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Characterization of Meibomian Gland Atrophy and the Potential Risk Factors for Middle Aged to Elderly Patients With Cataracts

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Purpose: To explore the characteristics of meibomian gland (MG) atrophy and its potential risk factors in the age-related cataract population.

Methods: Patients who underwent cataract surgery at age 40 or older were enrolled in this study. Preoperative clinical measurement records were obtained, including lipid layer thickness, tear meniscus height, noninvasive breakup time, and meiboscore. The meibomian gland atrophy ratio (MGAR) was measured by the ImageJ software. Univariate regression analysis and multivariate regression analysis were used to analyze the risk factors for MG atrophy.

Results: Female patients had less atrophy of the MG compared with male patients. The MGAR, meiboscore, tear meniscus height (TMH), and lipid layer thickness (LLT) gradually increased with age. However, the noninvasive breakup time decreased with age. The multivariate regression analysis indicated that dyslipidemia and increased triglyceride levels were identified as independent protective factors for MG atrophy. We further stratified the model by sex, and the following results showed only in the female patients with dyslipidemia and increased triglyceride had decreased MG atrophy. No significant correlation was observed between MG atrophy and tear film parameters including TMH, noninvasive breakup time, and LLT.

Conclusions: Our study suggests that age, sex, and diabetes are potential risk factors for MG atrophy. In addition, dyslipidemia and increased triglyceride levels are independent protective factors for MG atrophy in the elderly female population.

Translational Relevance: MG atrophy is the leading cause of meibomian gland dysfunction. To study the characteristics and risk factors of MG atrophy in cataract patients would be helpful to predict and prevent postoperative development of MGD.

Introduction

The meibomian glands (MG) are sebaceous glands found in the eyelids that consist of secretory acini.[1] The lipids secreted by the MGs are essential components of the tear film to maintain tear stability and thus for visual quality.

Obstruction of the terminal duct or changes in the quality or quantity of meibum leads to meibomian gland dysfunction (MGD).[2] Recent studies suggest that MG atrophy leads to tear film instability and is likely the main cause of MGD.[3] Therefore MG structure is an important index for the assessment of MGD.[4] The recent development of noncontact infrared meibography enables clear and noninvasive

observation of the morphologic characteristics of the meibomian glands.[5–7] The ratio of the MG atrophy could also be calculated by ImageJ software. This method is more accurate and sensitive than the conventional MG grading system.[8,9]

MGD is a major cause of patient dissatisfaction after cataract surgery.[10–12] Previous studies indicate that the prevalence of dry eye increases after cataract surgery.[10,13] Patients without dry eye before the operation often develop dry eye after cataract surgery.[10] Cataract surgical candidates are often older than 40 years old, which is an important factor for the development of MG atrophy. The MG atrophy increases with age, and the incidence of cataract surgery is also strongly age related.[14] However, few reports are available describing the MG health of this population.[10,11] Furthermore, the prevalence of dry eye and MGD in China is obviously higher than that of European countries.[15–18] A comprehensive understanding of the MG atrophy rate and the risk factors of the cataract patient population would be helpful to predict and prevent postsurgical development of MGD.

Various external and internal factors are associated with MGD, such as age,[5] sex,[19,20] surgery,[10] contact lenses wear,[7] and others. The influence of systemic factors, such as diabetes and dyslipidemia, on MG atrophy is still not fully understood.[21] The correlation between MGD and dyslipidemia has been studied by some previous studies. However, their conclusions were controversial. Some studies found that the prevalence of dyslipidemia in MGD patients was significantly higher compared with control subjects.[22–24] However, the retrospective case-controlled study by Dao et al.[25] suggests that low high-density lipoprotein (HDL) may be a protective factor for the development of MGD. And one study found that there was no difference for the prevalence of dyslipidemia between patients with MGD and those without MGD.[26] The relation between meibomian gland status and plasma lipid remains unclear in elder patients and warrants further investigation. The purpose of this study is to evaluate the MG atrophy measured by ImageJ and provide a deeper understanding of MG atrophy and the potential risk factors associated with cataract patients.

Methods

Study Population

This cross-sectional study was conducted at the eye hospital of Wenzhou Medical University, Hangzhou. Informed consent was obtained from the participants before their inclusion in the study. This study adhered to the tenets of the Declaration of Helsinki and was approved prospectively by the Investigational Review Board of School of Ophthalmology and Optometry and Eye Hospital at Wenzhou Medical University in Wenzhou, China.

This study enrolled patients older than 40 years old with cataracts. Exclusion criteria were as follows: a history of ocular surgery or trauma, ocular inflammation or infection, contact lenses use, pterygium, glaucoma, or any other disease known to affect the tear film, such as Sjögren's syndrome, Stevens-Johnson syndrome, and so on.

Study Protocol

An ophthalmic examination with slit-lamp biomicroscopy was first performed to exclude other ocular diseases. Then other clinical measurements were performed in the following order: (1) lipid layer thickness (LLT), (2) tear meniscus height (TMH), (3) noninvasive breakup time (NIBUT), and (4) meibography.

Subject Examination

Lipid layer thickness measurement was conducted with the LipiView interferometer (TearScience Inc., Morrisville, NC, USA). Briefly, the pupils of the subjects were positioned to the center of a live video screen, and the reflected image of the tear film was positioned within the green targeting rectangle. Participants were asked to fix on the internal target, and images were captured within a period of 20 seconds. Natural blinking was allowed during the examination. The LLT was reported as interferometric color units.

Tear meniscus height (TMH) and NIBUT were captured by a Keratograph 5M (K5M, Wetzlar, Germany). The inferior TMH was obtained five seconds after blinking. For NIBUT measurement, participants were instructed to blink twice and then maintain fixation on the target as long as possible. The average NIBUT (NIBUT-avg) that indicated the mean value of the tear film break-ups across the observed area was analyzed automatically by the software and was recorded.

Meibography was also captured by the Keratograph 5M. Images of both the upper and lower eyelids were captured by flipping the eyelids outward. Meiboscore and the ratio of meibomian gland atrophy area were calculated using these images. The meiboscore was calculated with the method described by Arita R, and both upper and lower eyelid were scored on scale of 0 to 3.[5] The meibomian gland atrophy ratio (MGAR) (the ratio of meibomian gland atrophy area compared with

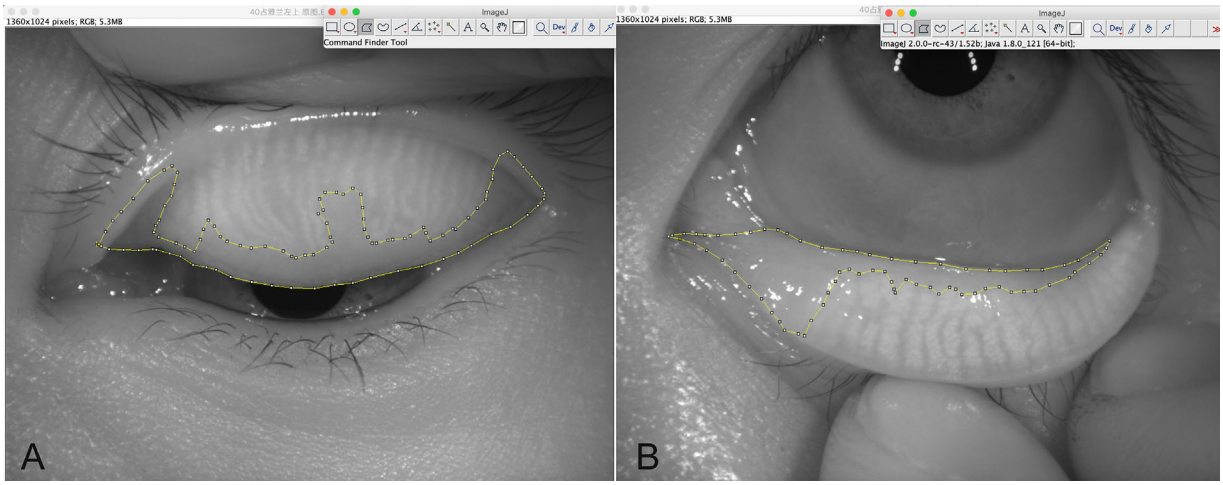

Figure. The meibomian gland atrophy ratio analyzed by ImageJ software. The "polygonselections" function of the ImageJ software was used to line out the edge of the atrophy area of the upper eyelid (A) and lower eyelid (B). The area of the whole tarsus was measured by the same method. The meibomian gland atrophy ratio was defined as the ratio of meibomian gland atrophy area compared to the total area of the tarsus.

the total area) was calculated using the polygon selection tool of ImageJ processing software (Fig.). The results are reported as the average MGAR of the upper eyelid and the lower eyelid.

Information about age (classified by a 10-year interval), sex, history of hypertension and diabetes, triglyceride, total cholesterol, HDL, low-density lipoprotein (LDL), weight, and height were also documented. Body mass index (BMI) was calculated by the formula: weight (kg)/height $(m)^2$. Patients were classified into three categories defined by the World Health Organization: <18.5 kg/ m^2, 18.5 to 25 kg/ m^2, and ≥ 25 kg/ m^2. Patients were defined as having dyslipidemia if meeting any one of the following four conditions: total cholesterol was above 200 mg/dL, triglycerides were higher than 150 mg/dL, HDL was lower than 40 mg/dL, or LDL was higher than 100 mg/dL.

Statistical Analysis

The mean $\pm$ standard deviation was used for statistical description of each parameter. The Pearson or Spearman correlation analysis was used to analyze the correlation between meiboscore, MGAR, and tear film parameters including NIBUT-avg, TMH and LLT. A two-step, multi-dimensional approach was used to distinguish the risk factors for MG atrophy. To screen the potential risk factors, β coefficient and 95% confidence intervals (CI) were evaluated using univariate analysis. The β coefficient was the regression coefficient that was the constant that represented the rate of change of one variable as a function of changes in the other. Using univariate analysis, age, sex, diabetes, triglycerides, and dyslipidemia were identified as potential influential factors for MG atrophy. Because advanced age and diabetes are universally acknowledged risk factors for MG atrophy and have been studied in our previous study,[27] we further analyzed dyslipidemia, HDL, LDL, triglyceride, and total cholesterol with adjusted multivariate models. The following models were used: Model I: adjusted for age and BMI; and Model II: adjusted for age, BMI, hypertension, and diabetes. Ultimately, only age, sex, diabetes, and dyslipidemia were identified as influential factors. Several previous studies suggested that sex is a risk factor for dyslipidemia, especially in postmenopausal women. Thus we finally stratified the model by sex. Because a majority of the patients were enrolled with both eyes, a generalized estimating equation was used for both univariate and multivariate analysis. All statistical tests were two-tailed at the 95% confidence level and were accomplished with R 3.4.3 (http://www.R-project.org). Values were considered statistically significant with P values less than 0.05.

Results

Subjects

In total, 1420 eyes (from 789 patients) were enrolled, including 333 male (42%) and 456 female (58%) subjects with a mean age of 72.90 $\pm$ 11.10 years (range 41–96 years) and 71.94 $\pm$ 9.61 years (range 41–92 years), respectively. Forty-eight eyes were excluded from meibomian gland atrophy measurement and

Table 1. Tear Film Function and Meibomian Gland Morphologic Evaluation between Different Subgroups

	MGAR	Meiboscore	NIBUT-Avg	TMH	LLT
Age, yrs					
40–50	28.98% ± 11.41%	2.81 ± 0.91	8.15 ± 4.43	0.19 ± 0.07	57.44 ± 20.41
50–60	31.53% ± 9.70%	2.88 ± 0.80	8.14 ± 4.75	0.19 ± 0.08	65.48 ± 20.62
60–70	31.60% ± 9.79%	2.83 ± 0.78	7.04 ± 4.74	0.21 ± 0.10	70.41 ± 20.84
70–80	32.73% ± 10.81%	2.96 ± 0.83	7.66 ± 5.46	0.21 ± 0.10	78.42 ± 20.08
80–90	33.52% ± 10.03%	2.96 ± 0.80	7.14 ± 5.56	0.23 ± 0.11	83.00 ± 19.81
≥90	34.11% ± 10.13%	2.95 ± 0.86	4.73 ± 3.95	0.21 ± 0.09	84.71 ± 20.73
Sex					
Man	33.69% ± 11.12%	2.99 ± 0.85	7.46 ± 5.25	0.22 ± 0.10	76.00 ± 21.70
Woman	31.86% ± 10.00%	2.88 ± 0.80	7.42 ± 5.20	0.21 ± 0.10	75.59 ± 21.04
BMI					
<18.5	33.54% ± 10.89%	2.98 ± 0.88	7.81 ± 5.79	0.21 ± 0.11	73.84 ± 23.52
18.5–24.9	32.28% ± 10.19%	2.92 ± 0.80	7.74 ± 5.29	0.21 ± 0.09	74.68 ± 21.29
≥25	33.41% ± 10.09%	2.97 ± 0.83	6.67 ± 4.80	0.22 ± 0.11	78.67 ± 19.51
Hypertension					
No	32.25% ± 10.18%	2.90 ± 0.80	7.62 ± 5.18	0.20 ± 0.09	71.92 ± 20.93
Yes	32.46% ± 10.49%	2.93 ± 0.83	7.26 ± 5.24	0.22 ± 0.10	79.24 ± 20.88
Diabetes					
No	32.06% ± 10.46%	2.89 ± 0.82	7.53 ± 5.30	0.21 ± 0.10	74.86 ± 21.14
Yes	33.77% ± 9.55%	3.01 ± 0.80	6.96 ± 4.77	0.23 ± 0.11	79.91 ± 21.13
Dyslipidemia					
No	32.99% ± 9.90%	2.97 ± 0.82	7.52 ± 5.36	0.21 ± 0.10	75.44 ± 21.51
Yes	31.76% ± 10.51%	2.86 ± 0.81	7.41 ± 5.11	0.22 ± 0.10	76.19 ± 20.73

further analysis due to poor meibomian gland picture quality of either the upper or lower eyelid. There were 415 (52.60%) patients with a history of hypertension and 119 (15.08%) patients with diabetes. There were 418 (54.15%) patients diagnosed with dyslipidemia.

In our study, the average MGAR of the upper eyelid was 31% ± 13%, and the lower eyelid was 34% ± 14%. In regard to the mean value of both eyelids, 98.76% of patients had a MG atrophy of more than 10%. A majority of patients had atrophy between 10% to 60%. Only 17 eyes (1.23%) presented with atrophy lower than 10%. A total of 609 eyes (44.39%) presented with atrophy between 10% to 30%, and 734 eyes (53.50%) had atrophy between 30% to–60%. Only 12 eyes (0.87%) had atrophy greater than 60%.

Association of Age, Sex, and Body Mass Index on MG Morphologic Evaluation

We categorized patients into different subgroups by age, sex, and BMI and found the association of these potential risk factors. This information is found in Table 1. The mean MGAR increased with age (40–50 years: 28.98% ± 11.41%; 50–60 years: 31.53% ± 9.70%; 60–70 years: 31.60% ± 9.79%; 70–80 years: 32.73% ± 10.81%; 80–90 years: 33.52% ± 10.03%; ≥90 years: 34.11% ± 10.13%). According to the univariate regression analysis by using a generalized estimating equation, the MGAR (β, 0.143, 95% CI [0.072, 0.215], $P < 0.001$) and meiboscore (β, 0.007, 95% CI [0.002, 0.013], $P = 0.006$) both showed a significantly age-related trend.

We also studied the association of sex. Results showed that female patients had significantly decreased meibomian gland atrophy compared to male patients (MGAR (β, −1.721, 95% CI [−3.239, −0.202], $P = 0.026$). The meiboscore was also significantly different (β, −0.111, 95% CI [−0.221, −0.002], $P = 0.046$). The results about the association of BMI showed that BMI was not a risk factor for MGAR or meiboscore ($P > 0.05$).

Association of Diabetes on MG Atrophy

In diabetic patients, the MGAR was 33.77% ± 9.55%, and in nondiabetic patients it was

Table 2. Univariate Logistic Regression of Systemic Factors Associated with Meibomian Gland Atrophy

	Meiboscore		MGAR	
Exposure	β Coefficient (95%CI)	*P*	β Coefficient (95%CI)	*P*
Age	0.007 (0.002, 0.013)	0.006	0.143 (0.072, 0.215)	<0.001
Sex				
Man	Reference	Reference	Reference	Reference
Woman	−0.111 (−0.221, −0.002)	0.046	−1.721 (−3.239, −0.202)	0.026
Hypertension				
No	Reference	Reference	Reference	Reference
Yes	0.029 (−0.078, 0.136)	0.600	0.333 (−1.159, 1.825)	0.662
Diabetes				
No	Reference	Reference	Reference	Reference
Yes	0.132 (−0.010, 0.275)	0.069	2.140 (0.075, 4.204)	0.042
BMI				
<18.5	Reference	Reference	Reference	Reference
18.5–24.9	−0.037 (−0.240, 0.166)	0.721	−1.110 (−3.963, 1.743)	0.446
≥25	−0.037 (−0.264, 0.189)	0.747	−1.075 (−4.176, 2.027)	0.497
Triglyceride	−0.066 (−0.121, −0.010)	0.020	−0.866 (−1.690, −0.041)	0.040
Total cholesterol	−0.017 (−0.071, 0.037)	0.546	−0.134 (−0.879, 0.610)	0.724
HDL	0.012 (−0.113, 0.137)	0.851	0.237 (−1.445, 1.918)	0.783
LDL	−0.017 (−0.077, 0.042)	0.569	−0.134 (−0.955, 0.688)	0.750
Dyslipidemia				
No	Reference	Reference	Reference	Reference
Yes	−0.157 (−0.264, −0.049)	0.004	−2.518 (−4.009, −1.028)	<0.001

*The table showed β coefficient (95%CI) and *P* value.

†Generalized estimate equation were used. In the analysis, the following variables were set as controls: man, no hypertension, no diabetes, BMI < 18.5, no dyslipidemia, therefore their values were "0."

32.06% ± 10.46%. Univariate regression analysis showed that diabetic patients had increased MGAR compared to non-diabetic patients (β, 2.140, 95% CI [0.075, 4.204], $P = 0.042$). Although the meiboscore was not significantly different (β, 0.132, 95% CI [−0.010, 0.275], $P = 0.069$) (Table 2).

Association of Dyslipidemia on MG Atrophy

Univariate analysis indicated that dyslipidemia is a potential influential factor for MG atrophy (Table 2). The MGAR was 31.76% ± 10.51% in patients with dyslipidemia, and it was 32.99% ± 9.90% in patients without dyslipidemia.

Patients with dyslipidemia had significantly decreased meibomian gland atrophy (MGAR (β, −2.518, 95% CI [−4.009, −1.028], $P < 0.001$). The difference in meiboscore was also significantly different (β, −0.157, 95% CI [−0.264, −0.049], $P = 0.004$). Then we analyzed the association of the four parameters of serum lipids, including triglyceride, total cholesterol, HDL, and LDL. Results showed that increased meibomian gland atrophy and meiboscore were both associated with decreased triglyceride levels (MGAR: β, −0.866, 95% CI [−1.690, −0.041], $P = 0.040$; meiboscore: β, −0.066, 95% CI [−0.121, −0.010], $P = 0.020$) (Table 2).

Multivariate regression analysis further studied the association of dyslipidemia and four parameters of serum lipids. When Model I adjusted for age and BMI, the results indicated that dyslipidemia and increased triglyceride are independent protective factors for meibomian gland atrophy. This is true not only for meiboscore (dyslipidemia: β, −0.139, 95% CI [−0.247, −0.031], $P = 0.012$; triglyceride: β, −0.065, 95% CI [−0.119, −0.011], $P = 0.018$), but also for MGAR (dyslipidemia: β, −0.022, 95% CI [−0.037, −0.007], $P = 0.003$; triglyceride: β, −0.799, 95% CI [−1.597, −0.002], $P = 0.050$).

When Model II was adjusted for age, BMI, hypertension, and fasting plasma glucose, these results were further confirmed (MGAR [dyslipidemia: β, −0.021,

95% CI {−0.036, −0.006}, $P = 0.006$; triglyceride: β, −0.766, 95% CI {−1.570, 0.037}, $P = 0.062$]; meiboscore [dyslipidemia: β, −0.133, 95% CI {−0.241, −0.025}, $P = 0.016$; triglyceride: β, −0.065, 95% CI {−0.119, −0.011}, $P = 0.019$]) (Table 3).

Several previous studies suggested that sex is a risk factor for dyslipidemia, especially in postmenopausal women. Thus we stratified these models by sex. Dyslipidemia and triglyceride were not influential factors for meibomian gland atrophy in male patients in the adjusted models I and II. The results are in Table 4. However, in female patients these results indicated a significant association in both models. Adjusted model I: MGAR (dyslipidemia: β, −0.024, 95% CI [−0.043, −0.004], $P = 0.017$; triglyceride: β, −0.911, 95% CI [−1.848, 0.026], $P = 0.057$); meiboscore (dyslipidemia: β, −0.160, 95% CI [−0.299, −0.021], $P = 0.024$; triglyceride: β, −0.072, 95% CI [−0.139, −0.005], $P = 0.034$). Adjusted model II: MGAR (dyslipidemia: β, −0.024, 95% CI [−0.044, −0.004], $P = 0.017$; triglyceride: β, −0.956, 95% CI [−1.926, 0.014], $P = 0.053$); meiboscore (dyslipidemia: β, −0.163, 95% CI [−0.304, −0.022], $P = 0.023$; triglyceride: β, −0.077, 95% CI [−0.145, −0.008], $P = 0.029$). These results suggest that in the female cataract population, dyslipidemia and increased triglycerides are independent protective factors for MG atrophy.

Correlation Between Meibomian Gland Atrophy and Tear Film Parameters

No significant correlation was found between meiboscore and tear film parameters including NIBUT-avg, TMH, and LLT ($P > 0.05$). There was also no significant correlation between MGAR and the same tear film parameters ($P > 0.05$).

Discussion

The aim of our study was to determine the characteristics of meibomian gland morphology in the age-related cataract population. Although a lot of research has been involved in this area, the present study has some new findings.

These results showed that 97.89% of patients had atrophy between 10% to 60%. Compared with previous studies, meibomian gland atrophy was more severe in this study. A study conducted by Cochener et al.[11] (342 eyes of 180 cataract patients; 56% female; mean age of 69.0 ± 10.68 years) reported that 44% patients had grade 0 atrophy, 30% patients had grade 1 atrophy, 19% patients had grade 2 atrophy, and 7% patients had grade 3 atrophy. The reason for the divergence between these two studies may be age, sex, and the constitution of the patients. The environment and eating or living habits between different regions may also influence the results. The average age in our study was slightly older. And this study included more female patients. Additionally, several studies have reported that air pollution reduces tear film stability,[28–31] which may contribute to the development of MG atrophy. Patients in our study were from Hangzhou, a city with severe air pollution in eastern China.

Our results indicate that age is associated with the atrophy of the MGs, which is in agreement with previous studies.[5,32] Many studies have suggested that the atrophy rate of the acini and the amount of meibomian lipids on the lid margin changes with age.[5,21] Our study also observed that the NIBUT-avg decreased with age. While the LLT and TMH increased with age. This is consistent with some previous studies. They found that tear production was increased in MGD patients.[33,34] The increased tear production may be a compensatory response to meibomian gland atrophy that has been demonstrated in previous experimental and clinical studies.[35] However, some studies found that tear production decreased with age in normal population and dry eye patients as the lacrimal gland function declined with age.[36–38] The reason for the contrary results may be that the patients in our study were most MG atrophy patients.

Our study also found that meibomian gland atrophy was more severe in older male patients compared with female patients. Studies by Arita et al.[5] and Den et al.[39] found similar findings in the elderly population. Males older than 60 years[5] or 70 years[39] tended to have more severe changes in meibomian gland morphology compared to females. Another study reported that sex hormones promoted keratinization, which was associated with MGD.[38] Androgens is considered to act as a protective factor on meibomian gland function.[40] In mouse studies, androgens promoted lipogenesis and downregulated genes related to keratinization.[41,42] However, estrogens play a negative effect on MG function.[40,43] For postmenopausal women, estrogens decrease rapidly, and they are under a more androgenic pattern of sex hormones.[44,45] Although men also have age-related hormonal changes, the sex hormonal changes are gradual compared with menopause.[46] Thus MGD would be more severe in older men. However, patient surveys indicate that the prevalence of dry eye is higher in elderly women.[47] This discrepancy may be due to the inclusion of both MGD and aqueous deficiency dry eye patients in these studies. Estrogens are considered to be a risk factor for dry eye.[48]

Table 3. Multivariate Analysis of the Associations Between Blood Lipid and Meibomian Gland Atrophy With Adjusted Models

	Meiboscore				MGAR			
	Model I		Model II		Model I		Model II	
Exposure	β (95%CI)	*P*	β (95%CI)	*P*	β (95%CI)	*P*	β (95%CI)	*P*
Triglyceride	−0.065 (−0.119, −0.011)	0.018	−0.065 (−0.119, −0.011)	0.019	−0.799 (−1.597, −0.002)	0.050	−0.766 (−1.570, 0.037)	0.062
Total cholesterol	0.007 (−0.048, 0.062)	0.799	0.006 (−0.049, 0.061)	0.823	0.271 (−0.474, 1.017)	0.476	0.244 (−0.501, 0.990)	0.521
HDL	0.038 (−0.090, 0.166)	0.558	0.035 (−0.093, 0.164)	0.589	0.530 (−1.195, 2.254)	0.547	0.422 (−1.321, 2.165)	0.635
LDL	0.001 (−0.059, 0.062)	0.964	0.001 (−0.059, 0.062)	0.970	0.192 (−0.627, 1.012)	0.645	0.177 (−0.646, 1.000)	0.673
Dyslipidemia								
No	Reference		Reference		Reference		Reference	
Yes	−0.139 (−0.247, −0.031)	0.012	−0.133 (−0.241, −0.025)	0.016	−0.022 (−0.037, −0.007)	0.003	−0.021 (−0.036, −0.006)	0.006

*The table showed β (95%CI) and P value. β, regression coefficient.
†Model I adjusted for age, BMI. And Model II adjusted for age, BMI, hypertension, and fasting plasma glucose.
‡Reference, control value. In the analysis, no dyslipidemia was set as a control and therefore its values was "0."

Table 4. Multivariate Analysis of the Associations Between Blood Lipid and Meibomian Gland Atrophy in Different Sexes

	Men		Women	
	β (95%CI)	*P*	β (95%CI)	*P*
Meiboscore				
Model I				
Triglyceride	−0.052 (−0.137, 0.032)	0.223	−0.072 (−0.139, −0.005)	0.034
Total cholesterol	−0.044 (−0.132, 0.044)	0.327	0.051 (−0.019, 0.121)	0.152
HDL	−0.036 (−0.206, 0.133)	0.674	0.106 (−0.074, 0.286)	0.249
LDL	−0.073 (−0.164, 0.017)	0.112	0.059 (−0.019, 0.138)	0.138
Dyslipidemia				
No	Reference	Reference	Reference	Reference
Yes	−0.095 (−0.266, 0.077)	0.279	−0.160 (−0.299, −0.021)	0.024
Model II				
Triglyceride	−0.053 (−0.137, 0.031)	0.214	−0.077 (−0.145, −0.008)	0.029
Total cholesterol	−0.050 (−0.137, 0.038)	0.263	0.050 (−0.021, 0.120)	0.168
HDL	−0.042 (−0.214, 0.130)	0.632	0.115 (−0.066, 0.297)	0.214
LDL	−0.076 (−0.166, 0.014)	0.100	0.058 (−0.021, 0.137)	0.148
Dyslipidemia				
No	Reference	Reference	Reference	Reference
Yes	−0.104 (−0.276, 0.068)	0.237	−0.163 (−0.304, −0.022)	0.023
MGAR				
Model I				
Triglyceride	−0.602 (−1.900, 0.696)	0.363	−0.911 (−1.848, 0.026)	0.057
Total cholesterol	−0.321 (−1.517, 0.874)	0.598	0.774 (−0.192, 1.741)	0.116
HDL	0.160 (−2.075, 2.395)	0.888	0.899 (−1.661, 3.458)	0.491
LDL	−0.809 (−2.063, 0.445)	0.206	0.947 (−0.124, 2.018)	0.083
Dyslipidemia				
No	Reference	Reference	Reference	Reference
Yes	−0.018 (−0.041, 0.006)	0.145	−0.024 (−0.043, −0.004)	0.017
Model II				
Triglyceride	−0.580 (−1.852, 0.692)	0.371	−0.956 (−1.926, 0.014)	0.053
Total cholesterol	−0.467 (−1.640, 0.706)	0.435	0.737 (−0.250, 1.724)	0.143
HDL	−0.049 (−2.354, 2.256)	0.967	1.036 (−1.540, 3.611)	0.431
LDL	−0.864 (−2.101, 0.373)	0.171	0.901 (−0.186, 1.988)	0.104
Dyslipidemia				
No	Reference	Reference	Reference	Reference
Yes	−0.019 (−0.042, 0.005)	0.122	−0.024 (−0.044, −0.004)	0.017

*The table showed β (95%CI) and *P* value. β, regression coefficient.
†Model I adjusted for age, BMI. And Model II adjusted for age, BMI, hypertension, and fasting plasma glucose.
‡Reference, control value. In the analysis, no dyslipidemia was set as a control and therefore its values was "0."

Additionally, the different constitution of age and sex may also influence the results.

Our findings suggest that dyslipidemia is an independent protective factor for meibomian gland atrophy in the elderly female population. The meibomian lipids are synthesized by acinar cells, taken up from the bloodstream, or both.[49] Therefore the components of the lipids in circulation may influence the quality and quantity of meibomian secretions. The pathophysiological and molecular mechanisms between MGD and dyslipidemia have not been fully understood. The study by Bu et al.[50] found that ApoE knockout mice that were a hypercholesterolemia animal model showed meibomian gland obstruction with meibomian gland atrophy. The ApoE knockout mice also showed increased inflammatory

cell infiltration, abnormal meibomian gland acinar cell proliferation, and excessive keratinization in the meibomian gland.[50] However, there is no molecular biology study to research the pathophysiological and molecular mechanisms in older patients. In this study, our subjects had an average age of 72.46 ± 10.30 years, which is the age in which the MG tends to atrophy. However, patients with dyslipidemia may synthesize and secrete more meibomian lipids, which may delay atrophy to some degree. On the other hand, in the elderly female population estrogen sharply decreases after menopause, which is an important factor in blood fat metabolism.[51,52] Thus dyslipidemia may be a potential protective factor in development of MG atrophy.

Moreover, our study finds that increased triglyceride is a protective factor for MG atrophy. However, the HDL, LDL, and total cholesterol have no significant association for MG atrophy. Although the retrospective case-controlled study by Dao et al.[25] suggests that low HDL may be a protective factor for the development of MGD. An animal experiment finds that knockout of Acyl-CoA:cholesterol acyltransferase, an enzyme for cholesterol esterification, has been shown to lead to atrophic acinar cells in the meibomian glands. In tissues of atrophic meibomian glands, cholesteryl esters are reduced, and free cholesterol is increased.[53] In another study the use of a special diet with limited lipid content induced MGD.[54] However, it has also been suggested that higher blood levels of increased total cholesterol and LDL are significantly associated with MGD.[24,25] Our findings need to be confirmed in future studies, in both fundamental and prospective studies, to understand the mechanisms. To the best of our knowledge, this is the first report concerning the protective effect of hyperlipidemia in the elderly female population.

Our study also observed that the meibomian gland atrophy rate was more severe in diabetic patients, whereas the difference was not significant for meiboscore. A reduction in corneal nerve density, and the abnormal morphology of the corneal nerve in diabetic patients leads to a decreased blink rate and influences meibomian gland function.[55] Furthermore, the increased inflammation associated with diabetes leads to meibomitis and MGD.[56] Several previous studies also reported that diabetes-related dry eye was associated with the duration of diabetes, poor metabolic glucose control, and the severity of proliferative diabetic retinopathy (PDR).[57] The diabetic patients enrolled in our study controlled metabolic glucose well, and none of them showed PDR which may make the difference of MG atrophy not obvious between diabetic patients and nondiabetic patients.

No significant correlation was observed between meibomian gland atrophy and tear film parameters in this study. The study of Giannaccare et al.[58] also found no significant correlation between meibomian gland atrophy and NIBUT, LLT. Although the study of Pult et al.[19] found a significant correlation between meibomian gland atrophy and tear film parameters including LLT and NIBUT. The reason may be that the population enrolled in this study were elder patients without obvious dry-eye–related symptoms. The relatively stable tear film may be a compensatory response in this population.

There are some limitations in our study. First, we only included patients from one clinic, which may have selection bias due to the homogeneity of race, region, culture, and lifestyle. Second, this study is a cross-sectional study that may have a potential selection bias because of the nonrandomization of the patients.

In conclusion, our study suggests that in this cataract population dyslipidemia and increased triglycerides are independent protective factors in the elderly female population, whereas age and sex are potential risk factors for meibomian gland atrophy. Future studies will provide a better understanding of the lipid changes and metabolic processes that occur in MGD patients with dyslipidemia.

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