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Meibomian gland loss area and its relationship with age and ocular surface disease index

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ABSTRACT

Purpose: Meibography images bring information about the status and integrity of the meibomian glands (MG). The aim of this study was to correlate the meibomian gland loss area (MGLA) with age and dry eye symptomatology. **Material and methods:** A total of 110 subjects were recruited for the study. From the Meibography images obtained with the Topcon® CA-800 topographer, MGLA was calculated as the difference between the total area of the tarsus and the MG presence area measured by using the ImageJ software. Before examination, all subjects completed an OSDI questionnaire. OSDI scores were grouped in 4 severity categories: normal (score ≤12), mild (score 12–22), moderate (score 22–32) and severe (score ≥32). Age were categorised in 3 subgroups: ≤25 years, from 25 to 45 years and ≥45 years. MGLA was also grouped in 4 categories of loss: ≤25 %, from 25 to 50%, from 50 to 75% and ≥75%. **Results:** Analysis was performed by dividing the sample in the 4 MGLA subgroups; these subgroups showed differences in age ($p=0.029$; Kruskal-Wallis test) and differences in OSDI scores ($p=0.001$; Kruskal-Wallis test). Sample was divided in 3 age subgroups and differences were obtained in MGLA values among subgroups ($p<0.001$; Kruskal-Wallis test). Samples was divided in 4 OSDI subgroups and differences were obtained in MGLA values among subgroups ($p=0.003$; Kruskal-Wallis test). Positive correlation (Spearman Correlation) were obtained for both, MGLA vs. age ($r=0.329$, $p<0.001$) and MGLA vs. OSDI ($r=0.380$, $p<0.001$). **Conclusion:** In the present study MGLA showed a relationship with age and OSDI.

Keywords: Meibomian Glands, Topcon CA-800 topographer, meibomian gland loss are, MGD, Dry eye symptomatology, ImageJ

1. INTRODUCTION

Meibomian Gland Dysfunction (MGD) is the first cause of evaporative dry eye, which is the most prevalent Dry Eye Disease (DED) type [1]. DED is defined by the Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop II (DEWS II) as "a multifactorial disease of the ocular surface characterised by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles". TFOS defined MGD as chronic and diffuse abnormality characterised by the quantitative or qualitative changes in the glandular secretion [2, 3].

The Meibography technique provides in-vivo images of the Meibomian Glands (MG) status and integrity [4-6]. These images are processed for calculating the percentage of MG loss. The Ocular Surface Disease Index (OSDI) questionnaire is a specific test for the DED diagnosis which was implemented to evaluate the patient's symptoms [2]. The aim of this study was to correlate the meibomian gland loss area (MGLA) with age and DED symptomatology.

2. MATERIAL AND METHODS

2.1 Participants

A total of 110 participants (80 woman and 30 men) of mean age 36 ± 16.41 (from 19 to 70 years old) were recruited from the Optometry Clinic in the Optics and Optometry Faculty of the Universidade de Santiago de Compostela, Spain. If subjects have a history of corneal, conjunctival or scleral disease, prior eye surgery, DMAE, glaucoma, diabetes mellitus or thyroid disorders, were excluded. Participants were not under any type of treatment or use artificial tears at the time of the sessions. This study is concerned into the tents of the Declaration of Helsinki and is approved by the Ethics Committee of the Universidade de Santiago de Compostela. Measurements were performed in the same laboratory

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with the same humidity and temperature conditions (temperature 20 – 23ºC, humidity 50-60%). All participants gave their written informed consent to be included in the study. Selected participants were scheduled for meibography images capture and OSDI questionnaire performance [2, 7], both accomplished in the same session.

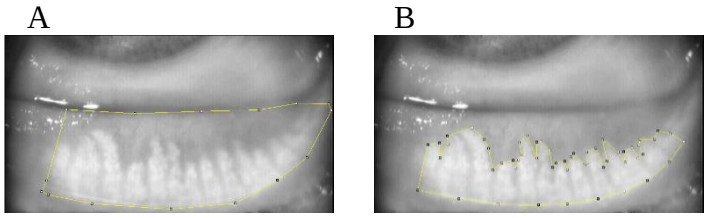
2.2 Ocular Surface Disease Index (OSDI)

Before eye examination, OSDI questionnaire was performed in all patients according to the manufacturer instructions. The OSDI was a simple test to classify dry eye patients according to their symptomatology [1]. It is compound by twelve questions, with five frequency categories each, about eye discomfort experimented in the last week. OSDI was classified in 4 categories, as well as done in other studies, based on patients symptomatology score: 0 – 12 (Normal), 13 – 22 (Mild), 23 – 32 (Moderate) and 33 – 10 (Severe) [1-4].

2.3 Meibography Images evaluation

Meibography images were captured by the Topcon® CA-800 topographer (TOPCON Corporation, Tokyo, Japan). It was provided with an infra-red (IR) camera which allows to observe the MG in-vivo [5, 6, 12]. To capture the MG images, patients were requested to place on the chinrest of the instrument, instructed to look up and the lower eyelid was everted; in this position, several images were taken.

MG images were evaluated with the open source software ImageJ (Wayne Rasband, Research Services Branch, National Institute of Mental Health, Bethesda, Maryland, USA) in order to calculate the MGLA [13]. First, the images were extracted from the CA-800 topographer and placed into a Windows 10 computer. Then, ImageJ software was used to enhance contrast and to measure the following areas; contrast was enhanced by clicking on *Plugins* > *Filters* > *Enhance local contrast* and using the default parameters (Figure 1).



$$\frac{Total\ tarsus\ Area - MG\ Area}{Total\ tarsus\ Area} \cdot 100 = MGLA$$

Figure 1. Enhance MG images contrast procedure with ImageJ software. A: Native CA-800 MG image (Pre-process), B: ImageJ post-process MG image.

Total tarsus area and MG Area were measured in order to calculate the MGLA, which was the difference between them expressed on a percentage (Figure 2). MGLA were calculated and data were categorized in four subgroups (MGLA-4) depending on the severity of the loss. These groups were: Grade 1 (< 25% of MGLA), Grade 2 (25 – 50% of MGLA), Grade 3 (50 – 75% of MLGA) and Grade 4 (< 75% of MGLA).

2.4 Statistical Analysis

Data analysis was performed with the IBM SPSS Statistics v.23 software (SPSS Inc., Chicago, IL) and significance was set at $p \leq 0.05$ for all tests. Kolmogorov-Smirnov test was performed to check if the data followed parametric or non-parametric distribution [14]. Age and OSDI follow normal distribution while MGLA did not. Therefore a non-parametric test Kruskal-Wallis was used for analyse the differences between subgroups. Non-parametric correlations were also calculated between variables by a Spearman correlation test.

3. RESULTS

Descriptive statistics of the present study were showed in Table 1. As data followed a non-parametric distribution, non-parametric descriptive statistics (median and inter-quartile range (IQR)) were displayed in Table 1; also maximum and minimum were included.

Table 1. Descriptive statistics. n = 110 subjects. SD: Standard Deviation, IQR: Inter-quartile Range. MGLA: Meibomian Gland Loss Area. OSDI: Ocular Surface Disease Index.

	Mean	SD	Median	IQR	Minimum	Maximum
Age [y]	35.51	16.41	25.50	21.00 – 51.25	19.00	70.00
MGLA [%]	37.63	18.24	35.00	21.80 – 50.38	2.51	84.49
OSDI	22.12	15.94	20.64	8.33 – 31.39	0.00	72.50

For the analysis, MGLA were categorized in 4 subgroups according to the percentage of loss. Differences in age ($p = 0.029$, Kruskal-Wallis test; Table 2) and OSDI scores ($p < 0.001$, Kruskal-Wallis test; Table 2) between MGLA subgroups were obtained.

Table 2. Differences in Age and Ocular Surface Disease Index scores between Meibomian Gland Loss Area subgroups. n = 110 subjects. SD: Standard Deviation, MGLA: Meibomian Gland Loss Area, OSDI: Ocular Surface Disease Index.

MGLA [%]	Subgroup by MGLA-4	n	Median	Mean ± SD	p
Age [y]	Grade 1	35	21.00	29.26 ± 13.15	0.029
	Grade 2	48	33.50	38.17 ± 17.71	
	Grade 3	22	34.00	38.23 ± 15.86	
	Grade 4	5	51.00	41.80 ± 18.58	
OSDI	Grade 1	35	12.50	14.92 ± 11.59	< 0.001
	Grade 2	48	25.00	22.05 ± 12.33	
	Grade 3	22	22.92	28.54 ± 21.51	
	Grade 4	5	54.55	44.77 ± 15.66	

The sample was divided into 3 age subgroups (< 25 years old, 25 – 45 years old and ≥ 45 years old) and differences in MGLA values according to age subgroups were obtained ($p < 0.001$, Kruskal-Wallis test; Table 3). The sample also was divided into 4 OSDI subgroups and differences in MGLA values according to OSDI subgroups were obtained ($p = 0.003$, Kruskal-Wallis test; Table 4).

Table 3. Differences in Meibomian Gland Loss Area values between Age subgroups. n = 110 subjects. SD: Standard Deviation, MGLA: Meibomian Gland Loss Area.

	Subgroup by Age-3	n	Median	Mean ± SD	p
MGLA [%]	Age < 25 years	50	28.37	31.39 ± 17.59	< 0.001
	Age 25 years, 45 years	21	34.38	36.51 ± 18.24	
	Age ≥ 45 years	39	45.50	46.24 ± 15.92	

Table 4. Differences in Meibomian Gland Loss Area values between the Ocular Surface Disease Index subgroups. n = 110 subjects. SD: Standard Deviation, MGLA: Meibomian Gland Loss Area, OSDI: Ocular Surface Disease Index.

	Subgroup by OSDI-4	n	Median	Mean ± SD	p
MGLA [%]	Normal	41	25.13	30.81 ± 16.31	0.003
	Mild	22	33.14	35.39 ± 18.42	
	Moderate	22	40.47	40.29 ± 12.26	
	Severe	25	49.56	48.44 ± 20.70	

Correlations between MGLA values, Age and OSDI scores were calculated. Positive but weak correlation between MGLA values and Age was obtained (Spearman Correlation: $r = 0.329$ and $p < 0.001$; Figure 3A), also positive but weak correlation between MGLA values and OSDI scores was obtained (Spearman Correlation: $r = 0.390$ and $p < 0.001$; Figure 3B).

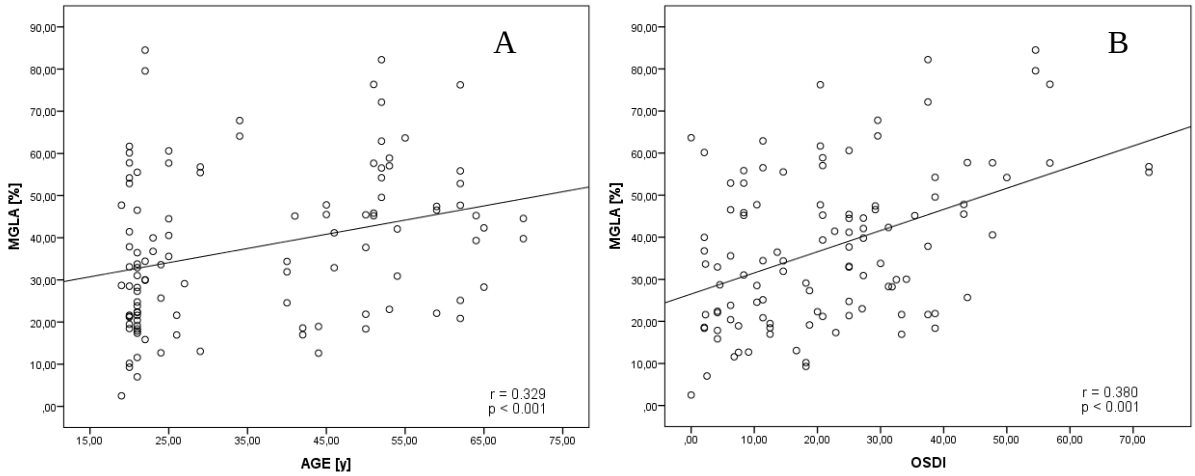


Figure 2. Spearman correlations between A) MGLA and Age, B) MGLA and OSDI. MGLA: Meibomian Gland Loss Area, OSDI: Ocular Surface Disease Index.

4. CONCLUSION

In the present study, it was found a difference in the MGLA value depending on the patient's age and symptomatology. When the sample was split by age, it was found that the older people shower higher meibomian gland loss (Table 3); in addition, when the sample was categorised by MG loss, the age value of the group with pathological levels was higher of those in the healthy or normal one (Table 2). Previous studies have been hypothesised that MG loss could be caused by factors like age, gender and hormones [15]. Studies showed a direct relationship between age and MG loss, which occur when MG were obstructed, atrophied and finally destructed [16]; this hypothesis is in concordance with present results.

Similar results were found regarding DED symptomatology; on the sample split by OSDI, severe symptomatic patients showed a higher level of meibomian gland loss (Table 4), whereas, when the sample was categorised by MGLA, OSDI score in the group with pathological levels of gland loss was higher of those in the considered normal patients (Table 3). The dry eye disease is characterised by inflation and damage of the ocular surface and adnexa that lead to symptomatology and impact in the quality of life [2]; MG have an important role in the homeostasis of the lacrimal functional unit, therefore, a damage in this piece of the system may enhance DED symptomatology [13].

In addition to the subgroup difference analysis, both symptomatology and age showed a correlation with MGLA: higher or lower MGLA values were directly related to an increase or decrease in the patient age and symptomatology (Figure 3). In conclusion, the present study showed that there is a close relationship between MG loss, age and symptomatology.

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REFERENCES

[1] J. P. Craig, K. K. Nichols, E. K. Akpek *et al.*, "TFOS DEWS II Definition and Classification Report," Ocul Surf, 15(3), 276-283 (2017).

[2] J. S. Wolffsohn, R. Arita, R. Chalmers *et al.*, "TFOS DEWS II Diagnostic Methodology report," Ocul Surf, 15(3), 539-574 (2017).

[3] J. D. Nelson, J. Shimazaki, J. M. Benitez-del-Castillo *et al.*, "The international workshop on meibomian gland dysfunction: report of the definition and classification subcommittee," Invest Ophthalmol Vis Sci, 52(4), 1930-7 (2011).
[4] H. Pult, and J. J. Nichols, "A review of meibography," Optom Vis Sci, 89(5), E760-9 (2012).
[5] R. Arita, K. Itoh, K. Inoue *et al.*, "Noncontact infrared meibography to document age-related changes of the meibomian glands in a normal population," Ophthalmology, 115(5), 911-5 (2008).
[6] H. Pult, and B. H. Riede-Pult, "Non-contact meibography: keep it simple but effective," Cont Lens Anterior Eye, 35(2), 77-80 (2012).
[7] L. Jones, L. E. Downie, D. Korb *et al.*, "TFOS DEWS II Management and Therapy Report," Ocul Surf, 15(3), 575-628 (2017).
[8] R. M. Schiffman, M. D. Christianson, G. Jacobsen *et al.*, "Reliability and validity of the Ocular Surface Disease Index," Arch Ophthalmol, 118(5), 615-21 (2000).
[9] M. H. Ring, D. F. Rabensteiner, J. Horwath-Winter *et al.*, "Introducing a new parameter for the assessment of the tear film lipid layer," Invest Ophthalmol Vis Sci, 53(10), 6638-44 (2012).
[10] K. L. Miller, J. G. Walt, D. R. Mink *et al.*, "Minimal clinically important difference for the ocular surface disease index," Arch Ophthalmol, 128(1), 94-101 (2010).
[11] A. F. G. B. de, M. R. Santhiago, M. N. de Azevedo *et al.*, "Evaluation of dry eye signs and symptoms in patients with systemic sclerosis," Graefes Arch Clin Exp Ophthalmol, 250(7), 1051-6 (2012).
[12] R. Arita, K. Itoh, S. Maeda *et al.*, "Efficacy of diagnostic criteria for the differential diagnosis between obstructive meibomian gland dysfunction and aqueous deficiency dry eye," Jpn J Ophthalmol, 54(5), 387-91 (2010).
[13] H. Pult, and B. Riede-Pult, "Comparison of subjective grading and objective assessment in meibography," Cont Lens Anterior Eye, 36(1), 22-7 (2013).
[14] R. A. Armstrong, L. N. Davies, M. C. Dunne *et al.*, "Statistical guidelines for clinical studies of human vision," Ophthalmic Physiol Opt, 31(2), 123-36 (2011).
[15] E. Knop, N. Knop, T. Millar *et al.*, "The international workshop on meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland," Invest Ophthalmol Vis Sci, 52(4), 1938-78 (2011).
[16] H. Pult, "Relationships Between Meibomian Gland Loss and Age, Sex, and Dry Eye," Eye Contact Lens, 44 Suppl 2, S318-S324 (2018).