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The Distribution of Intraocular Pressure and Its Association With Metabolic Syndrome in a Community

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Objectives: The current study was performed to assess the distribution of intraocular pressure (IOP) and its association with metabolic syndrome (MS) in a community.
Methods: We measured IOP and MS components from 446 adults, age 20 or more years old, who reside in a community in Kyunggi Province, South Korea. We compared the level of IOP according to the number of metabolic abnormalities and between normal and abnormal metabolic components. Linear regression analyses were used to determine the relationship between IOP and metabolic components.
Results: No significant difference in IOP (mean±SE) was found between men (12.24 ± 2.42) and women (12.55 ± 2.41 mmHg, $p > 0.1$), while IOP of men tended to decrease as age increased (p for trend < 0.01). After adjusting for age, IOP of subjects with abdominal obesity in men and high blood pressure in women were significantly higher than those without abdominal obesity or high blood pressure ($p < 0.05$). Female subjects with MS showed significantly higher IOP than those without MS. Participants with more metabolic disturbances tended to have a greater IOP elevation with a linear trend after adjusting for age and sex. In the univariate regression analysis, age and waist circumference were significantly associated with IOP in men, but systolic and diastolic blood pressure were associated with IOP in women. In final multiple regression model, age, systolic blood pressure, and triglyceride were associated with IOP in women, and age in men.
Conclusions: These findings suggest that MS and its components may be important determinants of elevated IOP.

Key words: Metabolic syndrome, Intraocular pressure, Insulin resistance, Obesity, Glaucoma
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INTRODUCTION

Glaucoma is an optic nerve disease that is associated with a disorder of blood supply and optic disc cupping [1] caused by elevated intraocular pressure (IOP) and one of the most frequent causes (12.3%) of blindness and visual loss in the world [2]. According to a previous study on the relationship between glaucoma and elevated IOP, when ocular hypotensive medication reduced IOP, the risk of a glaucoma incidence was decreased [3]. Other previous studies also showed that elevated IOP was prone to cause an incidence of glaucoma in various population groups [4,5]. In terms of preventing glaucoma, many researches on risk factors related to IOP were performed. They reported that elevated IOP is clearly associated with age [6-8], sex [9-11], hypertension [12,13], diabetes mellitus and impaired fasting glucose [13], and body mass index [14-17].

Considering that some metabolic disturbances, such as hypertension, diabetes mellitus, obesity and so on, are a part of the components of metabolic syndrome (MS), the correlation between MS and elevated IOP is expected. However, only one study [17] on this correlation was performed, and little is known about this correlation. The sample of the previous study consisted of visitors to the health promotion center at a general hospital, which served as a limiting factor.

Therefore, this study was conducted to assess that MS and its components have effect on the elevated on IOP.

METHODS

I. Subjects

We recruited 644 study participants, age 20 or above, who were from a community in Kyunggi Province, from July to August 2008, and voluntarily took part in the study. While recruiting the participants, we informed residents through conference with the representative of residents, home · market · community recreation center

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Table 1. Baseline characteristics in men and women

	Men (n=190)	Women (n=256)	p value*
Age (mean of y)	42.1±10.6	41.2±10.7	0.36
Body mass index (kg/m²)	24.4±3.0	23.2±3.3	<0.001
Regular physical activity (≥3/wk, %)	30.5	30.1	0.92
Current smoking (%)	39.64	1.32	<0.001
Current alcohol consumption (%)	66.1	35.1	<0.001
Income (%)			
≤ $ 2000	13.7	16.8	0.58
≤ $ 4000	60.5	54.5	
> $ 4000	25.8	28.7	
Marital status (%)			
Single, divorced, widow/widower	8.3	16.3	0.02
Married	91.7	83.7	
Education (%)			
None/Compulsory education	11.1	14.4	0.07
Upper secondary school	38.0	46.3	
College or above	50.9	39.3	
Metabolic syndrome components			
Waist circumference (cm)	90.8±6.8	85.0±7.9	<0.001
Fasting glucose (mg/dL)	103.3±26.9	99.9±20.8	0.15
Triglyceride (mg/dL)†	150.5±1.8	102.3±1.8	<0.001
HDL-cholesterol (mg/dL)†	41.1±1.2	46.8±1.2	<0.001
Systolic blood pressure (mmHg)†	122.5±1.1	113.7±1.2	<0.001
Diastolic blood pressure (mmHg)†	81.4±1.1	75.3±1.2	<0.001
Metabolic syndrome (%)	39.0	30.9	0.08
Intraocular pressure (mmHg)	12.24±2.42	12.55±2.41	0.17

mean ± standard deviation or proportions of subjects are presented, HDL: high-density lipoprotein, n=number of subject, $1=₩1,000
* p value for sex difference by t-test or chi-square test.
† Geometric mean ± geometric standard deviation.

visitations, and handing out flyers concerning this study, from several moth ago.

Subjects were excluded from analysis if they have cardiovascular disease, endocrine disorder including hyper-, hypo-thyroidism, eye disease, allergy, sinusitis, and common cold. Final data consisted of 446 subjects (190 men and 256 women) whose IOP of both eyes were investigated.

II. Ophthalmologic Examination

IOP was measured three times on each eye from the right side to the left side, with Kowa KT-800 tonometer (Kowa Company, Tokyo, Japan), and the mean value of the three measurements was taken. Then, we calculated the mean value of IOP of both eyes for analyzing. To minimize bias, all measurements were conducted between 1 and 7 P.M. by a single, well-trained technician. If the measurement of IOP was regarded unreliable by way of survey, we re-measured the unreliable IOP again.

III. Assessment of MS

According to the National Cholesterol Education Program-Adult Treatment Panel Ⅲ [18] with Korean-specific cutoffs for abdominal obesity [19], MS is defined as any three disturbances of following five metabolic components: 1) waist circumference ≥90 cm in men, 85 cm in women, 2) high-density lipoprotein (HDL)-cholesterol <40mg/dL in men, 50 mg/dL in women, 3) triglyceride ≥150 mg/dL, 4) blood pressure ≥130/85 mmHg, 5) fasting glucose ≥110 mg/dL or treatment of type 2 diabetes.

For diagnosing MS, height and weight were measured to 0.1cm and 0.1 kg using stadiometer and bodyweight, and waist circumference measurements were taken at the end of one or two times normal respirations at the middle point between the iliac crest and the lower border of the rib cage. Blood pressure was taken after a 5 min rest. Blood samples were collected after starvation for 12 hours, overnight, and analyzed with autoanalyzer-ADVIA 1650 (Siemens Medical Solutions, Erlangen, German).

IV. Statistical Analysis

Data were analyzed separately for men and women concerning the fact that there are significant differences between sex in the distribution and characteristics of

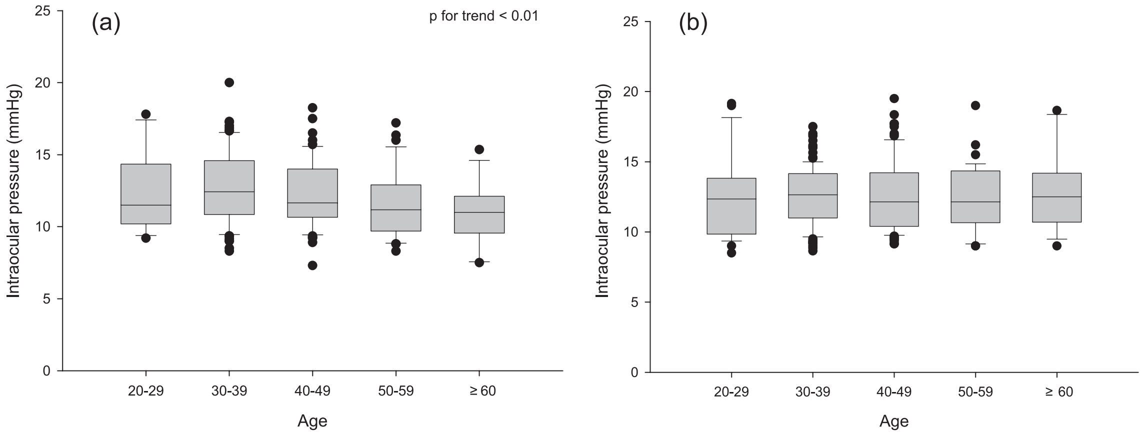

Figure 1. The distribution of mean (± standard errors) intraocular pressure according to the age groups in (a) men and (b) women.

Table 2. Age-adjusted least-square means (± standard errors) of intraocular pressure between normal and abnormal metabolic components

	Men			Women		
	Normal	Abnormal	p value	Normal	Abnormal	p value
Metabolic components						
Waist circumference	11.77 ± 0.25 (n=91)	12.66 ± 0.24 (n=99)	0.0101	12.37 ± 0.22 (n=125)	12.73 ± 0.21 (n=131)	0.25
Fasting glucose	12.18 ± 0.20 (n=147)	12.44 ± 0.38 (n=43)	0.5474	12.51 ± 0.17 (n=204)	12.74 ± 0.34 (n=52)	0.55
Triglyceride	12.05 ± 0.24 (n=102)	12.45 ± 0.25 (n=88)	0.2505	12.43 ± 0.18 (n=191)	12.91 ± 0.31 (n=65)	0.20
HDL-cholesterol	12.31 ± 0.22 (n=117)	12.12 ± 0.28 (n=73)	0.5848	12.35 ± 0.25 (n=93)	12.67 ± 0.19 (n=163)	0.31
Blood pressure	12.16 ± 0.23 (n=104)	12.33 ± 0.26 (n=86)	0.6262	12.30 ± 0.18 (n=182)	13.19 ± 0.29 (n=74)	0.01
Metabolic syndrome	12.00 ± 0.22 (n=116)	12.61 ± 0.28 (n=74)	0.0887	12.31 ± 0.19 (n=177)	13.10 ± 0.29 (n=79)	0.03

HDL: high-density lipoprotein.

Korean MS. We conducted unpaired student t-tests and chi-square tests to show the statistical differences of lifestyle, social economic status, MS and it components, and the distribution of IOP between both sexes, according to the characteristics of variables. Triglyceride, HDL-cholesterol, and blood pressure were log-transformed and analyzed because of its skewed distributions.

To determine the significant differences of IOP between participants with and without MS or MS components, we used covariance analysis with age adjusting and showed least square (LS) means. Univariate regression analysis was also performed to assess the individual effects of MS components and age on elevated IOP. A stepwise multiple linear regression analysis was then performed with backward elimination to select an appropriate model, and a p value > 0.20 was used for removal. To avoid the problem of multi-collinearity, we included independent variables in the models as only systolic blood pressure among systolic or diastolic blood pressure. All statistical analyses used SAS version 9.1 software package (SAS Institute Inc, Cary, NC, USA) for WINDOW, and we considered a p value < 0.05 to be significant for all analyses.

RESULTS

I. Characteristics of Subjects

The mean age of participants was 41.6 years old and, among them, the percentage of women was 57.4% (Table 1). There were not any significant differences in regular physical activity, income, education, and the proportion of MS between both sexes.

Figure 1 shows that the mean IOP (mean ± SE) of men was 12.24 ± 2.42 mmHg, but their IOP level was not significantly different from the level of women's (12.55 ± 2.41 mmHg, p>0.1). IOP in men was prone to decrease according to age (p for trend<0.01), but there was no tendency in women's aging.

II. IOP between Participants with and without Metabolic Disturbances

Table 2 shows that men with abdominal obesity and women with high blood pressure and MS had significantly higher IOP levels (p value<0.05), as compared to participants without those risk factors.

Table 3. Associations of intraocular pressure with age and metabolic variables by univariate linear regression analyses

Variables	Men		Women	
	β± SE	p value	β± SE	p value
Age (y)	-0.0433 ± 0.0164	0.009	-0.0073 ± 0.0141	0.60
Waist circumference (cm)	0.0578 ± 0.0258	0.03	0.0273 ± 0.0190	0.15
Fasting glucose (mg/dL)	-0.0055 ± 0.0066	0.40	0.0115 ± 0.0072	0.11
Triglyceride (mg/dL)*	0.4622 ± 0.2942	0.12	0.4916 ± 0.2587	0.06
HDL-cholesterol (mg/dL)*	0.2138 ± 0.9048	0.81	-0.3414 ± 0.7595	0.65
Systolic blood pressure (mmHg)*	2.4559 ± 1.7447	0.16	3.0479 ± 1.0503	0.004
Diastolic blood pressure (mmHg)*	0.9250 ± 1.5614	0.55	2.1061 ± 0.9951	0.04

HDL: high-density lipoprotein, SE: standard errors
* Log-transformed values were used for analysis

Table 4. Associations of intraocular pressure with metabolic variables by multiple linear regression analyses

Variables	Men			Women		
	β± SE	Partial R^2	p value	β± SE	Partial R^2	p value
Age (y)	-0.0473 ± 0.0169	0.0357	0.006	-0.0407 ± 0.0161	0.0146	0.01
Systolic blood pressure (mmHg)*	2.9308 ± 1.8176	0.0223	0.11	3.8168 ± 1.1531	0.0321	0.001
Waist circumference (cm)	0.0402 ± 0.0265	0.0115	0.13			
Triglyceride (mg/dL)*				0.5608 ± 0.2760	0.0154	0.04

SE: standard errors
* Log-transformed values were used for analysis

There was also significant difference in LSmean IOP between subjects with (13.10 ± 0.29) and without MS (12.31 ± 0.19) in women.

Participants with more MS factors (0, 1, 2, ≥ 3) had higher IOP (LSmean ± SE: 12.07 ± 0.29, 12.10 ± 0.23, 12.21 ± 0.23, 12.89 ± 0.20 mmHg) after adjusting for age and sex, and its linear trend was statistically significant (p for trend<0.05).

III. Regression Model Between IOP and MS Components with Age

In the univariate regression analysis between IOP and MS components with age (Table 3), age and waist circumference showed a significantly negative and positive association, respectively, with IOP in men. However, systolic and diastolic blood pressure had a positive association with IOP in women (p<0.05).

In the final multiple linear regression model (Table 4), age, systolic blood pressure, and triglyceride showed statistical significance with IOP in women, but age was the only variable significantly associated with IOP in men (p<0.05).

DISCUSSION

Some of studies performed in Asia, such as Korea [15], Taiwan [10,20], China [8], and Japan [6,12,14,16], reported that IOP varies with age. Despite variations in design and conduct of the studies, the overall results on the relationship of IOP with age were closely similar. In line with previous Asian studies, our study showed the negative association between IOP and age in men. However, the distribution of IOP between both sexes was not significantly different.

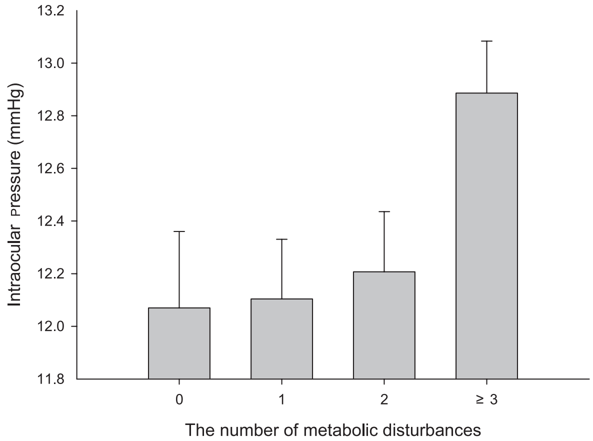

Figure 2. Least-square mean (± standard errors) intraocular pressure according to the number of metabolic disturbances. (p for trend < 0.05)

Table 2 indicated that subjects with metabolic disturbances are prone to have greater elevation in IOP than those without metabolic disturbances, and this result supported the conclusion that IOP was significantly correlated with the number of elements of

MS (Figure 2). Although, in both sexes, only waist circumference and blood pressure had significant effects on IOP among metabolic components, cumulative contributions of individual MS components might impact IOP elevation.

In terms of mechanism, the effect of individual MS components on IOP has already been studied in many previous reports. Some studies indicated the positive association of obesity with IOP [11,12,14-16]. Those results may be owed to the decrease of aqueous outflow and the increase of intraorbital adipose tissue, episcleral venous pressure, and blood viscosity following the increase in number of hemoglobin and hematocrit [16,17]. However, although abdominal obesity was prone to increase IOP in the result of univariate regression analyses of men, our final regression model on IOP (Table 4) showed smaller explanatory power for waist circumference (partial R^2: 0.012) than age (partial R^2: 0.036) in men; it was not statistically significant ($p > 0.1$). Women's result also did not show significant correlation between waist circumference and IOP in any analysis of this study.

In this study, the association between triglyceride and IOP was significant in women (Table 4). Other studies also reported the positive correlation on those variables [17,21], but there was no significant correlation between IOP and HDL-cholesterol. Although some previous studies reported those correlations to be significant [21], they were not significant enough to be verified.

In reporting the relationship between blood pressure and IOP, most studies have consistently shown a strong influence of blood pressure on IOP [10-14,22]. Increased blood pressure has been thought to elevate IOP by not only elevating ciliary artery pressure and consequently inducing an increase in production of aqueous humor, but also increased serum corticoids and sympathetic tone [23]. As a well-recognized risk factor, increased blood pressure had strong impacts on the elevated IOP (Table 4). In women, the explanatory power of blood pressure (partial R^2: 0.032) for IOP was higher than age (partial R^2: 0.015).

We analyzed the association of MS, related to the subsequent development of cardiovascular disease and diabetes [24], with IOP. Our study's strength is that this is the first study to assess the effect of MS and its components on IOP, based on community population, not visitors to a general hospital. However, we could not assess causality between IOP and MS because of the cross-sectional design of the current study.

In conclusion, we expect that IOP is influenced by MS in women. Although MS components had different effects according to the sex differences, a part of MS and its components also looks at the risk factors of IOP elevation in both sexes. However, its mechanism has not yet been clarified, so more studies are necessary to determine the exact cause-and-effect relationship of MS and IOP.

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