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Risk factors for normal tension glaucoma in a young population

40 세 미만 성인인구에서 정상안압녹내장의 위험인자 연구

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Risk factors for normal tension glaucoma in a young population

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Abstract
Risk factors for normal tension glaucoma in a young population

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Introduction*:* To identify systemic and ocular risk factors associated with normal tension glaucoma (NTG) in a young Korean population.

Methods*:* Retrospective, population based cross-sectional case-control study was performed. Between 2009 and 2010, among participants from 392 clusters representative of the Korean population from the Korea National Health and Nutrition

Examination Survey (KNHANES) (n =17,901), subjects between 19 to 39 years of age were included. Participants had structured interviews, blood pressure measurement, blood sampling and other measurements. The ophthalmologic examination included autorefraction, applanation tonometry, slit lamp examination and fundus photography. For participants meeting the glaucoma suspicion criteria, frequency doubling perimetry testing with the screening program N-30-1 was performed. NTG was diagnosed using International Society of Geographical and Epidemiological Ophthalmology criteria. The systemic and ocular risk factors for NTG were analyzed using univariate and multivariate comparisons.

Results: Eighty NTG patients and 4015 controls were included. In the univariate analysis, NTG group were more likely to have higher fasting plasma glucose (FPG) (98.04±33.16 vs. 89.74±12.65, p <0.001) and higher proportion of fasting capillary glucose (FCG) ≥200 mg/dL (p <0.001) than control. Multivariate analysis with logistic regression with stepwise selection of variables found that high myopia (OR, 3.54 [95% CI,1.34- 9.39], p=0.011), FCG≥200 mg/dL (OR, 12.65 [95% CI, 2.63, 60.94],p=0.002) and low high density lipoprotein cholesterol (HDL-C) (OR, 0.96 [95% CI, 0.94- 0.99],p=0.015) were associated with an increased risk of having NTG.

Conclusions: High myopia, FCG level ≥200mmol/L and low HDL-C level were significant risk factors for NTG in a young Korean population.

Key words: Normal Tension Glaucoma, Young Adult, Myopia, Diabetes Mellitus, Risk factors

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Introduction

Glaucoma is a progressive optic neuropathy where intraocular pressure (IOP) and other factors contribute to damage and in which there is a characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons. It is the leading cause of irreversible blindness worldwide[1] and can adversely impact quality of life for patients with visual field defects even if they are unaware of their diagnosis. The underlying pathogenesis of glaucoma is not completely understood and is likely influenced by both genetic and environmental factors. [2]

Normal tension glaucoma and its risk factors

Normal-tension glaucoma (NTG) is generally defined as visual field loss and optic nerve defects consistent with glaucoma and an IOP that does not exceed 21 mmHg. NTG accounts for a significant percentage of all forms of open-angle glaucoma, especially in Korea, Japan and among Asian Americans.[3-6] While high tension glaucoma, in which a certain level of intraocular pressure (IOP) is the predominant risk factor, additional IOP-independent factors are considered to be important in NTG.[7] Previously known ocular and systemic risk factors for NTG include myopia,[8,9] peripapillary atrophy,[10-12] disc hemorrhage,[13] migraine[13], obstructive sleep apnea syndrome,[14] thyroid disease[15] and cerebral infarction.[16] As glaucoma is considered to be a neurodegenerative disease and the prevalence increases with age,[17] most of the NTG prevalence and risk factor assessment studies have examined populations aged 40 years or older.[3,4,8,18,19] It is possible that the population with NTG is not a homogeneous group of patients with glaucoma, and the disease nature and pathogenesis could be different among the age groups,

especially in a young population.[20] However, few studies have investigated the risk factors of NTG in a young age group.

Myopia and glaucoma

Myopia is most common refractive error globally and the prevalence of it has increased during the 20th century, especially in East Asia including Korea, China and Japan.[21] Although the precise cause of myopia is unknown, previous studies have shown that myopia is influenced by both genetic and environmental mechanisms.[22] Epidemiological studies have suggested that sustained near-work activities are associated with axial elongation and myopia. On possible link between myopia and near-work is that children may have suboptimal accommodation during near work (accommodative lag) leading to hyperopic defocus of the retina that results in axial elongation.[23] Also, many studies suggest that time spent outdoors decreases the risk of developing myopia and its progression. [24,25] According to the recent eye disease prevalence study in South Korea,[26] the prevalence of myopia between 19 to 39 years was 68.8%, considerably higher than in the elderly population. Myopia has been increasing at a rapid rate in the younger population and it is postulated that increased time spent schooling, reading and other near-work activities and decreasing time outdoors in these days might contribute to the increasing prevalence of myopia.

Myopia is known to be a risk factor for several sight threatening eye diseases including retinal detachment, myopic retinopathy and glaucoma.[27] Many clinical and fundamental studies have shown that high myopia and glaucoma are closely associated. There are several hypotheses which explain the association between the two disorders: individuals with axial myopia have weaker scleral support at the optic

nerve, and this contributes to a greater susceptibility of the optic nerve to glaucomatous damage.

The aim of the study

If myopia is also a risk factor for NTG in young population, it is presumed that increasing myopia in this age group could lead to increasing prevalence of NTG in the future. However, there is no published data of population based NTG risk factor assessment study in young population under 40.

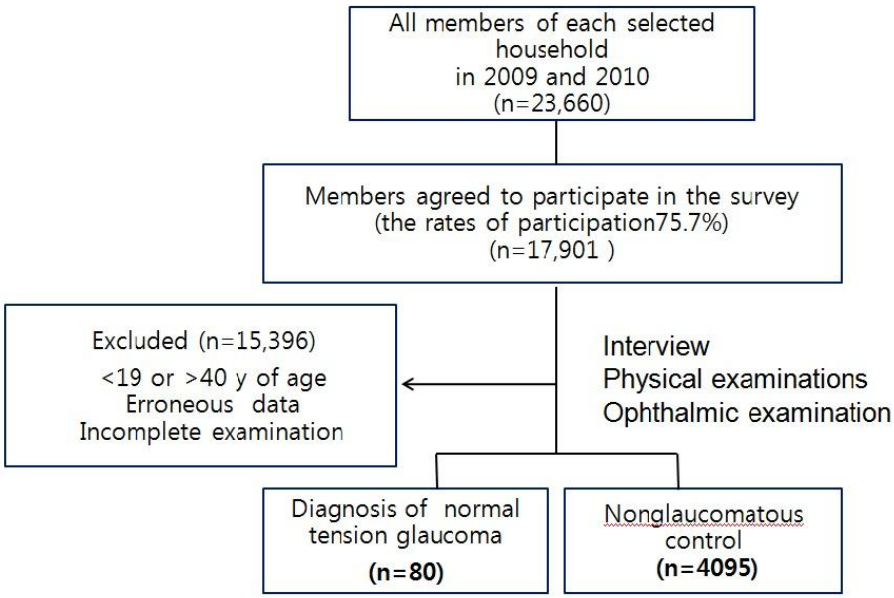
The aim of the current study was to investigate the ocular and systemic risk factors of NTG in a population aged between 19 and 39 with a cross-sectional multivariable analysis in a representative sample of the adult Korean population using the Korean National Health and Nutrition Examination Survey (KNHANES) 2009–2010 data.

Materials and Methods

Sample and population

This study was based on data obtained from the 2009-2010 Korean National Health and Nutrition Examination Survey (KNHANES), a cross-sectional and nationally representative survey that was conducted by the Ministry of Health and Welfare of the Republic of Korea. In total, 392 sampling units, comprising 7,253 households were randomly sampled. Sampling units were households that were selected through a stratified, multistage, probability-sampling design that was based on geographic area, gender, and age from a database of household registries. Of the total target population of 23,660, 17,901 participants (response rate:75.7%) underwent the examinations and the medical interviews (9,760 participants of the 12,722 target population (76.7%) in 2009, and 8,141 of the 10,938 (74.4%) in 2010). Of these 17,901 participants, 4,116 who were younger than 19 years were excluded. Also excluded were 354 participants who had missing data (figure). Weights indicating the probability of being sampled were assigned to each participant, enabling the results from this study to represent the entire Korean population. This study has followed the Tenets of the Declaration of Helsinki and as all the data of KNHANES is opened to the public after removal of personal identifiers and being anonymized, the Institutional Review Board of Seoul National University Hospital determined that this study was exempt from requiring their approval.

Figure 1. Selection of eligible subjects for the analysis



Survey components

Participants completed four parts of a questionnaire, composed of a Health Interview Survey, Health Behavior Survey, Health Examination Survey, and Nutrition Survey. The interview included a questionnaire about having diabetes mellitus, hypertension, migraine, cold extremity and a family history of glaucoma. Physical examinations were performed by trained investigators following a standardized procedure. Body weight and height were measured in light indoor clothing without shoes to the nearest 0.1 kg and 0.1 cm. Body mass index (BMI) was calculated as the ratio of weight/height^2 (kg/m^2). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured on the right arm using a standard mercury sphygmomanometer (Baumanometer, Baum, Copiague, NY, USA). The average of

two systolic and diastolic blood pressure readings, recorded at an interval of five minutes, was used for analysis. Subjects were defined as having hypertension if they had a history of taking anti-hypertensive medication or when measured SBP was ≥ 140 mmHg or diastolic BP was ≥90 mmHg. Systemic hypotension was defined when DBP < 65 mmHg. Mean ocular perfusion pressure (MOPP) was calculated as 2/3 [DBP + 1/3 (SBP-DBP)] –IOP. After 12 hours of overnight fasting, blood samples were obtained from the antecubital veins of the study subjects. Fasting plasma glucose, insulin, total cholesterol, triglyceride (TG), high density lipoprotein cholesterol (HDL-C), blood urea nitrogen (BUN) and creatinine levels were measured using a Hitachi 7600-110 chemistry analyzer (Hitachi, Tokyo, Japan). Blood hemoglobin was measured with an XE-2100D (Sysmex, Tokyo, Japan). Subjects who had been diagnosed with diabetes by physicians or had a fasting plasma glucose level ≥126mg/dL were defined as having diabetes mellitus. White blood cell (WBC) and red blood cell (RBC) counts were quantified by an automated blood cell counter (ADVIA 120, Bayer, NY, USA). Subjects were categorized as having anemia if the level of hemoglobin was <12g/dL in nonpregnant, <11d/gL in pregnant women and <13g/dL in men.

Subjects underwent a detailed eye examination, which included autorefraction using an autorefractor-keratometer (KR8800; Topcon, Tokyo, Japan);slit-lamp examination, including assessment of peripheral anterior chamber depth by the Van Herick method (Haag-Streit model BQ-900; Haag-Streit AG, Koeniz, Switzerland); IOP, measured by Goldmann applanation tonometry (GAT; Haag-Streit; Haag-Streit AG, Koeniz, Switzerland) by ophthalmologists; fundus photographs with a digital

nonmydriatic fundus camera (TRC-NW6S,Topcon,Tokyo,Japan) and a Nikon D-80 digital camera (Nikon, Tokyo, Japan).

If the participants had elevated IOP ≥22 mmHg or a glaucomatous optic disc [(1)horizontal or vertical CD ratio≥0.5, or (2) violation of the ISNT rule (the neuroretinal rim thickness order of inferior > superior > nasal >temporal), or (3) presence of optic disc hemorrhage, or (4) presence of a retinal nerve fiber layer defect], frequency doubling perimetry testing (FDT) with the screening program N-30-1 was carried out.

Spherical equivalent refractive error was calculated as (sphere + cylinder/2) measured in diopters (D). Myopia was defined when myopic spherical equivalent of the eye (SE) was <-0.5. Low myopia was defined in eyes with a myopic SE > -0.5 D to ≤ -3.0. Moderate myopia was defined in eyes with an SE of the eye of >-3.0 D to ≤-6.0 D and high myopia was defined as SE > -6.0D.

All fundus photographs were assessed for severity of diabetic retinopathy. Existences of microaneurysm, dot hemorrhage, hard exudates, cotton wool spot, venous loop or beading, clinically significant macular edema, neovascularization, vitreous or retinal hemorrhage, fibrous proliferation, tractional retinal detachment, previous laser treatment were evaluated.

Definition of Normal-Tension Glaucoma and Nonglaucoma Control

The definition of NTG was based on the International society of Geographical and Epidemiological Ophthalmology (ISGEO) criteria and the previous study[28,29]

Patients were defined as NTG if IOP≤21mmHg (The cutoff normal IOP of 21 mmHg were based on the healthy population in the KNHANES, correlating with the

99.5th percentile), the presence of an open angle (peripheral anterior chamber depth >1/4 corneal thickness) and any one of the following category I or category II diagnostic criteria were met.

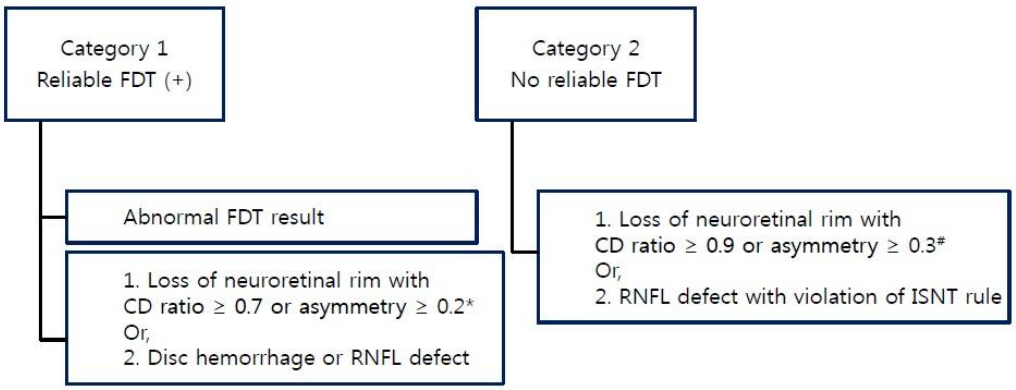
Category I criteria ; The presence of FDT testing results and fixation error and false positive error ≤1: (1) loss of neuroretinal rim with vertical or horizontal cup-disc ratio ≥0.7 or asymmetry of vertical cup-disc ratio ≥0.2 (both values determined by ≥97.5th percentile for the normal population in the KNHANES) or presence of optic disc hemorrhage or presence of retinal nerve fiber layer defect and (2) the presence of an abnormal FDT testing result (at least one location of reduced sensitivity)

Category II criteria; Absence of FDT testing results or fixation error or false positive error≥2, (1) loss of neuroretinal rim with vertical cup-disc ratio≥0.9 or asymmetry of vertical cup-disc ratio≥0.3 (both values determined by ≥99.5th percentile for the normal population in the KNHANES) or (2) the presence of retinal nerve fiber layer defect with violation of the ISNT rule (the neuroretinal rim thickness order of inferior > superior > nasal >temporal).

Non-glaucomatous subjects were those who met all of the following criteria in both eyes. (1) IOP ≤21mmHg, (2) the presence of an open angle (peripheral anterior chamber depth >1/4 corneal thickness), (3) non-glaucomatous optic disc (vertical and horizontal cup-disc ratio <0.7 and inter-eye difference of vertical and horizontal cup-disc ratio <0.2), (4) absence of optic disc hemorrhage or retinal nerve fiber layer defect) and (5) optic disc satisfying the ISNT rule. Only one eye of each subject was considered for the statistical analyses. Data of the eye diagnosed with NTG were used in the NTG subjects and one eye was selected randomly when both eyes were

eligible. For controls, one eye was randomly chosen.

Figure 2 The definition of normal tension glaucoma was based on the International society of Geographical and Epidemiological Ophthalmology (ISGEO) criteria. Subjects with intraocular pressure ≤21mmHg, the presence of an open angle and any one of the following category I or category II diagnostic criteria.



FDT = frequency doubling perimetry; CD = cup to disc; RNFL = retinal nerve fiber layer

*,# values determined by * ≥97.5th & # ≥99.5th percentile for the healthy population in the Korean National Health and Nutrition Examination Survey

Data Analysis

The data were analyzed using SAS (version 9.2; SAS Institute, Cary, NC, USA). Participant characteristics were summarized for the entire sample using means and standard deviations for continuous variables and frequencies and percentages for categorical variables. For univariate analysis each parameter was compared between

the NTG group and the control group. Differences between groups were evaluated using Student's t-test and the chi-square test and to minimize type 1 error, Bonferroni correction for multiple comparisons were used to compare both groups. For multivariate analysis, logistic regression analysis was performed. Variables were stepwise selected according to the statistical significance affecting the discrimination between groups. Statistical significance was defined as a probability value of <5% for the comparison between groups and stepwise variable selection in logistic regression analysis. Odds ratio (OR) and 95% confidence intervals (CI) are presented

Results

Of 13,431 participants who were at least 19 year old and completed ophthalmic and medical examination, 80 subjects were diagnosed as NTG and 4015 were categorized as non-glaucomatous control between 19 to 39 years of age.(Figure 1)

The mean vertical and horizontal cup-disc ratio was significantly different between NTG and control groups (NTG group vs. control group: horizontal cup-disc ratio; 0.58±0.12 vs. 0.33±0.11, p<0.001, vertical cup-disc ratio; 0.56±0.20 vs. 0.34 ±0.11, p<0.001, t-test). Diabetic retinopathy findings existed 2 (2.5%, one with cotton wool spots, and 1 with microaneurysm) in the NTG group and 6 (0.15%, four with microaneurysms and hard exudates, 2 with cotton wool spots) in the control groups. There was no severe diabetic retinopathy with significant ischemia or neovascularization in the eyes of both groups.

Table 1 shows the results of the comparison of ocular and systemic parameters between NTG and non-glaucomatous control aged from 19 to 39 years. Subjects with NTG were more likely to have higher fasting plasma glucose (98.04±33.16 vs. 89.74±12.65, p <0.001) and higher proportion of fasting capillary glucose ≥200 mg/dL (p <0.001) after Bonferroni correction. All the parameters were in included in the multivariate regression analysis with stepwise selection of variables and it demonstrated that high myopia (OR, 3.54 [95% CI,1.34- 9.39], p=0.011), FCG≥200 mg/dL (OR, 12.65 [95% CI, 2.63, 60.94], p=0.002) and low HDL-C (OR, 0.96 [95% CI, 0.94-0.99], p=0.015) significantly associated with increased risk for having NTG. Moderate myopia marginally increased the risk of NTG (OR, 2.18 [95% CI, 0.93-5.12]), p=0.075) (Table 2).

Table 1. Comparing of parameters for Normal-Tension Glaucoma (NTG) and control between 19 to 39 years of age.

	NTG (n=80)	**Control (N=4015)**	**Unadjusted Odds Ratio (95% CI)**	**p-value**
Systemic				
Age	32.34±5.14	30.63±5.86	1.050 (1.000, 1.102)	0.050
Gender(male-female)	40-40	1681-2334	0.769 (0.455, 1.300)	0.327
BMI (kg/m^2).	23.21±3.27	22.88±3.67	1.004 (0.953, 1.058)	0.878
SBP (mmHg)	109.25±10.44	107.83±11.86	1.007 (0.990, 1.024)	0.438
DBP (mmHg)	73.21±9.39	71.19±9.83	1.019 (0.996, 1.042)	0.110
FPG (mg/dL)	98.04±33.16	89.74±12.65	1.015 (1.007, 1.024)	**<0.001**
FCG(mg/dL) ≥ 200	3/71 (4.23)	9/3549 (0.25)	17.805 (4.183, 75.779)	**<0.001**
Insulin(μIU/dL)	11.19±7.57	10.26±5.56	1.013 (0.988, 1.037)	0.311
Total Cholesterol (mg/dL)	178±33.99	176.53±33.21	0.999 (0.989, 1.009)	0.829
HDL-C (mg/dL)	46.55±8.55	50.00±10.79	0.964 (0.94, 0.988)	0.004
TG (mg/dL)	112.18±75.74	112.32±103.02	1.000 (0.998, 1.002)	0.790
BUN (mg/dL)	12.62±3.45	12.35±3.37	1.040 (0.972, 1.113)	0.258
Creatinine (mg/dL)	0.81±0.15	0.80±0.20	0.923 (0.345, 2.470)	0.873
WBC (cells/μL)	6.21±1.76	6.13±1.67	0.937 (0.785, 1.118)	0.470
RBC (cells/μL)	4.75±0.45	4.7±0.48	0.914 (0.550, 1.519)	0.728
Diabetes mellitus	3/80 (3.75)	21/4015 (0.52)	7.318 (2.044, 26.203)	0.002
Hypertension	1/80 (1.25)	56/4015 (1.39)	0.853 (0.113, 6.415)	0.877
Hypotension	14/80 (17.50)	949/4015 (23.64)	0.575 (0.305, 1.084)	0.087
Migraine	10/80 (12.5)	535/4013 (13.33)	0.813 (0.405, 1.631)	0.043
Cold extremity	6/80 (7.5)	725/4013 (18.07)	0.395 (0.161, 0.970)	0.560
Anemia	7/77 (9.09)	345/3864 (8.93)	1.620 (0.536, 4.899)	0.393
Family history of glaucoma	5/19 (26.32)	90/877 (10.26)	3.604 (1.135, 11.448)	0.030
Ocular				
IOP (mmHg)	14.08±2.67	13.84±2.70	1.022 (0.937, 1.115)	0.622

MOPP (mmHg)	42.74±6.06	41.76±6.84	1.018 (0.987, 1.051)	0.255
Myopia				
Low (-3D≤SE<-0.5D)	29/80 (36.25)	1734/4015 (43.29)	0.980 (0.499, 1.924)	0.953
Moderate (-6D≤SE<-3D)	20/80 (25.00)	740/4015 (18.47)	1.669 (0.759, 3.673)	0.203
High (<-6D)	13/80 (16.25)	287/4015 (7.16)	3.424 (1.526, 7.683)	0.003

CI = confidence interval; IOP = intraocular pressure; MOPP = mean ocular perfusion pressure; SE = spherical equivalence; D = diopter; BMI = body mass index; SBD= systolic blood pressure; DBP = diastolic blood pressure; FPG = fasting plasma glucose; FCG = fasting capillary blood glucose; TG = triglyceride; HDL-C=high-density lipoprotein cholesterol; BUN = blood urea nitrogen; WBC = white blood cell; RBC = red blood cell

Significant values ($P < 0.0018$, corrected for multiple comparisons (0.05/27).

Table 2. Multivariate Logistic Regressions of Risk Factors for Normal-Tension Glaucoma (NTG) between 19 to 39 years of age.

Parameter	Odds Ratio (95% CI)	P value
Myopia		
Low (-3 D≤SE<-0.5 D)	1.11 (0.52, 2.37)	0.797
Moderate(-6 D≤ SE <-3 D)	2.18 (0.93, 5.12)	0.075
High (<-6 D)	3.54 (1.34, 9.39)	0.011
FCG(mg/dL) ≥200	12.65 (2.63, 60.94)	0.002
HDL-C (mg/dL)	0.96 (0.94, 0.99)	0.015

CI = confidence interval; SE = spherical equivalence; FCG = fasting capillary blood glucose; HDL-C=high-density lipoprotein cholesterol

Discussion

In normal tension glaucoma, both IOP-dependent and IOP-independent mechanisms play a role in optic nerve damage.[30] Although IOP is a risk factor for progressive visual field loss in NTG, other risk factors may also be important in disease progression. In the present study, we found some significant risk factors other than IOP for NTG in a young population.

Myopia has been consistently associated with primary open angle glaucoma (POAG) in populations over 40 years of age in other population based studies.[8,9,31-34]

In the Tajimi study, where most POAG subjects (92.3%) had NTG,[4] myopia was also a risk factor.[8] Our study found that in a young population, high myopia (SE < -6 D) was a significant risk factor for NTG with an odds ratio of 3.54 (95% CI,1.34-9.39). The prevalence of myopia is relatively higher in Asian than Western countries.[35-37] In a recent study in Korea,[26] the prevalence of myopia in adult Koreans over 40 years of age was 35.7%, higher than Western Europe and United States and similar to China and Japan. In the same study, the prevalence of myopia between 19 to 39 years was 68.8%, considerably higher than in the elderly population. If there is a positive correlation between myopia and NTG, the higher prevalence of myopia in a young age population could lead to an increased risk of NTG in this age group in Korea.

It has been believed that compared with high-pressure POAG, NTG occurs at an older age.[30] The mean age of NTG patients in the Low-Pressure Glaucoma Treatment Study was 64.9 years where the enrolled inclusion criteria was patients with age of 30 years or older.[38] However, in other hospital-based NTG studies of

Korean subjects, mean age of patients was relatively younger (51.8 to 55.6 years)[20,39,40]and the myopic NTG group was significantly younger than the nonmyopic NTG group.[39] Therefore, the relatively younger onset of NTG in Korea might be related to the high prevalence of myopia in a young population.

In our study,a higher level of FPG was significant risk factors in univariate analysis and FCG (mg/dL) ≥200 was a significant risk factor in both univariate and multivariate analysis. The association of diabetes mellitus with open-angle glaucoma was not consistently seen in epidemiologic studies. Diabetes may increase the risk of POAG by elevating IOP.[41] However, the relationship between NTG and diabetes demonstrated in our study suggest that other IOP independent factors in diabetes may also be important in the development of glaucoma. Kim et al[42] showed that diabetes mellitus was more common in subjects with bilateral NTG than with unilateral involvement. They suggested that diabetes mellitus may influence eyes to become more susceptible to glaucomatous damage. Although the etiologic link between diabetes and NTG is not clearly understood, many clinical and experimental observations suggest a role for diabetes mellitus in NTG. For example, in rats with chronically elevated IOP, chemically induced diabetes augmented retinal ganglion cell apoptosis.[43] Also, it had been suggested that diabetes mellitus is associated with impaired autoregulation,[44] which is considered to be important mechanism of eye damage in glaucoma. Vascular dysregulation, leading to both low perfusion pressure and insufficient autoregulation may lead to unstable ocular perfusion and thereby to ischemia and reperfusion damage to the optic nerve.[45]

Dyslipidemia, which is usually defined as high levels of total cholesterol, TG

and/or low level of HDL-C, is one of the most important modifiable risk factors for cardiovascular diseases.[46] Due to its pronounced impact on many organs of the body, dyslipidemia has also been indirectly or directly linked to a wide range of eye diseases, including age-related macular degeneration, glaucoma, retinal vein occlusions and hypertensive and diabetic retinopathy.[47] Also, open-angle glaucoma patients are significantly more likely to have hyperlipidemia.[48] In the present study, low HDL-C was significantly associated with NTG. This is in line with recent studies in which statin and other lipid lowering agent use may have a protective effect against the development of open angle glaucoma[49,50] and visual field stabilization in patients with NTG.[51] Although we could not include the subjects' use of statin in the analysis, we suggest that low HDL-C level could be a candidate for modifiable risk factor for NTG.

Elevated IOP is a risk factor for progressive visual field loss in NTG[52] and the average IOP of POAG subject in Tajimi study was higher than that of normal control. However, in our study, there was no significant different of IOP between NTG and control subjects. The relationship between NTG and IOP has been debated by many researchers. Although there are some studies which demonstrated that NTG patients with asymmetric IOPs have worse visual field loss in the eye with higher IOP,[53,54] the Low-Pressure Glaucoma Treatment Study did not find a relationship between IOP asymmetry and visual field asymmetry.[55] This finding of current study might support that IOP-independent mechanisms is more important in the development of NTG in our study population.

Hypertension, hypotension, level of blood pressure and MOPP were not related with NTG in our study population. Evidence for the effect of blood pressure on

glaucoma remains controversial. Although there are some studies which showed relationship between low DPB, high SBP and low MOPP with a high prevalence of open angle glaucoma[56] and low DBP with the progression of NTG,[57] other epidemiologic studies failed to found significant association with hypertension and glaucoma.[15] As our study subjects consisted of adults under 40 years old, we presume that the relationship between blood pressure or ocular perfusion pressure and NTG is not clear in this age group.

Some known risk factors, including a family history of glaucoma, migraine and cold hands, were not identified in the multivariate analysis. The absence of such factors should be interpreted with caution because the relevant information here was obtained solely by interview. In the previous study, NTG was associated with a lower body mass index.[58] However, we could not find significant difference in our study population. This could be due to the difference of ethnicity and age of the study population.

This study has some limitations. First, although central corneal thickness is one of the risk factors for open angle glaucoma and this may have an impact on the measure of IOP, we did not include it in the analysis as this information was not available in KNHANES. Second, due to the limitation of epidemiological study setting of KNHANES, we couldn't evaluate gonioscopy data which is the gold standard of determining angle status. Instead, we used peripheral anterior chamber depth >1/4 corneal thickness as a definition of open angle. Thirds, as this is a cross-sectional study, we cannot establish that the risk factors were present before the onset of glaucoma had occurred.

Conclusion

In conclusion, high myopia, FCG level ≥200mmol/L and low HDL-C level were significant risk factors for NTG in a young Korean population. The result could be used as useful data not only for early detection of the NTG in a high risk group, but also for the investigation of new treatments.

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국문 초록

서론: 40 세 미만의 한국인에서 정상안압녹내장의 전신적 및 안과적 위험인자가 무엇인지 알아보고자 하였다.

방법: 본연구는 후향적, 단면적 역학연구이며 2009년에서 2010년 사이에 대한민국 인구를 대표하는 392 군락을 무작위 표본추출하여 조사한 자료에서 19세에서 39세 사이를 대상으로 하였다. 모든 참가자를 대상으로 병력청취 및 혈압측정, 혈액표본추출등을 포함한 전신검사를 시행하였다. 자동굴절검사, 골드만압평안압측정, 세극등 검사 및 안저촬영등을 포함한 자세한 안과 검사도 시행하였다. 이상의 안과검사에서 녹내장 의심 범주에 들어가는 경우에는 시야검사를 시행하였다. 정상안압녹내장은 국제지역역학안과협회에서 정한 범주에 따라 진단하였다. 전신적, 안과적 위험인자와 정상안압 녹내장 사이의 관계는 단변수 및 다변수분석을 시행하여 알아보았다.

결과: 80명의 정상안압녹내장 환자와 4015명의 정상대조군이 연구에 포함되었다. 단변수분석에서는 높은 공복혈장포도당농도 및 200mmol/L 이상의 간이공복혈당농도가 정상안압녹내장과 유의한 관련이 있었다. 로지스틱 회귀분석을 이용한 다변수 분석에서는 고도근시 (OR, 3.54 [95% CI,1.34- 9.39]), 간이공복혈당농도가 200 mg/dL 이상인 경우 (OR, 12.65 [95% CI, 2.63, 60.94]), 고밀도지질단백질농도가 낮은 경우 (OR, 0.96 [95% CI,

0.94- 0.99]) 가 정상안압녹내장의 유병과 유의한 관계가 있었다.

결론: 대한민국의 40세 미만의 성인에서 고도근시, 200mmol/L 이상의 간이공복혈당농도, 낮은 고밀도지질단백질농도는 정상안압녹내장의 유의한 위험인자였다.

주요어 : 정상안압녹내장, 젊은연령성인, 근시, 당뇨, 위험인자

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