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Association between pterygium and obesity status in a South Korean population

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Abstract

This study examined the association between pterygium and obesity status by examining a nationally representative sample of South Korean adults.

This population-based, cross-sectional study comprised 16,234 adults (aged ≥19 years) who had participated in the fifth annual Korea National Health and Nutrition Examination Survey from 2010 to 2012. The enrolled subjects underwent interviews, clinical examinations, and laboratory investigations. We compared body mass index (BMI) and waist circumference (WC), according to the presence of pterygium. Multiple logistic regression analysis was conducted to examine the associations of each obesity parameter with pterygium after adjusting for age, smoking status, alcohol consumption, physical activities, educational levels, outdoor occupation, area of residence, and daily sun exposure duration.

The prevalence rate of pterygium tended to increase as the BMI increased only in women, and both male and female subjects with higher WC were likely to have more pterygium in both sexes. In the multivariate analysis, overweight women had an odd ratio (OR) (95% confidence interval (CI)) of 1.16 (0.86–1.55) and obese women had an OR (95% CI) of 1.35 (1.02–1.77) compared to women with normal weight (*P* for trend for ORs = 0.04). Compared to women without abdominal obesity, abdominally obese women had an OR (95% CI) of 1.26 (1.01–1.58). There was no significant association between obesity and pterygium in men.

The present study provides epidemiologic evidence of an association between obesity and pterygium in women. Further studies are needed to examine the sex difference in the pathogenesis of pterygium.

Abbreviations: BMI = body mass index, BP = blood pressure, CIs = confidence intervals, FPG = fasting plasma glucose, KCDC = Korea Centers for Disease Control and Prevention, KNHANES = Korea National Health and Nutrition Examination Survey, NO = nitric oxide, ORs = odds ratios, ROS = reactive oxygen species, SE = standard error, TAS = total antioxidant status, UVB = ultraviolet-B, WC = waist circumference.

Keywords: obesity, population-based, pterygium

1. Introduction

Pterygium is a benign mass with fibrovascular growth of the conjunctiva and Tenon capsule, commonly encroaching onto the cornea.[1] Several risk factors including older age, male gender, outdoor occupation, rural residence, and low educational levels have been proposed to increase the risk of pterygium.[2–7] Although the pathogenesis of pterygium formation is still not clarified, pterygium has been reported to be strongly linked with ultraviolet-B (UVB) light exposure.[8,9] People with increased UVB exposure, such as those living near the equator, have an increased risk of pterygium formation.[10] UVB exposure and the resultant oxidative stress play a primary role in the pathogenesis of pterygium.[11–13]

Obesity, a known threat to health, is a prominent cause of chronic vascular and pulmonary diseases, cancer, and hepatic and renal dysfunction.[14–16] Obesity can induce systemic oxidative stress, which causes the complications associated with obesity.[17,18] Other factors also contribute to oxidative stress in obese patients, including hyperleptinemia, low antioxidant defense, chronic inflammation, and l reactive oxygen species (ROS) generation.[17–20]

Based on the previous findings that oxidative stress may be a common denominator in the pathogenesis of pterygium and obesity, we hypothesized that the association between pterygium and obesity status might differ among individuals. In the present study, we analyzed the association between pterygium and obesity via a population-based survey conducted by the Korean government. We focused on the association between pterygium and obesity status, including body mass index (BMI) and waist circumference (WC).

2. Methods

2.1. Survey and subjects

This population-based, cross-sectional study was based on the data obtained from the fifth annual Korea National Health and

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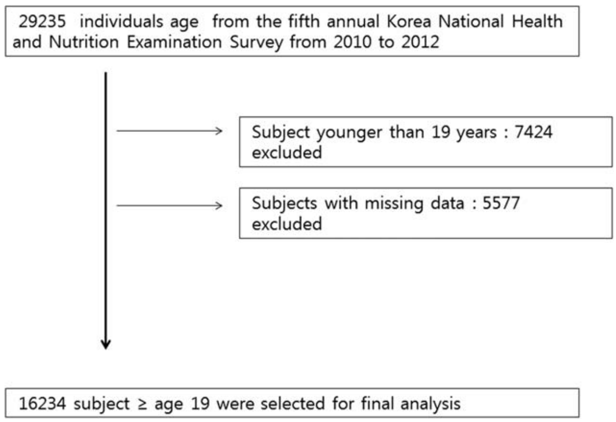

Figure 1. Stepwise approach to final selection of study population.

Nutrition Examination Survey (KNHANES) from 2010 to 2012. The KNHANES has been conducted annually since 1998 by the Division of Chronic Disease Surveillance, Korea Centers for Disease Control and Prevention (KCDC), and the Korean Ministry of Health and Welfare. The detailed design of the KHANES has been described previously.[21] The survey was designed to assess the health and nutritional status of the noninstitutionalized civilian population of South Korea and consists of 3 surveys including health interview, health examination, and nutritional examination surveys. Participants were selected from sampling household units based on the population and housing consensus from the National Census Registry in Korea using a stratified, multistage, and probability based sampling design with proportional allocation.

Of 29,235 participants sampled initially, 7424 individuals aged <19 years and 5577 with any missing data were excluded. And then, a total of 16,234 subjects (6990 men and 9244 women) were included in the final analyses (Fig. 1). All participants in the survey signed an informed consent form before participation. This survey was reviewed and approved by the Institutional Review Board of the KCDC.

2.2. Measurement of obesity parameters and definitions

Trained staffs performed anthropometric measurements of the subjects. Body weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, with the subjects wearing indoor clothing without shoes. BMI was calculated using the formula: body weight (kg)/height^2 (m^2). Normal BMI was defined as $18.5 \leq \text{BMI} < 23\,\text{kg/m}^2$. The presence of overweight was defined as $23 \leq \text{BMI} < 25\,\text{kg/m}^2$ and general obesity as $\text{BMI} \geq 25\,\text{kg/m}^2$ and overweight as $23 \leq \text{BMI} < 25\,\text{kg/m}^2$.[22] WC was measured at the midpoint between the lower border of the rib cage and the iliac crest at the end of a normal expiration with the subjects in a standing position. The cutoff point of abdominal obesity was defined as WC ≥90 cm for men and WC ≥80 cm for women.[23,24]

2.3. Assessment of pterygium

Study ophthalmologists performed a structured slit-lamp examination (Haag-Streit model BQ-900; Haag-Streit AG, Koeniz, Switzerland) to assess diseases in the anterior segment of the eye. A presence of pterygium was defined as a radially oriented fibrovascular lesion crossing the nasal or temporal limbus. We diagnosed as pterygium when the patients had it in at least 1 eye as previously defined.[25] The length of pterygium was measured by measuring the longest horizontal length from the limbus with horizontal slit illumination. Subtypes of pterygium were based on the visibility of the underlying episcleral blood vessels. The atrophic subtype was defined as pterygium in which the episcleral vessels underlying the body of pterygium were clearly distinguished. The fleshy subtype was defined as thick pterygium was completely obscured. All other pterygia that did not satisfy the definitions of above two categories were defined as intermediate type.[26]

2.4. Covariates

The detailed methodologies of these studies have been summarized in a previous report.[21,27] All subjects were asked about their sociodemographic and lifestyle characteristics by trained interviewers. Educational level was classified as 2 groups according to the number of schooling year: more than 12 years (high school graduate) or less. The areas of residence were classified into urban areas (administrative division of "dong") and rural areas (administrative division of "eup" or "myeon"). The type of occupation was categorized as 6 groups such as "manager and specialized job," "office job," "service and sales job," "agriculture, fishery, and forestry job," "blue-collar laborer job," and "unemployed." The groups of "agriculture, fishery, and forestry job" and "blue-collar laborer job" were defined as outdoor occupation. Daily sun exposure duration was categorized as <5 and ≥5 hours. Subjects were categorized into 3 groups according to the average alcohol amount (g) of consumed per day for a month before the interview: nondrinkers, light to moderate drinkers (1–30 g/day), and heavy drinkers (>30 g/day).[28] Subjects were categorized into 3 groups according to the response on the self-report questionnaire: nonsmokers (those who had never smoked or had smoked <100 cigarettes in their lifetimes), ex-smokers (those who had smoked more than 100 cigarettes in the past but do not smoke currently), and current smokers (those who were smoking currently, and had smoked ≥100 cigarettes in their lifetimes). Physical activity was assessed using the modified form of International Physical Activity Questionnaire for Koreans. Subjects were considered regular physical exercisers if they performed moderate exercise more than 5 times per week for over 30 minutes per session or performed vigorous exercise more than 3 times per week for over 20 minutes per session.[29]

Blood pressure (BP) was measured 3 times with 5-minute intervals on the right arm in the seated position using a mercury sphygmomanometer (Baumanometer, WA Baum Co., Copiague, NY), and the mean value of the second and third measurements was used in the analysis. Hypertension was defined as a systolic BP ≥ 140 mm Hg, a diastolic BP ≥ 90 mm Hg, or treatment with antihypertensive medications.[30]

Blood samples were obtained after fasting for at least 8 hours. They were appropriately processed and immediately refrigerated and transported in cold storage to the Central Testing Institute in Seoul Korea. Serum levels of fasting plasma glucose (FPG) were measured using a Hitachi Automatic Analyzer 7600 (Hitachi, Tokyo, Japan) by enzymatic methods using commercially available kits (Daiichi, Tokyo, Japan). Type 2 diabetes mellitus was defined by an FPG level ≥126 mg/dL, treatment with insulin or oral hypoglycemic agents, or diagnosis by a physician.[31]

2.5. Statistical analysis

The survey procedure of SAS version 9.2 for Windows (SAS Institute, Cary, NC) was used for all statistical analyses to

Table 1

Baseline characteristics of study subjects according to the presence of pterygium.

	Men			Women		
	No	**Yes**	**P^***	**No**	**Yes**	**P^***
N	6420	570		8667	577	
Age, y	42.9±0.3	59.3±0.7	<0.001	45.2±0.3	64.5±0.7	<0.001
Body mass index, kg/m^2	24±0	23.7±0.1	0.052	23.1±0.1	24.3±0.2	<0.001
Waist circumference, cm	83.8±0.2	84.6±0.4	0.056	77.5±0.2	82.6±0.5	<0.001
Hypertension, %	30.5 (0.8)	49.8 (2.6)	<0.001	23 (0.6)	50.2 (2.9)	<0.001
Diabetes mellitus, %	8.7 (0.4)	12.6 (1.7)	0.01	7 (0.4)	15.5 (1.9)	<0.001
Current smoker, %	46 (0.7)	35 (2.4)	<0.001	6.3 (0.4)	4.4 (1.2)	0.205
Heavy alcohol drinker, %	18.4 (0.6)	19.8 (2.1)	0.505	2.2 (0.2)	1.1 (0.5)	0.135
Regular physical activity, %	27.9 (0.7)	27.6 (2.4)	0.902	22.4 (0.7)	25.4 (2.2)	0.148
Educational level (≥12 y), %	79.2 (0.7)	41.9 (2.6)	<0.001	65.3 (0.8)	14.2 (2)	<0.001
Rural residence, %	19.1 (1.8)	33.8 (3.4)	<0.001	19.1 (1.7)	42.5 (3.7)	<0.001
Outdoor occupation, %	34.1 (1)	53 (2.6)	<0.001	16.4 (0.7)	32.5 (2.9)	<0.001
Sun exposure duration (≥5 h)	27.4 (0.9)	39.9 (2.6)	<0.001	13.1 (0.7)	30.7 (3.0)	<0.001
Length, mm		1.8±0.1			1.8±0.1	
Recurrence (yes), %		26.6 (2.2)	—		29.9 (2.2)	—
Subtype of pterygium, %						
Atrophic	—	52.5 (2.9)		—	53.1 (3.1)	
Intermediate	—	35.4 (2.7)		—	36.1 (2.7)	
Fleshy	—	12.1 (1.8)		—	10.8 (1.7)	

Data are presented as means±standard error (SE) or percentage (SE).

* P values were calculated by using Chi-square test for categorical variables or independent t test for continuous variables.

account for the complex sampling design. Two-sided P values <0.05 were considered statistically significant. Data are presented as mean±standard error (SE) or as percentage (SE). Independent t test and Chi-square test for continuous and categorical variables respectively were used to compare the baseline characteristics according to the presence of pterygium in both sexes. The prevalence rates of pterygium according to obesity parameters or obesity status were compared by using Chi-square test. Hierarchical multivariable logistic regression analyses were used to estimate the associations between pterygium and obesity parameters. Odds ratios (ORs) and 95% confidence intervals (CIs) for the presence of pterygium according to obesity status were obtained after adjusting for age in Model 1. Model 2 was adjusted for age, smoking status, alcohol consumption, and physical activity and then Model 3 was adjusted for all variables in Model 2 plus educational level, outdoor occupation, area of residence, and daily sun exposure duration.

3. Results

3.1. Baseline characteristics of study subjects according to the presence of pterygium

The baseline characteristics of subjects according to the presence of pterygium in both sexes are described in Table 1. The mean age of men with pterygium was 59.3±0.7 years, while that of men without pterygium was 42.9±0.3 years ($P<0.001$). The mean age of women with and without pterygium was 64.5±0.7 and 45.2±0.3 years, respectively ($P<0.001$). Women with pterygium had higher BMI and WC than women without pterygium ($P<0.001$ for both BMI and WC). However, in men, the obesity parameters were not significantly different according to the presence of pterygium. In both sexes, the prevalence rates of hypertension and type 2 diabetes were higher among subjects with pterygium than among those without pterygium. The rate of men without pterygium who were current smokers was higher than that of men with pterygium who were current smokers ($P<0.001$). The rates of current smoking in women and in those with heavy alcohol consumption and regular physical activity in both sexes were not different according to the presence of pterygium. In both men and women, subjects without pterygium had a significantly higher educational level than those with pterygium and the rates of rural residence, outdoor occupation, and daily sun exposure duration of more than 5 hours were significantly higher in subjects with pterygium than in those without pterygium ($P<0.001$).

3.2. Prevalence rates of pterygium in relation to obesity

Figure 2 shows the prevalence rates of pterygium according to the obesity parameters. The prevalence rate of pterygium in women tended to increase as the BMI increased; however, it was not associated with the BMI in men. With respect to WC, both male and female subjects with abdominal obesity were likely to have higher prevalence of pterygium. Figure 3 shows the prevalence rates of pterygium according to the obesity status. The pterygium rates were significantly different according to the presence of general obesity or abdominal obesity in both men and women ($P=0.024$ in men and $P<0.001$ in women). Also, in both sexes, the rates were higher in subjects with only abdominal obesity than that in those with only general obesity.

3.3. Risks of pterygium according to obesity parameters

Table 2 shows the ORs (95% CIs) of pterygium according to obesity parameters. In women, after adjustment for age (Model 1), subjects with overweight ($23 \le \text{BMI} < 25\,\text{kg/m}^2$) and obesity ($\text{BMI} \ge 25\,\text{kg/m}^2$) had OR (95% CI) of 1.2 (0.9–1.6) and 1.43 (1.09–1.87), respectively, compared to those with normal weight ($18.5 \le \text{BMI} < 23\,\text{kg/m}^2$). The ORs exhibited significantly increasing trends (P for trend=0.008). After a further adjustment for smoking status, alcohol consumption, and physical activity

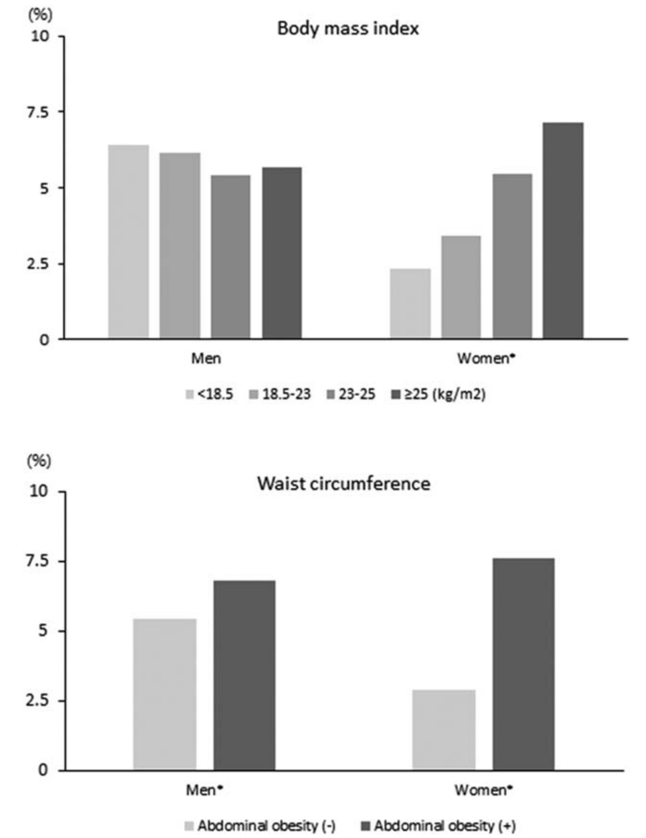

Figure 2. Prevalence rates of pterygium according to the obesity parameters (*P for trend <0.05).

(Model 2), overweight women had an OR (95% CI) of 1.11 (0.83–1.49) and obese women had an OR (95% CI) of 1.34 (1.03–1.76) compared to women with normal weight (P for trend for ORs = 0.03). These associations persisted even after an additional adjustment for educational level, outdoor occupation, residential area, and daily sun exposure duration (P for trend for ORs = 0.04 in Model 3). Compared to women without abdominal obesity, women with abdominal obesity had an OR (95% CI) of 1.39 (1.11–1.74) in Model 1, 1.3 (1.04–1.63) in

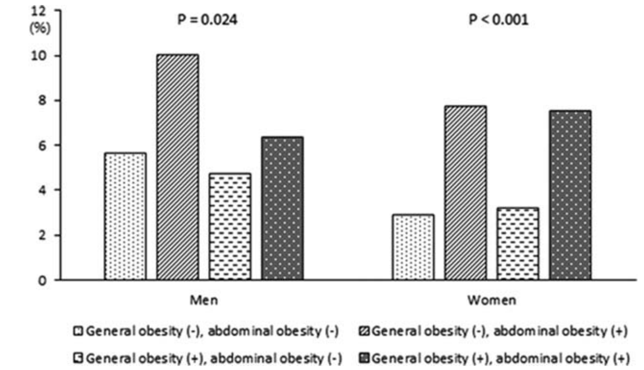

Figure 3. Prevalence rates of pterygium according to the obesity status (P values were calculated by Chi-square test).

Model 2, and 1.26 (1.01–1.58) in Model 3, respectively. Meanwhile, in men, the risk of pterygium was not significantly associated with either BMI or WC, irrespective of adjustment for confounding variables.

Table 3 presents the mean length, recurrence rates, and subtypes of pterygium according to the obesity parameters. In men, mean length and subtypes of pterygium did not significantly differ according to obesity parameters. However, men with general obesity or abdominal obesity were less likely to have recurrence. In women, mean length, recurrence rates, and subtypes of pterygium were not significantly different according to the obesity parameters.

4. Discussion

To the best of our knowledge, this is the first population-based study investigating the association between obesity and pterygium. In the present study, high BMI and high WC were positively associated with the risk of pterygium in Korean women. This association was independent of possible confounding factors including age, smoking, alcohol drinking, physical activity, outdoor occupation, area of residence, and daily sun exposure duration. Interestingly, there was no significant association between BMI and pterygium in men.

Table 2

ORs (95% CIs) of having pterygium in relation to obesity parameters.

	Men			Women		
	Model 1†	Model 2‡	Model 3§	Model 1†	Model 2‡	Model 3§
Body mass index, kg/m^2						
<18.5	0.78 (0.46–1.31)	0.81 (0.48–1.37)	0.84 (0.5–1.41)	0.99 (0.54–1.83)	1 (0.54–1.85)	1.09 (0.59–2.02)
18.5–23	1	1	1	1	1	1
23–25	0.9 (0.67–1.21)	0.89 (0.66–1.2)	0.92 (0.67–1.25)	1.2 (0.9–1.6)	1.11 (0.83–1.49)	1.16 (0.86–1.55)
≥25	1.08 (0.84–1.39)	1.06 (0.82–1.38)	1.13 (0.87–1.47)	1.43 (1.09–1.87)	1.34 (1.03–1.76)	1.35 (1.02–1.77)
P for trend*	0.999	0.684	0.68	0.008	0.03	0.04
Waist circumference, cm						
Men <90 or women <80	1	1	1	1	1	1
Men ≥90 or women ≥80	1.06 (0.83–1.35)	1.02 (0.8–1.3)	1.05 (0.82–1.35)	1.39 (1.11–1.74)	1.3 (1.04–1.63)	1.26 (1.01–1.58)
P*	0.637	0.877	0.676	0.004	0.021	0.045

CIs = confidence intervals, ORs = odds ratios.
* P values were calculated by using hierarchical multivariable logistic regression analysis and P for trend was obtained from general linear model.
† Model 1 was adjusted for age.
‡ Model 2 was adjusted for age, smoking status, alcohol consumption, and physical activity.
§ Model 3 was adjusted for variables in Model 2 plus educational level, outdoor occupation, area of residence, and daily sun exposure duration.

Table 3

Mean length, recurrence rates, and subtype of pterygium according to the obesity parameters.

	Length, mm		Recurrence, %			Type, %			
	Mean ± SE	P^*	No	Yes	P^*	Atrophic	Intermediate	Fleshy	P^*
Men									
Body mass index, kg/m^2		0.529			0.04				0.461
<18.5	2 ± 0.2		3.6 (1)	3 (1.2)		2.8 (1)	4.6 (1.7)	2.8 (1.5)	
18.5–23	1.8 ± 0.1		34.6 (2.9)	46.4 (4.4)		35.6 (3.6)	37 (4.1)	50 (6.9)	
23–25	2 ± 0.3		23.1 (2.6)	24.5 (4)		25.7 (3.3)	21.1 (3.5)	19 (5.4)	
≥25	2 ± 0.2		38.7 (3.1)	26.2 (3.7)		35.8 (3.4)	37.3 (4.4)	28.2 (7.1)	
Waist circumference, cm		0.083			0.021				0.18
Men <90 or women <80	2 ± 0.2		68.3 (2.9)	79 (3.3)		73 (3.2)	66 (4)	80.8 (6.9)	
Men ≥90 or women ≥80	1.7 ± 0.1		31.7 (2.9)	21 (3.3)		27 (3.2)	34 (4)	19.2 (6.9)	
Women									
Body mass index, kg/m^2		0.467			0.693				0.516
<18.5	1.8 ± 0.4		2.6 (0.7)	4.6 (2.6)		1.9 (0.7)	5.4 (2.2)	2.5 (2)	
18.5–23	1.7 ± 0.1		31.6 (3)	34.6 (4.5)		31.5 (3)	33.2 (3.9)	34.7 (7.1)	
23–25	2 ± 0.2		24.9 (2.7)	22.9 (3.8)		23.8 (3)	25.6 (3.5)	23.4 (5.9)	
≥25	1.9 ± 0.2		40.9 (3.2)	37.9 (4.1)		42.8 (4)	35.9 (3.7)	39.4 (7.5)	
Waist circumference, cm		0.746			0.451				0.992
Men <90 or women <80	1.9 ± 0.1		35.6 (2.9)	39.6 (4.5)		37 (3.3)	36.3 (4)	36.8 (7.3)	
Men ≥90 or women ≥80	1.8 ± 0.1		64.4 (2.9)	60.4 (4.5)		63 (3.3)	63.7 (4)	63.2 (7.3)	

Data are presented as means ± standard error (SE) or percentage (SE).

* *P* values were calculated by using independent *t* test, analysis of variance, or Chi-square test.

Obesity as a chronic inflammatory disease is defined as a state of oxidative stress.[32] Increased levels of proinflammatory cytokines in obesity are known to be responsible for the overproduction of ROS and nitrogen species that lead to oxidative stress.[32] Oxidative stress is a condition caused by a harmful increase in the production of ROS, resulting from the imbalance between ROS levels and host antioxidant defenses and involving every tissue in the body.[33] Local and systemic oxidative stress may represent the link between pterygium and obesity. Research on local exposure to UVB has largely focused on pterygium pathogenesis; however, there is controversial evidence that local oxidative stress, alone, does not explain pterygium development.

It is believed that UV-induced free radicals, through a photochemical reaction, are crucial factors in the development of pterygium.[34–36] Although still not clear, ROS generated by exposure to UV light have been reported to be trigger factors for conjunctival diseases, including pterygium and there are various studies on the association between oxidative stress and antioxidant defense.[37,38] Kormanovski et al[37] showed an increase in nitric oxide (NO) and total antioxidant status (TAS) levels, as well as a tendency toward a decrease in the levels of all antioxidant enzymes in the primary pterygium group compared to the control group. Also, they reported that there was a significant decrease in the levels of TAS and antioxidant enzymes in the recurrent pterygium group.[37] These results support the idea that oxidative stress plays a prominent part in the pathogenesis and recurrence of pterygium. In this context, we also assume the possible association of obesity and pterygium through oxidative stress.

We found sex differences in the association between obesity and pterygium. Previous epidemiologic studies found differences in pterygium development between female and male subjects.[2–7] Differences in UVB and occupational exposure may be a significant environmental factor; however, this hypothesis remains controversial. Sex differences in occupational and sunlight exposure do not explain the persistent 4-fold increased risk of pterygium in men. This suggests that other unknown factors may have contributed to the sex differences. The sex differences in the association of obesity and pterygium may be explained by oxidative stress and the antioxidant defense response. Kormanovski et al showed that the correlation is different between men and women when analyzing the parameters of oxidative stress and those of antioxidant defense in normal conjunctival tissue. This raises the possibility that there exist sex differences regarding the response and to oxidative stress. We previously reported that the prevalence of flesh type pterygium was significantly lower in menopausal women receiving estrogen replacement therapy.[38] As estrogen has the ability to protect against oxidative stress,[39] estrogen in the tear film may protect against the development of flesh type pterygium by blocking oxidative stress-induced inflammation. These data also support the causal link between oxidative stress and development of pterygium.

The clinical implications of these results include the identification of potentially modifiable factors other than ultraviolet exposure. One strength of this study is its large sample size with standardized ocular assessment by an ophthalmologist and the comprehensive assessment of associated factors. Moreover, Koreans have relatively uniform genetic and environmental influences; racial differences may not have influenced the results. However, the cross-sectional analysis limits the ability to explain causality, and an assessment of ultraviolet exposure is relatively crude as the common limitation of other population-based study. In conclusion, the results of this study indicate that the risk of pterygium is significantly associated with BMI irrespective of adjustments for confounding factors in women. Our findings regarding the association between obesity and pterygium may allow physicians to counsel patients about modifiable factors. Further prospective studies are necessary to investigate the interrelationships among obesity, pterygium, sex differences, and oxidative stress.

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