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Evaluation of the effect of eyelid disorder surgeries on tears and anterior segment parameters with meibography and corneal topography

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Ethics Committee Approval
Ethics committee approval was obtained for the study with decision number 202184 at the meeting on 09.04.2021 by the decision of the Afyonkarahisar Health Sciences University Clinical Research Ethics Committee.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Abnormalities of eyelid shape, including ptosis, entropion, ectropion, lagophthalmos, and dermatochalasis, can occur at any age and affects the patient's life quality, visual functions, and comfort. These abnormalities can be regarded as illnesses and can be cured medically and surgically. Meibomian glands are large sebaceous glands located in the lower and upper eyelids. Our study aimed to observe changes in anterior cornea segment parameters and meibomian glands of patients undergoing surgery for eyelid shape abnormalities.

Methods: Our sample comprised 31 patients, who were operated on at Afyonkarahisar Health Sciences University Hospital, were examined with respect to cornea topographic measurements and the drop-out of meibomian glands at the pre-operative and first-month post-operative processes and post-operative third month. In this prospective cohort method study, the surgical eyes of the patients were determined as the study group and the healthy eyes as the control group.

Results: Surgical and healthy eyes of 31 patients were included in this study (N=62). The sample comprised 18 male and 13 female patients. The average age and standard deviation values of patients were determined as 66.50 (17.315) in males and 65.92 (13.714) (P = 0.659) in females. In terms of anterior cornea segment parameters (K1, K2, ACA, ACD, ACV, and CCT), no prominent differences were found in pre-operative and post-operative results (K1, K2, ACA, ACD, ACV, and CCT) in both the study and control groups. Meibography revealed that the increased meibomian gland drop-out of surgical eye measurements of pre- and post-operative was statistically significant (P < 0.001), whereas the change seen in healthy eyes was not statistically significant (P = 0.051). Furthermore, although the change through meibomian glands of entropion patients was not significant (P = 0.066), the drop-out of the meibomian gland of the other surgery cases (ptosis, ectropion, lagophthalmos, blepharoplasty, and dermatochalasis surgery) was found to be statistically significant (P = 0.038).

Conclusion: Surgeries to correct abnormalities in eyelid shape can lead patients to meibomian gland drop-out. Pre-operative assessment of patients whose surgeries are planned, and post-operative monitoring, must be done meticulously in order to minimize the likelihood of symptoms and avoid meibomian gland dysfunction.

Keywords: Eyelid surgeries, Meibography, Meibomian gland dysfunction, Corneal topography

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Introduction

Eyelid deformity is a congenital condition or an acquired condition that can occur at any age. The medical and surgical treatment options for this condition can affect the person functionally and aesthetically. Eyelid deformities include ptosis, entropion, ectropion, lagophthalmos, and dermatochalasis. A normal blink reflex and complete eyelid closure are essential for a stable tear film and protection of the ocular surface. The risk of dry eyes, changes in the meibomian glands, exposure to keratopathy, corneal ulcers, and even corneal perforation increases because of insufficient protection of the cornea due to eyelid deformities and lack of stable tear film [1].

Meibomian gland dysfunction (MGD) is the most common cause of dry eye syndrome, and it causes morphological changes in meibomian glands. MGD also results in glandular stasis, ductal dilatation, and glandular drop-out. Many techniques have been introduced in recent years to demonstrate MGD, among which evaporimetry is the least invasive. According to invasiveness (i.e., most to least invasive), these methods can be listed as follows: Interferometry, Meibometry, evaluation of glandular morphology, quantitative and qualitative characteristics of secreted lipids, and Meibography. Although meibography allows the evaluation of meibomian glands *in vivo*, ducts can be evaluated in more detail with specific illumination techniques [1]. Normal meibomian glands appear grape-like, with hypoilluminated acini. The ducts and orifices transmit light and are visualized as hyperilluminescent regions surrounded by gland acini [2]. There are two types of meibography; namely, translumination of the everted lid and direct illumination, a technique called non-contact meibography.

In the translumination technique, which was first introduced by Tapie, the light source (e.g., white light from the Finoff Transluminator) is placed on the eyelid skin, and the lid is everted to observe the meibomian glands from the palpebral conjunctival surface [3]. A similar method using infrared (IR) imaging can be done. Jester et al. documented the morphological changes in the meibomian glands with IR imaging using translumination (white light) and a Zeiss photo and slit-lamp microscope [2]. Because of the disadvantages of analog IR photography (e.g., expensive, images can only be seen after film processing), Mathers et al. introduced video technology [4]. It was shown that higher-quality gland imaging is possible with the video method by recording the images of each meibomian gland using a single-chip IR video camera, a hand-held transluminescent light source, and a video monitor.

The non-contact meibography technique was first used by Arita et al. in 2008 [5]. The IR light source and the camera do not come into contact with the patient during this method. The meibomian glands were visualized by everting the eyelid (without contact with the light probe) using an IR video camera and a slit-lamp biomicroscope equipped with an IR filter. The contrast of light and dark in the meibomian gland images obtained with this technique is the opposite of the one obtained in the translumination technique.

Applications with different light spectra may provide additional information in meibography. For example, the visibility of gland morphology increases with IR hyper-reflective/hypoilluminescent monitoring of glands in the IR technique. However, it remains unclear whether a correlation exists between the severity of the IR reflex and gland secretion, and no correlation or change is expected because of the long wavelength (i.e., relatively low energy). However, further studies examining the relationship between gland morphology and secretion with light spectra are needed [6].

There is no gold standard for the classification of meibomian glands. Some evaluate the number of glands, while others evaluate partial gland percentage, gland dropout, duct dilatation, or hypertranslucent scars and cysts [7-10]. There are only a few assessment scales in this respect.

In the present study, the purpose was to evaluate the effect of eyelid deformity surgeries on tear and anterior cornea segment parameters with meibography and corneal topography. We also aimed to examine any changes in the meibomian glands and anterior cornea segment parameters of the surgery by comparing the operated eye with the other, healthy eye.

Materials and methods

This study was conducted at Afyonkarahisar Health Sciences University Hospital Ophthalmology Polyclinic. Ethics committee approval was obtained for the study (decision no. 202184) at the meeting held on April 9, 2021 by the decision of the Afyonkarahisar Health Sciences University Clinical Research Ethics Committee. The study's methodologies complied with the ethical principles set forth in the Helsinki Declaration. Patients aged 18–75 years who were diagnosed with eyelid deformity (ptosis, entropion, ectropion, lagophthalmos, or dermatochalasis) in Afyonkarahisar Health Sciences University Eye Clinic between January 2020 and January 2021 were included in the study. Those who had previously undergone unilateral or bilateral valve surgery were excluded. Patients who were operated on both eyelids were also excluded. Pre-operative, post-operative first month, and post-operative third month meibography and corneal topography measurements were performed in both eyes of each patient. All of the measurements were made by a single individual. Four patients who could not attend the third-month follow-up and one patient whose corneal topography measurements could not be obtained were excluded from the study. Consent for the study was obtained from each patient.

All surgeries were performed under local anesthesia. Ptosis surgery was performed in 10 patients, entropion surgery in 7 patients, ectropion surgery in 4 patients, surgery because of lagophthalmos in 4 patients, and blepharoplasty surgery because of dermatochalasis in 6 patients. Each group was evaluated individually and together. The surgeries were performed by the same person.

Routine topical medications were prescribed to all patients after the surgeries. Corneal topographic measurements and non-contact meibography measurements were made before the surgery and in the first and third months after the surgery.

Corneal topography and non-contact meibography measurements were made with the same device (Sirius Topographer). The anterior segment parameters K1, K2, ACA, ACD, ACV, and CCT were evaluated before and after the surgery and during the first and third months of the corneal topography measurements. The drop of the meibomian glands was noted as a percentage of the patients before the operation in the first and third month in the meibography measurements (Table 1).

Table 1: Grading scales in meibography

Pflugfelder et al. [30]	Grade 0, No Gland Drop-out.	Grade 1, 33% Gland Drop-out.	Grade 2, 33-66% Gland Drop-out.	Grade 3, >66% Gland Drop-out.	
Nichols et al. [31]	Grade 1, Partial Gland not Visualized.	Grade 2, <25% Presence of Partial Gland.	Grade 3, 25-75% Presence of Partial Gland.	Grade 4, >75% Presence of Partial Gland.	
Arita et al. [32]	Grade 0, No MG Drop-out.	Grade 1, <1/3 Drop-out in Total MG Area.	Grade 2, 1/3-2/3 Drop-out in Total MG Area	Grade 3, >2/3 Drop-out in Total MG Area.	
Pult & Riede-Pult [33]	Grade 0, Drop-out Area 0%.	Grade 1, Drop-out Area 25%.	Grade 2, Drop-out Area 25-50%.	Grade 3, Drop-out Area 50-75%.	Grade 4, Drop-out Area 75%.

In the mutual evaluation of meibography measurements, the upper eyelid of the patients who underwent ptosis and upper lid blepharoplasty surgery was compared with the upper eyelid of the other, healthy eye (Figure 1). The changes in the meibomian glands of both lower eyelids were compared in patients who underwent eyelid surgery because of ectropion, entropion, and lagophthalmos (Figure 2). When making the measurements, both eyelids were everted with a pencil or cotton swab. The ratio of the drop of meibomian glands to the area of the everted valve was measured at each follow-up. The percentages of meibomian gland drop were noted at each measurement. A total of 3–5 images were taken for each valve, and the clearest image was included in the study for each patient.

Figure 1: Non-contact meibography images showing varying degrees of meibomian gland drop in the normal population

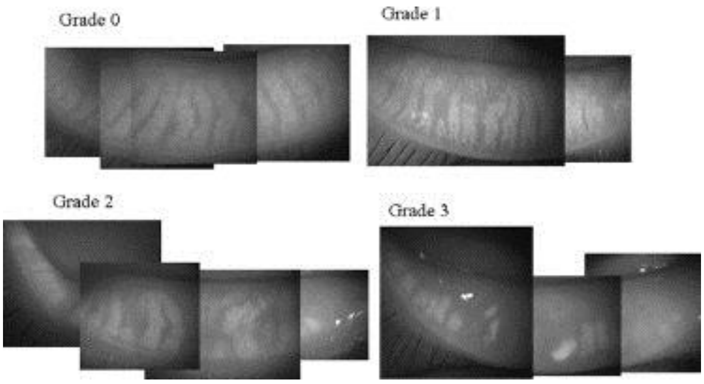
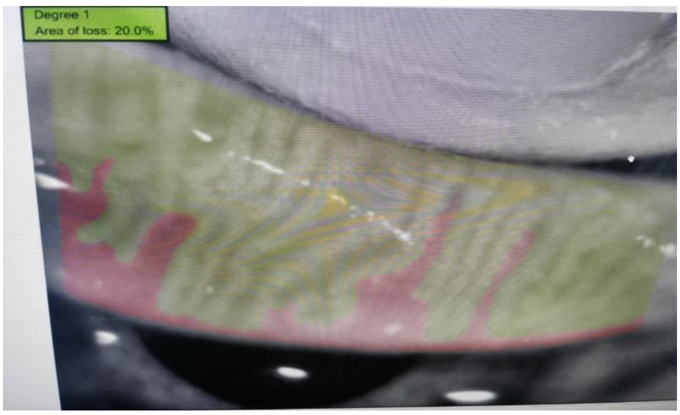


Figure 2: Upper lid meibography measurement in a patient undergoing ptosis surgery



From the corneal anterior segment parameters, K1 (flat keratometric value), K2 (vertical keratometric value), ACA (anterior chamber angle), ACD (anterior chamber depth), ACV (anterior chamber volume), and CCT (central corneal thickness) were measured and compared at each control. The measurements were made by the same researcher in a dimly-lit room. The inspections, such as contact methods (e.g., applanation tonometry) and examination of the ocular surface staining with fluorescein using a slit lamp, were performed before the topographic measurements. The patients were asked to place their heads on the chin-rest, in a sitting position, and look at the fixation light at the center of the device. The shots were applied 3 times for each patient, and the clearest image was included in the study.

Statistical analysis

Numbers and percentages were calculated for qualitative data, and arithmetic means and standard deviations were calculated for quantitative data as descriptive statistics. The Friedman test was used because the data did show a normal distribution in the evaluation of the variables with repeated measurements. In cases where the hypothesis was accepted as a result of the Friedman test, Dunn's multiple comparison tests were used to determine the group or groups responsible for the difference. The Spearman correlation coefficient was used to determine whether there were relationships between the variables. Whether the data had a normal distribution was determined with the Shapiro–Wilk test. The significance level was set at $P < 0.05$ and SPSS v. 26.0 (IBM Corp., Armonk, NY) software was used to evaluate the data

Results

The eyes of 31 patients who underwent surgery, including the non-operated, healthy eye, were included in the present study. Eighteen of 31 patients were male and 13 were female. The mean (standard deviation) age of male patients was found to be 66.50 (17.315) years, and the mean age of female patients was 65.92 (13.714) years ($P = 0.659$). The mean age of all patients included in the study was 66.26 (15.659) years.

Regarding the keratometric values measured in the study (K1, K2, ACD, ACV, ACA, and CCT), no significant differences were detected between consecutive measurements of healthy (control group) eyes and between consecutive measurements of eyes that underwent surgery ($P > 0.05$) (Table 2, 3).

Table 2: Mean, standard deviation, and *P*-values of anterior segment parameters in the healthy eye group (controls)

	Healthy eye (control group; n = 31)					
	K1	K2	ACV	ACA	ACD	CCT
Pre-op measurement	42.17 (2.04)	43.48 (2.35)	143.58 (36.22)	46.65 (8.57)	3.71 (0.68)	539.26 (35.84)
Post-op 1st-month measurement	42.67 (1.99)	43.86 (2.23)	146.52 (36.08)	45.71 (9.81)	3.74 (0.60)	542.32 (43.22)
Post-op 3rd-month measurement	42.86 (1.50)	44.02 (2.09)	145.71 (36.11)	46.26 (8.70)	3.75 (0.60)	542.74 (45.40)
P-value	0.081	0.58	0.19	0.27	0.84	0.94

Table 3: Mean, standard deviation, and *P*-values of anterior segment parameters in the surgical group

	Surgical eye (study group; n = 31)					
	K1	K2	ACV	ACA	ACD	CCT
Pre-op measurement	42.46 (2.34)	43.72 (2.35)	143.55 (33.86)	45.52 (8.47)	3.69 (0.62)	542.97 (52.28)
Post-op 1st-month measurement	42.45 (2.09)	43.81 (1.91)	137.06 (34.62)	44.19 (8.48)	3.72 (0.62)	540.68 (50.95)
Post-op 3rd-month measurement	42.79 (1.71)	43.94 (1.64)	136.06 (28.16)	44.00 (8.05)	3.69 (0.57)	541.39 (52.04)
P-value	0.053	0.67	0.34	0.58	0.32	0.16

When the percentages of meibomian gland drop-out were evaluated, no significant differences were detected in the consecutive measurements of the healthy control group, but the drop-out of the meibomian glands in the surgical eyes was significant ($P < 0.001$) (Table 2, 3). The keratometric values, the changes in the percentage drop-out in the meibogram glands, and the *P*-values in the consecutive measurements are given in the table 2-4.

Table 4: The mean, standard deviation, and *P*-values of meibomian gland drop-out changes in the control and study group

Meibomian gland dropout, %	Control group (healthy eye) 31 Eyes	Study group (operated eyes) 31 Eyes
Pre-op measurement	35.771 (18.540)	34.503 (18.808)
Post-op 1st-month measurement	36.613 (16.583)	44.648 (18.289)
Post-op 3rd-month measurement	39.135 (17.248)	45.381 (19.882)
P-value	0.051	<0.001

The changes in keratometric values and meibomian gland drop-out were not found to be significant until the third post-operative month. However, as an exception to these, the change in the K1 value of the healthy eyes of the patients who underwent ectropion surgery was found to be significant (P = 0.039). Changes were detected in the K1 values of the eyes of the patients who underwent entropion surgery and who were included in the surgical study group (P = 0.018). A change was detected in the central corneal thickness (CCT) in the surgical study eyes of the patients who were operated on for lagophthalmos (P = 0.018).

Although the changes in meibomian gland drop-out in healthy eyes were not found to be significant in all five surgical groups, those in the surgical group were significant.

Discussion

Dry eye disease is one of the most common ophthalmological diseases. Although dry eye disease is multifactorial, one of the most important causes is meibomian gland dysfunction. Meibomian gland dysfunction causes evaporative dry eye indirectly by disrupting the tear film lipid layer. This evaporation can cause hyperosmolarity in the tears and trigger dry eye disease. There is a strong association between dry eye disease and meibomian gland dysfunction [11]. Surgery may also affect the function of the meibomian glands and lacrimal glands and result in postoperative dry eye disease [12].

Evaporative dry eye disease can be caused by conditions affecting the eyelid, such as meibomian gland dysfunction and other eyelid diseases. Meibomian gland dysfunction is seen in approximately 60% of dry eye patients and is responsible for 20% of dry eye disease cases because of aqueous insufficiency [11].

When the literature was reviewed, it was found that surgical procedures cause drop-out in meibomian glands. Chang et al. [13] reported that 40 patients who underwent cataract surgery had significant drop-out rates after surgery. Similarly, a study by Klein-Theyer et al. [14], who used the Hughes procedure for valve reconstruction, found an increase in meibomian gland drop-out, fluorescein staining, and ocular surface disease index (OSDI) scores of the patients who were followed-up after surgery. The results of this and similar studies corroborate our hypothesis that drop-outs of meibomian glands will occur as a result of the valve surgeries.

In the literature, the number of studies reporting meibomian gland drop-out due to eyelid deformities is small. We posit that the drop-out of meibomian glands observed in our study can be attributed to anatomical changes post-surgery, obstruction in the orifices of the meibomian glands post-surgery, and/or increased inflammation in the eyelids.

The most important finding of our research is that surgeries related to eyelid deformities can cause the drop-out of meibomian glands. No significant differences were detected in meibomian gland drop-out rates between pre- and post-operative measurements of patients who had only entropion surgery, when separated according to surgical groups.

Yang et al. [15] reported no significant differences in the drop-out rate of meibomian glands, according to pre-operative measurements in the follow-up performed up to the fifth month in patients who were operated on for marginal entropion. The reason why this difference was not detected can be explained by the abnormal positioning of the orifices of the meibomian glands in the eyelids of patients with marginal entropion. Similarly, in the study that was conducted by Vaidya et al. [16], which included 8 patients who had been operated on for involutional entropion, no differences were detected between pre- and post-operative meibomian gland drop-out rates in surgical eyes. These studies support the proposition that surgery causes no differences in the drop-out of meibomian glands in entropion patients, a result which was also found in our study.

Additionally, no significant differences were found in our study in pre- and post-operative keratometric values in patients who underwent ptosis and upper eyelid blepharoplasty procedures; likewise, no differences were detected in a study by Ceylan et al., who also reported significant changes in the K2 value in the first month in the Levator approach ptosis surgery group [17]. Considering that the patients were followed-up in the last 3 months in our study, it can be understood why no significant changes were detected in the keratometric values, given that the measurements yielded more accurate data over a longer period.

In a study by Zinkernagel et al. [18], changes were detected in the corneal topographic values of patients who underwent blepharoplasty and ptosis surgery. These authors also contended that such a surgery would impair vision levels. Similarly, a positive correlation was detected between the increased fat removed with blepharoplasty and corneal topographic changes. The fact that no significant topographical changes were detected in the present study could be related to the surgical method used and to our less aggressive approach.

Significant decreases were reported in the mean keratometric values and corneal astigmatism values in the post-operative evaluations of the eyes of 17 patients with ptosis surgery in a study by Savino et al. [19]. No significant differences were detected in the central corneal thicknesses of these patients. Similarly, no differences were found in pre- and post-operative central corneal thicknesses in our study. The results regarding the changes in keratometric values were different from the results of our study. This can be explained by the fact that there were fewer ptosis patients in our present study (10 patients), or by the fact that Savino et al. included congenital ptosis patients in their sample. Similarly, Assadi et al. [20] found statistically significant changes in post-operative K2 values in 21 patients who underwent congenital ptosis correction.

In contrast, Youssef et al. [21] reported no significant difference in keratometric values in the first month post-operation in patients who had undergone ptosis surgery. However, significant decreases were detected in the mean K values of ptosis patients who were controlled until the third postoperative month. In our study, there was no significant difference in pre- and postoperative keratometric values in patients who underwent ptosis and upper eyelid blepharoplasty; contrary to this result, it is possible to think that early ptosis surgeries had a greater effect on keratometric values, because the mean age was significantly lower (24.7 [7.9] years) in the study of Youssef et al. [21].

Similarly, in their study, as in the present study, Nalci et al. [22] found no significant changes in K1 and K2 values in the third postoperative- month of patients who had blepharoplasty surgery relative to the pre-operative period. It is remarkable that a similar mean age was detected in the patients of both our study and the study by Nalci et al. Similar to our study, the fact that the results of the blephroplasty surgery did not cause a significant change on the keratometric values can be explained by the fact that the ages of the patients who underwent surgery in our study and Nalci et al.'s study were similar.

In a study by Eshraghi et al. [23], in 19 eyes that had lateral tarsal strip application because of entropion and ectropion, no differences were detected in K1, K2, and mean keratometric values. Unlike their study, significant differences were found in K1 values after entropion surgery in our surgery. Similarly, significant changes were found in the K1 values in the control group after ectropion surgery in our study, which may be because of the insufficient number of entropion patients included in the study. As is already known, the robustness of the results of a given study increases along with increasing sample size. Also, in a retrospective analysis of 25 patients who underwent lateral tarsal strip application for involutional entropion, Yunoki et al. [24] reported no significant differences in K1 and K2 values.

Furthermore, the changes in corneal topographic values were examined in 23 patients who had blepharoplasty surgery for upper lid dermatochalasis in a study by Şimşek et al. [25] According to this study, the changes in post-operative corneal astigmatism values (0.15D) were statistically significant, finding that there might be slight changes in the visual level of the patients after blepharoplasty surgery. For this reason, in the presence of a concomitant valve pathology in every patient for whom refractive surgery is considered, firstly, correcting the valve pathology may come to mind. The changes in K1 and K2, which are the anterior segment parameters that were evaluated in the present study, were not statistically significant. The difference between these studies may be that Şimşek et al. considered the astigmatic changes as a whole instead of evaluating the anterior segment parameters separately.

In a larger study by Monga et al. [26], which was conducted with 51 patients operated on due to upper eyelid entropion, the change in flat and vertical keratometric values was not found to be significant. In a study by El-Ghany Mohammed et al. [27], which included 50 eyes that underwent ptosis surgery, changes in central corneal thickness were not statistically significant, similar to our study. As in the present study, Koçer et al. [28] examined the changes in anterior chamber depth (ACD) and patients who had undergone upper eyelid blepharoplasty surgery, and, as in our study, changes in the anterior chamber were not found to be significant.

The literature review revealed many studies evaluating the effects of eyelid surgeries on keratometric values. The majority of these studies support the present hypothesis that the flat (K1) and vertical (K2) keratometric values and changes in central corneal thickness (CCT) values, which were predicted in the study, are not significant [27-29].

It is important for the accuracy of the results of the study that the other eye of the same patient was used as the control group, that the surgical procedures were performed by the same surgeon, and that the meibography procedure was performed by the same person. The limitations of our study are that the number of surgical cases in the study is small, and the post-operative follow-up period is relatively short. Our data should be supported by studies with larger sample sizes and longer follow-up periods.

Conclusion

The surgical methods available for eyelid deformities may cause meibomian gland to drop out in patients. Pre-operative evaluation and post-operative follow-up must be performed with care in patients who are scheduled for surgery to avoid possible symptoms and meibomian gland dysfunction. However, larger studies are required to support the accuracy of the present results.

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