정상 성인 한국인에서 대사증후군의 인자와 안구 관류압 사이의 상관관계

The Association between Metabolic Abnormalities and Ocular Perfusion Pressure in Healthy Korean Adults

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Purpose: To evaluate the influences of metabolic abnormalities on mean ocular perfusion pressure (MOPP) in the Korean population.

Methods: This cross-sectional study involved 40,193 healthy subjects aged 20-89 years who visited the Health Promotion Center of a general hospital. The participants underwent automated multiphasic tests, including non-contact tonometry, automated perimetry, fundus photography, blood samplings for lipid profiles, and measurement of height and weight for body mass index (BMI). National Cholesterol Education Program Adult Treatment Panel III with a Korean specific guideline for waist circumference was used to define metabolic syndrome (MS).

Results: The mean age of participants was 48.38 ± 10.58 years. The MOPP of men (62.71 ± 8.51 mmHg) was significantly higher than that of women (59.95 ± 8.87 mmHg). In univariate analysis between the MOPP and number of components in MS, participants with more MS components had a significantly higher MOPP for both men ($r = 4.017 \pm 0.048$, $p < 0.0001$) and women ($r = 3.549 \pm 0.047$, $p < 0.0001$). In multiple linear regression analysis, age, high-density lipoprotein, triglyceride (TG), waist circumference, and blood glucose were significantly associated with MOPP in men; MOPP had a significant association with age, total cholesterol, TG, waist circumference, blood glucose, and BMI in women.

Conclusions: In the Korean population, both men and women with components of MS were more likely to have a higher MOPP after adjusting for confounding factors. There were significant positive correlations between BMI and MOPP among women, but not among men.

Key words: Body mass index; Mean ocular perfusion pressure; Metabolic syndrome

Introduction

Glaucoma is defined as a progressive optic neuropathy, in which specific damage to the optic nerve and visual field defect are present.¹ Although the exact mechanisms of the anatomic and functional damage in glaucoma are unknown, the most important risk factor of glaucoma is elevated intraocular pressure (IOP).²⁻⁴ Many previous studies demon-

strated systemic risk factors of higher IOP.⁵⁻⁹ Oh et al.⁵ and Imai et al.⁶ showed that metabolic syndrome (MS), a cluster of obesity, hypertension, hyperglycaemia, and hyperlipidaemia, was a risk factor for elevated IOP. Jaen-Díaz et al.⁷ described the relationship between hyperlipidaemia and higher IOP. In addition, obesity and elevated body mass index (BMI) have been associated with elevated IOP.⁸ Therefore, MS, or a component thereof, may influence elevated IOP.⁹

Studies have provided conflicting information regarding factors associated with glaucoma.¹⁰⁻¹³ Some large population-based studies have shown that hypertension and diabetes mellitus are positively correlated with open-angle glaucoma (OAG). There was no association between hypertension and OAG or diabetes mellitus and OAG shown in other

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studies. Furthermore, several studies demonstrated that a higher BMI was associated with a lower risk of OAG.¹⁴⁻¹⁶

Recently, mean ocular perfusion pressure (MOPP) has been found to be an important risk factor for OAG, because a vascular factor may play a critical role in the pathogenesis of normal tension glaucoma.¹⁷⁻¹⁹ To our knowledge, there are no reports on the relationship between MOPP and anthropometric measures. Since there are differing results in previous studies about whether MS or components of MS are associated with a higher or lower risk of OAG, we performed this study to evaluate not only the influence of age and sex but also of BMI and the components of MS on MOPP in the Korean population (as a representative oriental country).

Materials and Methods

We examined 40,193 healthy subjects visiting the Health Promotion Center. The majority of the subjects were office workers and their families who resided in Busan City (population: 3.5 million). The participation rate was 1.1% of the total population of Busan City. Informed consent was obtained from all participants. The study was performed following the tenets set forth in the Declaration of Helsinki and was approved by the Institutional Review Board at Pusan National University Hospital (IRB No. 1702-030-052).

For this study, we used seven age groups divided by decades ranging from 20 to 29 years to 80 plus years. Before testing, each participant was interviewed about previous health problems and medical history, including ocular disease, by a physician and an ophthalmologist. Participants having a history of intraocular disease or surgery at least in one eye and receiving medical treatment for glaucoma, hyperlipidaemia, hypertension, or diabetes mellitus were excluded.

The test schedule of the automated multiphasic tests consisted of 40 items, including best-corrected visual acuity by Snellen chart, non-contact tonometry (NCT), Humphrey automated perimetry (central 30-2 program, Zeiss Humphrey, Dublin, CA, USA), fundus photography (30-degree colour stereo photographs) for the optic disc and macula, and blood

sampling for total cholesterol, High-density lipoprotein (HDL) cholesterol, triglyceride (TG), and glucose, occurred on the same day. Height and weight were measured with the subjects wearing a light-weight hospital gown in a standing position without shoes. BMI was calculated as weight (kg) divided by height (m) squared. IOP was determined by the mean value of three successive readings of both eyes by NCT (Canon T-2, Canon, Tokyo, Japan) between the hours of 09:00 and 11:00, to minimize the effect of diurnal variation. To avoid interexaminer and inter-tonometer variances, all IOP measurements were taken by the same trained paramedical assistant without applying a topical anaesthetic. Mean arterial pressure (MAP) was calculated as follows: $\text{MAP} = \text{diastolic blood pressure (DBP)} + [1/3 \times (\text{systolic blood pressure (SBP)} - \text{DBP})]$. It was thus possible to calculate MOPP from the difference between MAP and IOP substituted for venous pressure as follows: $\text{MOPP} = 2/3 \times (\text{MAP} - \text{IOP})$.^{19,20} Blood samples were taken after fasting for eight hours to obtain total cholesterol, HDL, and TG.

According to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) with the Korean specific guideline for waist circumference,^{5,9,21} MS was defined as having three or more of the following five risk factors: 1) serum triglycerides ≥ 150 mg/dL, 2) serum HDL-cholesterol < 40 mg/dL for men and < 50 mg/dL for women, 3) systolic/diastolic blood pressure $\geq 130/85$ mmHg, 4) fasting glucose ≥ 110 mg/dL, and 5) waist circumference ≥ 90 cm for men and 85 cm for women.

A cross-sectional analysis was based on data obtained from each subject. Data were analysed separately for men and women because the characteristics of Korean MS between men and women are significantly different. We performed a student's *t*-test and an analysis of variance test to show the relationship between the MOPP and age, gender, total cholesterol, TG, HDL, glucose, BMI, and MS. To investigate whether there are significant differences in MOPP between participants with and without MS or MS components, a covariance analysis was used to show age-adjusted, least-square means. Univariate and multivariate linear regression analyses were conducted to assess the effect of total cholesterol, TG, HDL, glucose, BMI, and MS with age

on MOPP. *p*-values less than 0.05 were considered statistically significant. All data were processed and analysed by

the SPSS version 18.0 software for Windows (SPSS Inc., Chicago, IL, USA).

Table 1. Distribution of age and sex in the study population

Age (years)	Value		
	Men	Women	Total
20-29	739 (1.85)	699 (1.75)	1,438 (3.6)
30-39	3,250 (8.10)	3,469 (8.6)	6,719 (16.7)
40-49	6,697 (17.4)	7,296 (18.2)	14,293 (35.6)
50-59	5,688 (14.15)	5,765 (14.35)	11,453 (28.5)
60-69	2,553 (6.35)	2,859 (7.15)	5,412 (13.5)
70-79	432 (1.10)	400 (1.00)	832 (2.1)
≥80	15 (0.04)	31 (0.06)	46 (0.1)
Total	19,674 (48.89)	20,519 (51.11)	40,193 (100)

Values are presented as number (%).

Results

The present study consisted of 40,193 healthy Korean participants (19,674 men and 20,519 women). Table 1 shows the distribution of subjects by age and gender. The mean age of the participants was 48.38 ± 10.58 years (range 20-89 years) for men and 48.29 ± 10.52 years (range 20-88 years) for women. There were significant differences in total cholesterol, HDL, TG, waist circumference, BMI, and MOPP between men and women (Table 2).

The measurement of MOPP in men (62.71 ± 8.51) was

Table 2. General features of some selected variables of the study subjects

Variable	Men	Women	<i>p</i> -value between men and women
Age (years)	48.38 ± 10.58	48.29 ± 10.52	0.089*
Total cholesterol (mg/dL)	206.15 ± 36.52	193.09 ± 34.45	<0.0001*
HDL (mg/dL)	50.57 ± 12.46	57.48 ± 13.76	<0.0001*
TG (mg/dL)	147.50 ± 96.21	107.56 ± 147.50	<0.0001*
Waist circumference	85.49 ± 7.99	79.27 ± 8.60	<0.0001*
BMI (kg/m^2)	24.42 ± 4.14	24.11 ± 3.40	0.009*
MOPP (mmHg)	62.71 ± 8.51	59.95 ± 8.87	<0.0001*

Values are presented as mean $\pm$ standard deviation.

HDL = high-density lipoprotein; TG = triglyceride; BMI = body mass index; MOPP = mean ocular perfusion pressure.

**p*-value by student *t*-test.

Figure 1. Mean ocular perfusion pressure (MOPP) in the male (A) and female (B) according to the age in the study population.

significantly higher than that in women (59.95 ± 8.87 , $p < 0.0001$). In addition, the level of MOPP in both genders was significantly different according to age groups ($p < 0.0001$) (Fig. 1).

Men with abnormal levels of serum TG, serum HDL, blood pressure, fasting glucose, or waist circumference had significantly higher MOPP than those without components of MS. Compared to women participants without risk factors of MS, women with high levels of serum TG, blood pressure, fasting glucose, or waist circumference had elevated MOPP.

In addition, there was also a significant difference in the least-square means of MOPP between participants with and without MS in both genders ($p < 0.0001$) (Table 3). In univariate analysis between MOPP and the number of com-

ponents of MS, participants with more components of MS had significantly higher MOPP in men ($r = 4.017 \pm 0.048$, $p < 0.0001$) and in women ($r = 3.549 \pm 0.047$, $p < 0.0001$).

In univariate linear regression analysis between MOPP and TG, HDL, glucose, total cholesterol, BMI, and age, MOPP had a positive association with total cholesterol, TG, waist circumference, glucose, BMI and age; MOPP had a negative association with HDL in men ($p < 0.0001$). MOPP was positively associated with all variables in women. However, HDL was not a significant factor of elevated MOPP ($p = 0.073$) (Table 4). In multiple linear regression analysis, age, HDL, TG, waist circumference, and glucose showed statistical significance with MOPP in men ($p < 0.0001$); MOPP had significant association with age, total cholesterol, TG, waist circumference, glucose, and BMI in women

Table 3. Age-adjusted least-square means of MOPP between normal and abnormal metabolic components

Variable	Men			Women		
	Normal	Abnormal	<i>p</i> -value*	Normal	Abnormal	<i>p</i> -value*
HDL	66.65 $\pm$ 0.16	67.23 $\pm$ 0.07	0.001	66.30 $\pm$ 0.19	66.27 $\pm$ 0.18	0.880
TG	66.58 $\pm$ 0.14	67.29 $\pm$ 0.09	<0.0001	66.02 $\pm$ 0.15	66.54 $\pm$ 0.21	0.003
Glucose	66.58 $\pm$ 0.07	67.29 $\pm$ 0.16	<0.0001	65.69 $\pm$ 0.08	66.87 $\pm$ 0.25	<0.0001
BP	59.73 $\pm$ 0.1	74.14 $\pm$ 0.14	<0.0001	74.06 $\pm$ 0.22	58.50 $\pm$ 0.14	<0.0001
Waist circumference	66.44 $\pm$ 0.11	67.43 $\pm$ 0.14	<0.0001	65.71 $\pm$ 0.23	66.85 $\pm$ 0.12	<0.0001
MS	63.91 $\pm$ 0.07	69.96 $\pm$ 63.91	<0.0001	62.89 $\pm$ 0.14	69.68 $\pm$ 0.22	<0.0001

Values are presented as mean $\pm$ standard deviation.

MOPP = mean ocular perfusion pressure; HDL = high-density lipoprotein; TG = triglyceride; BP = blood pressure; MS = metabolic syndrome.

**p*-value by student *t*-test.

Table 4. Univariate linear regression analysis for relationship between MOPP and some selected variables in study population

Variable	Men		Women	
	$\beta \pm SE$	<i>p</i> -value*	$\beta \pm SE$	<i>p</i> -value*
Age (years)	0.317 $\pm$ 0.006	<0.0001	0.118 $\pm$ 0.006	<0.0001
Total cholesterol (mg/dL)	0.016 $\pm$ 0.002	<0.0001	0.004 $\pm$ 0.002	0.014
HDL (mg/dL)	-0.066 $\pm$ 0.005	<0.0001	0.009 $\pm$ 0.005	0.073
TG (mg/dL)	0.030 $\pm$ 0.001	<0.0001	0.014 $\pm$ 0.001	<0.0001
Waist circumference (cm)	0.369 $\pm$ 0.007	<0.0001	0.282 $\pm$ 0.007	<0.0001
Glucose (mg/dL)	0.103 $\pm$ 0.003	<0.0001	0.052 $\pm$ 0.002	<0.0001
BMI (kg/m ²)	0.007 $\pm$ 0.002	<0.0001	0.391 $\pm$ 0.014	<0.0001

MOPP = mean ocular perfusion pressure; SE = spherical equivalent; HDL = high-density lipoprotein; TG = triglyceride; BMI = body mass index.

**p*-value by univariate Pearson correlation.

($p < 0.0001$, $p = 0.033$, $p < 0.0001$, $p < 0.0001$, $p < 0.0001$, $p < 0.0001$) (Table 5).

Discussion

The present study showed that individuals with components of MS were more likely to have higher MOPP after adjusting for confounding factors. In addition, we found a significant positive correlation between BMI and MOPP among women, but not among men.

Although many previous studies demonstrated the positive association of BMI with IOP,^{8,22-24} obesity with IOP, and diabetes mellitus with IOP, there were some population-based studies concerned with the positive correlation between BMI and OAG.^{12,16,25} The Singapore Malay Eye Study showed that BMI had a protective association against glaucoma, with those with a higher BMI being at lower risk of glaucoma.²⁵ In addition, in this population-based study, despite the positive relationship between cholesterol level and IOP, metabolic abnormalities were not significant risk factors for glaucomatous optic neuropathy. Pasquale et al.¹⁶ showed a significant inverse relationship between a higher BMI and OAG, with an IOP of 21 mmHg or less among women. However, in another studies, persons with hyperlipidaemia alone had a protective association against glaucoma.^{26,27} Other components of MS, as well as obesity, were risk factors for developing glaucoma. The conflicting results among studies may be explained by the differences

in ethnicity, sample size, and measurement method.

The present study applied MOPP for measuring ocular perfusion, not diastolic perfusion pressure (diastolic pressure-IOP). Choi et al.¹⁹ suggested MOPP would be more appropriate for measuring ocular perfusion than diastolic perfusion pressure because MOPP integrates IOP, systolic, and diastolic blood pressure together. Population-based studies showed that MOPP, as well as IOP, were important risk factors for OAG.^{25,28} Since there was discordance between the associations of anthropometric measures for IOP and MOPP, it might be overestimated that persons with MS, based on the relationship between MS and elevated IOP, had a risk for developing glaucoma. Further studies are needed to understand the complicated relationship of anthropometric parameters with the risk of OAG.

Previous reports suggested the mechanism of the protective effect of obesity on developing glaucoma. Pasquale et al.¹⁶ suggested that adipose tissue, which secretes oestrogen that has a neuroprotective effect, may be the protective mechanism of higher IOP against OAG. Therefore, a higher BMI in women had a protective influence against OAG by producing more oestrogen in the adipose tissue. Since oestrogen affects direct vasodilatory actions, previous reports demonstrated that oestrogen might also play a role in the enhancement of ocular blood flow.^{16,20,29} Given that persons at risk of glaucoma tend to have a lower MOPP,^{17,19,30} our findings might support that persons with components of MS, or women with a

Table 5. Multivariate linear regression analysis for relationship between MOPP and some selected variables in study population

Variable	Men		Women	
	$\beta \pm SE$	p -value*	$\beta \pm SE$	p -value*
Age (years)	0.213 $\pm$ 0.006	<0.0001	0.099 $\pm$ 0.005	<0.0001
Total cholesterol (mg/dL)	-	-	0.003 $\pm$ 0.002	0.033
HDL (mg/dL)	0.019 $\pm$ 0.004	<0.0001	-	-
TG (mg/dL)	0.013 $\pm$ 0.001	<0.0001	0.009 $\pm$ 0.001	<0.0001
Waist circumference (cm)	0.222 $\pm$ 0.007	<0.0001	0.188 $\pm$ 0.009	<0.0001
Glucose (mg/dL)	0.046 $\pm$ 0.003	<0.0001	0.031 $\pm$ 0.002	<0.0001
BMI (kg/m ²)	-	-	0.141 $\pm$ 0.017	<0.0001

MOPP = mean ocular perfusion pressure; SE = spherical equivalent; HDL = high-density lipoprotein; TG = triglyceride; BMI = body mass index.

* p -value by enter method.

higher BMI, have a protective effect against glaucoma. There were several limitations in our study. The first was the inaccuracy of NCT for the measurement of IOP. Although the variation of IOP measurement using NCT was greater than that using Goldmann applanation tonometry (GAT), it was reported that NCT is reliable within normal IOP range.³¹ In addition, NCT has been shown to correlate well with GAT.^{32,33} Second, the calculation of MOPP based on the theoretical formula may not reflect the real physiological status of ocular perfusion. Direct measurement of ocular blood flow could result in a different outcome.

In conclusion, individuals with metabolic abnormalities and women with higher BMI tend to have a higher MOPP. Based on the results of the present study, investigating the mechanism of how metabolic abnormalities affect ocular perfusion may help find the precise associations of anthropometric measures with glaucoma.

Competing interests

The authors report no conflict of interest.

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국문초록

정상 성인 한국인에서 대사증후군의 인자와 안구 관류압 사이의 상관관계

목적: 한국인을 대상으로 대사이상인 평균 안구 관류압에 미치는 영향을 알아보고자 한다.

대상과 방법: 종합병원 건강증진센터에 방문한 40,193명의 건강한 한국인을 대상으로 횡단적 단면연구를 하였다. 참가자들은 비접촉 안압측정, 험프리 자동시야측정, 컬러 안저촬영, 지질대사지표에 대한 혈액검사, 체질량지수 계산을 위한 키, 몸무게 측정, 허리둘레 측정 등을 시행하였다. 미국 콜레스테롤 교육 프로그램(NCEP ATP III)의 진단기준을 이용하여 대사증후군을 정의하였으며, 남성과 여성을 분리하여 자료를 분석하였다.

결과: 평균 나이는 남성 48.38 ± 10.58세, 여성 48.29 ± 10.52세였으며, 남성의 평균 안구 관류압(62.71 ± 8.51 mmHg)이 여성(59.95 ± 8.87 mmHg)에 비해 유의하게 높았다. 단변량 분석에서 대사 증후군의 인자를 많이 가지는 경우, 남성($r=4.017 \pm 0.048$, $p<0.0001$)과 여성($r=3.549 \pm 0.047$, $p<0.0001$) 모두 평균 안구 관류압이 유의하게 높게 나타났다. 다변량회귀분석에서 남성의 경우 나이, HDL, TG, 허리둘레, 혈당이 평균 안구 관류압과 유의하게 관련이 있는 것으로 나타났고, 여성의 경우 나이, 총 콜레스테롤, TG, 허리둘레, 혈당, 체질량지수가 평균 안구 관류압과 유의하게 관련이 있었다.

결론: 한국인에서 남성과 여성 모두 대사 증후군의 인자를 가진 경우 안구 관류압이 높게 나타났다. 여성에서는 체질량지수와 평균 안구 관류압 사이에 유의한 상관관계가 있었으나 남성은 관계가 없었다.