocular medical histories were retrospectively reviewed on past charts. (systemic diseases or status including diabetes, cardiovascular diseases, Hypertension, hypotension, migraine, neurologic diseases, Raynaud phenomenon, rheumatic diseases, thyroid diseases, hypercholesterolemia, obstructive sleep apnea, previous significant blood loss requiring blood transfusion, long standing steroid medication history). Family history of glaucoma in first degree relatives was also reviewed. Insufficient information was asked during interview in outpatient clinic or by telephone.

Cigarette smoking status was classified to current /past /none smoker. quantity and duration of cigarettes smoking among present smokers and quiting time among past smokers were also evaluated. during lifetime, subjects smoking less than 100 cigarettes were regarded as none smokers.[21] Adherence was investigated by self-report of patients. Adherence was measured as dates of taking eye drop medication in a week averagely.[22]

Criteria for glaucoma progression were similar to those of the Collaborative NTG Study[23-24]: Deepening, enlargement, new defect.

a defect was considered to have deepened or enlarged if 2 points or more within or adjacent to an existing scotoma had worsened by at least 10 dB; these 2 progressing points had to be adjacent and if 3 points or more within or adjacent to an existing scotoma had worsened by at least 5 dB; these 3 progressing points had to be adjacent (at least one of which had deteriorated by $\geq$10 dB) on 2 consecutive perimetric examination. A new defect also was part of progression and was defined as a cluster of at least 3 points meeting the criteria for a VF defect occurring in a previously normal part of the field. Any field progression

had to be verified on at least 1 subsequent field with no other explanation on clinical examination for deterioration.

Statistical analysis

All analyses were performed using SPSS for windows version 18.0 (SPSS, Inc., Chicago, IL). All continuous variables were contented with normal distribution assumption with the Shapiro-Wilk test. Univariate analysis was performed with variables compared between those with and without visual field progression with the independent sample 2-tailed t test . All minimal expected frequency were under 5. so, categorical variables were analyzed with Fisher's exact test. Multivariate analysis was performed with Cox proportional hazards regression analysis and is expressed as hazard ratio (HR) with 95% confidence intervals (95% CI). Variables that were candidates for multivariate testing included all variables that might be considered to be associated with visual field progression, including age, refraction, central corneal thickness (CCT), mean IOP of untreated status, mean IOP during follow up after treatment, mean IOP during follow up (mmHg), magnitude of IOP fluctuation during follow-up, level of initial visual field damage (MD, PSD), and occurrence of disc hemorrhage, presence of beta-zone parapapillary atrophy (β-PPA), Family history of glaucoma in first degree relatives, cigarette smoking, adherence. The magnitude of IOP fluctuation was calculated as the difference between maximum IOP and minimum IOP.

Independent variables were chosen based on both empirical and statistical (from univariate results) associations with progression. Variables with statistical significance of less than 0.20 on univariate analysis were included in multivariate modeling

Follow-up time was defined as the time over which chart notes and visual field testing were available for review. For Kaplan– Meier survival analysis and Cox regression, the end point in the progressing group was the first worsened visual

field, and in the non-progressing group the end point was the last available visual field. The critical value of significance was set at $P<0.05$ for all analyses.

III. RESULTS

A total of 27 eyes, 22 persons from NTG patients were recruited. . Clinical characteristics of subjects are shown in table 1. Mean duration of follow-up was 71.85±15.07 months. Seventeen patients (63%) showed VF progression until the last follow up, and 37% of patients were remained VF stable. According to the survival analysis, at the time of 36 months past, 37% were visual field defect progressed. At the time of 60 months past, 58% were visual field defect progressed (Figure 1).

Univariate analysis were performed between patients with VF progression and those with no progression. No variables showed significant differences between 2 groups (Table 2).

Among 22 NTG patients, 17 patients have unilateral NTG. Axial length, refraction, CCT, mean IOP of untreated status were compared NTG eyes to healthy eyes. There were no significant differences between NTG eyes and healthy eyes (Table 3).

For Cox proportional hazards regression analysis, several variables were chosen. Presence of β-PPA with statistical significance of 0.128 on univariate analysis was included in multivariate model. Age, mean IOP of untreated status, refraction, CCT, baseline PSD were chosen based on empirical significance. Presence of β-PPA (hazard ratio [HR], 29.46; 95% confidence interval [CI], 1.14-764.69; P=0.04) was associated with field progression. Other variables were not significantly different in the regression model (Table 4).

In addition, survival analysis were performed about previously known risk factors. In the survival analysis of patient with CCT>540 ㎛ versus CCT≤540 ㎛, during overall follow up, 39% subjects were VF stable in the CCT>540 ㎛ group and 39% subjects were VF stable in the CCT≤540 ㎛ group. There was no significant differences (Mentel-Cox log rank, p=0.228; Breslow statistics, p=0.053; Tarone-Ware, p=0.106). But, at time of 36 months past, 87% in

CCT>540 ㎛ versus 38% in CCT≤540 ㎛ were VF stable. This result showed significant differences (p=0.009). At time of 60 months past, 48% in CCT>540 ㎛ versus 38% in CCT≤540 ㎛ were VF stable. This was not significantly different (p=0.667) (Figure 2).

In the survival analysis of patient with presence of beta-zone parapapillary atrophy (β-PPA) versus absence of β-PPA, during overall follow up, 50% subjects were VF stable in the absence of β-PPA and 25.1% subjects were VF stable in the presence of β-PPA. This was not significantly different (Mentel-Cox log rank, p=0.098; Breslow statistics, p=0.066; Tarone-Ware, p=0.070) (Figure 3).

In the survival analysis of patient with high teens pretreatment intraocular pressure (20≥ IOP>15 mmHg) versus low teens pretreatment IOP (15≥ IOP>10 mmHg), there was no significant differences (Mentel-Cox log rank, p=0.995; Breslow statistics, p=0.942; Tarone-Ware, p=0.977) (Figure 4).

Table 1. Characteristics of patients with normal-tension glaucoma (n=27)

Characteristics	NTG eyes (n=27)
Age (years)	30.59 ± 4.38
Sex (number, male : female)	18 : 9
Duration of follow-up (months)	71.85 ± 15.07
Axial length (mm)	26.60 ± 1.43
Refraction (diopters)	-6.23 ± 2.74
CCT (㎛)	556.04 ± 34.59
Baseline MD (decibels)	-5.58 ± 3.89
Baseline PSD (decibels)	7.28 ± 4.96
Mean IOP of untreated status (mmHg)	15.17 ± 2.15
Mean IOP during follow up after treatment (mmHg)	12.72 ± 1.35
Mean IOP during follow up (mmHg)	13.34 ± 1.38
The magnitude of IOP (mmHg)	6.68 ± 1.78
Lowering IOP (%)	15.47 ± 8.06
DH (number, positive/negative)	2/27 (7.4%)
β-PPA (number, presence/absence)	23/27 (85.2%)
Family history of glaucoma	4/23 (17.4%)
Cigarette smoking (in male)	11/17 (64.7%)
Pregnancy (in female)	3/9 (33.3%)
Adherence	5.52±1.95

Continuous values are presented as means ± standard deviation.

CCT, central corneal thickness; MD, mean deviation; PSD, pattern standard deviation; IOP, intraocular pressure; DH, disc hemorrhage; β-PPA, beta-zone parapapillary atrophy

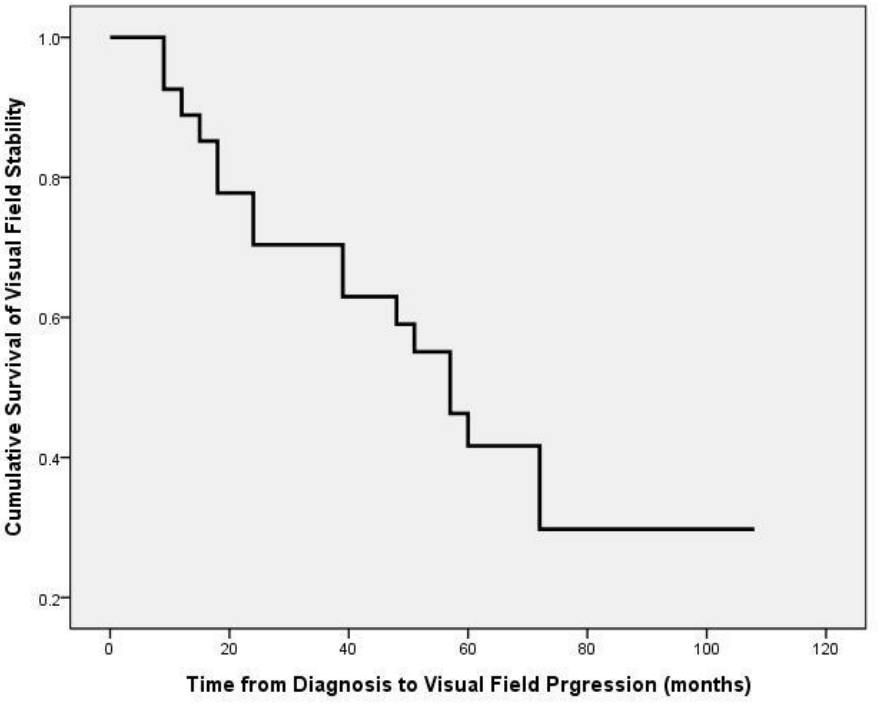

Figure 1. Kaplan-Meier survival analysis for visual field stability in young normal-tension glaucoma patient.
Overall follow-up, 30% were remained VF stable. At the time of 36 months past, 37% were VF defect progressed. At the time of 60 months past, 58% were VF defect progressed.

Table 2. Univariate analysis of risk factors between patients with visual field progression (progressor) and those with no visual field progression (non-progressor)

Risk factors	Progressor (n=17 , 63%)	Non-progressor (n=10 , 37%)	p-value
Age (years)	30.47 ± 3.95	30.80 ± 5.25	0.855*
Female/male	6/17 (35.3%)	3/10 (30.0%)	1.000§
Axial length (mm)	26.85 ± 1.01	26.35 ± 1.81	0.542*
Refraction (diopters)	-6.04 ± 2.92	-6.49 ± 2.60	0.706*
CCT (μm)	552.23 ± 26.51	561.00 ± 44.04	0.559*
Baseline MD (decibels)	-5.65 ± 3.73	-5.45 ± 4.36	0.899*
Baseline PSD (decibels)	8.01 ± 4.76	6.03 ± 5.28	0.326*
Mean IOP of untreated status (mmHg)	15.10 ± 2.00	15.28 ± 2.48	0.854*
Mean IOP during follow up after treatment (mmHg)	12.53 ± 1.15	12.99 ± 1.63	0.440*
Mean IOP during follow up (mmHg)	13.33 ± 1.00	13.36 ± 1.87	0.966*
The magnitude of IOP (mmHg)	6.77 ± 1.36	6.56 ± 2.35	0.790*
Lowering IOP (%)	16.21 ± 9.55	14.40 ± 5.63	0.617*
DH (number, positive/negative)	2/17 (11.8%)	0/10 (0.0%)	0.516§
β-PPA (number, positive/negative)	16/17 (94.1%)	7/10 (70%)	0.128§
Family history of glaucoma	2/13 (15.4%)	2/10 (20.0%)	1.000§
Cigarette smoking status (in male) (present and past)	7/10 (70%)	4/7 (57.1%)	0.644§
Pregnancy (in female)	2/6 (33.3%)	1/3 (33.3%)	1.000§
adherence	5.41 ± 1.71	5.65 ± 2.27	0.786*

CCT, central corneal thickness; MD, mean deviation; PSD, pattern standard deviation; IOP, intraocular pressure; DH, disc hemorrhage; β-PPA, beta-zone parapapillary atrophy

Continuous values are presented as means ± standard deviation.

Continuous variables were analyzed with the independent t-test.
Categorical variables were analyzed with Fisher's exact test.
*Independent t-test

§Fisher's exact test

Table 3. Paired analysis between glaucomatous eye and healthy eye in unilateral normal-tension glaucoma patients (n=17)

Variable	glaucomatous eye	Healthy eye	P value
Axial length (mm)	25.54 ± 1.32	25.67 ± 1.33	0.157
Refraction (diopters)	-5.51 ± 2.72	-4.95 ± 2.46	0.250
CCT (μm)	562.67 ± 38.40	556.33 ± 44.18	0.195
Mean IOP of untreated status (mmHg)	15.30 ± 2.39	15.13 ± 2.39	0.611

CCT, central corneal thickness; IOP, intraocular pressure

Values are presented as means ± standard deviation

The paired T-test analysis was used. *p<0.05

Table 4. Cox proportional hazards regression analysis of risk factors for visual field progression

Risk factors	Hazard ratio	95% confidence interval	P value
Age (years)	0.86	0.68-1.10	0.229
Mean IOP of untreated status (mmHg)	1.06	0.73-1.54	0.773
Refraction (diopters)	1.57	0.94-2.63	0.08
CCT (per 40μm thickening)	0.58	0.20-1.72	0.326
β-PPA	29.46	1.14-764.69	0.04*
Baseline PSD (decibels)	1.17	0.93-1.47	0.17

IOP, intraocular pressure; CCT, central corneal thickness; β-PPA, beta-zone parapapillary atrophy; PSD, pattern standard deviation

*p<0.05

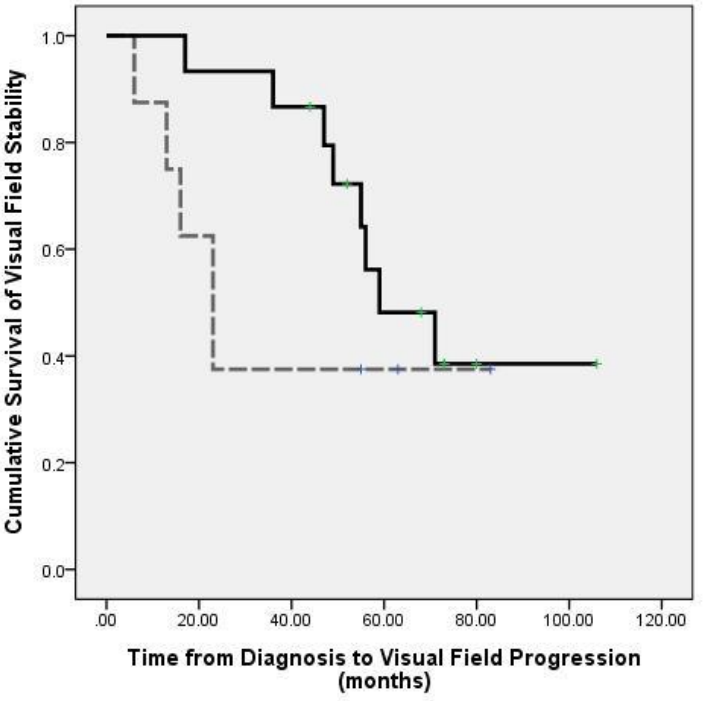

Figure 2. Kaplan-Meier survival analysis of patient with CCT>540 ㎛ versus CCT≤540 ㎛. During overall follow up, 39% subjects were visual field stable in the CCT>540 ㎛ group and 39% subjects were VF stable in the CCT≤540 ㎛ group. There was no significant differences (Breslow statistics, p=0.053). But, at time of 36 months past, 87% in CCT>540 ㎛ versus 38% in CCT≤540 ㎛ were VF stable. This result showed significant differences (p=0.009)
(Solid line: CCT>540 ㎛, dashed line: CCT≤540 ㎛)

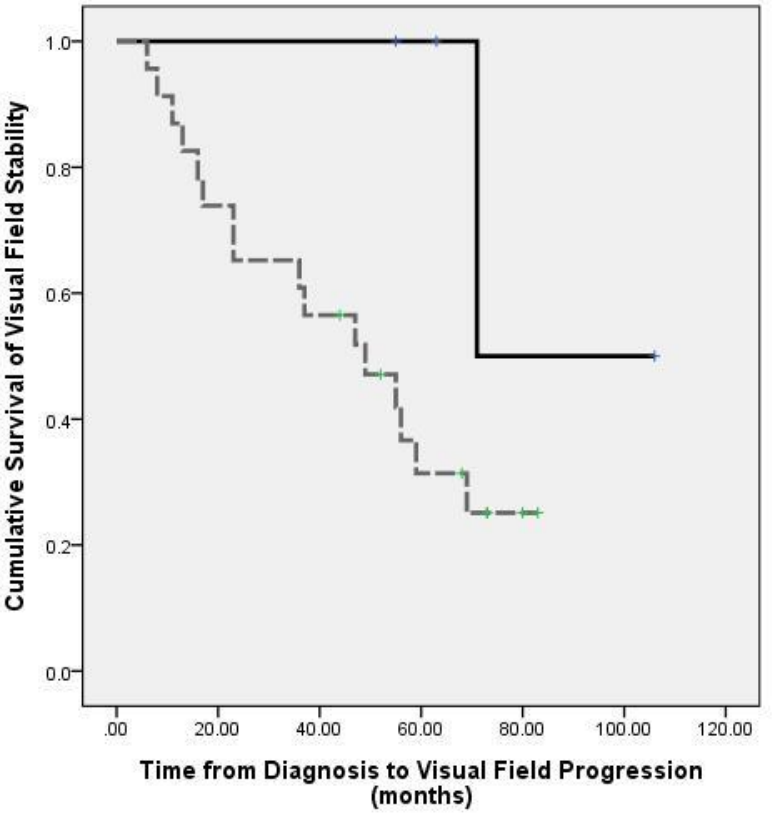

Figure 3. Kaplan-Meier survival analysis of patient with presence of beta-zone parapapillary atrophy versus absence of β-PPA. During overall follow up, 50% subjects were visual field stable in the absence of β-PPA and 25.1% subjects were visual field stable in the presence of β-PPA. This was not significantly different (Breslow statistics, p=0.066)
(Solid line: absence of β-PPA, dashed line: presence of β-PPA)

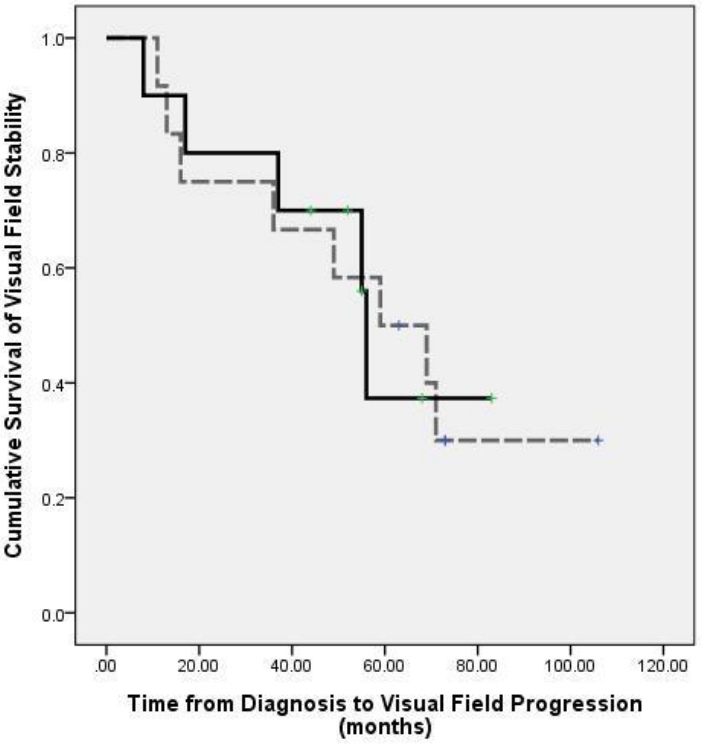

Figure 4. Kaplan-Meier survival analysis of patient with high teens pretreatment intraocular pressure (20≥IOP>15 mmHg) versus low teens pretreatment IOP (15≥IOP>10 mmHg). There was no significant differences (Mentel-Cox log rank, p=0.995; Breslow statistics, p=0.942; Tarone-Ware, p=0.977).
(Solid line: high teens NTG , dashed line: low teens NTG)

IV. DISCUSSION

The Collaborative Normal Tension Glaucoma Study (CNTGS) was the only large multi-centered randomized clinical trials about risk factors for the progression of NTG. The range of ages in CNTGS were 20~90 years old (mean age 63.6 years). In CNTGS, 65% of NTG patients did not show any progression despite not receiving any treatment. Conversely, 12% of NTG patients showed progression in spite of aggressive reduction of IOP by over 30%.[25] Disease progression was defined as optic disc progression or visual field loss. Also, suggesting genetic influence, Asians had a slower rate of progression than Caucasians (p=0.0057). only 1 of total 20 asians had reached end-point.[26]

In this study, only under 40 years old NTG patients were enrolled. mean age was 30.59 years. All patients were Koreans. All patients used at least more than 1 topical antiglaucoma medication, mean IOP lowering percent was 15.47%. An overall survival analysis revealed that 70% NTG patients showed visual field progression. Until 5 years follow-up, 58% patients showed disease progression.

Despite lowering about 15% IOP, these visual field progression rates were much higher than disease progression rate reported in CNTG untreated arm. It could be assumed that young NTG progresses faster than elderly NTG.

Univariate analysis, comparing between patients with visual field progression and those with no VF progression, did not show any significant differences in various factors like age, refraction, central corneal thickness (CCT), mean IOP of untreated status, mean IOP during follow up after treatment, Mean IOP during follow up (mmHg), magnitude of IOP fluctuation during follow-up, level of initial visual field damage (MD, PSD), and occurrence of disc hemorrhage, presence of β-PPA, family history of glaucoma in first degree relatives, cigarette smoking, adherence. Because some variables have been shown to be risk factors of development or progression of OAG in previous studies, we performed additional analysis.

Mean refraction was -6.23 diopter (D), ranged from -10.87 to 0 D. except only one emmetropia patient, all patients were myopia. 13 of 24 eyes (54%) have high myopic eye (under -6.00 D). In Korea and Japan, myopia is more prevalent than western area. According to over 50000 people enrolled survey of 19 years-old healthy Koreans, the prevalence of high myopia (under -6.00 D) was 12.39%.[27] Rate of high myopia in young NTG patients was much higher than previous large survey. Recent article reported that myopia is not related with NTG VF progression.[28] In this study, refraction showed no statistical significance in univariate analysis and Cox regression model.

Optic disc hemorrhage has been associated with NTG in several studies and has also been shown to be a predictive factor for NTG progression.[30-31] It is related with vascular insufficiency as possible pathogenesis of NTG. Only 2 eyes showed more than 1 episode of optic disc hemorrhage. That is because, exclusively young NTG patients were enrolled. Frequency of hemorrhage is thought to be lower than elderly patients. There is no statistical significance between progressor and non-progressor.

Visual field progression in patients with OAG was significantly associated with thinner CCT.[32] But, there has been no definite report only about NTG cases. An overall survival analysis revealed that the rate of visual field progression did not show significant differences between CCT>540 ㎛ group and CCT≤540 ㎛ group [Breslow statistics (p=0.053)]. But, at time of 36 months past, 87% in CCT>540 ㎛ group versus 38% in CCT≤540 ㎛ group were visual field stable. This was statistically significant (p=0.009). According to figure 2, CCT thinner group showed visual field progressions earlier than CCT thicker group progressions. Thicker CCT might be protective for visual field progression at least in the initial stages. This result is similar to previous studies. In survival analysis, as subjects have been excluded after progression, two survival curves might show no differences as time goes by.

Relation between initial visual field damage and progression of VF is a subject

of debate in previous OAG studies. A more advanced visual field score appeared to be protective in the Advanced Glaucoma Intervention Study (AGIS)[5], whereas a more severe visual field mean deviation was a prognostic factor in the Early Manifest Glaucoma Trial (EMGT)[6]. Initial mean deviation and pattern standard deviation showed no significance in univariate analysis and Cox regression model.

IOP and age are most important factors in the NTG. While we know both factors influence prevalence of NTG, but not definite in disease progression of NTG. In CNTGS, neither age nor the untreated level of IOP affected the rate of untreated disease progression. In this study, mean age was not significantly different between progressor and non-progressor. Also, the rate of progression did not have differences between twenties and thirties. Between progressor and non-progressor, there were no significant differences in Mean IOP of untreated status, Mean IOP during follow up after treatment, Mean IOP during follow up, the magnitude of IOP, and Lowering IOP (%). Survival curves between high teens NTG group and low teens NTG group showed no differences (Figure 4). This is similar result with previous study.[33] Despite of about 15% lowering IOP, 58% young NTG patients (<40 years old) have shown visual field deterioration in 5 years follow up. This result, comparing with previous study, was much higher. Only 35% of NTG patients showed disease progression in 5 years even though in CNTGS untreated arm. Current IOP lowering strategy for treating NTG may not be sufficient to manage young aged NTG patients. Surely, unlike CNTGS, lowering IOP percent could not reach the over 30%.

Beta-zone parapapillary atrophy (β-PPA) is known to be highly related with high myopia. Recent report said that eyes with β-PPA are at increased risk for glaucoma progression.[29] In this study, 23 of total 27 (85.7%) patients have β-PPA. Average refraction was -6.55 D in presence of β-PPA group and -4.12 in absence β-PPA group. In Cox proportional hazards regression analysis, presence of β-PPA (hazard ratio [HR], 29.46; 95% confidence interval [CI], 1.14-764.69;

P=0.04) was associated with field progression. But, only 4 patients did not have β-PPA.

Limitation of this study is lack of enough number of subjects. Only 22 patients of total 1489 NTG patients were enrolled. First, under 40 years old NTG patients are uncommon. and Second, inclusion and exclusion criteria were strict. In previous studies, because of learning effect, first two examinations usually were excluded. but not in this study as VF reliability in younger ages are higher than older ages.

Early aged developed NTG patients may have essentially different intrinsic vulnerability comparing to late developed NTG. Besides IOP and vascular insufficiency, it can be related to genetic and structural vulnerability of eye. Results of this study are not fully explained by previous knowledge about NTG. It is assumed that high myopia and β-PPA are highly related to young aged NTG patients. High myopic eyes have thinner RNFL than non-myopic eyes. In case of young glaucoma patients, life expectancy is remained longer than older patients. As there will be more chances of irreversible progression, more strict and steady examination and treatment are needed. According to this result, current IOP lowering strategy for treating NTG may not be sufficient to manage young aged NTG patients. More knowledge and new additional treatment strategy will be needed.

V. CONCLUSION

In this study, despite of about 15% lowering IOP, 58% young NTG patients (<40years old) have shown visual field deterioration in 5 years follow up. This result, comparing with previous study, was much higher. In CNTGS, only 35% of NTG patients showed disease progression in 5 years without any treatments.

Almost eyes have myopic refractive error. 54% eyes were high myopia (under -6.00 D). and Rate of high myopia in young NTG patients was much higher than previous large survey. β-PPA were prevalent in young aged NTG patients (85.7%). In Cox proportional hazards regression analysis, presence of β-PPA (HR=29.46; P=0.04) was associated with visual field progression. It is assumed that high myopia and β-PPA are highly related to young aged NTG patients. Current IOP lowering strategy for treating NTG may not be sufficient to manage young aged NTG patients.

Besides IOP and vascular insufficiency, it can be related to genetic and structural vulnerability of eye. More knowledge and new additional treatment strategy will be needed.

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ABSTRACT(IN KOREAN)

젊은 정상 안압 녹내장 환자에서 시야 결손 진행의 위험 인자

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이 준 원

녹내장의 유병률은 나이가 들수록 증가한다. 젊은 나이에 발생한 녹내장 환자는 흔치 않고 나이는 교정 불가능한 요소이기 때문에, 젊은 나이 개방각 녹내장 환자를 대상으로 한 연구는 지금까지 없었다. 젊은 나이의 녹내장 환자의 경우, 기대 수명이 많이 남아 있기 때문에, 녹내장성 비가역적 변화를 겪을 기회가 많이 남아 있다. 그러므로, 보다 엄격하고 꾸준한 검사와 치료가 필요하다.

본 연구의 목적은 18세에서 40세 사이의 젊은 정상 안압 녹내장 환자에서 시야 결손 진행의 위험 인자에 대해 알아 보는 것이다.

세브란스 병원과 강남 세브란스 병원에서 1998년부터 2008년까지 정상 안압 녹내장으로 진단 받은 1489명의 환자를 후향적으로 분석하였다. 1489명 중 22명, 27안이 본 후향적 연구에 포함되었다. 시야 결손 진행의 기준은 the Collaborative NTG study 의 기준과 유사하였다. 시야 결손이 진행한 군과 진행하지 않은 군 사이에 단변량 분석을 시행하였고, 추가적으로 콕스 비례 위험 회귀 분석과 생존 분석을 시행하였다.

22명, 27안이 연구에 포함되었다. 평균 15% 정도 안압 하강을 하였음에도, 5년 까지의 58%의 정상 안압 녹내장 환자에서 시야 결손 진행을 보였다. 대부분의 환자가 근시였다. 또한 54%의 환자가 -6.00 디옵터 이하의 고도 근시 환자였다. 베타 유두 주위

위축은 85.7% 에서 나타났다. 또한 콕스 비례 위험 모형에서 베타 유두 주위 위축의 시야 결손 진행에 대한 비례 위험도는 29.46 으로 유의하게 나타났다. (p=0.04)

결론적으로, 젊은 나이 정상 안압 녹내장 환자에서는 고도 근시와 베타 유두 주위 위축이 높은 빈도로 나타났으며, 베타 유두 주위 위축은 시야 결손과 관련이 있었다. 젊은 나이 녹내장의 병리 기전을 밝히기 위해서는 추가적인 연구가 요구된다.

핵심되는 말 : 젊은 나이, 정상 안압 녹내장, 고도 근시, 베타 유두 주위 위축