임상의과학 석사 학위 논문

Metabolic Syndrome : A Risk Factor for Normal Tension Glaucoma?

대사증후군: 정상안압녹내장의 위험요인인가?

2013 년 2 월

서울대학교 대학원

의과대학 임상의과학과

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Abstract (English)

Introduction: To determine whether normal tension glaucoma (NTG) is associated with metabolic syndrome and to evaluate which components of metabolic syndrome are related to NTG.

***Methods*:** This study included 18,244 Korean adults aged 40 years or older who underwent health checkups including fundus photography and intraocular pressure measurements between September 2010 and August 2011. For NTG diagnosis, all participants with findings suggestive of glaucoma completed a comprehensive glaucoma evaluation, including applanation tonometry, gonioscopy, stereoscopic disc photography, retinal nerve fiber layer photography, and standard automated perimetry. The National Cholesterol Education Program Adult Treatment Panel III guideline was used to characterize metabolic syndrome.

***Results*:** Of the 18,244 participants, 3636 (19.9%) had metabolic syndrome and 300 (1.6%) were diagnosed with NTG. The presence of metabolic syndrome was associated with NTG, which had borderline

significance by logistic regression analysis (OR, 1.28; *P*=0.0667). Of the individual components of metabolic syndrome, hypertension and impaired glucose intolerance (IGT) were found to be significantly associated with NTG (OR, 1.53; *P*=0.0005 and OR, 1.47; *P*=0.0063). Individuals with both of these conditions showed an increased association with NTG (OR, 2.42; *P*=0.0001). None of the other components of metabolic syndrome were significantly associated with the incidence of NTG. NTG was positively associated with the number of metabolic syndrome components (OR, 1.10; *P*=0.0398).

***Conclusions*:** Of the metabolic syndrome components, hypertension and IGT contributed to an increased risk of NTG. These findings suggest that components of metabolic syndrome play an important role in the pathogenesis of NTG.

Keywords: Metabolic syndrome, Normal tension glaucoma, Hypertension, Impaired glucose intolerance

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Introduction

Normal tension glaucoma (NTG), a subset of glaucoma, is an entity with progressive glaucomatous optic neuropathy and corresponding visual field defects, but with intraocular pressure (IOP) within the statistically normal range. Because patients with NTG have normal IOP, vascular abnormalities such as vasospasms or ischemia are thought to play a more important role in the pathogenesis of NTG than IOP.(1) Epidemiologic data have shown that while high IOP is a major and strong risk factor for glaucoma, low ocular perfusion pressure is also a strong and consistent risk factor, with some studies also finding associations with low blood pressure.(2) Disc hemorrhages, which are often found in NTG patients, are thought to be a cause of microinfarctions and optic nerve head damage.(3)

Metabolic syndrome is a cluster of atherosclerotic risk factors that are strongly associated with cardiovascular morbidity and mortality. Metabolic syndrome consists of factors including impaired glucose tolerance (IGT) of diabetes, hypertension, hyperlipidemia, and obesity, which may cause widespread microvascular and autonomic dysfunction and hemodynamic disturbances. Previous studies have provided

conflicting evidence regarding whether components of metabolic syndrome increase or decrease the risk of open angle glaucoma (OAG).The Singapore Malay Eye study(4) documented no association between any single or combination of metabolic syndrome components with OAG. In contrast, Newman-Casey et al.(5) reported an association between OAG and diabetes and hypertension. However, there is little information on associations between NTG and metabolic syndrome. This controversy poses several fundamental questions. Are patients with metabolic syndrome at a greater risk of developing NTG? If metabolic syndrome is associated with NTG, what is the etiology of this increased risk? These are critical issues for ophthalmologists because of significant increases in the incidence of hypertension, diabetes, hyperlipidemia, and obesity in recent years.

The purpose of this study was to determine whether NTG is associated with metabolic syndrome and to evaluate which components of metabolic syndrome are related to NTG.

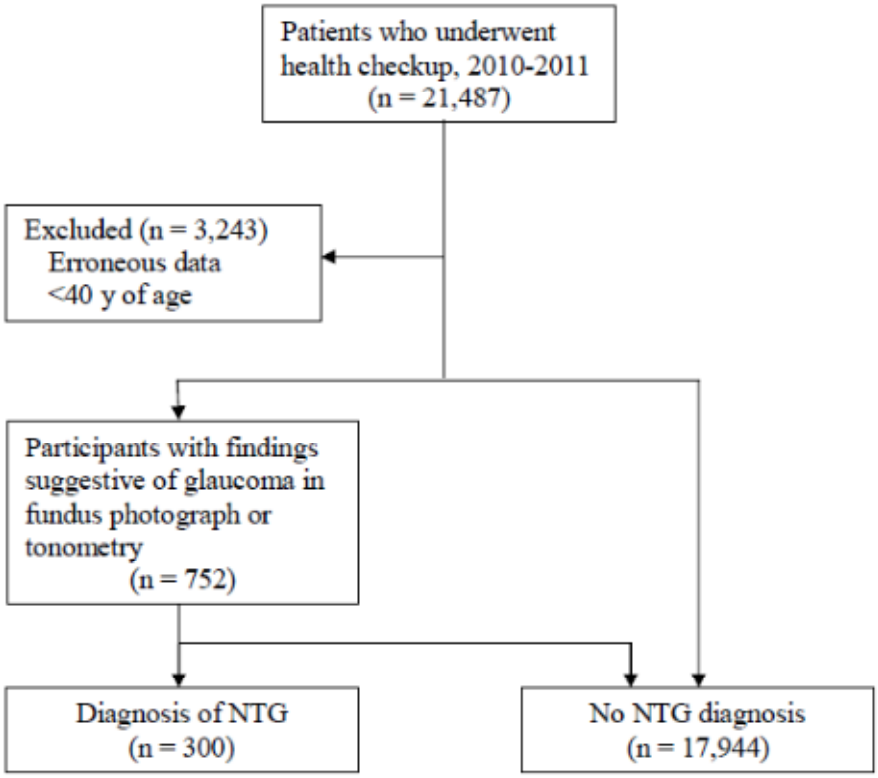
Materials and Methods

Study population

We performed a cross-sectional study involving participants who attended a regular health checkup at The Healthcare Gangnam Center of Seoul National University Hospital between September 2010 and August 2011. Figure 1 demonstrates the derivation of the subject for analysis. Of the 21,487 Korean subjects aged 20 to 94 years who underwent examination, including color fundus photography using a 45° digital non-mydriatic fundus camera (Canon EOS D60; Canon Inc, Utsunomiya, Japan), 18,244 (84.9%) participants were aged 40 years or older. Since glaucoma in young patients is occasionally associated with additional congenital malformations, participants 40 years of age or younger were excluded.(6) All data, including age, gender, blood pressure, body mass index (BMI), height, weight, waist circumference measurements, lipid profiles, fasting serum glucose, laterality, and IOP measured by non-contact pneumatic tonometry (CT-60NCT, Topocon, Tokyo, Japan) were collected from subjects' medical records. IOP measurements were obtained 3 times for each eye, and the mean value of these measurements was used for analysis. The study followed the

tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of the Seoul National University Hospital.

Figure 1. Selection of eligible subjects for the analysis.



Assessment of Normal Tension Glaucoma

For NTG diagnosis, all participants with findings suggestive of glaucoma on non-mydriatic color fundus photography or non-contact tonometry were referred to the glaucoma clinic. Three glaucoma specialists independently evaluated color fundus photographs to detect

suspicious findings, such as glaucomatous optic disc appearance or nerve fiber layer defect. The criteria for suspicious findings were as follows: (1) disc suspect –a cup-disc ratio of the optic disc of ≥0.5, cup-disc ratio asymmetry of ≥0.2, vertical cupping of the optic disc, rim width at superior position (11 to 1 o'clock) or inferior position (5 to 7 o'clock) of ≤0.2 of the disc diameter, or disc hemorrhage; and/or (2) retinal nerve fiber layer (RNFL) suspect – RNFL defects having a width at the disc edge larger than that of a major retinal vessel or diverging in an arcuate or wedge shape; and/or (3) an IOP of ≥22 mmHg.

All participants with findings suggestive of glaucoma underwent a comprehensive glaucoma evaluation, including IOP measurements by Goldmann applanation tonometry, slit-lamp examination, gonioscopy, dilated fundus examination with a 78D lens, color disc photography, red-free RNFL photography (VX-10, Kowa Optimed, Tokyo, Japan), and Swedish interactive thresholding algorithm (SITA) 30-2 perimetry (Humphrey field analyzer II, Carl Zeiss Meditec, Dublin, CA).

NTG was defined as the presence of an open anterior chamber angle, an IOP level below 22mmHg, and 2 of the following 3 features:

(1) evidence of characteristics or compatible glaucomatous optic disc damage on disc stereophotographs and/or (2) RNFL defect on RNFL photographs and/or (3) glaucomatous visual field defect on automated static perimetry.

Definition of metabolic syndrome and hyperlipidemia

Measurements of height, weight, and waist circumference (WC) were obtained for all participants. BMI was calculated as weight in kilograms divided by height in meters squared. Systolic and diastolic blood pressures were also measured with an automated sphygmomanometer.

Metabolic syndrome is defined by the presence of 3 or more of the following the criteria, according to the Regional Office for the Western Pacific Region of the World Health Organization criteria of the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) guidelines:(7, 8) (1) Abdominal obesity (WC≥90cm for men or WC≥80cm for women) (2) Hypertriglyceridemia (triglyceridelevel≥150 mg/dL); (3) Low level of high-density lipoprotein cholesterol (HDL)(HDL <40 mg/dL in men or HDL<50

mg/dL in women); (4) Hypertension (130/85 mmHg or greater or the use of blood pressure medication); and (5) IGT (fasting glucose level of 110 mg/dL or greater, or physician diagnosis of diabetic mellitus and use of diabetes medication).

Diabetes mellitus was defined as a fasting plasma glucose level of 126 mg/dL or greater on at least 2 occasions, plasma glucose of 200 mg/dL or greater 2 hours after a 75-g oral glucose tolerance test, requirement of insulin or glucose-lowering medication to control glucose levels, or a medical history of diet-controlled diabetes. In this study, hyperlipidemia was defined as total serum cholesterol over 220mg/dL or a calculated value of low-density cholesterol upwards of 140mg/dL, according to Japan Atherosclerosis Society guidelines.(9)

Analyses

Statistical analyses were performed with SAS version 9.1 software packages (SAS Institute, Cary, NC, USA). Two groups of subjects were compared using the unpaired *t*-test and the chi-square test, and a *P*-value of <0.05 was accepted as significant. Logistic regression models were used to analyze associations between the incidence of NTG and

any metabolic syndrome components alone or in combination, while adjusting for age and sex. The adjusted odds ratio (OR) and 95% confidence intervals (CIs) were calculated.

We also evaluated the influence of systemic parameters, such as age, gender, BMI, mean blood pressure (mean value of systolic and diastolic blood pressure), presence of NTG, and history of diabetes, on IOP using a single regression model. The IOP of both eyes was used in analyses. In a final, stepwise multiple regression analysis, data were analyzed separately for men and women and for the right and left eye after checking for interactions between variables, which were confirmed as significant through single regression analysis. With variable selection, multiple regression analysis was conducted to control for multicollinearity among independent variables. Linear association between dependent variables and continuous independent variables were analyzed through fractional polynomials.(10)

Results

Among a total of 21,487 Korean participant underwent screening, 3243 subjects were excluded since the age of 40 years or younger and their insufficient data. Of the remaining 18,244 subjects (10375 men and 7869 women), 752 with findings suggestive of glaucoma in fundus photograph or tonometry were referred for further diagnostic examination. According to color fundus photography, 511 participants had glaucomatous optic disc appearance, 309 were RNFL suspect and 105 had both suspicious conditions. Thirty seven participants had an IOP of ≥22 mmHg without abnormal fundus finding. Of these, 300 subjects (1.6% of the study population) were finally diagnosed with NTG (Figure 1).

Basic Subject Characteristics

Of the 18,244 participants, 3636 (19.9%) had metabolic syndrome. Demographic and clinical data are presented in Table 1. Patients with NTG were significantly older (54.2±8.2years vs. 52.8±8.4, $P = 0.0028$) and had a higher mean IOP in both eyes (14.2± 2.9 mmHg vs. 13.4±2.7mmHg in the right eye, $P < 0.0001$; 14.4± 2.9mmHg vs. 13.7±

2.7mmHg in the left eye, $P < 0.0001$). Patients with NTG had a higher serum fasting glucose (102.9 ±22.6 mg/dL vs. 98.8 ±18.4 mg/dL, $P = 0.0073$). The proportion of females was significantly lower among subjects with NTG than among those without NTG (32.0% vs.43.3%, $P = 0.0001$).

Table 1. Characteristics of the Study Population.

Characteristics	All subjects (n=18,244)	Subjects without NTG (n = 17,944)	Subjects with NTG (n = 300)	*P*-value
Mean (SD)				
Age, y	52.8 (8.4)	52.8 (8.4)	54.2 (8.2)	0.0028*
IOP (OD), mm Hg	13.4 (2.7)	13.4 (2.7)	14.2 (2.9)	< 0.0001*
IOP (OS), mmHg	13.7 (2.7)	13.7 (2.7)	14.4 (2.9)	< 0.0001*
Systolic BP, mmHg	117.8 (15.2)	117.8 (15.2)	120.6 (16.3)	0.0595*
Diastolic BP, mmHg	75.7 (11.3)	75.7 (11.4)	77.2 (12.0)	0.3830*
Fasting glucose, mg/dL	98.7 (18.3)	98.8 (18.4)	102.9 (22.6)	0.0073*
Body mass index, kg/㎡	23.7 (2.8)	23.7 (2.8)	24 (2.8)	0.8803*
Waist Circumference				
Male	87.6 (6.8)	87.6 (6.8)	87.5 (6.8)	0.6585*
Female	81.9 (7.5)	81.8 (7.5)	83.4 (7.8)	0.3158*
Triglyceride, mg/dL	120.3 (74.2)	120.2 (74.2)	128 (77.7)	0.3678*
HDL, mg/dL				
Male	50.2 (11.8)	50.2 (11.9)	50 (11.3)	0.7076*

Female	59.6 (14)	59.6 (14.0)	59.5 (14.8)	0.8230*
No. (%)				
Age group, y				
40-49	7367 (40.4)	7274 (40.5)	93 (31.0)	0.0208†
50-59	7002 (38.4)	6869 (38.3)	133 (44.3)	
60-69	3142 (17.2)	3080 (17.2)	62 (20.7)	
70-79	666 (3.7)	655 (3.7)	11 (3.7)	
≥80	67 (0.4)	66 (0.4)	1 (0.3)	
Gender (female)	7869 (43.1)	7773 (43.3)	96 (32.0)	0.0001†

NTG = normal tension glaucoma; SD = standard deviation; IOP = intraocular pressure; OD = right eye; OS = left eye; BP = blood pressure; HDL = high-density lipoprotein cholesterol.

*P-values were calculated using independent sample t-test.

†P-values were calculated using chi-square test.

Association between Metabolic Syndrome and Normal Tension Glaucoma

The prevalence of metabolic syndrome, as defined by NCEP-ATP III, was 19.8% in subjects without NTG and 25.7% in subjects with NTG. The presence of metabolic syndrome was associated with NTG, which had borderline significance by logistic regression analysis (OR, 1.28; 95% confidence interval [CI], 0.98–1.67; $P = 0.0667$).Table 2 shows the ORs for NTG by presence of each individual component and the combination of metabolic abnormalities, calculated by adjusted

logistic regression analysis. There were significant associations of NTG with hypertension and IGT among the individual components of metabolic syndrome (age/gender-adjusted OR, 1.53; 95% CI, 1.20–1.94; $P = 0.0005$; OR, 1.47; 95% CI, 1.12–1.94; $P = 0.0063$, respectively). The OR was greater for persons with hypertension and IGT than for persons with each of these conditions individually (age/gender-adjusted OR, 2.42; 95% CI, 1.54–3.80; $P = 0.0001$). By contrast, persons with low HDL cholesterol levels showed a negative tendency for an increasing risk of developing NTG, but this negative association was not statistically significant (OR, 0.76; 95% CI, 0.56–1.04; $P = 0.0823$). There was no significant association between NTG and several other combinations of metabolic syndrome components.

Table 2. Association of Normal Tension Glaucoma with Metabolic Syndrome Components.

	Subjects without NTG (n = 17,944)	**Subjects with NTG (n = 300)**	**Adjusted OR (95% CI)**	**P-value**
Metabolic syndrome				
Yes, n (%)	3559 (19.8)	77 (25.7)	1.28 (0.98,1.67)	0.0667

Metabolic syndrome components				
Abdominal obesity, n (%)	8591 (47.9)	143 (47.7)	1.05 (0.83,1.33)	0.7000
Hypertriglyceridemia, n (%)	4198 (23.4)	80 (26.7)	1.09 (0.83,1.41)	0.5419
Low HDL cholesterol, n (%)	3720 (20.7)	48 (16)	0.76 (0.56,1.04)	0.0823
HTN, n (%)	7015 (39.1)	158 (52.7)	1.53 (1.20,1.94)	0.0005
IGT, n (%)	2791 (15.6)	72 (24)	1.47 (1.12,1.94)	0.0063
Combinations of Metabolic syndrome components				
HTN + IGT, n(%)	483 (2.7)	22 (7.3)	2.42 (1.54,3.80)	0.0001
HTN + Hyperlipidemia, n(%)	814 (4.5)	17 (5.7)	1.18 (0.72,1.94)	0.5177
IGT + Hyperlipidemia, n(%)	210 (1.2)	5 (1.7)	1.29 (0.53,3.17)	0.5751
HTN + IGT + Hyperlipidemia, n(%)	86 (0.5)	3 (1)	1.95 (0.61,6.21)	0.2594

NTG = normal tension glaucoma; OR = odds ratio; CI = confidence interval; HDL = high-density lipoprotein cholesterol; HTN = hypertension; IGT = impaired glucose tolerance.

All values were adjusted for age and gender.

P-values were calculated using logistic regression analysis.

Table 3 presents the association between NTG and the number of metabolic syndrome components. An increasing number of metabolic

syndrome components showed a positive association with NTG (age/gender-adjusted OR, 1.103; 95% CI, 1.01–1.21; $P = 0.0398$). The prevalence of NTG tended to be proportional to the number of metabolic abnormalities present (Figure 2).

Table 3. Association between Normal Tension Glaucoma and the Number of Metabolic Syndrome Components.

	Patients without NTG (n = 17,944)	**Patients with NTG (n = 300)**	**P-value**	**OR (95% C.I.)**	**OR* (95% C.I.)**
Number of metabolic syndrome components					
0, n (%)	4451 (24.8)	65 (21.7)			1.10 (1.01,1.21)
1, n (%)	5544 (30.9)	79 (26.3)	0.7055	0.94 (0.67,1.31)	
2, n (%)	4390 (24.5)	79 (26.3)	0.5046	1.12 (0.80,1.57)	
3, n (%)	2430 (13.5)	50 (16.7)	0.2672	1.24 (0.85,1.81)	
4, n (%)	944 (5.3)	21 (7)	0.2459	1.37 (0.82,2.22)	
5, n (%)	185 (1)	6 (2)	0.1284	1.94 (0.83,4.56)	

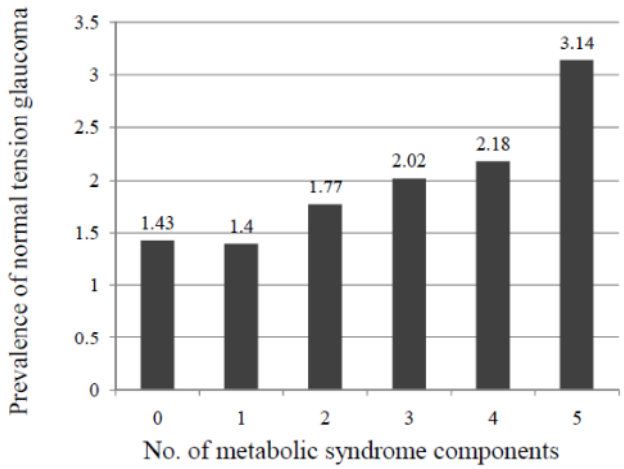
NTG = normal tension glaucoma; OR = odds ratio.

All values were adjusted for age and gender.

P-values were calculated using logistic regression analysis.

*OR is defined as the odds ratio for NTG by one-factor increase in the number of metabolic syndrome components.

Figure 2. Prevalence of normal tension glaucoma according to the number of metabolic syndrome components. The prevalence of normal tension glaucoma tends to be proportional to the number of metabolic abnormalities.



Factors Affecting Intraocular Pressure

Since the IOP was highly correlated between right and left eyes (r = 0.873, $P = 0.001$), one eye from each subject was randomly selected for analysis. In the single regression analysis, several systemic variables, including BMI, mean blood pressure, and history of diabetes, showed a significant association with the IOP in men and women (all, P for trend <0.0001). In the interaction analyses, a significant interaction between

IOP and gender was confirmed ($P< 0.0001$, data not shown). Therefore, we conducted separate stepwise multiple regression analyses for men and women. In the final multiple regression model, BMI, mean blood pressure, and history of diabetes also showed statistical significance with IOP in all participants ($P< 0.05$) (Table 4).

Table 4. Factors Affecting Intraocular Pressure.

Variables	Men (n = 10,375)		Women (n = 7,869)	
	Beta	***P*-value**	**Beta**	***P*-value**
Single regression analysis				
Body mass index, kg/m^2	0.122	<.0001	0.088	<.0001
Mean blood pressure, mmHg*	0.036	<.0001	0.040	<.0001
History of diabetes	0.452	<.0001	1.194	<.0001
Multiple regression analysis				
Body mass index, kg/m2	0.076	<.0001	0.030	0.0049
Mean blood pressure, mmHg*	0.035	<.0001	0.036	<.0001
History of diabetes	0.562	<.0001	0.928	<.0001

*Mean blood pressure is defined as the mean value of systolic and diastolic blood pressure.

Discussion

This study was designed to determine whether NTG is associated with metabolic syndrome and to evaluate which components of metabolic syndrome are related to NTG. By including a large sample of subjects and by adjusting for significant confounding variables, this study has demonstrated that high blood pressure and IGT contribute to an increased risk of NTG. Our results show that hypertension and IGT are independently associated with NTG (adjusted OR, 1.53 and 1.47, respectively). Subjects with both hypertension and IGT had an even higher OR (adjusted OR, 2.42) for developing NTG than when considering each condition individually.

In the present study, IGT was shown to be associated with NTG. This corresponds well with earlier studies, which reported that diabetes contributes to an increased risk of developing OAG.(5, 11-15)Although the association between diabetes and OAG was not consistently demonstrated in epidemiologic studies, many observations suggest that diabetes plays a role in the pathophysiology of NTG. Diabetes causes microvascular damage and may affect vascular autoregulation of the retina and optic nerve. Because impaired autoregulation is considered

to be an important mechanism for the development of glaucoma, it is reasonable to suggest that diabetes may be associated with glaucoma.(16-18) Moreover, another experimental study has reported that oxidative DNA damage from diabetes causes glaucomatous injury.(19) Our results suggest an additional clinical observation, supporting a possible role of diabetes in the pathogenesis of NTG.

Whether hypertension is involved in developing of OAG continues to be debated. In our analysis, the prevalence of NTG was 53% higher in subjects with hypertension than in those without, and the association was even stronger for comorbid conditions with diabetes. These data obtained in our study are in agreement with those of a previous longitudinal cohort study by Newman-Casey et al.,(5) in which individuals with both hypertension and diabetes had an increased hazard of developing OAG relative to individuals with no components of metabolic syndrome. Although an increase in mean blood pressure by 10mmHg resulted in only a 0.34–0.36mmHg increase in IOP in our study, systemic hypertension may increase IOP by increased aqueous humor production resulted from increased ciliary perfusion or an increase in episcleral venous pressure.(20) Other explanations for the

association between hypertension and glaucoma have been proposed in previous reports.(21, 22) Caprioli et al.(2) suggested that the resultant microangiopathy of long-term hypertension can produce harmful effects on the retina and optic nerve. Moreover, during episodic hypotension (nocturnal dips) accompanied by antihypertensive treatments, drop of optic nerve head perfusion pressure below a critical level may result in further optic nerve ischemia and OAG.(23) On the contrary, Barbados Eye Study(24) reported hypertension has a protective role in developing of OAG by maintaining an adequate perfusion for the optic nerve. In other study, diastolic blood pressure was positively related to OAG, whereas systolic blood pressure tended to have a negative relationship.(25) Other studies have implied that ocular perfusion pressure seems more pertinent to glaucoma than BP alone and relationship of BP and OAG may be affected by many complex factors.(2, 22, 26-28)

Our results suggest that lipid abnormalities are not a significant risk factor for NTG. Previous studies have reported discordant results.(4, 5, 29, 30) McGwinet al.(30) demonstrated a protective association of hyperlipidemia against OAG. The potential antiapoptotic,

neuroprotective, and retinal circulatory effects of statins may modify the risk of OAG.(31-33) Experimental research has revealed that statins can increase aqueous outflow capacity by inducing cellular changes in trabecular meshwork structure.(34) Further studies are necessary to better understand the relationship between hyperlipidemia, cholesterol-lowering medications, and the risk of NTG.

In this study, a history of diabetes showed a significant association with IOP of both eyes. Patients with diabetes have been shown to have greater central corneal thickness, which may increase IOP readings measured by Goldmann applanation tonometry.(35, 36)Therefore, it should be noted that corneal stiffening resulted from glycation-induced corneal collagen modification and subsequent increase in central corneal thickness may lead to overestimation of IOP.(37-39)

Interestingly, as the number of metabolic syndrome components increased, the prevalence of NTG tended to increase linearly. Logistic regression analysis showed a significant increase of 10% in the risk of developing NTG with the presence of each additional metabolic syndrome components. Our results are inconsistent with those of a previous study; the Singapore Malay Eye Study(4) reported that the

prevalence of OAG had a U-shaped relationship with the number of metabolic abnormalities. Our observations support the current understanding that IOP-independent factors play an important role in the pathogenesis of NTG.

Hospital-based studies may have detection biases because individuals with comorbidities like diabetes or hypertension are apt to receive more frequent eye examinations than the general population and are therefore more likely to be diagnosed with glaucoma. Since we analyzed data from participants receiving regular health checkups, our results may be relatively free from the aforementioned selection bias compared to the results of most hospital-based studies. Moreover, the strength of this study is that our sample size is considerably larger than those of similar studies. The large sample size increases the precision of the estimate and enables adjustments for numerous confounding variables.

Our study had the following limitations. IOP was initially measured by noncontact tonometer in the health checkup program. Other drawbacks may include limited interpretation of the implication of IOP values because of unmeasured central corneal thickness. Thus, we are

unable to control for the potential confounding effect of central corneal thickness. Although we demonstrated a relationship between several metabolic syndrome components and NTG in various analyses, the cross-sectional study design limited our ability to confirm a causal relationship between these diseases. Moreover, the dose-response relationship between metabolic syndrome and NTG was not explored by the lack of details regarding severity of glaucomatous damage and metabolic syndrome. Further studies, therefore, should overcome these limitations in clarifying whether metabolic syndrome is a true risk factor for NTG.

In conclusion, of the metabolic syndrome components that we studied, high blood pressure and IGT contributed to an increased risk of NTG. These findings suggest that components of metabolic syndrome play an important role in the pathogenesis of NTG.

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초록

서론: 대사증후군의 정상안압녹내장과 관련성과 대사증후군 중 어떤 요인이 정상안압녹내장과 관련이 있는지 알아보고자 하였다.

방법: 2010 년 9 월부터 2011 년 8 월까지의 기간동안 안저사진 및 안압측정을 포함한 건강검진을 받은 40 세 이상의 18,244 명의 한국인을 대상으로 분석하였다. 정상안압녹내장의 진단을 위해 녹내장 의증 환자들을 대상으로 압평안압계측정, 전방각검사, 시신경유두입체촬영검사, 시신경섬유층촬영 및 시야검사를 시행하였다. 대사증후군은 The National Cholesterol Education Program Adult Treatment Panel III 에 따라 정의하였다.

결과: 18,244 명의 환자 중 3636 명 (19.9%)이 대사증후군으로, 300 명 (1.6%)가 정상안압녹내장 환자로 진단되었다. 로지스틱회귀분석을 통해 대사증후군의 유병 여부가 정상안압녹내장과 관련성이 있음을 알 수 있었다(OR, 1.28; *P*=0.0667). 대사증후군의 구성요소 중 고혈압과 내당능장애가 정상안압녹내장과 유의한 관계를 보였다(OR, 1.53; *P*=0.0005 and OR, 1.47; *P*=0.0063). 그러나 이외의 구성요소는 유의한 관련성이 없었다.

대사증후군의 구성요소의 수가 많을수록 정상안압녹내장에 함께 유병될 가능성이 높아지는 경향을 보였다(OR, 1.10; *P*=0.0398).

결론: 대사증후군의 구성요소 중 고혈압과 내당능장애가 정상안압녹내장 유병 위험성을 높임을 알 수 있었다. 이는 대사증후군의 구성요소들이 정상안압녹내장의 발생에 기여할 가능성을 시사한다.

주요어: 대사증후군, 정상안압녹내장, 고혈압, 내당능장애

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