Prevalence of and Risk Factors Associated With Dry Eye: The Korea National Health and Nutrition Examination Survey 2010–2011

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• PURPOSE: To investigate the prevalence of and risk factors associated with dry eye syndrome (DES) in South Korea.

• DESIGN: Cross-sectional study.

• METHODS: In 2010 and 2011, 11,666 subjects, ranging in age from 19 to 95, were randomly selected as nationally representative participants in the Korea National Health and Nutrition Examination Survey (KNHANES). Subjects were divided into 2 groups: 1 with clinically diagnosed DES and 1 with symptoms of dry eye. We determined the prevalence of and risk factors for dry eyes in a Korean population. Health-related quality of life (HRQoL), measured by the EuroQoL-5 dimension (EQ-5D), was evaluated in patients with dry eyes.

• RESULTS: The mean age was 49.9 years. The overall prevalence of diagnosed DES was 8.0% (95% confidence interval [CI], 7.3% to 8.7%), and of dry eye symptoms the prevalence was 14.4% (95% CI, 13.1 to 15.7). Age (adjusted odds ratio [aOR] = 1.8, 1.6), female (aOR = 2.8, 1.9); history of eye surgery (aOR = 2.6, 2.2); stress (aOR = 1.7, 1.6); thyroid disease (aOR = 1.7, 1.5); and high education level (aOR = 1.6, 1.5) were common risk factors in the groups. Subjects who had undergone ptosis, cataract or refractive surgery were more likely to have dry eye than subjects with no history of eye surgery. Means of pain and anxiety dimensions in the EQ-5D and the Euro Quality of Life Visual Analog Scale (EQ-VAS) were significantly higher in the group with diagnosed DES than in the normal group.

• CONCLUSIONS: The risk factors were mostly similar in both groups. It is thought there are more patients with DES who have not been diagnosed by doctors. Doctors should identify whether a patient has any risk factors for dry eye. Patients need to be educated about the modifiable factors of DES. (Am J Ophthalmol 2014;158:1205–1214. © 2014 by Elsevier Inc. All rights reserved.)

DRY EYE SYNDROME (DES) IS THE MOST COMMON disease causing patients to visit ophthalmology clinics.[1] The concept of DES has been understood as a multifactorial disease of the tears and ocular surface that is accompanied by increased osmolality of the tear film and inflammation of the ocular surface.[2] The symptoms of DES are worse than simply discomfort; the condition disrupts activities of daily living and negatively affects quality of life.[3] Thus, dry eye has recently been recognized as an important public health problem.[3] A large-scale study of the prevalence of and risk factors for the disease is essential for planning therapeutic methods and prevention of the disease.[4] The prevalence of DES has been reported in many studies to range from 5.5% to 33.7% and is generally known to be higher in Asians than Westerners.[5–11] Typical risk factors for dry eye have been reported to include old age, female gender, smoking, and contact lens use.[7,10,11] Most studies have reported prevalence of and risk factors for specific ages or within specific regions, but no data are available about the general population.

Thus, this study was conducted to analyze groups with dry eye prevalence and risk factors based on the data collected from a large-scale population study to find methods to prevent dry eye and improve patient quality of life.

METHODS

THE SOUTH KOREA CENTER FOR DISEASE CONTROL AND Prevention conducted the Korea National Health and Nutrition Examination Survey (KNHANES) studies I, II and III in 1998, 2001 and 2005 to examine the general health and nutrition status of South Koreans. KNHANES V (2010–2012) involved a population-based random sampling of households across 576 national districts

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(192 per year), selected by a panel to represent the South Korean population using a stratified, multistage, clustered sampling method based on 2009 National Resident demographics. Detailed methodologies of these studies have been reported previously.[4] This survey was reviewed and approved by the Institutional Review Board of the South Korea Centers for Disease Control and Prevention. All participants provided written informed consent. This cross-sectional prevalence study was conducted in accordance with the Declaration of Helsinki.

The KNHANES studies were divided into 3 parts: a health interview survey, a health examination survey and a nutrition survey. For the health interview survey, a trained interviewer asked questions directly of individuals 12 years of age and older.

Because the South Korean Ophthalmological Society participated in the survey, starting in July 2008, ophthalmologic interviews and examinations of the same participants have also been conducted. In 2010, to evaluate risk factors for dry eye specifically, interviews were conducted about dry eye. All members of each selected household were asked to participate in the survey; the rate of participation was, in fact, 82.0%. Participants older than 19 years of age underwent full ocular examinations, including auto refraction, visual acuity testing and slit-lamp examinations. This study included 11,666 adults 19 of age and older who completed a questionnaire regarding independent risk factors and underwent slit-lamp examinations.

Subjects were asked the following question: To date, have you ever before been diagnosed by a physician as having a dry eye (either eye)? The possible responses were yes or no. To make data collection more accurate, subjects were also asked the following question: Until now, have you ever had dry eye symptoms before; for example, dryness of the eye or a sense of irritation? Then the subjects were asked the question above with an emphasis on "by a physician."

The independent variables were divided into 4 categories: (1) sociodemographic factors; (2) health examination variables; (3) health behavior risk factors; and (4) variables regarding the eye. The income per adult equivalent was calculated using the formula household income/square root of the number of people in the household.[12] Binge alcohol users were defined as males who consumed more than 7 drinks on a single occasion or females who consumed more than 5 drinks on a single occasion at least once per month.[13] Lifetime smokers included respondents who reported that they were current smokers and had smoked at least 100 cigarettes in their lifetimes. Medical histories of diseases, such as hypertension, rheumatoid arthritis, thyroid disease, and surgical history of the eyes, were obtained by health interviewers. Detailed definitions of other diseases were based on previously reported papers[14–17] and are briefly described in the Figure.

The Euro quality of life-5 dimensions (EQ-5D) was also analyzed for an objective investigation of health status. The EQ-5D questionnaire is a standardized generic instrument for describing and evaluating health; it was designed by the EuroQol group, an international research network established in 1987.[18] The EQ-5D self-reported questionnaire consists of a 5-dimensional descriptive system and a visual analog scale (EQ-VAS) together with brief demographic questions. The descriptive system defines health in term of 5 dimensions: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Each dimension is divided into 3 levels, indicating no problem, some or moderate problems, or extreme problems.

• **STATISTICAL METHODS:** Descriptive statistics are reported for each response. To determine the prevalence of dry eye in South Korea according to age groups, the prevalence was calculated using the weights defined by the guidelines of KNHANES V. To calculate the weights according to KNHANES V in accordance with the guidelines for the 2010 South Korean population (in accordance with the 2010 census of South Korea), a poststratification adjustment was performed, based on response and extraction rates, to include the distribution of the 2010 South Korean population according to gender and age groups at 5-year intervals. Finally, the sum of the weights according to KNHANES V is equal to the South Korean population of 2010.

Unfortunately, the data for high-density lipoprotein (HDL) cholesterol disclosed to the public were flawed because the test methods were changed in October 2011, and the HDL cholesterol data in 2011 needed additional validation. Regarding HDL cholesterol in this study, only data from 2010 were used for the multivariate logistic regression (number of subjects = 4640). We did not provide the entire multivariate analysis result set from the 2010 data and have simply inserted the result in the table because HDL cholesterol was ultimately not significant and did not affect other odds ratios significantly.

A 2-step, multidimensional approach was used to identify risk factors for dry eye. First, to identify risk factors associated with dry eye, odds ratios and 95% confidence intervals (CIs) were calculated using univariate logistic regression analysis. Second, multivariate logistic regression analysis was used to determine risk factors with each variable after adjusting for the variables that were significant (with P values of <0.05) in the univariate analyses. Some variables could be confounded by age, so multivariate analysis was performed to adjust for age. Ultimately, the final model included age, gender, monthly household income, education, residential area, occupation, hypertension, obesity, hypercholesterolemia, HDL-hypocholesterolemia, hypertriglyceridemia, rheumatoid arthritis, thyroid disease, lifetime smoker, binge alcohol user, sleep duration, stress, and history of eye surgery.

To evaluate which kinds of eye surgery were associated with dry eye, as diagnosed by a physician, or dry eye symptoms, adjusted proportions were calculated based on

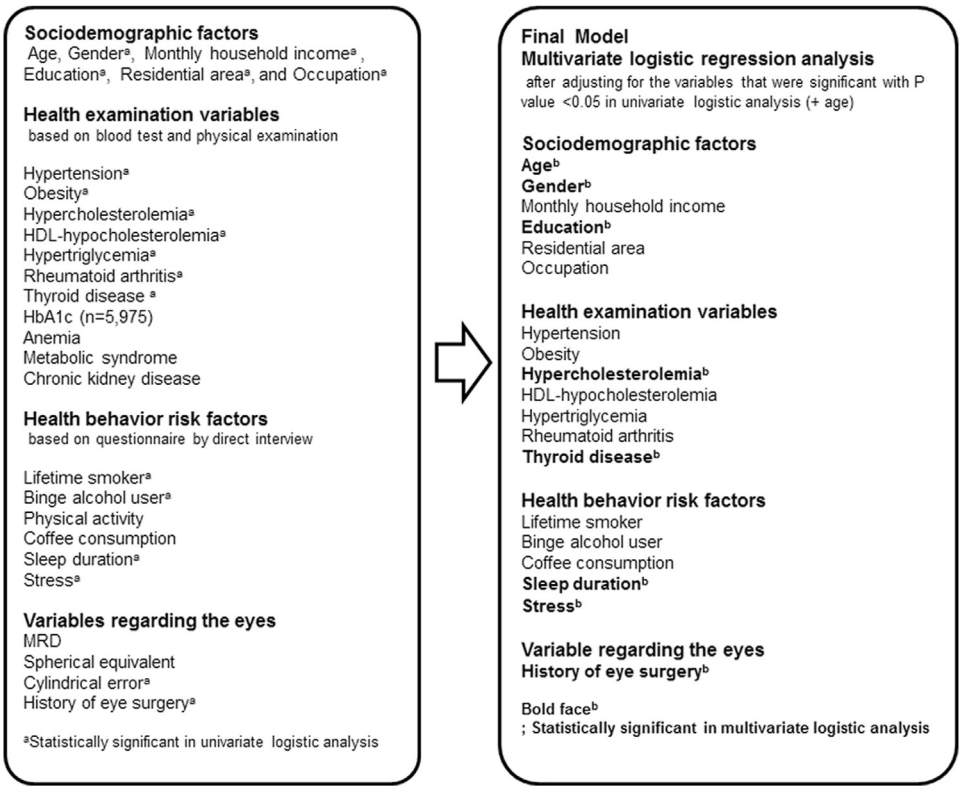

FIGURE. Flowchart of the step approach for identifying risk factors for dry eye in South Korea using univariate and multivariate analysis. The independent variables were divided into 4 categories: (1) sociodemographic factors; (2) health examination variables based on blood tests and physical examinations; (3) health behavior risk factors based on questionnaires via direct interviews; and (4) variables based on ophthalmologic interviews and examinations. HbA1C = glycated hemoglobin; HDL = high density lipoprotein; MRD = marginal reflex distance.

multivariable linear regression after adjusting for age, gender, education, thyroid disease, hypercholesterolemia, sleep duration, and stress, which were significant variables in the final model. The relationship between dry eye and EQ-5D was identified using unadjusted and adjusted means, based on linear regression analysis. All statistical tests were 2-sided at the 95% CI level and were performed using the Stata/SE 12.1 software (StataCorp, College Station, Texas, USA).

RESULTS

THE MEAN AGE OF THE 11,666 PARTICIPANTS 19 YEARS OF age or older was 49.9 (SD, 16.7) years. Of the participants, 42.8% were males, and 78.5% were living in urban areas. Supplemental Table 1 provides the characteristics of the study population in greater detail.

The overall prevalence of patients with dry eye—with real diagnoses or with symptoms—was 16.0% (95% CI = 14.6% to 17.3%). The overall prevalence of dry eye diagnosed by a physician and dry eye symptoms was 8.0% (95% CI, 7.3% to 8.7%) and 14.4% (95% CI, 13.1% to 15.7%), respectively. The prevalence of patients with dry eye symptoms or with a diagnosis at the age of 40 or older was 10.7% for males (95% CI = 9.1 to 12.2) and 20.6% (95% CI = 18.5 to 22.7) for females. Table 1 shows the prevalence of dry eye by age and gender.

The independent risk factors associated with dry eye in the univariate analyses are marked by an *a* ([a]) in the left column of the Figure. Supplemental Table 2 reports the results of the univariate analyses in detail with unadjusted odds ratios and 95% CIs. Gender, monthly household income, education, residential area, occupation, hypertension, obesity, hypercholesterolemia, hypo-HDL-cholesterolemia, hypertriglyceridemia, rheumatoid arthritis, thyroid disease, smoking, binge alcohol user, sleep duration, stress, and history of eye surgery were statistically significant in the univariate logistic regression analyses. The right column in the Figure provides the factors associated with dry eye as diagnosed by a physician or as the experiencing of dry eye symptoms in the multivariate analysis for each variable, after adjusting, based on the final model. Table 2 provides a list of risk factors based on the final model of combined multivariate analyses using age and all factors that were statistically significant in the univariate analysis. Old age (adjusted odds ratio [aOR] = 1.8 and 1.6, respectively; both $P < 0.01$); females (aOR = 2.8 and 1.9, respectively;

TABLE 1. The Prevalence of Dry Eyes for Specific Ages and Genders in South Korea

	Diagnosed DES		Symptoms of DES		Diagnosed DES or Symptoms of DES	
	%	95% CI	%	95% CI	%	95% CI
All						
19–29	8.3	(6.8–10.1)	15.1	(12.9–17.6)	16.8	(14.5–19.4)
30–39	7.8	(6.4–9.4)	13.8	(11.9–15.9)	15.5	(13.5–17.8)
40–49	7.1	(6.0–8.4)	12.9	(10.9–15.1)	14.6	(12.5–17.0)
50–59	8.9	(7.5–10.5)	15.2	(13.2–17.5)	17.1	(14.9–19.5)
60–69	9.1	(7.6–10.9)	16.2	(13.9–18.8)	17.0	(14.6–19.7)
70–	6.7	(5.4–8.2)	14.1	(11.7–16.7)	15.0	(12.7–17.8)
Men						
19–29	3.6	(2.3–5.8)	9.9	(7.6–12.8)	10.1	(7.4–12.8)
30–39	3.7	(2.5–5.3)	9.5	(7.4–12.1)	10.3	(7.9–12.7)
40–49	3.5	(2.5–5.0)	8.8	(6.7–11.5)	9.8	(7.3–12.2)
50–59	3.2	(2.2–4.7)	8.6	(6.6–11.2)	9.5	(9.3–13.2)
60–69	5.9	(4.1–8.2)	11.4	(8.8–14.7)	12.3	(9.6–15.7)
70–	4.9	(3.5–6.7)	13.1	(10.1–16.7)	13.9	(10.9–17.6)
Women						
19–29	13.3	(10.8–16.3)	20.7	(17.4–24.4)	23.8	(20.1–27.6)
30–39	12.0	(9.8–14.7)	18.1	(15.4–21.2)	20.8	(17.7–23.9)
40–49	10.8	(8.9–13.0)	17.0	(14.3–20.2)	19.7	(16.5–22.8)
50–59	14.5	(12.2–17.2)	21.7	(18.7–25.1)	21.1	(18.7–23.5)
60–69	12.1	(9.8–14.7)	20.3	(17.1–24.0)	21.2	(17.9–24.9)
70–	7.8	(6.0–10.0)	14.7	(11.8–18.1)	15.7	(12.7–19.3)

CI = confidence interval; DES = dry eye syndrome.

both $P < 0.01$); history of eye surgery (aOR = 2.6 and 2.2, respectively; both $P < 0.01$); stress (aOR = 1.7 and 1.6; $P = 0.01$ and 0.02, respectively); thyroid disease (aOR = 1.7 and 1.5; $P < 0.01$ and 0.01, respectively); and high education level (aOR = 1.6 and 1.5; $P = 0.05$ and 0.02, respectively) were significant risk factors in the group with diagnosed DES and in the group with symptoms of dry eye (Table 2).

The association between dry eye and type of surgery is shown in Table 3. Subjects who had histories of ptosis surgery (OR = 5.6 and 4.2, respectively; $P < 0.01$ and 0.02); refractive surgery (OR = 3.4 and 2.6, respectively; both $P < 0.01$); or cataract surgery (OR = 2.2 and 2.2, respectively; both $P < 0.01$) were more likely to have dry eye as opposed to subjects with no history of eye surgery.

Means of pain, discomfort/anxiety, depression dimensions, and EQ-VAS in the EQ-5D were significantly higher in the group diagnosed with DES than in the normal group (all $P < 0.01$) (Table 4).

DISCUSSION

THE PREVALENCE OF DES HAS BEEN REPORTED DIFFERENTLY in each study.[5–11] Thus, it is difficult to compare results directly in simple numeric terms. Generally, the prevalence of DES is known to increase with age, and most large-scale studies of DES prevalence have been conducted in elderly subjects.[7,19] However, considering the characteristics of South Korea, where refractive surgery is being marketed actively, and the use of computers and smart phones is increasing, in this study, we recruited people older than 19 years of age as subjects. Age-dependent prevalence was compared, and the total prevalence of the patients with dry eye symptoms or those who were diagnosed with DES was 16.8% in the 19- to 29-year-old group, 17.1% in 50- to 59-year-old group, and 17.0% in 60- to 69-year-old group, showing a double peak. The prevalence of patients with dry eye symptoms or diagnosis at age 40 or older was 10.7% for males and 20.6% for females. This was slightly lower than, but similar to, the results of the Koumi study in Japan: 12.5% and 21.6%, respectively.[11] Risk factors for DES that have been reported commonly include old age, being female, use of contact lenses, video display use, and systemic medications, but other factors did not show correlations in some studies.[7,10,11]

This study also found old age to be a significant risk factor for dry eye compared with the 19- to 29-year age group. But their similar prevalence may be associated with use of contact lenses, increased computer-based work, increasing smart-phone use, higher numbers of attempted refractive surgeries, and other factors.[20–22] With aging, lacrimal gland function reduces, causing decreased tear secretion and an increase in cases of dry eye.[11,23] On the other hand, visual display terminal users' tear break-up time was found to be significantly shortened. This was reported to be related

TABLE 2. Risk Factors for Dry Eyes in South Korea (N = 11 666): Multivariate Analysis According to Final Model

	Diagnosed DES (n = 1031)			Symptoms of DES (n = 1731)		
	OR	95% CI	*P*	OR	95% CI	*P*
Sociodemographic factors						
Age						
19–29	1.0 (ref)			1.0 (ref)		
30–39	1.0	(0.7–1.5)	0.84	1.1	(0.8–1.4)	0.62
40–49	1.2	(0.9–1.7)	0.23	1.1	(0.9–1.5)	0.34
50–59	1.8	(1.2–2.7)	<0.01[a]	1.5	(1.1–2.1)	0.01[a]
60–69	1.7	(1.1–2.7)	0.02[a]	1.6	(1.1–2.3)	<0.01[a]
70–	1.0	(0.6–1.7)	0.93	1.2	(0.8–1.9)	0.34
Gender						
Men	1.0 (ref)			1.0 (ref)		
Women	2.8	(2.1–3.7)	<0.01[a]	1.9	(1.5–2.4)	<0.01[a]
Monthly household income						
Lowest quintile	1.0 (ref)			1.0 (ref)		
2nd–4th quintile	1.1	(0.8–1.6)	0.53	1.2	(0.9–1.6)	0.14
Highest quintile	1.2	(0.8–1.8)	0.39	1.2	(0.9–1.6)	0.28
Education						
Elementary school	1.0 (ref)			1.0 (ref)		
Middle school	1.3	(0.8–2.0)	0.24	1.1	(0.8–1.4)	0.65
High school	1.5	(1.0–2.2)	0.06	1.0	(0.8–1.4)	0.93
University or higher	1.6	(1.0–2.4)	0.05[a]	1.5	(1.1–2.0)	0.02[a]
Residential area						
Urban	1.0 (ref)			1.0 (ref)		
Rural	1.0	(0.7–1.3)	0.90	1.1	(0.8–1.5)	0.63
Occupation						
Farming, fishing, and forestry occupations	1.0 (ref)			1.0 (ref)		
Administrator, management, professional	1.5	(0.8–2.9)	<0.17	1.4	(0.8–2.3)	0.20
Business and financial operations occupations	1.3	(0.7–2.6)	<0.37	1.6	(0.9–2.6)	0.09
Sales and related occupations	0.9	(0.5–1.7)	0.86	1.2	(0.7–1.9)	0.54
Installation, maintenance and repair occupations/technicians	1.3	(0.7–2.5)	0.45	1.3	(0.8–2.2)	0.35
Laborer	1.3	(0.7–2.4)	0.48	1.4	(0.8–2.2)	0.22
Unemployed	1.5	(0.9–2.7)	0.14	1.5	(0.9–2.3)	0.09
Health examination variables						
Hypertension						
No	1.0 (ref)			1.0 (ref)		
prehypertension	0.9	(0.7–1.1)	0.30	1.0	(0.8–1.2)	0.92
Hypertension	0.8	(0.6–1.0)	0.07	0.9	(0.7–1.1)	0.23
Obesity						
Underweight	1.0 (ref)			1.0 (ref)		
Normal	0.9	(0.6–1.4)	0.75	1.2	(0.8–1.7)	0.31
Obesity	0.8	(0.6–1.3)	0.40	1.0	(0.7–1.4)	0.99
Hypercholest-erolemia						
No	1.0 (ref)			1.0 (ref)		
Yes	1.2	(0.9–1.6)	0.13	1.4	(1.1–1.7)	<0.01[a]
HDL- hypo-cholesterolemia (2010 data only)						
No	1.0 (ref)			1.0 (ref)		
Yes	1.1	(0.8–1.5)	0.63	0.8	(0.6–1.1)	0.16

Continued on next page

TABLE 2. Risk Factors for Dry Eyes in South Korea (N = 11 666): Multivariate Analysis According to Final Model (*Continued*)

	Diagnosed DES (n = 1031)			Symptoms of DES (n = 1731)		
	OR	95% CI	*P*	OR	95% CI	*P*
Hypertriglycemia						
No	1.0 (ref)			1.0 (ref)		
Yes	0.9	(0.7–1.3)	0.66	0.9	(0.7–1.2)	0.50
Rheumatoid arthritis						
No	1.0 (ref)			1.0 (ref)		
Yes	1.3	(0.8–2.2)	0.29	0.9	(0.5–1.5)	0.66
Thyroid disease						
No	1.0 (ref)			1.0 (ref)		
Yes	1.7	(1.2–2.4)	<0.01[a]	1.5	(1.1–2.0)	0.01[a]
Health behavior risk factors						
Lifetime smoker						
No	1.0 (ref)			1.0 (ref)		
Yes	0.7	(0.6–1.0)	0.09	0.9	(0.7–1.1)	0.30
Binge alcohol user						
Never drink alcohol	1.0 (ref)			1.0 (ref)		
Not a binge alcohol user	1.0	(0.8–1.2)	0.82	1.2	(1.0–1.4)	0.09
Yes	1.0	(0.7–1.3)	0.89	1.1	(0.9–1.4)	0.30
Sleep duration						
6–8 hrs	1.0 (ref)			1.0 (ref)		
<6 hrs	1.1	(0.9–1.5)	0.34	1.3	(1.0–1.6)	0.03[a]
>8 hrs	0.7	(0.5–1.1)	0.10	0.9	(0.6–1.2)	0.48
Stress						
Least stressful	1.0 (ref)			1.0 (ref)		
Moderately stressful	1.3	(1.0–1.7)	0.07	1.3	(1.0–1.6)	0.03[a]
Extremely stressful	1.7	(1.1–2.6)	0.01[a]	1.6	(1.1–2.3)	0.02[a]
Variable regarding the eyes						
History of eye surgery						
No	1.0 (ref)			1.0 (ref)		
Yes	2.6	(2.0–3.3)	<0.01[a]	2.2	(1.8–2.7)	<0.01[a]

CI = confidence interval; DES = dry eye syndrome; HDL = high density lipoprotein; hrs = hours; n = number; OR = odds ratio; ref = reference.
[a]Multivariate logistic regression analysis; statistical significance $P < 0.05$.

to the evaporative type of DES such as meibomian gland dysfunction (MGD).[22] In the group of subjects 70 years of age and older, the prevalence of dry eye was slightly lower. Such a result was also shown in the Koumi study of Japan.[11] Other systemic diseases may have made them underevaluate their dry eyes, and/or cornea sensitivity reduction may affect their ability to sense dryness of the ocular surface.[11]

Regarding gender, the prevalence was about twice as high in females as in males, as has been reported previously.[7] It could be that sex hormones affect the lacrimal glands, meibomian glands, conjunctival goblet cell density, and ocular surface sensitivity.[24]

Many studies have reported a relationship between ocular surgery and dry eye.[25–29] In this study, those in the group who had had cataract, refractive or ptosis surgeries had significantly higher risks for DES when compared with those in the group who had no history of surgery. There are several complex factors in relation to ocular surgery that may cause dry eye. First, most ocular surgeries are performed using a microscope, and the continuous exposure to the strong light of the microscope by the ocular surface during the surgery is considered to be related to DES development.[25] Also, the anesthetic eyedrops used in such surgeries contain preservatives such as benzalkonium chloride, which can be harmful to the corneal epithelium.[30] Benzalkonium chloride has cytotoxic effects on the cornea, causing reduced cell proliferation and viability and increased epithelial permeability.[30] Along with the anesthetic, medications used after surgery can affect the ocular surface. Surgeries that damage the corneal nerve in any way may desensitize the cornea and delay its recovery and may induce pathologic corneal changes.[26,28] Its role is not fully understood, but the corneal nerve is involved in tear secretion and is believed to contribute to the recovery of corneal epithelium when its structure is damaged.[28] Thus, corneal sensory denervation results in decreased epithelial metabolic activity, loss of cytoskeletal structure associated with cellular adhesion, and decreased tear secretion.[26,28]

TABLE 3. The Association Between Type of Eye Surgery and Dry Eye Diagnosis or Symptoms of Dry Eye in South Korea: Univariate and Multivariate Logistic Regression Analysis

	Type of Surgery	Univariate OR	Multivariate OR	95% CI	*P*
Diagnosed DES	No	1.0 (ref)	1.0 (ref)		
	Glaucoma surgery	2.0	1.7	(0.3–10.8)	0.54
	Cataract surgery	2.0	2.2	(1.6–3.0)	<0.01[a]
	Strabismus surgery	0.6	0.6	(0.1–4.0)	0.58
	Ptosis surgery	4.8	5.6	(1.6–19.3)	<0.01[a]
	Retinal surgery	0.9	1.5	(0.2–9.8)	0.67
	Refractive surgery	4.1	3.4	(2.4–4.8)	<0.01[a]
	Others	1.8	1.7	(1.2–2.6)	<0.01[a]
	More than 2 surgeries	4.9	1.9	(0.8–4.8)	0.16
Symptoms of DES	No	1.0 (ref)	1.0 (ref)		
	Glaucoma surgery	1.6	1.8	(0.3–10.2)	0.52
	Cataract surgery	1.9	2.2	(1.7–3.0)	<0.01[b]
	Strabismus surgery	1.8	2.0	(0.7–5.8)	0.20
	Ptosis surgery	4.2	4.2	(1.2–14.5)	0.02[b]
	Retinal surgery	0.6	1.0	(0.2–5.1)	0.91
	Refractive surgery	3.4	2.6	(2.0–3.5)	<0.01[b]
	Others	1.6	1.5	(1.1–2.1)	<0.01[b]
	More than 2 surgeries	2.2	0.4	(0.1–1.3)	0.13

CI = confidence interval; DES = dry eye syndrome; OR = odds ratio; , ref = reference.

[a]Multivariate logistic regression analysis after adjusting for all variables in final model. including age, gender, education, thyroid disease, stress. Statistically significant $P < 0.05$

[b]Multivariate logistic regression analysis after adjusting for all variables in final model, including age, gender, education, hypercholesterolemia, thyroid disease, sleep duration, stress. Statistical significance $P < 0.05$

TABLE 4. Means of Health-Related Quality of Life Between Normal Eye and Clinically Diagnosed Dry Eye Group Using EuroQoL 5-Dimension[a] in South Korea

	Normal Eye Group (n = 10 635)		Dry Eye Group (n = 1031)		
EQ-5D Category	Mean	95% CI	Mean	95% CI	*P*
Mobility	1.17	(1.16–1.18)	1.19	(1.16–1.22)	0.20
Self-care	1.05	(1.05–1.06)	1.06	(1.04–1.07)	0.69
Usual activities	1.12	(1.11–1.13)	1.13	(1.11–1.15)	0.55
Pain or discomfort	1.26	(1.26–1.28)	1.33	(1.29–1.36)	<0.01[b]
Anxiety or depression	1.12	(1.11–1.13)	1.16	(1.13–1.19)	<0.01[b]
EQ-VAS scores	79.56	(77.02–82.11)	73.90	(71.87–75.92)	<0.01[b]

CI = confidence interval; EQ-5D = EuroQoL 5-dimension; EQ-VAS = EuroQoL visual analog scale; n = number.

[a]Adjusted for age, gender, income, education, occupation, and residential area.

[b]Linear regression analysis; statistical significance $P < 0.05$.

The most typical case is keratorefractive surgery. Keratorefractive surgeries have been reported to disturb ocular surface homeostasis by causing decreased corneal sensitivity, tear film instability, decreased aqueous tear production, and corneal and conjunctival epitheliopathy.[27] The dry eye that occurs after keratorefractive surgery results mostly from damage to corneal sensory nerves.[31] Refractive surgeries flatten the corneal surface and result in a rough corneal surface, which may change the blinking pattern, disturb corneal tear fluid flow, and cause persistent breakup of the tear film.[32]

Cataract surgery is another ophthalmic intervention that can lead to DES.[25] There are many factors that might affect the ocular surface environment after cataract surgery. Dry eye in patients after cataract surgery is due mainly to the disruption of corneal nerves that may potentially disrupt the neural loop and also to elevated inflammatory factors in the tear film due to ocular surface irritation.[26]

In this study, the surgery that had the highest risk for DES was ptosis surgery. A previous study reported a 26.5% rate of dry eye after lid surgery.[29] After surgery, temporary lagophthalmos can promote dryness of the cornea.[33]

It is a well-known clinical phenomenon that desiccation occurs in the exposed cornea in consistent partial blinkers.[34] Incomplete blinking appears likely to contribute to lipid layer deficiencies and results in reduced opportunities for the tarsal goblet cells to contribute to the integrity of the mucin layer of the exposed cornea and tear film.[34] As a result, it leads to inferior punctate keratopathy and exacerbates eyelid wiper epitheliopathy.[35]

DES is known to affect physical and mental functions negatively, and studies have suggested that stress and dry eye may be related.[3,19] In a study that researched the relationship between DES and psychiatric diagnoses in Veterans Affairs, subjects with depression or post-traumatic stress disorder had higher risk factors for DES.[36,37] Of course, their antidepressant drugs may have affected DES, and dry eye symptoms may have affected their emotional states and caused their psychiatric illnesses; any cause-and-effect relationship is far from clear.[37] Also, previous reports suggest a role for psychological stress in triggering the onset of autoimmunity.[38] Long-term psychological stress can be a stimulus, resulting in hypofunction of the hypothalamic pituitary-adrenal axis and the sympathetic-adrenal axis.[38] This can change the serum level of cortisol and cause autoimmune disorders by interacting with the immune system.[38] Not all subjects who answered that they were under severe stress would suffer from autoimmune disease, and the patients with DES who were diagnosed with autoimmune disease were not researched separately in this study. However, stress is known to enhance immune responses, and stress may act as a risk factor for DES anyway.[39] Thus, it is meaningful that in this study, stress was found to be a related risk factor in both groups.

Several factors are considered to cause dry eye in thyroid disease: exophthalmos, increased palpebral fissure height, lagophthalmos, and reduced tear production.[40] However, there is ambiguity in the literature regarding the identification of any association between thyroid disease and DES.[41] However, in this study, we showed a significant relationship between dry eye and thyroid disease.

Higher education levels were shown to be significant risk factors in both groups. However, household income and residential area did not show a significant correlation in the multivariate analysis. It is deemed that residential areas and economic gaps did not work as barriers to medical service access in South Korea because South Korea is a small country, and the entire population is provided with national medical insurance.[42] Societal awareness of DES would be likely to correlate with more frequent diagnosis of disease, given the equal access to health care.[42,43] As for occupation, the office-based service group that used video display devices was found in the univariate analysis to have a closer relationship with dry eye than the farming group. However, this was not found to be significant in multivariate analysis, possibly due to the complexity of intraoccupation-group, gender, age, area of living, and so forth.

Short sleep duration and hypercholesterolemia were significantly related to symptoms of dry eye. Some have suggested that rapid eye movement during sleep serves not only to increase lacrimal secretions but also to humidify and lubricate the ocular surface. Thus, lack of sleep may be associated with dry eye.[44] Hypercholesterolemia is considered to be related to MGD.[45] One study reported that the patients with moderate to severe MGD had significantly higher total cholesterol than the controls.[45] It was suggested that the increased concentration of cholesterol increased viscosity and induced meibomian plugging, aggravating MGD.[45,46] It is well known that severe MGD can induce dry eye symptoms.[46] More research on the relationships between serum lipid levels, tear film lipid levels and dry eye is needed.

Cigarettes or alcohol were reported in previous studies[6] to be risk factors for dry eye,[7,47,48] but other studies did not show the relationship.[11] The multivariate analysis did not show significant differences in this study, although they were identified as significant risk factors in univariate analyses. As for caffeine, it has been reported, in some cases, to increase tear production and work as a protective factor for DES.[7,49] But in other reports, it is said to decrease tear function.[49] Coffee was assumed to be the primary source of caffeine intake. However, coffee has many other components; thus, consumption of coffee does not necessarily assess the relationship between caffeine and DES. In this study, coffee consumption did not show any significant correlation with DES.

We found that DES was associated with HRQoL, especially in terms of pain and mood. DES is a chronic disease, like hypertension and diabetes, and it can affect a patient's mental status. Many studies have shown the relationship between dry eye and anxiety and depression disorder using various questionnaires about QOL.[50] Anxiety and depression disorders are common diseases in the psychiatric clinic but are often ignored in nonpsychiatric clinics.[50] Eye physicians should not forget the mental status of their patients.

This study has several limitations. First, it involved only South Koreans. Circumstances may differ in other countries, leading to different results. However, this aspect of involving only South Koreans may also be strength because few studies have examined Asian populations. Second, DES was diagnosed based on patients' subjective symptoms, objective signs and abnormal dry eye test results. Unfortunately, the study design did not include direct physical examination to define dry eye using a slit-lamp because this survey was large, and its main purpose was to evaluate the prevalence of and risk factors for, dry eye. To increase accuracy, we first asked the interviewee whether he or she had symptoms and then asked again if he or she had been diagnosed by a physician as having dry eye. Because of these limitations, we did not focus on age-dependent prevalence but, rather, on independent risk factors for DES. Third, because this was a cross-sectional study, temporal cause-and-effect relationships could not be determined. Fourth, because factors such as the use of contact

lenses or drugs that possibly affect dry eyes were not included in the variables, there could be additional confounding factors or risk factors that were not identified in the study. Finally, some factors such as self-reported health status and stress have greatly subjective aspects, and personal biases may have been included.

Nevertheless, this study is meaningful because it is the first large-scale population-based study of the prevalence of and risk factors for DES in South Korea. The patients who were not diagnosed with dry eye by a physician but had the symptoms, in fact, had risk factors similar to those who had been diagnosed by physicians. This means that most of the patients with symptoms of dry eye would probably be diagnosed with DES if and when they visited a physician. DES is known to affect daily activities and the quality of life, and patients who do not use artificial tears have been reported to have twice the problems with daily activities of those who do use artificial tears.[3] Thus, it is important to help people who have dry eye symptoms to get appropriate treatments. Additionally, it is important to educate patients who are diagnosed with DES to be cautious about the risk factors and to improve their lifestyles. In particular, educating patients before surgery about possible future dry eye symptoms and treatments is important. More accurate information about the prevalence of DES through objective tests and continued research into longitudinal relationships with DES and improving patients' quality of life are needed.

ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE FORM FOR DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST, and none were found. Data in this study are from the Korean Ophthalmological Society. Design of study (K.Y.S., K.C.Y., J.M.A.); Conduct of study (K.Y.S., K.C.Y, J.M.A.); Collection, management, analysis, and interpretation of data (J.M.A., S.H.L., H.T.R., R.J.P.); Literature search (K.Y.S., K.C.Y., J.M.A. S.H.L., H.S.Y., T.I.K.); Preparation of manuscript (J.M.A., S.H.L.); Critical revision of manuscript (K.Y.S., K.C.Y., J.M.A); Final approval of manuscript (K.Y.S., K.C.Y., J.M.A.).

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Biosketch

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SUPPLEMENTAL TABLE 1. The Number and Percentage of Variables Used in the Korea National Health and Nutrition Examination Survey 2010–2011 in South Korea (n = 11 666)

	n	Percentage (%)
Sociodemographic factors		
Age		
19–29	1348	11.6
30–39	2205	18.9
40–49	2093	17.9
50–	6020	51.6
Gender		
Male	4990	42.8
Female	6676	57.2
Monthly household income		
Lowest quintile	1614	14.0
2nd–4th quintile	6763	58.7
Highest quintile	3142	27.3
Education		
Elementary school	2976	26.0
Middle school	1263	11.1
High school	3782	33.1
University or higher	3413	29.9
Residential area		
Urban	9156	78.5
Rural	2510	21.5
Occupation		
Administrator, management, professional	1420	12.45
Business and financial operations occupations	911	7.99
Sales and related occupations	1409	12.36
Farming, fishing and forestry occupations	983	8.62
Installation, maintenance and repair occupations/technicians	1074	9.42
Laborer	946	8.3
Unemployed	4660	40.87
Health examination variables		
Hypertension		
No (SBP $<$120 and DBP $<$80)	4346	40.4
Prehypertension (120 $\leq$SBP $<$140 or 80 $\leq$DBP $<$90)	2687	25.0
Hypertension (SBP $>$140 or DBP $>$90)	3732	34.7
Obesity		
Underweight (BMI $<$18.5 kg/m^2)	541	4.7
Normal (18.5 kg/m^2 $\leq$BMI $<$25 kg/m^2)	7388	63.9
Obesity (BMI $\geq$25 kg/m^2)	3634	31.4
Hypercholesterolemia		
No	8541	84.8
Yes ($\geq$240 mg/dL)	1530	15.2
HDL-hypocholesterolemia (data from 2010 only)		
No	3451	74.4
Yes ($<$40 mg/dL)	1189	25.6
Hypertriglycemia		
No	7245	84.7
Yes ($\geq$200 mg/dL)	1311	15.3
Rheumatoid arthritis		
No	11 200	97.9
Yes	242	2.1
Thyroid disease		
No	10 966	95.84
Yes	476	4.16

Continued on next page

SUPPLEMENTAL TABLE 1. The Number and Percentage of Variables Used in the Korea National Health and Nutrition Examination Survey 2010–2011 in South Korea (n = 11 666) (*Continued*)

	n	Percentage (%)
HbA1C (n = 523)		
No	4735	76.5
Yes(≥6.5 mU/L)	1452	23.5
Anemia		
No	10 008	90.8
Yes(men <13, women <12, pregnant <11)	1014	9.2
Metabolic syndrome		
No	8493	72.8
Yes	3173	27.2
Chronic kidney disease		
No	11 374	97.5
Yes	292	2.5
Health behavior risk factors		
Lifetime smoker		
No	6967	60.9
Yes	4480	39.1
Binge alcohol user		
Never drink alcohol	3156	27.6
Not a binge alcohol user	4726	41.3
Yes	3564	31.1
Physical activity of moderate intensity		
Never and <5 times in a week	11 156	97.5
≥5 times in a week	287	2.5
Coffee consumption		
Never	1058	10.6
1–6 cups per week	2417	24.3
≥7 cups per week	6484	65.1
Sleep duration		
6–8 hrs	8779	76.7
<6 hrs	1777	15.5
>8 hrs	889	7.8
Stress		
Least stressful	1838	16.1
Moderately stressful	9108	79.6
Extremely stressful	502	4.4
Variables regarding the eyes		
MRD (mm) in right eye		
1–1.9	798	7.0
2–2.9	1805	15.9
3–3.9	4053	35.6
≥4.0	4726	41.5
Spherical equivalent in right eye		
''−1.0D≤ & <0.0D''	3690	48.9
''−2.0D≤ & <−1.0D''	1554	20.6
''−4.0D≤ & <−2.0D''	1200	15.9
''−6.0D≤ & <−4.0D''	649	8.6
''<−6.0D''	459	6.1
Cylindrical error in right eye		
0D	1449	12.6
''−1.0D≤ & <0.0D	6999	61.0
''−2.0D≤ & <−1.0D''	2324	20.2
''−4.0D≤ & <−2.0D''	617	5.4
''<−4.0D''	92	0.8

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SUPPLEMENTAL TABLE 1. The Number and Percentage of Variables Used in the Korea National Health and Nutrition Examination Survey 2010–2011 in South Korea (n = 11 666) (*Continued*)

	n	Percentage (%)
History of eye surgery		
No	10 021	85.9
Yes	1645	14.1
Dry eye diagnosed by physician		
No	10 635	91.2
Yes	1031	8.8
Dry eye symptoms		
No	9251	84.2
Yes	1731	15.8

BMI = body mass index; DBP = diastolic blood pressure; HbA1C = glycated hemoglobin; HDL = high density lipoprotein; hrs = hours; MRD = marginal reflex distance; n = number; SBP = systolic blood pressure; D = diopter.

SUPPLEMENTAL TABLE 2. Factors Associated With Dry Eye in South Korea: Univariate Analysis (n = 11 666)

	Diagnosed DES			Symptoms of DES		
	OR	95% CI	*P*	OR	95% CI	*P*
Sociodemographic factors						
Age						
19–29	1.0 (ref)			1.0 (ref)		
30–39	0.9	(0.7–1.2)	0.56	0.9	(0.7–1.1)	0.35
40–49	0.8	(0.7–1.1)	0.22	0.8	(0.7–1.0)	0.11
50–59	1.1	(0.9–1.4)	0.62	1.0	(0.8–1.3)	0.93
60–69	1.1	(0.8–1.5)	0.49	1.1	(0.9–1.4)	0.49
70–	0.8	(0.6–1.1)	0.14	0.9	(0.7–1.2)	0.50
Gender						
Male	1.0 (ref)			1.0 (ref)		
Female	3.4	(2.8–4.1)	<0.01[a]	2.2	(1.9–2.5)	<0.01[a]
Monthly household income						
Lowest quintile	1.0 (ref)			1.0 (ref)		
2nd–4th quintile	1.3	(1.0–1.5)	0.04[a]	1.0	(0.9–1.2)	0.26
Highest quintile	1.3	(1.1–1.7)	<0.01[a]	1.1	(0.9–1.3)	0.34
Education						
Elementary school	1.0 (ref)			1.0 (ref)		
Middle school	1.0	(0.8–1.3)	0.92	0.8	(0.6–1.0)	0.07
High school	1.0	(0.9–1.3)	0.95	0.8	(0.7–1.0)	0.03[a]
University or higher	1.0	(0.9–1.3)	0.99	1.0	(0.8–1.2)	0.66
Residential area						
Urban	1.0 (ref)			1.0 (ref)		
Rural	0.7	(0.6–1.0)	0.02[a]	0.8	(0.6–1.1)	0.13
Occupation						
Farming, fishing and forestry occupations	1.0 (ref)			1.0 (ref)		
Administrator, Management, Professional	2.9	(2.0–4.2)	<0.01[a]	1.4	(1.1–1.8)	<0.01[a]
Business and financial operations occupations	2.6	(1.7–3.9)	<0.01[a]	1.3	(1.0–1.7)	0.04[a]
Sales and related occupations	3.1	(2.1–4.6)	<0.01[a]	1.3	(1.0–1.6)	0.07
Installation, maintenance, and repair occupations/technicians	1.6	(1.1–2.5)	0.03	0.9	(0.7–1.2)	0.34
Laborer	3.3	(2.2–4.8)	<0.01[a]	1.2	(0.9–1.6)	0.15
Unemployed	7.7	(5.5–10.9)	<0.01[a]	1.6	(1.3–2.0)	<0.01[a]
Health examination variables						
Hypertension						
No (SBP <120 and DBP <80)	1.0 (ref)			1.0 (ref)		
Prehypertension (120 ≤SBP <140 or 80 ≤DBP<90)	0.7	(0.5–0.8)	<0.01[a]	0.8	(0.7–1.0)	0.02[a]
Hypertension (SBP >140 or DBP >90)	0.7	(0.6–0.8)	<0.01[a]	0.8	(0.7–0.9)	<0.01[a]
Obesity						
Underweight (BMI <18.5 kg/m^2)	1.0 (ref)			1.0 (ref)		
Normal (18.5 kg/m^2 ≤BMI <25 kg/m^2)	0.7	(0.5–1.0)	0.04[a]	0.9	(0.7–1.2)	0.60
Obesity (BMI ≥25 kg/m^2)	0.6	(0.4–0.8)	<0.01[a]	0.7	(0.5–0.9)	0.02[a]
Hypercholest-erolemia						
No	1.0 (ref)			1.0 (ref)		
Yes (≥240 mg/dL)	1.3	(1.0–1.6)	0.04[a]	1.2	(1.0–1.5)	0.05[a]
Hypo-HDL-cholesterolemia (result from 2010 data only)						
No	1.0 (ref)			1.0 (ref)		
Yes (<40 mg/dL)	0.7	(0.6–0.9)	<0.01[a]	0.7	(0.6–0.9)	<0.01[a]
Hypertriglycemia						
No	1.0 (ref)			1.0 (ref)		
Yes (≥200 mg/dL)	0.7	(0.5–0.9)	<0.01[a]	0.8	(0.6–1.0)	0.03[a]
Rheumatoid arthritis						
No	1.0 (ref)			1.0 (ref)		
Yes	1.5	(1.0–2.2)	0.03[a]	1.2	(0.9–1.7)	0.21

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SUPPLEMENTAL TABLE 2. Factors Associated With Dry Eye in South Korea: Univariate Analysis (n = 11 666) (*Continued*)

	Diagnosed DES			Symptoms of DES		
	OR	95% CI	*P*	OR	95% CI	*P*
Thyroid disease						
No	1.0 (ref)			1.0 (ref)		
Yes	2.2	(1.7–2.9)	<0.01[a]	1.8	(1.4–2.2)	<0.01[a]
HbA1c (n = 533)						
No	1.0 (ref)			1.0 (ref)		
Yes(≥6.5 mU/L)	0.8	(0.6–1.0)	0.08	0.9	(0.7–1.1)	0.21
Anemia						
No	1.0 (ref)			1.0 (ref)		
Yes (men <13, women <12, pregnant <11)	1.1	(0.9–1.5)	0.40	1.2	(1.0–1.4)	0.10
Metabolic syndrome						
No	1.0 (ref)			1.0 (ref)		
Yes	0.8	(0.7–1.0)	0.09	0.9	(0.8–1.0)	0.13
Chronic kidney disease						
No	1.0 (ref)			1.0 (ref)		
Yes	1.3	(0.8–2.1)	0.35	1.1	(0.7–1.6)	0.71
Health behavior risk factors						
Lifetime smoker						
No	1.0 (ref)			1.0 (ref)		
Yes	0.4	(0.3–0.4)	<0.01[a]	0.5	(0.5–0.6)	<0.01[a]
Binge alcohol user						
Never drink alcohol	1.0 (ref)			1.0 (ref)		
Not a binge alcohol user	0.9	(0.7–1.1)	0.20	1.0	(0.9–1.2)	0.97
Yes	0.5	(0.4–0.7)	<0.01[a]	0.7	(0.6–0.9)	<0.01[a]
Physical activity of moderate intensity						
Never and <5 times in a week	1.0 (ref)			1.0 (ref)		
≥5 times in a week	1.0	(0.6–1.8)	0.92	1.1	(0.7–1.7)	0.64
Coffee consumption						
Never	1.0 (ref)			1.0 (ref)		
1–6 cups per week	1.0	(0.7–1.4)	0.98	1.0	(0.8–1.3)	0.95
≥7 cups per week	0.8	(0.6–1.1)	0.21	0.8	(0.6–1.0)	0.08
Sleep duration						
6–8 hrs	1.0 (ref)			1.0 (ref)		
<6 hrs	1.1	(0.9–1.4)	0.25	1.3	(1.1–1.5)	<0.01[a]
>8 hrs	0.9	(0.6–1.2)	0.45	1.0	(0.8–1.3)	0.93
Stress						
Least stressful	1.0 (ref)			1.0 (ref)		
Moderately stressful	1.4	(1.1–1.9)	<0.01[a]	1.3	(1.1–1.6)	<0.01[a]
Extremely stressful	2.0	(1.3–2.9)	<0.01[a]	1.7	(1.2–2.4)	<0.01[a]
Variables regarding the eyes						
MRD (mm) in right eye						
1–1.9	1.0 (ref)			1.0 (ref)		
2–2.9	0.9	(0.6–1.3)	0.49	1.1	(0.8–1.5)	0.64
3–3.9	1.1	(0.8–1.5)	0.67	1.1	(0.8–1.5)	0.69
≥4.0	1.2	(0.8–1.8)	0.29	1.1	(0.8–1.5)	0.67
Spherical equivalent in right eye						
''−1.0D≤ & <0.0D	1.0 (ref)			1.0 (ref)		
''−2.0D≤ & <−1.0D''	0.8	(0.6–1.0)	0.07	1.0	(0.8–1.2)	0.82
''−4.0D≤ & <−2.0D''	0.9	(0.7–1.2)	0.64	1.0	(0.8–1.3)	0.96
''−6.0D≤ & <−4.0D''	0.9	(0.6–1.3)	0.48	1.0	(0.7–1.2)	1.00
''<−6.0D''	1.2	(0.8–1.7)	0.44	1.2	(0.9–1.7)	0.26
Cylindrical error in right eye						
0D	1.0 (ref)			1.0 (ref)		

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SUPPLEMENTAL TABLE 2. Factors Associated With Dry Eye in South Korea: Univariate Analysis (n = 11 666) (*Continued*)

	Diagnosed DES			Symptoms of DES		
	OR	95% CI	*P*	OR	95% CI	*P*
''−1.0D≤ & <0.0D	0.9	(0.7–1.2)	0.51	1.1	(0.9–1.3)	0.45
''−2.0D≤ & <−1.0D''	1.0	(0.7–1.3)	0.80	1.1	(0.8–1.4)	0.66
''−4.0D≤ & <−2.0D''	1.0	(0.6–1.6)	0.96	1.5	(1.1–2.1)	0.01[a]
''<−4.0D''	0.4	(0.1–1.2)	0.09	0.6	(0.2–1.4)	0.22
History of eye surgery						
No	1.0 (ref)			1.0 (ref)		
Yes	2.7	(2.3–3.2)	<0.01[a]	2.2	(1.9–2.6)	<0.01[a]

BMI = body mass index; CI = confidence interval; DES = dry eye syndrome; DBP = diastolic blood pressure; n = number; HbA1c = glycated hemoglobin; HDL = high density lipoprotein; hrs = hours; MRD = marginal reflex distance; OR = odds ratio; ref = reference; SBP = systolic blood pressure; D = diopter.

[a]Univariate logistic regression analysis; statistical significance $P < 0.05$.