·Investigation·

Association between metabolic syndrome and age-related cataract

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Abstract

• AIM: To determine the effect of metabolic syndrome on age-related cataract formation.

• METHODS: We analyzed data for 2852 subjects [41.8% men and 58.2% women; mean (±SD) age, 52.9±13.9y], taken from the Korea National Health and Nutrition Examination Survey 2008. Metabolic syndrome was diagnosed by criteria proposed by the Joint Interim Societies. Cataract was diagnosed by using the Lens Opacities Classification System III. The association between metabolic syndrome and cataract was determined using age-adjusted and multivariable logistic regression analyses.

• RESULTS: In multivariable analyses, men with metabolic syndrome had a 64% increased risk of nuclear cataract [odds ratio (OR), 1.64; 95% confidence interval (CI), 1.12-2.39]. Women with metabolic syndrome had a 56% increased risk of cortical cataract (OR, 1.56; 95% CI, 1.06-2.30). Men and women with metabolic syndrome had a 46% (OR, 1.46; 95% CI, 1.01-2.12) and 49% (OR, 1.49; 95% CI, 1.07-2.08) increased risk of any cataract, respectively. The prevalence of nuclear and any cataract significantly increased with an increasing number of disturbed metabolic components in men, and prevalence of all types of cataracts increased in women. Men using hypoglycemic medication had an increased risk of nuclear (OR, 2.62; 95% CI, 1.41-4.86) and any (OR, 2.27; 95% CI, 1.14-4.51) cataract, and women using antidyslipidemia medication had an increased risk of cortical (OR, 2.18; 95% CI, 1.12-4.24) and any (OR, 2.21; 95% CI, 1.14-4.26) cataract.

• CONCLUSION: Metabolic syndrome and its components, such as abdominal obesity, high blood pressure, and impaired fasting glucose, are associated with age-related cataract formation in the Korean population.

• **KEYWORDS:** cataract; metabolic syndrome; obesity; diabetes mellitus; hypertension
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INTRODUCTION

Cataract is considered to be a global public health problem, and approximately 30% of blindness is caused by cataract [1]. As a cluster of metabolic disorders such as abdominal obesity, impaired fasting glucose, dyslipidemia, and high blood pressure (BP), metabolic syndrome (MS) has been recently known as the fastest growing disorder [2]. Numerous prior studies have shown the associations of MS-related diseases, such as obesity [3-7], diabetes mellitus[3,5,7,8], dyslipidemia [7,9-12], and hypertension [12], with cataract incidence. However, only a few studies have evaluated the association between MS and age-related cataract[3,7,11-13].

MS has been variously defined by several professional and public health organizations after being firstly defined by the World Health Organization (WHO) in 1998 [14]. The most commonly accepted definition is the criteria proposed by the National Heart, Lung, and Blood Institute (AHA/NHLBI)[15]. There are two other widely accepted definitions suggested by the National Cholesterol Education Program Adult Treatment Panel III (NCEP)[16] and the International Diabetes Federation (IDF) [17]. The above three definitions are commonly approached by evaluating five factors [waist circumference (WC), triglyceride, high-density lipoprotein cholesterol (HDL-C), BP, and glucose], but each definition adopts the different application of some metabolic components: using ethnic specific WC cut-off point (IDF) or not (NCEP; AHA/NHLBI), using different cut-off points for fasting glucose (NCEP: ⩾110 mg/dL; AHA/NHLBI, IDF: ⩾100 mg/dL), and making the presence of abdominal obesity mandatory (IDF) or not (NCEP; AHA/NHLBI) for diagnosing MS. Recently, the Joint Interim Societies (JIS) MS definition was proposed for unifying the above three definitions which lacked an uniformed and accepted definition [18]. However, to our knowledge, previous studies did not use the AHA/NHLBI or

JIS definition itself for evaluating the association between MS and cataract. Moreover, most of the previous studies did not evaluate WC but did evaluate body mass index (BMI) to diagnose MS [3,7], although WC is a more important indicator for eye health [19] than BMI. Another benefit of using standardized MS definitions is that it is possible to compare the risk magnitudes of cataract with those of other diseases. Therefore, there is a need to evaluate the impact of MS on cataract formation as diagnosed by the JIS definition. Moreover, previous studies had some limitations: most reported studies, except for one study [3], that were interested in the association between MS and cataract were conducted in Western countries[7,11-13]. Almost all subjects of those studies were limited to the population of a couple of cities or a certain part of a country.

Thus, we conducted this study to assess the association of JIS-defined MS and its components with age-related cataract using nationally representative Korean data taken from the Korea National Health and Nutrition Examination Survey (KNHANES) 2008.

SUBJECTS AND METHODS

This study is a continuation of a preliminary report by Park and Lee[20] that used interview data about life experience with cataract and showed the possible relationships of cataract formation with MS and its components. Data for the present study were derived from the KNHANES 2008 performed by the Korea Centers for Disease Control and Prevention [21]. KNHANES is a nationwide cross-sectional study to select a representative sample of the Korean population. This survey employed stratified multi-stage design based on age, sex, and residence geographic area. The protocol of KNHANES was approved by the Korean Ministry of Health and Welfare. KNHANES was conducted according to the Ethical Principles for Medical Research Involving Human Subjects defined by the Declaration of Helsinki. Informed written consent was obtained from all subjects before their participation. KNHANES staff administered dietary and health interviews and performed physical examinations. Ophthalmologic examinations have been performed since the 2008 survey in KNHANES, and thus ophthalmology studies using KNHANES data could be performed based on ophthalmologists' diagnosis, not interview questions. The details of this survey are described elsewhere [21]. A total of 2944 subjects (≥31y) were examined for every single component of MS and age-related cataract. Subjects were excluded if they were pregnant (n=6) or they did not fast for 8h (n=86). Therefore, 2852 subjects [41.8% men and 58.2% women; mean (±SD) age, 52.9±13.9y] remained for this study.

BMI was calculated as the weight in kg divided by the square of height in meters. WC was measured using a tape measure at the midpoint between the tops of the iliac crest and the lowest rib at the level of the navel, kept parallel to the floor, with minimal respiration. BP was measured three times using sphygmomanometer after participants were seated for 5min, and the average of the last two determinations for systolic BP and diastolic BP was used. Analysis of fasting triglyceride, HDL-C, and glucose were conducted using enzymatic methods with an auto-analyzer (Hitachi Automatic Analyzer 7600, Hitachi, Japan).

MS was defined by JIS criteria [18]. Subjects who had at least three of the following five metabolic disorders were considered to have MS: 1) abdominal obesity: WC ≥90 cm in men or ≥85 cm in women, using the Korean-specific standard[22]; 2) high triglyceride: triglyceride ≥150 mg/dL or treatment; 3) low HDL-C: HDL-C <40 mg/dL in men or <50 mg/dL in women or treatment; 4) high BP: systolic BP ≥130 mm Hg or diastolic BP ≥85 mm Hg or treatment; 5) impaired fasting glucose: fasting plasma glucose ≥100 mg/dL or treatment. Dyslipidemia was defined based on the report of NCEP [16] as HDL-C <40 mg/dL, low-density lipoprotein cholesterol ≥160 mg/dL, total cholesterol ≥240 mg/dL, triglyceride ≥200 mg/dL, or current use of antidyslipidemia medication. Diabetes mellitus was defined as glucose ≥126 mg/dL or current use of hypoglycemic medication [16]. Hypertension was defined as systolic BP ≥140 mm Hg, diastolic BP ≥90 mm Hg, or current use of antihypertensive medication[16].

Lens opacities were examined by using a slit-lamp microscope (Haag-Streit model BQ-900; Haag-Streit, Koeniz, Switzerland). Lens status was classified into anterior subcapsular [Lens Opacities Classification System III (LOCS III) score ≥0.6], posterior subcapsular (LOCS III score ≥2), cortical (LOCS III score ≥4), nuclear (LOCS III score ≥4 for nuclear opalescence or ≥4 for nuclear color), mixed cataract (more than one type), and normal eye status compared with photographic standards [23]. Any cataract was defined as the presence of any of the above five types of age-related cataract.

Statistical Analysis Differences between subjects with and without MS were tested by using the Wilcoxon rank sum test, Chi-square test, and Fisher's exact test. Associations of MS with anterior and posterior subcapsular cataracts were not analyzed in detail due to the low prevalence (0.9% and 0.7%, respectively). Any cataract and specific types of cataract were estimated according to the number of MS components (0, 1, 2, and ≥3). The Cochran-Armitage trend test was used to determine whether the increasing number of MS disturbances was associated with cataract prevalence. Age-adjusted and multivariable logistic regression analyses were conducted to assess the association of cataract formation with MS, its components, and 3 severe metabolic disturbances (*e.g.* dyslipidemia, diabetes mellitus, and hypertension). In the multivariable logistic regression

Table 1 Characteristics of subjects by metabolic syndrome

Variables	Men (*n*=1191)			Women (*n*=1661)		
	No metabolic syndrome (*n*=862;72.4%)	Metabolic syndrome (*n*=329; 27.6%)	[a]*P*	No metabolic syndrome (*n*=1169; 70.4%)	Metabolic syndrome (*n*=492; 29.6%)	*P*
Age	51.3±13.7	55.7±13.3	<0.001	49.6±13.5	61.4±11.8	<0.001
Body mass index (kg/m^2)	23.1±2.8	25.7±2.8	<0.001	22.7±2.9	25.6±3.1	<0.001
Lifestyle						
Vigorous physical activity (min/d)	23.4±50.3	17.8±39.5	0.120	16.5±40.5	14.0±39.1	0.001
Smoking amount (pack-years)	18.1±18.7	22.9±21.6	0.002	0.7±4.0	1.3±5.1	<0.001
Alcohol consumption (g/d)	12.9±18.8	15.0±22.7	0.805	1.8±6.2	1.5±6.0	0.396
Sun exposure (≥5 h/d, %)	41.4	40.3	0.739	22.5	28.6	0.010
Family history of eye disease (%)	19.6	15.3	0.091	22.3	17.9	0.045
Cataract (%)						
Cortical	8.7	10.9	0.234	7.4	15.0	<0.001
Nuclear	14.6	26.4	<0.001	13.9	29.5	<0.001
Anterior subcapsular	1.2	1.3	1.000	0.7	1.1	0.544
Posterior subcapsular	0.7	0.0	0.196	0.7	1.0	0.544
Mixed	4.1	5.5	0.345	4.5	11.8	<0.001
Any	31.3	45.9	<0.001	28.8	63.2	<0.001
Metabolic components						
Waist circumference (cm)	82.1±8.1	91.4±6.9	<0.001	77.2±8.4	87.6±8.3	<0.001
Triglycerides (mg/dL)	128.9±86.0	230.2±146.8	<0.001	97.9±65.0	197.1±117.2	<0.001
HDL-cholesterol (mg/dL)	50.6±11.5	42.7±10.0	<0.001	56.4±11.9	46.3±10.8	<0.001
Systolic blood pressure (mm Hg)	114.6±14.4	124.7±15.3	<0.001	110.3±15.9	127.0±17.6	<0.001
Diastolic blood pressure (mm Hg)	74.5±9.7	80.7±11.9	<0.001	70.8±10.0	77.3±10.9	<0.001
Fasting plasma glucose (mg/dL)	96.8±22.6	113.3±29.1	<0.001	92.9±13.5	110.4±29.9	<0.001

HDL-cholesterol: High-density lipoprotein cholesterol. [a]Tested by Wilcoxon rank sum test, Chi-square test, or Fisher's exact test.

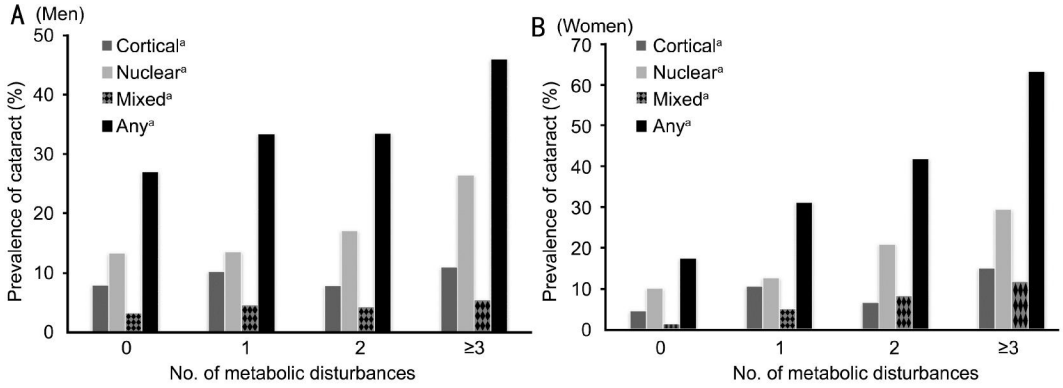

Figure 1 Prevalence of cataract by increasing number of metabolic disturbances in men (A) and women (B) [a]*P* for trend <0.001.

analyses, we adjusted the following potential confounders: age; daily time spent in vigorous physical activity; the total pack-years of smoking (the total number of years spent smoking the number of cigarette packs smoked daily); the amount of daily alcohol consumption; daily sun exposure (≥5 or <5 h/d); family income (<500, 500 to 999, 1000 to 1999, 2000 to 2999, or ≥3000 $/mo); occupational status (blue collar or white collar); marital status (married or single/divorced/widow/widower); and family history of eye disease (*e.g.* glaucoma, cataract, strabismus, retinopathy, blepharoptosis, or other eye diseases). The risks of cataract formation in subjects using medication for metabolic disorders were additionally analyzed after adjusting to age and multiple potential confounders. Statistical analyses were performed for men and women separately, because there was a significant difference between models including and excluding sex ×MS interaction term. Data analyses were conducted using SAS 9.2 software package (SAS Institute Inc., Cary, North Carolina, USA). *P* values less than 0.05 were considered significant.

RESULTS

The mean (±SD) age of the study subjects was 52.9±13.9 years old (Table 1). The prevalence of MS and age-related cataract were 28.8% and 37.5%, respectively. The most prevalent cataract type was nuclear cataract of which 18.1% of the study population suffered. The subjects with MS were significantly older and had higher cataract prevalence and unhealthier metabolic components than those without MS. Figure 1 indicates that nuclear and any cataract in men significantly increased according to the number of MS

Table 2 Odds ratio and 95% confidence interval for cataract formation among subjects with metabolic disturbances compared to subjects without those

Variables	Age-adjusted model		Multivariable model[1]	
	Men	Women	Men	Women
Cortical cataract				
Metabolic components				
Abdominal obesity	0.80 (0.51, 1.27)	1.18 (0.83, 1.67)	0.98 (0.60, 1.61)	1.24 (0.85, 1.82)
High triglyceride	1.23 (0.80, 1.88)	0.81 (0.56, 1.17)	1.26 (0.79, 1.99)	1.04 (0.71, 1.55)
Low HDL-cholesterol	0.95 (0.60, 1.53)	0.95 (0.67, 1.34)	1.17 (0.70, 1.96)	1.02 (0.70, 1.49)
High blood pressure	1.23 (0.81, 1.87)	1.37 (0.94, 1.99)	1.16 (0.74, 1.83)	1.67 (1.10, 2.54)[a]
Impaired fasting glucose	0.71 (0.47, 1.09)	0.91 (0.63, 1.31)	0.75 (0.47, 1.19)	1.08 (0.73, 1.61)
Metabolic syndrome	0.99 (0.64, 1.54)	1.17 (0.82, 1.67)	1.07 (0.65, 1.74)	1.56 (1.06, 2.30)[a]
Severe metabolic disturbances				
Dyslipidemia	0.97 (0.64, 1.46)	1.08 (0.76, 1.53)	1.24 (0.79, 1.95)	1.26 (0.86, 1.86)
Diabetes mellitus	0.66 (0.34, 1.28)	1.21 (0.74, 1.98)	0.72 (0.35, 1.47)	1.35 (0.78, 2.34)
Hypertension	1.14 (0.75, 1.75)	1.62 (1.12, 2.34)[a]	1.00 (0.63, 1.59)	1.96 (1.30, 2.96)[a]
Nuclear cataract				
Metabolic components				
Abdominal obesity	1.40 (1.00, 1.97)[a]	1.09 (0.83, 1.45)	1.24 (0.85, 1.81)	1.17 (0.86, 1.60)
High triglyceride	1.13 (0.80, 1.57)	1.30 (0.98, 1.72)	1.08 (0.75, 1.57)	1.26 (0.92, 1.72)
Low HDL-cholesterol	1.12 (0.78, 1.62)	1.22 (0.93, 1.60)	1.02 (0.67, 1.54)	1.25 (0.92, 1.70)
High blood pressure	0.96 (0.69, 1.34)	1.03 (0.76, 1.38)	0.92 (0.64, 1.33)	0.91 (0.65, 1.27)
Impaired fasting glucose	1.82 (1.31, 2.52)[a]	1.21 (0.91, 1.60)	1.61 (1.12, 2.31)[a]	1.22 (0.89, 1.67)
Metabolic syndrome	1.73 (1.24, 2.42)[a]	1.34 (1.01, 1.77)[a]	1.64 (1.12, 2.39)[a]	1.28 (0.93, 1.75)
Severe metabolic disturbances				
Dyslipidemia	1.02 (0.74, 1.41)	0.94 (0.71, 1.24)	0.91 (0.63, 1.31)	0.89 (0.65, 1.23)
Diabetes mellitus	2.28 (1.48, 3.52)	0.86 (0.57, 1.31)	1.96 (1.21, 3.18)[a]	0.88 (0.55, 1.41)
Hypertension	0.98 (0.70, 1.38)	1.00 (0.74, 1.35)	1.00 (0.69, 1.46)	0.92 (0.66, 1.29)
Mixed cataract				
Metabolic components				
Abdominal obesity	0.91 (0.47, 1.76)	1.65 (1.10, 2.49)[a]	0.78 (0.36, 1.67)	1.48 (0.93, 2.36)
High triglyceride	0.60 (0.30, 1.19)	1.09 (0.72, 1.65)	0.66 (0.31, 1.42)	1.22 (0.76, 1.95)
Low HDL-cholesterol	0.43 (0.20, 0.93)	1.16 (0.77, 1.76)	0.45 (0.18, 1.13)	1.23 (0.77, 1.97)
High blood pressure	0.93 (0.51, 1.71)	1.28 (0.82, 2.00)	1.14 (0.58, 2.25)	1.37 (0.82, 2.28)
Impaired fasting glucose	1.84 (1.01, 3.36)[a]	1.55 (1.03, 2.35)[a]	1.78 (0.90, 3.54)	1.60 (1.00, 2.56)[a]
Metabolic syndrome	0.95 (0.51, 1.79)	1.35 (0.89, 2.05)	1.14 (0.55, 2.37)	1.45 (0.90, 2.32)
Severe metabolic disturbances				
Dyslipidemia	0.79 (0.43, 1.46)	0.89 (0.59, 1.36)	1.00 (0.49, 2.01)	0.99 (0.61, 1.59)
Diabetes mellitus	1.92 (0.91, 4.05)	1.06 (0.59, 1.89)	2.25 (0.97, 5.22)	1.04 (0.53, 2.06)
Hypertension	0.85 (0.46, 1.56)	0.98 (0.64, 1.51)	1.09 (0.55, 2.14)	1.10 (0.68, 1.81)
Any cataract				
Metabolic components				
Abdominal obesity	1.03 (0.74, 1.45)	1.11 (0.82, 1.50)	0.96 (0.67, 1.39)	1.20 (0.87, 1.66)
High triglyceride	1.01 (0.73, 1.41)	1.02 (0.75, 1.39)	1.00 (0.71, 1.42)	1.05 (0.76, 1.46)
Low HDL-cholesterol	0.91 (0.63, 1.33)	1.01 (0.75, 1.35)	0.98 (0.65, 1.47)	1.04 (0.76, 1.42)
High blood pressure	1.05 (0.76, 1.45)	1.13 (0.83, 1.54)	1.03 (0.73, 1.46)	1.18 (0.85, 1.65)
Impaired fasting glucose	1.43 (1.04, 1.98)[a]	1.51 (1.11, 2.05)[a]	1.31 (0.93, 1.85)	1.74 (1.25, 2.42)[a]
Metabolic syndrome	1.46 (1.03, 2.06)[a]	1.41 (1.03, 1.91)[a]	1.46 (1.01, 2.12)[a]	1.49 (1.07, 2.08)[a]
Severe metabolic disturbances				
Dyslipidemia	0.94 (0.68, 1.30)	0.94 (0.70, 1.27)	0.97 (0.69, 1.38)	1.00 (0.73, 1.39)
Diabetes mellitus	1.67 (1.05, 2.67)[a]	1.74 (1.08, 2.80)[a]	1.66 (1.00, 2.74)[a]	1.69 (1.02, 2.81)[a]
Hypertension	1.05 (0.75, 1.48)	1.24 (0.90, 1.70)	1.02 (0.71, 1.47)	1.36 (0.97, 1.91)

HDL-cholesterol: High-density lipoprotein cholesterol. [1]Adjusted for age (continuous), daily time spent in vigorous physical activity (continuous), the total pack-years of smoking (continuous), the amount of daily alcohol consumption (continuous), daily sun exposure (≥5 or <5 h/d), family income (<500, 500 to 999, 1000 to 1999, 2000 to 2999, or ≥3000 US$/mo), occupational status (blue collar or white collar), marital status (married or single/divorced/widow/widower), and family history of eye disease. [a]*P* value <0.05.

components present, and all types of cataracts and any cataract in women significantly increased.

In the multivariable logistic regression analyses, in men, MS was significantly associated with higher risks of nuclear [odds ratio (OR), 1.64; 95% confidence interval (CI), 1.12-2.39] and any (OR, 1.46; 95% CI, 1.01-2.12) cataract (Table 2). In women, MS was significantly associated with higher risks of cortical (OR, 1.56; 95% CI, 1.06-2.30) and any (OR, 1.49; 95% CI, 1.07-2.08) cataract. Impaired fasting glucose of men was significantly associated with higher risks

Table 3 Odds ratio and 95% confidence interval for cataract formation among subjects using medication compared to not-using subjects in each group having metabolic disturbances

Variables	Age-adjusted model			Multivariable model[1]		
	High TG or low HDL-C[2]	High blood pressure	Impaired fasting glucose	High TG or low HDL-C	High blood pressure	Impaired fasting glucose
Men						
Cortical	1.92 (0.76, 4.83)	0.77 (0.43, 1.39)	1.00 (0.44, 2.31)	1.74 (0.64, 4.73)	0.60 (0.30, 1.20)	1.29 (0.53, 3.16)
Nuclear	1.06 (0.45, 2.47)	1.10 (0.68, 1.79)	2.75 (1.61, 4.72)[a]	1.02 (0.41, 2.55)	1.60 (0.92, 2.79)	2.62 (1.41, 4.86)[a]
Mixed	0.58 (0.07, 4.78)	0.87 (0.37, 2.03)	1.23 (0.45, 3.42)	0.79 (0.08, 7.53)	0.79 (0.29, 2.20)	1.14 (0.32, 4.01)
Any	1.40 (0.61, 3.18)	0.70 (0.42, 1.17)	2.30 (1.23, 4.31)[a]	1.25 (0.52, 2.99)	0.82 (0.47, 1.43)	2.27 (1.14, 4.51)[a]
Women						
Cortical	2.02 (1.10, 3.70)[a]	1.02 (0.64, 1.63)	1.42 (0.75, 2.68)	2.18 (1.12, 4.24)[a]	1.03 (0.62, 1.72)	1.41 (0.70, 2.86)
Nuclear	1.32 (0.78, 2.24)	1.14 (0.77, 1.69)	0.68 (0.40, 1.16)	1.38 (0.76, 2.52)	1.14 (0.72, 1.78)	0.81 (0.44, 1.47)
Mixed	0.61 (0.23, 1.58)	1.07 (0.62, 1.85)	0.84 (0.42, 1.70)	0.90 (0.33, 2.45)	1.14 (0.61, 2.16)	0.87 (0.38, 2.02)
Any	1.95 (1.06, 3.58)[a]	1.29 (0.83, 2.02)	1.73 (0.93, 3.22)	2.21 (1.14, 4.26)[a]	1.39 (0.86, 2.26)	1.54 (0.77, 3.07)

TG: Triglyceride; HDL-C: High-density lipoprotein cholesterol. [1]Adjusted for age (continuous), daily time spent in vigorous physical activity (continuous), the total pack-years of smoking (continuous), the amount of daily alcohol consumption (continuous), daily sun exposure (≥5 or <5 h/d), family income (<500, 500 to 999, 1000 to 1999, 2000 to 2999, or ≥3000 US$/mo), occupational status (blue collar or white collar), marital status (married or single/divorced/widow/widower), and family history of eye disease. [2]Either a high TG (≥150 mg/dL or treatment) or a low HDL-C (<40 mg/dL in men or <50 mg/dL in women or treatment). [a]P <0.05.

of nuclear cataract (OR, 1.61; 95% CI, 1.12-2.31). High BP and impaired fasting glucose of women were significantly associated with higher risks of cortical (OR, 1.67; 95% CI, 1.10-2.54) and any (OR, 1.74; 95% CI, 1.25-2.42) cataract, respectively. In the age-adjusted analyses, abdominal obesity was significantly associated with higher risks of nuclear and mixed cataracts in men and women, respectively.

The risks for nuclear and any cataract formation were significantly increased when subjects used medications under high triglyceride or low HDL-C and impaired fasting glucose status (Table 3). However, interestingly, the subjects using medications for high triglyceride or low HDL-C (34 men and 79 women) had healthier triglyceride (men and women using medications, 188.8±132.8 mg/dL and 153.9±93 mg/dL; not using medications, 228.7±131.9 mg/dL and 174.2±114.5 mg/dL; P values of Wilcoxon rank sum test, 0.005 and 0.034) and HDL-C blood levels (men and women using medications, 46.2±10.5 mg/dL and 52.4±13.3 mg/dL; not using medications, 42.6±9.5 mg/dL and 44.6±7.8 mg/dL; P values of Wilcoxon rank sum test, 0.022 and <0.001) as compared with those not using medications (539 men and 775 women) (data not shown). Although many subjects with impaired fasting glucose (74 of 449 men and 102 of 479 women) and high blood pressure (219 of 464 men and 362 of 582 women) also used medications, we did not find any unusual results related to fasting glucose and blood pressure levels.

DISCUSSION

Our study showed that MS was significantly associated with age-related cataract, especially cortical, nuclear, and any cataract. Among MS components, abdominal obesity, high BP, and high fasting glucose were shown to be major contributors to this association. Furthermore, using medication of the subjects for treating high triglyceride or low HDL-C was significantly related to high cataract formation, although those using medication had healthier triglyceride and HDL-cholesterol blood levels than the others not using medication. Previous studies on the association between MS and cataract achieved similar findings to some degree[3,7,11-13].

Obesity and abdominal obesity have been suggested as risk factors for age-related cataract in several populations. A recent review study by Cheung and Wong [6] showed that obesity is consistently associated with cortical and posterior subcapsular cataract but not associated with other types of cataract. In several studies, subjects with high BMI decreased or did not increase the risk of some type of cataract or cataract surgery[3-5]. A study by Sabanayagam *et al* [3] showed that the obesity (≥25 kg/m^2) was positively related to cortical cataract but negatively related to nuclear cataract. In another KNHANES study [4] using Korean-specific obesity definition[24], compared to the normal weight (18.5-22.9 kg/m^2), the overweight (23.0-24.9 kg/m^2) was significantly associated with the lower risk of cataract formation. Studies on the association between abdominal obesity and cataract also showed inconsistent results [8,11-13], similar to that of obesity studies using BMI. Our study showed that abdominal obesity increased nuclear cataract formation in men and mixed cataract formation in women when adjusting age. Among metabolic components, abdominal obesity has been emphasized because visceral fat accumulation is closely associated with cardiovascular disease[25]. Visceral fat obesity has a higher correlation with insulin resistance than subcutaneous fat obesity does [26], and WC was a better indicator to predict a higher intraocular pressure than BMI[19].

Our study found that high triglyceride and low HDL-C was not significantly associated with any type of cataract. Some studies demonstrated the significant associations of high triglyceride or low HDL-C with cataract [7,9-11], but others did not [3,5]. Oxidative stress and inflammation resulting from abnormal triglyceride or HDL-C levels can possibly induce cataract formation [27,28]. In contrast, it is possible that the significant associations are caused by different genetic or environmental factors or chance. Interestingly, among our subjects with problems of triglyceride or HDL-C levels, women using antidyslipidemia medication had higher prevalence of cortical and any cataract than women not using medication (Table 3), although a subject taking medication had healthier triglyceride and HDL-C levels compared to those not taking medication. It is difficult to identify a possible biologic mechanism for this result, because statins, widely used to control serum cholesterol, have antioxidant activity and reduce the risk of cataract [29]. Nevertheless, a previous study showed that shorter-term use of statin (<5y) was associated with the increased risk of cataract surgery[30]. Another study showed the possibility that risk of posterior subcapsular cataract can be increased with high statin doses in some animal models [31]. Alternatively, we guessed that the association between using antidyslipidemia medication and higher prevalence cataract might be caused by that 88.0% of subjects using antidyslipidemia medication also used antihypertensive medication (data not shown) which is known as a risk factor for cataract formation [5]. Indeed, the significant association between antidyslipidemia medication and cataract disappeared after adjusting for the use of antihypertensive medication. Because our study did not clarify the cause of the association between antidyslipidemia medication intake and the increased risk of cortical and any cataract formation in women, future epidemiology study should be conducted to elucidate the causes of this association.

Our study showed the significant associations of impaired fasting glucose or diabetes mellitus with nuclear, mixed, and any cataract formation in both sexes, as documented in many epidemiologic studies [3,5,7,8]. Advanced glycation of lens proteins has been suggested to play a pathogenic role in cataract formation[32]. Cataract formation may also be initiated by hyperosmotic effect through the aldose reductase pathway that converts blood glucose into sorbitol in lens [33]. Increased interleukin-6, fibrinogen, and C-reactive protein levels, as markers of inflammation, in subjects with impaired fasting glucose or diabetes mellitus may be another pathway to form cataract [34]. In our study, taking hypoglycemic medications was significantly associated with cataract formation. In the Beaver Dam Eye Study, use of oral hypoglycemic agents or insulin was associated with cortical cataract and posterior subcapsular cataract formation [35]. However, subjects taking medication had a higher fasting glucose level, compared to subjects not taking medication. Considering that significant associations between hypoglycemic medications and cataract remained after glucose level, medication independently had an effect on cataract formation.

High BP and hypertension were significantly associated with cortical cataract in women. Previous studies documented inconsistent findings for those associations [3,5,8,11,12]. For example, the associations of high BP with cortical, nuclear, posterior subcapsular, and any cataract formation were shown in the previous studies [3,11], but other studies did not show the significance [7]. Studies on hypertension have reported similar results to the studies on high BP [5,8,12]. Although the mechanism explaining the association of high BP and hypertension with cataract is not clear, endothelial dysfunction and inflammation may play a role in this association [36]. Previous studies showed that subjects using antihypertensive medication had a higher incidence of nuclear cataract [5]. However, our results did not show any significant effect of antihypertensive medication on cataract formation. It may be due to the use of antihypertensive and antidyslipidemia medication in made some trade-off.

Finally, our findings demonstrated a significant association between MS and any cataract formation, consistent with previous studies [3,7,11-13] despite their application of different MS definitions. Regarding the specific type of age-related cataract, MS was significantly associated with cortical cataract in women and nuclear cataract in both sexes. In Australian studies, MS increased 10-year incidence of cortical, nuclear, and posterior subcapsular cataract [5], and increased 5-year incidence of cortical and posterior subcapsular cataract [7]. However, MS was significantly associated with only cortical and nuclear cataract in Singaporean[3] and Lithuanian[11] populations, respectively. In our study, the association between MS and any cataract was mainly influenced by abdominal obesity, high BP, and impaired fasting glucose among metabolic components. Moreover, we assumed that this association might be influenced by cumulative contributions of individual metabolic components. Although there is no clear explanation for pathophysiological mechanisms between MS and cataract formation, inflammation, oxidative stress, and endothelial dysfunction may contribute to the association between MS and cataract[27,36].

To our knowledge, this is the first study that investigated the association between MS and age-related cataract formation

among nationwide representative population and simultaneously evaluated the effects of using every MS-related medication on a specific type of cataract. Our results were demonstrated according to the sex, so we found that there were different effects of MS on cataract formation by sex. However, we could not assess causality because our findings were based on a cross-sectional design. We are cautious to apply our findings to other populations, because we focused on one ethnic population in Asia. Another limitation of our study was that we could not analyze dose-response effects of specific MS-related medications and treatment-period effects of those on cataract formation because of insufficient data. In conclusion, our findings showed that MS and its components, abdominal obesity, high BP, and impaired fasting glucose, were associated with age-related cataract formation. Additionally, age-related cataract formation may be influenced by MS-related medications. Thus, one of the effective tools for prevention of age-related cataract formation is to avoid the development of MS.

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REFERENCES

1 Jonas JB, George R, Asokan R, Flaxman SR, Keeffe J, Leasher J, Naidoo K, Pesudovs K, Price H, Vijaya L, White RA, Wong TY, Resnikoff S, Taylor HR, Bourne RR; Vision Loss Expert Group of the Global Burden of Disease Study. Prevalence and causes of vision loss in Central and South Asia:1990-2010. *Br J Ophthalmol* 2014;98(5):592-598

2 Foreyt JP. Need for lifestyle intervention: how to begin. *Am J Cardiol* 2005;96(4A):11E-14E

3 Sabanayagam C, Wang JJ, Mitchell P, Tan AG, Tai ES, Aung T, Saw SM, Wong TY. Metabolic syndrome components and age-related cataract: the Singapore Malay eye study. *Invest Ophthalmol Vis Sci* 2011;52 (5): 2397-2404

4 Park S, Kim T, Cho SI, Lee EH. Association between cataract and the degree of obesity. *Optom Vis Sci* 2013;90(9):1019-1027

5 Tan JS, Wang JJ, Mitchell P. Influence of diabetes and cardiovascular disease on the long-term incidence of cataract: the Blue Mountains eye study. *Ophthalmic Epidemiol* 2008;15(5):317-327

6 Cheung N, Wong TY. Obesity and eye diseases. *Surv Ophthalmol* 2007; 52(2):180-195

7 Ghaem Maralani H, Tai BC, Wong TY, Tai ES, Li J, Wang JJ, Mitchell P. Metabolic syndrome and risk of age-related cataract over time: an analysis of interval-censored data using a random-effects model. *Invest Ophthalmol Vis Sci* 2013;54(1):641-646

8 Lindblad BE, Hakansson N, Philipson B, Wolk A. Metabolic syndrome components in relation to risk of cataract extraction: a prospective cohort study of women. *Ophthalmology* 2008;115(10):1687-1692

9 Heydari B, Kazemi T, Zarban A, Ghahramani S. Correlation of cataract with serum lipids, glucose and antioxidant activities: a case-control study. *West Indian Med J* 2012;61(3):230-234

10 Rim TH, Kim MH, Kim WC, Kim TI, Kim EK. Cataract subtype risk factors identified from the Korea National Health and Nutrition Examination survey 2008-2010. *BMC Ophthalmol* 2014;10;14:4

11 Paunksnis A, Bojarskiene F, Cimbalas A, Cerniauskiene LR, Luksiene DI, Tamosiunas A. Relation between cataract and metabolic syndrome and its components. *Eur J Ophthalmol* 2007;17(4):605-614

12 Galeone C, Petracci E, Pelucchi C, Zucchetto A, La Vecchia C, Tavani A. Metabolic syndrome, its components and risk of age-related cataract extraction: a case-control study in Italy. *Ann Epidemiol* 2010;20 (5): 380-384

13 Bojarskiene F, Cerniauskiene LR, Paunksnis A, Luksiene DI. Association of metabolic syndrome components with cataract. *Medicina (Kaunas)* 2006;42(2):115-122

14 Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 1998;15(7):539-553

15 Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr, Spertus JA, Costa F; American Heart Association; National Heart, Lung, and Blood Institute. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 2005;112(17):2735-2752

16 National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. *Circulation* 2002;106(25):3143-3421

17 Alberti KG, Zimmet P, Shaw J; IDF Epidemiology Task Force Consensus Group. The metabolic syndrome-a new worldwide definition. *Lancet* 2005;366(9491):1059-1062

18 Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, Fruchart JC, James WP, Loria CM, Smith SC Jr; International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; International Association for the Study of Obesity. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009;120(16):1640-1645

19 Park SS, Lee EH, Paek D, Cho SI. Body mass index compared with waist circumference indicators as a predictor of elevated intraocular pressure. *J Korean Oph Opt Soc* 2010;15(3):293-297

20 Park SS, Lee EH. Relations of cataract to metabolic syndrome and its components-based on the KNHANES 2005, 2007. *J Korean Oph Opt Soc* 2009;14(3):103-108

21 Oh K, Lee J, Lee B, Kweon S, Lee Y, Kim Y. Plan and operation of the 4th Korea National Health and Nutrition Examination Survey (KNHANES IV). *Korean J Epidemiol* 2007;29(2):139-145

22 Lee SY, Park HS, Kim DJ, Han JH, Kim SM, Cho GJ, Kim DY, Kwon HS, Kim SR, Lee CB, Oh SJ, Park CY, Yoo HJ. Appropriate waist circumference cutoff points for central obesity in Korean adults. *Diabetes Res Clin Pract* 2007;75(1):72-80

23 Karbassi M, Khu PM, Singer DM, Chylack LT Jr. Evaluation of lens opacities classification system III applied at the slitlamp. *Optom Vis Sci* 1993;70(11):923-928

24 Oh SW, Shin SA, Yun YH, Yoo T, Huh BY. Cut-off point of BMI and obesity-related comorbidities and mortality in middle-aged Koreans. *Obes Res* 2004;12(12):2031-2040

25 Matsuzawa Y, Funahashi T, Nakamura T. The concept of metabolic syndrome: contribution of visceral fat accumulation and its molecular mechanism. *J Atheroscler Thromb* 2011;18(8):629-639

26 Nagaretani H, Nakamura T, Funahashi T, Kotani K, Miyanaga M, Tokunaga K, Takahashi M, Nishizawa H, Kishida K, Kuriyama H, Hotta K, Yamashita S, Matsuzawa Y. Visceral fat is a major contributor for multiple risk factor clustering in Japanese men with impaired glucose tolerance. *Diabetes Care* 2001;24(12):2127-2133

27 Selin JZ, Lindblad BE, Rautiainen S, Michaëlsson K, Morgenstern R, Bottai M, Basu S, Wolk A. Are increased levels of systemic oxidative stress and inflammation associated with age-related cataract? *Antioxid Redox Signal* 2014;21(5):700-704

28 Tabet F, Rye KA. High-density lipoproteins, inflammation and oxidative stress. *Clin Sci(Lond)* 2009;116(2):87-98

29 Chodick G, Heymann AD, Flash S, Kokia E, Shalev V. Persistence with statins and incident cataract: a population-based historical cohort study. *Ann Epidemiol* 2010;20(2):136-142

30 Fong DS, Poon KY. Recent statin use and cataract surgery. *Am J Ophthalmol* 2012;153(2):222-228

31 Gerson RJ, MacDonald JS, Alberts AW, Chen J, Yudkovitz JB, Greenspan MD, Rubin LF, Bokelman DL. On the etiology of subcapsular lenticular opacities produced in dogs receiving HMG-CoA reductase inhibitors. *Exp Eye Res* 1990;50(1):65-78

32 Stevens VJ, Rouzer CA, Monnier VM, Cerami A. Diabetic cataract formation: potential role of glycosylation of lens crystallins. *Proc Natl Acad Sci USA* 1978;75(6):2918-2922

33 Pollreisz A, Schmidt-Erfurth U. Diabetic cataract-pathogenesis, epidemiology and treatment. *J Ophthalmol* 2010;2010:608751

34 Hayashino Y, Jackson JL, Hirata T, Fukumori N, Nakamura F, Fukuhara S, Tsujii S, Ishii H. Effects of exercise on C-reactive protein, inflammatory cytokine and adipokine in patients with type 2 diabetes: a meta-analysis of randomized controlled trials. *Metabolism* 2014;63 (3): 431-440

35 Klein BE, Klein R, Lee KE, Danforth LG. Drug use and five-year incidence of age-related cataracts: The Beaver Dam Eye Study. *Ophthalmology* 2001;108(9):1670-1674

36 Klein BE, Klein R, Lee KE, Knudtson MD, Tsai MY. Markers of inflammation, vascular endothelial dysfunction, and age-related cataract. *Am J Ophthalmol* 2006;141(1):116-122