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Meibomian Gland Dysfunction and Dry Eye are Similar, but Different based on a Population-Based Study (Hirado-Takushima Study) in Japan

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ABSTRACT

PURPOSE: To evaluate the prevalence and risk factors of and the relation between meibomian gland dysfunction (MGD) and dry eye (DE) in Japan.

DESIGN: A population-based cross-sectional study.

METHODS: Participants filled in questionnaires regarding ocular symptoms, systemic diseases, and lifestyle factors. Meibomian gland-related parameters and tear film–related parameters were evaluated. Risk factors for MGD and DE were analyzed with univariate and multivariate logistic regression. Age-specific prevalence of MGD and DE was estimated with a general additive model with degree-3 natural splines. The structural relation between MGD and DE was assessed by factor analysis with the principal components method and promax rotation.

RESULTS: A total of 356 residents of Takushima Island (133 males, 223 females) with a mean ±SD age of 55.5 ± 22.4 years (range, 6 to 96 years). were participated. The prevalence of MGD and DE was 32.9% and 33.4%, respectively, with a coexistence rate of 12.9%. The prevalence of MGD was associated with male sex (odds ratio [OR], 2.42), age (OR per decade increment,1.53), and oral intake of lipid-lowering agents (OR, 3.22). The prevalence of DE was associated with female sex (OR, 3.36), contact lens wear (OR, 2.84), conjunctivochalasis (OR, 2.57) and lid margin abnormalities (OR, 3.16). The age-specific prevalence of MGD and DE differed, and factor analysis for 16 parameters showed that MGD and DE had independent hidden sources (interfactor correlation, –0.017).

CONCLUSION: MGD and DE are common in this population. Although their ocular symptoms are similar, the pathogenesis of MGD differs from that of DE.

Full-Length Article–Manuscript

Meibomian Gland Dysfunction and Dry Eye are Similar, but Different based on a Population-Based Study (Hirado-Takushima Study) in Japan

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Short title: Meibomian gland dysfunction and dry eye in Japan

Meibomian glands are large sebaceous glands located in the eyelid that secrete lipid (meibum) into the tear film in order to prevent excessive evaporation of tear fluid.[1] They are thus implicated in diseases related to the eyelid (blepharitis) or to the tear film (dry eye).[2] MGD can be considered as a cause of posterior blepharitis.[2, 3] The term MGD was first used in 1980 by Korb and Henriquez[4] and is considered to refer to a functional abnormality of meibomian glands. In 2011, the report of an international workshop on MGD organized by the Tear Film and Ocular Surface Society defined MGD as "a chronic abnormality of meibomian glands characterized by terminal duct obstruction or qualitative or quantitative changes in the glandular secretion, which can result in alteration of the tear film, inflammation, ocular surface disease, and symptoms of eye irritation."[3] MGD has subsequently attracted attention as a leading cause of dry eye (DE),[3, 5] which has emphasized the important role of meibomian glands in homeostasis of the tear film and ocular surface.[3, 6, 7] Although MGD is a common disease worldwide, it is still overlooked clinically and considered to be less prevalent than DE. Whereas the etiology of MGD may differ from that of DE, the two conditions share many symptoms including ocular fatigue, dryness, burning sensation, itchy sensation, and foreign body sensation.[3] Indeed, the ocular symptoms of MGD and DE are too similar to allow discrimination between the two diseases on the basis of symptoms alone. This similarity is likely one reason that MGD has been overlooked in clinical practice.

Nine population-based studies and six hospital-based studies have examined the prevalence of MGD over the last 20 years,[8-10] whereas 24 population-based studies and 14 hospital-based studies have examined that of DE over the past 10 years.[8] Among the 15 previous epidemiologic studies of MGD,[8-10] only five mentioned MGD instead of DE in their titles,[9-13] with the remainder focusing on aspects of DE rather than MGD. Moreover, MGD patients and DE patients tended to be confused in some studies for which inclusion criteria were based on ocular symptoms alone.[8] In addition, most of the populations examined in previous epidemiologic studies of MGD were over the age of 40.[8] As far as we are aware, no previous population-based study of MGD or DE investigated the similarities and differences between MGD and DE in the same cohort.

We have now performed a population-based study including younger individuals (aged 6 and older) in Japan in order to investigate the prevalence, risk factors, and systemic disease associations of MGD and DE separately. The

similarities and differences between MGD and DE were also compared and analyzed.

Methods

Subjects and study design

This is a population-based cross-sectional study. All study procedures complied with the tenets of the Declaration of Helsinki regarding human studies. This clinical study was approved by the Institutional Review Board of Itoh Clinic and registered in the University Hospital Medical Information Network database (UMIN 000028310). Written informed consent was obtained from all subjects before inclusion in the study. Out of 628 residents in Takushima island, of which 616 individuals were aged ≥6 years and therefore eligible for the study. The details are described in supplement.

Questionnaires

Participants completed Questionnaires related general information, systemic condition, and ocular symptoms using the Dry Eye–Related Quality-of-Life Score (DEQS) questionnaire.[14] Details are described in supplementary data.

Examinations

Assessments of ocular surface of both eyes were performed according to standardized protocols by a team of seven ophthalmologists with expertise in DE and MGD (members of the Lid and Meibomian Gland Working Group). Tear meniscus height, the lipid layer thickness of the tear film determined with the LipiView interferometer, lipid layer grade and noninvasive breakup time of the tear film,[15] lid margin abnormalities,[16] the tear film breakup time with fluorescein (FTBUT), corneal-conjunctival fluorescein staining score,[17] the absence or presence of conjunctivochalasis, pterygium, or conjunctival papillae, the grading of meibum[18]observed by a slitlamp, the meiboscore determined by noncontact meibography (Topcon, Tokyo, Japan),[19] the absence or presence of *Demodex*, and the Schirmer's test without anesthetic were evaluated. The details are shown in supplementary data.

Definition of MGD

MGD was defined[20] as (1) the presence of any chronic ocular symptom[14]; (2) more than one lid margin abnormality among vascularity, displacement of the

mucocutaneous junction (MCJ), and irregularity; and (3) obstruction of meibomian glands as revealed by the detection of plugging and reduced meibum expression in response to moderate digital pressure[18] in at least one eye. The ophthalmologists performing the examinations were masked to the results of tests performed by others.

Definition of DE

DE was defined according to the Japanese criteria of (1) the presence of any DE symptom[14] and (2) an FTBUT of≦5 s.[21] DE definition is irrelevant of meibum quality or tear secretion. This definition included both those who had normal MG function and abnormal MG function.

Statistical Analysis

Chi-squared test was applied to compare the degree of DEQS between subjects with MGD and those with DE. Univariate and multivariate logistic regression was used to evaluate the association of background variables and tear film-related variables with MGD/DE risk. For the multivariate models, stepwise selection method with $P = 0.15$ as the selection criteria was used. For the factor analysis, variables with $P < 0.1$ on univariate logistic analysis were selected as candidates possibly influencing on MGD/DE risk. A P value of < 0.05 was considered statistically significant other than the selection criteria for multivariate analysis and factor analysis. All statistical analysis was performed by independent statistician with SAS version 9.4 (SAS Institute, Cary, NC). The details are shown in supplementary data.

Results

Subjects

A total of 384 subjects (141 males, 243 females), with a mean ± SD age of 55.5 ± 22.4 years (range, 6 to 96 years), agreed to participate in the study (overall participation rate, 62.3%). After exclusion of those who could not use a chin rest for the ocular examinations, who terminated their participation, or who were not able to understand the procedure, the final study cohort included 356 subjects (133 males, 223 females) with a mean ±SD age of 55.5 ± 22.4 years (range, 6 to 96 years).

Comparison of Ocular symptoms between MGD and DE

Chi-squared test showed no significant differences in the degree of ocular symptoms between subjects with MGD and those with DE. (Table 1)

Prevalence and Risk Factors of MGD

The prevalence of symptomatic MGD (based on Japanese diagnostic criteria) was 32.9% for the entire study cohort, 41.4% for individuals aged 40 years or older, and 44.5% for those aged 50 years or older (Table 2). The prevalence was significantly higher for males than for females (42.1% versus 27.4%, P = 0.0051). The age-standardized prevalence of MGD is shown in Table 2, with the highest prevalence being apparent in individuals aged 80 years or older and prevalence increasing with age in both males and females (P < 0.0001). The estimated distribution of MGD prevalence according to age for males and females is also shown in Figure 1.

In univariate logistic regression, male sex, age, the meiboscore, and the presence of *Demodex*, showed statistically significant association with the prevalence of MGD, and oral intake of lipid-lowering agents and daily hours of outdoor work or computer use showed possible association (Table 3). Subsequent multivariate logistic regression analysis showed that male sex, age, and oral intake of lipid-lowering drugs were independently and significantly (P < 0.05) associated with a higher risk of MGD (Table 3).

Prevalence and Risk Factors of DE

The prevalence of DE in the study cohort was 33.4% and was significantly higher in females than in males (41.7% versus 19.5%, P < 0.0001) (Table 4). The age-standardized prevalence of DE is shown in Table 4, with the prevalence increasing with age in both males and females (P = 0.0019 and 0.0056, respectively). The estimated distribution of DE prevalence according to age for males and females is also shown in Figure 2.

In univariate logistic regression, female sex, current smoking and the presence of conjunctivochalasis and lid margin abnormalities showed statistically significant association with the prevalence of DE, and contact lens wear and use of sleeping pills showed possible association (Table 5). Subsequent multivariate logistic regression analysis showed that female sex, contact lens wear, and the presence of conjunctivochalasis or lid margin abnormalities were independently and significantly (P < 0.05) associated with a higher risk of DE (Table 5).

Relationship Between MGD and DE

The prevalence of MGD was 32.9% (117/356) and that of DE was 33.4% (119/356), with the rate of coexistence of both MGD and DE being 12.9% (46/356). Forty-six (38.7%) of the 119 subjects with DE were thus diagnosed with MGD, and 46 (39.3%) of the 117 subjects with MGD also had DE. The prevalence of MGD was zero in males or females younger than 20 years, but it increased to 0.8%, 16.9%, 49.1%, and 71.5% in men and to 4.4%, 15.7%, 29.0%, and 47.0% in women at 20, 40, 60, and 80 years, respectively (Table 2, Fig 1). On the other hand, the prevalence of DE in males was lower than that in females at all ages. In males, the prevalence of DE remained almost constant at ~10% between 6 and 40 years of age and then increased according to a J-shaped curve, with values of 10.1%, 17.2%, and 34.2% at 40, 60, and 80 years, respectively (Table 4, Fig 2). The prevalence of DE in females increased with age according to an S-shaped curve, with a peak at 40 years and values of 16.8%, 29.3%, 41.2%, 45.6%, 43.6%, and 45.7% at 10, 20, 30, 40, 60, and 80 years, respectively (Table 4, Fig 2). Overall, the estimated distribution pattern of MGD and DE were completely different.

Factor analysis for 16 parameters showed that MGD and DE had independent hidden sources (interfactor correlation, –0.017). Factor 1 (*y*-axis) corresponds to MGD-related parameters, whereas Factor 2 (*x*-axis) corresponds to DE-related parameters (Fig 3, Table 6). MGD ($x = 0.008$, $y = 0.657$) was thus independent of DE ($x = 0.831$, $y = 0.106$). The parameters contributing most to MGD were age followed by displacement of the MCJ, irregularity and vascularity of the lid margin, meibum grade, meiboscore, plugging of meibomian gland orifices, and the presence of conjunctivochalasis. Given that the definition of MGD in the present study was based on ocular symptoms, more than one lid margin abnormality (among vascularity, MCJ displacement, and irregularity), and meibomian gland obstruction (plugging and reduced meibum expression), our results suggest that age, meiboscore, and conjunctivochalasis are additional key factors for MGD. On the other hand, the parameters contributing most to DE were FTBUT, corneal-conjunctival fluorescein staining score, and female sex. Given that the definition of DE in the present study was based on symptoms and FTBUT, the corneal-conjunctival fluorescein staining score and female sex are additional key factors for DE. Of note, the DEQS score (symptom questionnaire) was not substantially

associated with MGD or DE in this analysis (Fig 3, Table 6).

Discussion

As far as we are aware, our study, performed with individuals aged 6 or older across nine decades, is the first population-based analysis of the prevalence and risk factors of both MGD and DE. In addition, we analyzed and compared parameters associated with MGD or DE. Our results indicate that, even though it is not possible to distinguish between the two conditions on the basis of ocular symptoms alone, the pathogenesis of MGD is distinct from that of DE.

We found that the prevalence of MGD (based on Japanese diagnostic criteria[20]) was 32.9% in our Japanese cohort of individuals aged 6 years or older. The prevalence of DE was 33.4%. Multivariate analysis revealed that male sex, age, and the use of lipid-lowering drugs were independent factors in the development of MGD, whereas female sex, contact lens wear, conjunctivochalasis, and lid margin abnormalities were independent factors for the development of DE. The coexistence rate for both MGD and DE was 12.9%. MGD and DE were thus both common in this cohort. Age- and sex- specific prevalence rates differed between MGD and DE. Moreover, factor analysis for MGD- or DE-related parameters showed that MGD and DE were independent conditions. Together, these results thus indicate that MGD and DE are distinct conditions in terms of their etiology and pathogenesis, despite the overlap in their ocular symptoms.

We found that the prevalence of MGD was 32.9% among all subjects aged 6 years or older, 41.4% among those aged 40 years or older, and 44.5% among those aged 50 years or older. Nine population-based studies and six hospital-based studies have previously examined the prevalence of MGD across different age, sex, and race cohorts.[8-10] The reported prevalence based on clinical signs (including telangiectasia, plugging, and meibum quality or quantity) alone in populations over the age of 40 ranged from 3.6% to 68.0%. In general, rates tended to be higher in Asian population cohorts[9, 12, 22-25] than in Caucasians.[11, 26] The highest reported prevalence for MGD in previous population-based studies is 60.8% for a Chinese population aged 65 years or older in Taiwan,[22] followed by 56.3% in Singapore[12] and 51.8% for those aged at least 65 in Korea.[25] The prevalence of MGD in the present study is likely lower than these previous estimates because our cohort included individuals as young as 6 years old and we defined MGD on the basis of ocular symptoms, lid

margin abnormalities, and reduced meibum expression, whereas the previous population-based studies examined cohorts aged at least 40 or 65 years and diagnosed with MGD on the basis of looser criteria such as the presence of only plugging or telangiectasia. In addition, our study showed only 38.5% of women aged over 60 years had MGD. Lemp et al reported over 85% of patients seen in a DE clinic were found to have MGD.[5] As our study was a population-based study, the study performed by Lemp et al.[5] was a clinic-based retrospective study. Our study included the normal subjects. The enrolled subjects seemed to be different in those two studies. Moreover, the definition of DE in our study was different from that of Lemp.[5] That's why for the discrepancy between ours and those of Lemp.[5]

In the present study, multivariate analysis revealed that male sex and age were significant factors in the development of MGD. Whereas some previous studies have detected a higher rate of MGD in men,[11-13, 22] others have not seen a sex difference[9, 10] or detected a higher prevalence in women.[24, 25] This discrepancy might be due to confusion between MGD and DE in some studies. Effects of sex hormones such as androgens and estrogens on meibomian glands have been described,[27] and recent studies have detected a higher prevalence of MGD in adolescent boys than in girls.[28, 29] In the present study, the prevalence of MGD in men was especially high in those aged 40 years or older, which might correspond to onset of the "male menopause[30]."An imbalance of sex hormones might thus affect the pathogenesis of MGD in men, as the loss of androgens is also believed to contribute to the pathogenesis of MGD in women.[31]

Most population-based studies of DE have been based on only ocular symptoms.[8] The Asia Dry Eye Society now recommends that DE be diagnosed on the basis of both ocular symptoms and a short FTBUT.[21] Previous population-based studies adopted a definition of DE based on the presence of both symptoms and signs, and they reported an overall prevalence ranging from 8.7% to 30.1%.[11, 13, 32, 33] Our estimate of DE prevalence (33.4%) is most similar to that of a Chinese study (30.1%)[34] based on symptoms and either an FTBUT of <5 s, a Schirmer test value of <5 mm, or corneal staining.

Multivariate analysis revealed that female sex was a significant factor for the development of DE in the present study. Female sex has repeatedly been found to be associated with DE, although some studies have found otherwise.[8, 31] In the present study, the prevalence of DE was higher in females

than in males at all ages, although this difference had largely disappeared at advanced ages. The prevalence of DE in females increased with age, peaking at ~40 years. Estrogens are thought to be a risk factor for DE,[31] and they peak in women at ~30 to 40 years of age.[35] Another population-based study performed with British female twins obtained a similar result, with the prevalence of DE showing a significant increase per age decade and peaking in the 40- to 50-year-old age group.[33] On the other hand, estrogen levels increase in men after the male menopause.[35] Several hormonal mechanisms related to progesterone, androgens, and prolactin in addition to estrogens have been proposed to explain the age dependence of DE prevalence in both men and women.[31] Although estrogen levels decrease with advanced age in women,[35] aging has also been thought to be a risk factor for DE in both men and women.[8] In addition, our multivariate analysis revealed that contact lens wear was a significant factor for the development of DE. Previous studies have also found that contact lens wear is associated with a higher prevalence of DE.[8] In the present study, contact lens wear was common among women in their 20s to 40s. A significant effect of age on the prevalence of DE was not detected in the present study, probably because of the high prevalence apparent in women in their 30s and 40s. This latter finding is consistent with some[8] but not all previous studies, with discrepancies again possibly being due to confusion between MGD and DE.

We found that the use of lipid-lowering agents was also a significant independent contributing factor to MGD (odds ratio of 3.22, with a 95% confidence interval of 1.05 to 9.87). Previous studies have also found an association between MGD and dyslipidemia.[36-40] MGD is considered to be a major cause of evaporative dry eye[41] and posterior blepharitis.[42] In fact, meibomian glands are large sebaceous glands[27] and MGD is characterized by an altered composition or amount of meibum.[43] Individuals with MGD have been found to have a higher incidence of elevated total blood cholesterol than the general population,[36] and cholesterol esters may play a role in the development of MGD.[44] Other studies have suggested the possibility that increased amounts of cholesterol in the glandular secretion may play a role in the pathogenesis of MGD.[43, 45] Hypercholesterolemia is a risk factor for ischemic heart, cerebrovascular, and peripheral vascular disease.[46, 47] MGD has been proposed as a potential marker of hypercholesterolemia, and, like MGD, the risk factors for cardiovascular disease include male sex and age.[46, 48,

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The presence of *Demodex* mites was more frequent in subjects with MGD than in those without this condition. However, multivariate logistic regression analysis did not confirm the presence of *Demodex* as an independent factor associated with an increased risk of MGD, likely because it was also associated with age, male sex, and the meiboscore (data not shown). A previous study found that the presence of *Demodex* was related to MGD pathophysiology.[50] Our population-based study supports an association between MGD and *Demodex* and suggests that attention to the presence of these mites is warranted.

The population of Takushima is not representative of the entire Japanese population with regard to geographic location, age distribution, or occupation. Takushima is located in the southwestern region of Japan, and the time spent working outdoors (3.5 ± 2.3 h per day as determined in the present study) is likely higher than that for urban areas. The time spent using a computer (1.6 ± 2.4 h a day) and the proportion of contact lens wearers (0.7%) are also likely lower than for the entire country. Environmental risk factors for DE—including time spent in air-conditioned rooms, computer use, and contact lens wear—are thus likely less prevalent in Takushima. Nevertheless, the prevalence of both DE and MGD was similar to that determined in previous studies of Asian cohorts, with Asian race itself being thought to be a critical risk factor for both conditions.

There are several limitations to our study. First, the number of participants younger than 18 years was small, which is not unusual for an isolated rural island in Japan. Second, the symptom questionnaire was developed for DE rather than MGD. A more appropriate questionnaire might provide a more accurate determination of symptomatic MGD prevalence. Third, the slitlamp diagnostic criteria were relatively subjective, even though the members of our working group are specialists with regard to both MGD and DE. Standardization of such criteria should also allow more accurate comparisons between studies. Fourth, blood tests such as those for total cholesterol or triglyceride levels were not performed in our study. We therefore cannot conclude that MGD is directly associated with dyslipidemia itself. Lipid-lowering drugs might affect MGD by other mechanisms, with further studies thus being necessary to investigate the relations among MGD, dyslipidemia, and the use of lipid-lowering agents. Lastly, the prevalence rates might be slightly different

when our study are applied to the criteria of other countries other than Japan, due to the definition of MGD/DE. In addition, the environmental factors, such as humid, temperature or air pollution, and dietary proclivity might affect the results.

In conclusion, our population-based study of the prevalence of MGD and DE in individuals aged 6 years and older has revealed that both MGD and DE are common conditions in Japan, with an estimated prevalence of 32.9% and 33.4%, respectively. Male sex, age, and the use of lipid-lowering agents were significantly associated with MGD, whereas female sex, contact lens wear, and the presence of conjunctivochalasis or lid margin abnormalities were significantly associated with DE. The coincidence rate of MGD and DE was 12.9%. Although their ocular symptoms are similar, the principal factors such as the risk factors, etiology, and pathogenesis of MGD and DE are different. MGD may be caused in part by dyslipidemia and may give rise to posterior blepharitis or DE.

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Figure Captions

Figure 1. Distribution of age-specific prevalence of meibomian gland dysfunction (MGD) for males and females estimated by a general additive model with degree-3 natural splines.

Figure 2. Distribution of age-specific prevalence of dry eye (DE) for males and females estimated by a general additive model with degree-3 natural splines.

Figure 3. Factor analysis of the relations among meibomian gland dysfunction (MGD), dry eye (DE), and various clinical parameters shown in Table 6. Abbreviations: MCJ, mucocutaneous junction (displacement of); CFS, corneal-conjunctival fluorescein staining score; DEQS, Dry Eye–Related Quality-of-Life Score; FTBUT, fluorescein breakup time of the tear film.

Table 2. Total and age-specific prevalence of meibomian gland dysfunction with 95% confidence intervals.

Age group (years)	Total	Male	Female
Total	117/356 (32.9%, 28.0%-38.0%)	56/133 (42.1%, 33.6% - 51.0%)	61/223 (27.4%, 21.6% - 33.7%)
6-9	0/13 (0.0%, 0.0% - 24.7%)	0/9 (0.0%, 0.0% - 33.6%)	0/4 (0.0%, 0.0% - 60.2%)
10 - 19	0/33 (0.0%, 0.0% - 10.6%)	0/15 (0.0%, 0.0% - 70.8%)	0/18 (0.0%, 0.0% - 18.5%)
20 - 29	2/17 (11.8%, 1.5% - 36.4%)	0/3 (0.0%, 0.0% - 70.8%)	2/14 (14.3%, 1.8% -42.8%)
30 - 39	1/18 (5.6%, 0.1% - 27.3%)	0/6 (0.0%, 0.0% - 45.9%)	1/12 (8.3%, 0.2% - 38.5%)
40 - 49	8/37 (21.6%, 9.8% - 38.2%)	2/7 (28.6%, 3.7% - 71.0%)	6/30 (20.0%, 7.7% - 38.6%)
50 - 59	21/64 (32.8%, 21.6% - 45.7%)	9/23 (39.1%, 19.7% - 61.7%)	12/41 (29.3%, 16.1% - 45.5%)
60 - 69	31/74 (41.9%, 30.5% - 53.9%)	18/30 (60.0%, 40.6% - 77.3%)	13/44 (29.5%, 16.8% - 45.2%)
70 - 79	31/64 (48.4%, 35.8% - 61.3%)	15/24 (62.5%, 40.6% - 81.2%)	16/40 (40.0%, 24.9% -56.7%)
≥80	23/36 (63.9%, 46.2% - 79.2%)	12/16 (75.0%, 47.6% - 92.7%)	11/20 (55.0%, 31.5% - 76.9)

The trend *P* value for age in all, male, or female subjects was <0.0001 as calculated by logistic regression. The *P* value for sex in all subject was 0.0051 as calculated by logistic regression.

Table 3. Risk factors for meibomian gland dysfunction evaluated by univariate and multivariate logistic regression.

	Univariate analysis		Multivariate analysis	
Independent variable	Crude odds ratio (95% CI)	*P* value	Adjusted odds ratio (95% CI)	*P* value
Sex (male/female)	2.33 (1.41-3.87)	0.001	2.42 (1.25-4.67)	0.009
Age (per decade increment)	1.53 (1.24-1.88)	<0.001	1.53 (1.21-1.94)	<0.001
Meiboscore	1.35 (1.15-1.58)	<0.001		
Antihypertensive drugs	1.38 (0.84-2.56)	0.201		
Lipid-lowering agents	2.56(0.89-7.42)	0.083	3.22 (1.05-9.87)	0.041
Demodex	2.10 (1.21-3.65)	0.008		
Outside work time	1.13 (1.02-1.26)	0.017		
Computer use time	0.77 (0.58-1.02)	0.068		

CI, confidence interval.

Table 4. Total and age-specific DE prevalence with 95% confidence intervals.

Age group (years)	Total	Male	Female
Total	119/356 (33.4%, 28.5%-38.6%)	26/133 (19.5%, 13.2% - 27.3%)	93/223 (41.7%, 35.2% - 48.5%)
6-9	1/13 (7.7%, 0.2% - 36.0%)	1/9 (11.1%, 0.3% - 48.2%)	0/4 (0.0%, 0.0% - 60.2%)
10 - 19	4/33 (12.1%, 3.4% - 28.2%)	1/15 (6.7%, 0.2% - 31.9%)	3/18 (16.7%, 3.6% - 41.4%)
20 - 29	7/17 (41.2%, 18.4% - 67.1%)	0/3 (0.0%, 0.0% - 70.8%)	7/14 (50.0%, 23.0% -77.0%)
30 - 39	6/18 (33.3%, 13.3% - 59.0%)	1/6 (16.7%, 0.4% - 64.1%)	5/12 (41.7%, 15.2% - 72.3%)
40 - 49	15/37 (40.5%, 24.8% - 57.9%)	1/7 (14.3%, 0.4% - 57.9%)	14/30 (46.7%, 28.3% - 65.7%)
50 - 59	21/64 (32.8%, 21.6% - 45.7%)	3/23 (13.0%, 2.8% - 33.6%)	18/41 (43.9%, 28.5% - 60.3%)
60 - 69	24/74 (32.4%, 22.0% - 44.3%)	6/30 (20.0%, 7.7% - 38.6%)	18/44 (40.9%, 26.3% - 56.8%)
70 - 79	24/64 (37.5%, 25.7% - 50.5%)	7/24 (29.2%, 12.6% - 51.1%)	17/40 (42.5%, 27.0% -59.1%)
≥80	17/36 (47.2%, 30.4% - 64.5%)	6/16 (37.5%, 15.2% - 64.6%)	11/20 (55.0%, 31.5% - 76.9)

The trend *P* value for age in all, male, or female subjects was 0.0041, 0.0019, and 0.0056, respectively, as calculated by logistic regression. The *P* value for sex in all subject was <0.0001 as calculated by logistic regression.

Table 5. Risk factors for dry eye evaluated by univariate and multivariate logistic regression

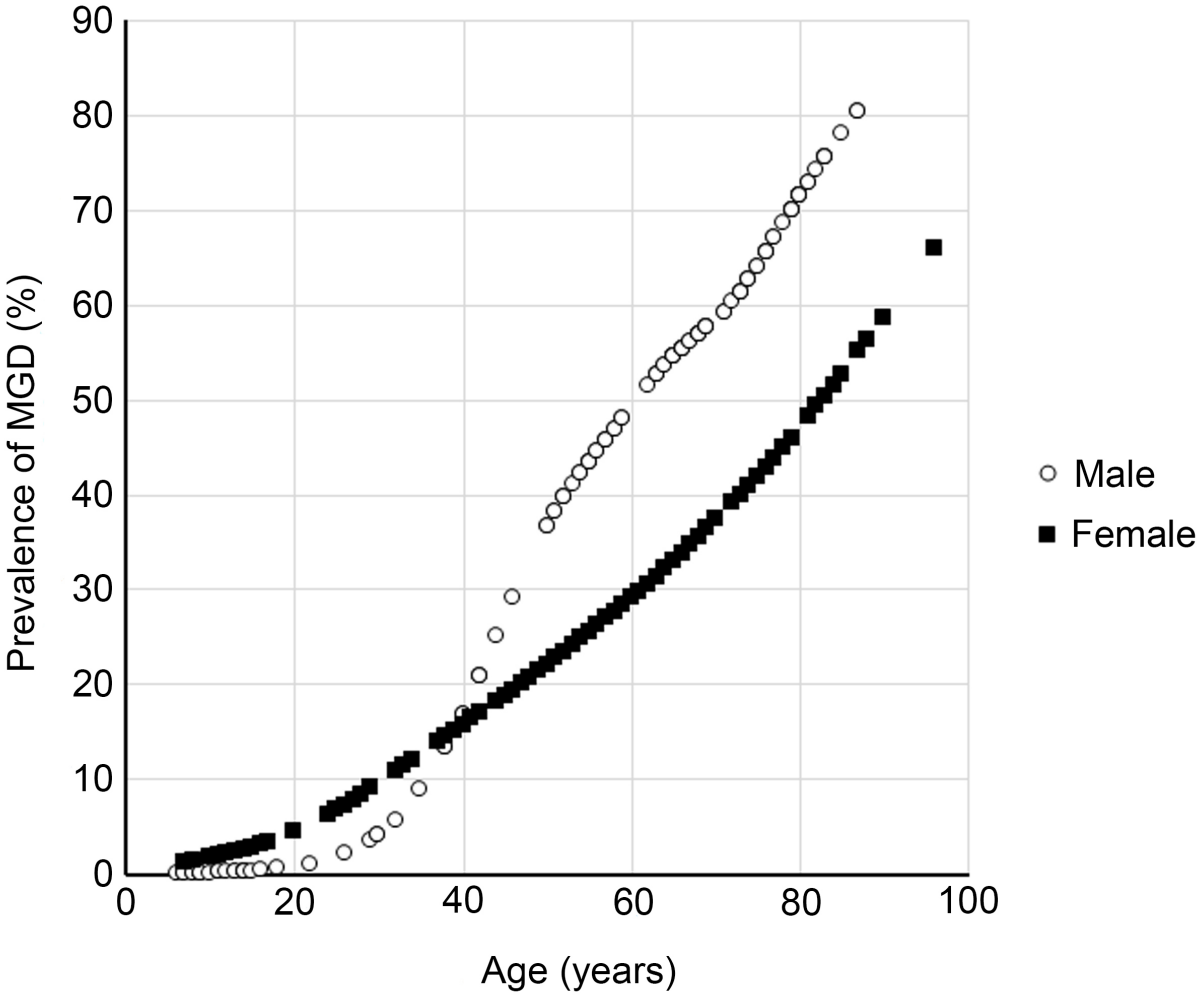
	Univariate analysis		Multivariate analysis	
Independent variables	Crude odds ratio (95% CI)	*P* value	Adjusted odds ratio (95% CI)	*P* value
Sex (male/female)	0.32 (0.18-0.57)	<0.001	3.36 (1.85-6.07)	<0.0001
Eye makeup use	1.81 (0.80-4.08)	0.152		
Current smoking	0.25 (0.07-0.85)	0.026		
Contact lens wear	2.17 (0.91-5.18)	0.083	2.84 (1.08-7.43)	0.034
Hypertension	1.44 (0.90-2.33)	0.139		
Sleeping pills	2.43 (0.91-6.50)	0.077		
Conjunctivochalasis	2.93 (1.62-5.30)	0.000	2.57 (1.35-4.88)	0.004
Conjunctival papillae	1.51 (0.92-2.47)	0.101		
Lid margin abnormality (plugging, vascularity,or irregularity)	2.31 (1.11-4.83)	0.025	3.16 (1.38-7.23)	0.007

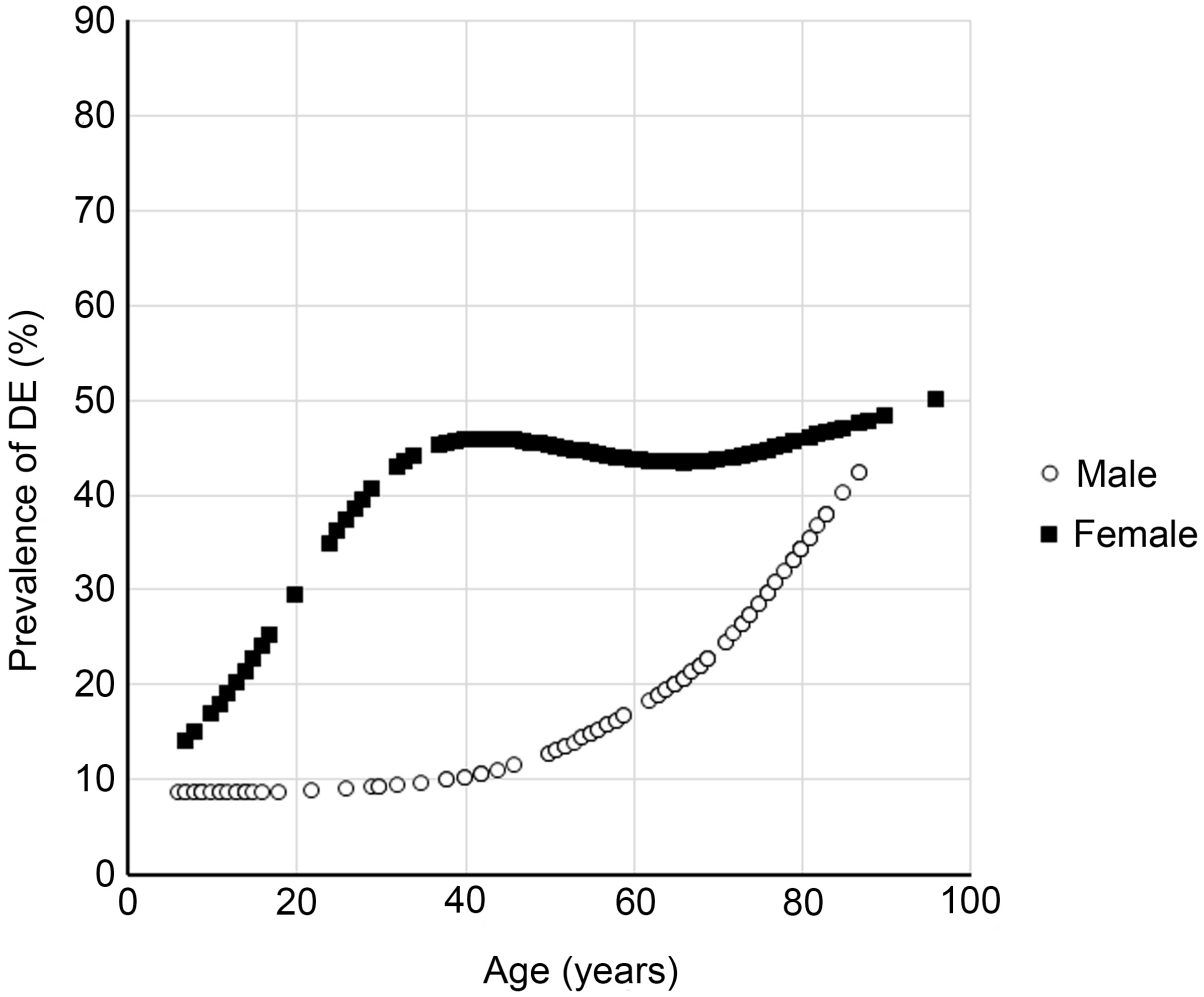
CI, confidence interval.

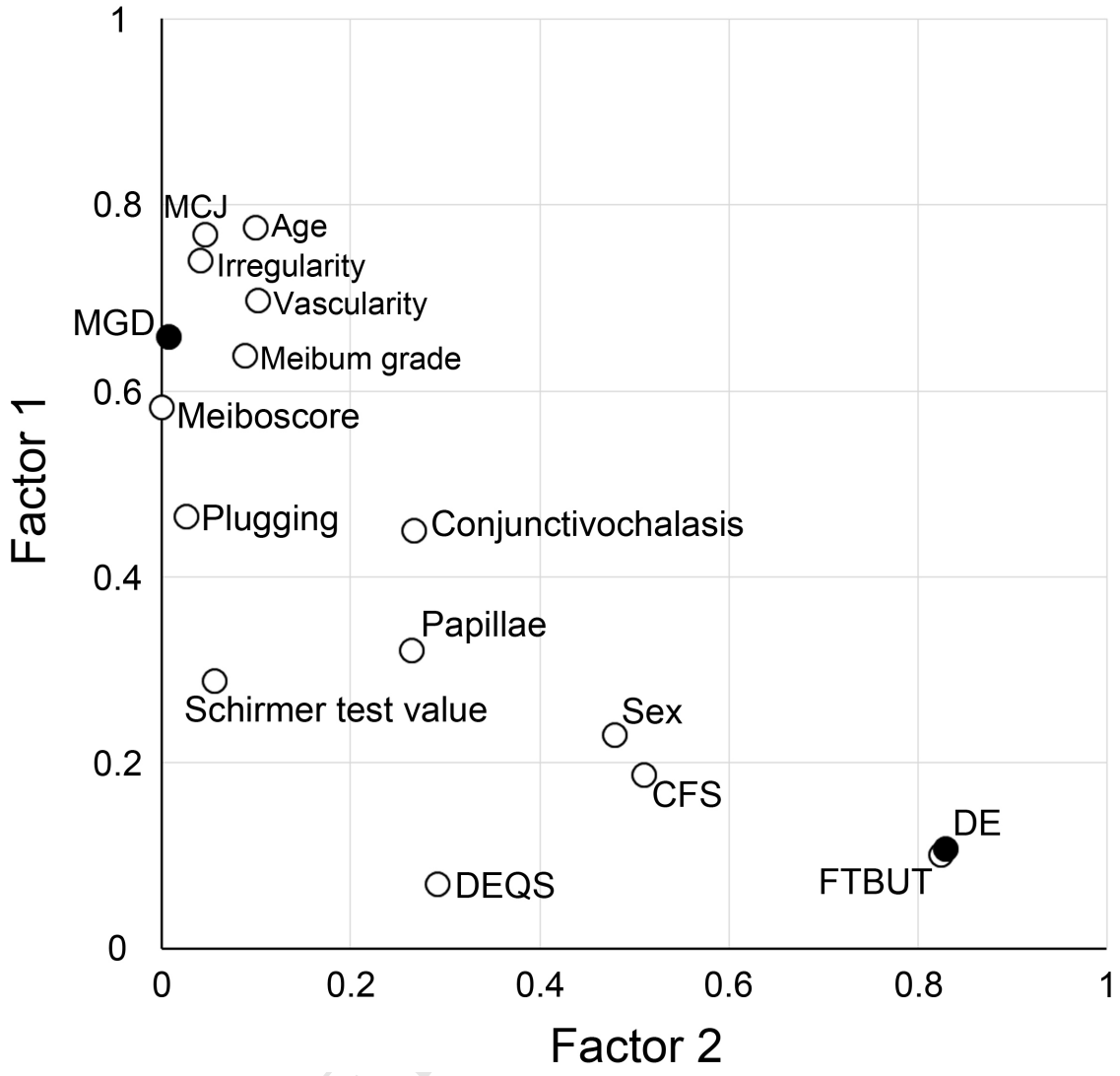
Table 6. Relations among meibomian gland dysfunction, dry eye, and clinical parameters according to factor 1 and factor 2.

Parameter	Factor 1	Factor 2
MGD	0.657	0.008
DE	0.106	0.831
Age	0.776	-0.100
Sex	0.230	-0.479
DEQS	0.070	0.293
Plugging	0.466	0.026
Vascularity	0.698	-0.102
Displacement of MCJ	0.768	-0.046
Irregularity	0.740	0.041
Meiboscore	0.583	-0.001
Meibum grade	0.638	-0.088
FTBUT	-0.101	-0.824
CFS	-0.187	0.510
Schirmer test value	-0.288	-0.056
Conjunctivochalasis	0.450	0.267
Papillae	-0.321	0.264

MGD, meibomian gland dysfunction; DE, dry eye; DEQS, Dry Eye-Related Quality-of-Life Score; MCJ, mucocutaneous junction; FTBUT, fluorescein tear film breakup time, CFS, corneal·conjunctival fluorescein staining score.


Prevalence of MGD (%)
90
80
70
60
50
40
30
20
10
0
0
20
40
60
80
100
Age (years)
Male
Female


90
80
70
60
50
40
30
20
10
0
Prevalence of DE (%)
0
20
40
60
80
100
Age (years)
Male
Female


1
0.8
0.6
0.4
0.2
0
Factor 1
0
0.2
0.4
0.6
0.8
1
Factor 2
MCJ
Age
Irregularity
Vascularity
MGD
Meibum grade
Meiboscore
Plugging
Conjunctivochalasis
Papillae
Schirmer test value
Sex
CFS
DE
DEQS
FTBUT

Highlights

•A population-based study of meibomian gland dysfunction (MGD) and dry eye (DE) was performed in Japan
•The prevalence, risk factors, and age and sex distribution differed between MGD and DE
•Although their ocular symptoms are similar, MGD and DE appear to be essentially distinct diseases