Relationship Between Eyelid Pressure and Ocular Surface Disorders in Patients With Healthy and Dry Eyes

Masahiko Yamaguchi1,2 and Atsushi Shiraishi2

1Department of Ophthalmology, Ehime Prefectural Central Hospital, Kasuga-cho, Matsuyama, Ehime, Japan
2Department of Ophthalmology, Ehime University Graduate School of Medicine, Shitsukawa, Toon, Ehime, Japan

PURPOSE. To determine whether an eyelid pressure measurement device, called a blepharo-tensiometer, can detect changes in the eyelid pressure in different types of ocular surface disorders.

METHODS. First, the repeatability of the blepharo-tensiometer was determined by measuring the eyelid pressures on 3 separate days from healthy volunteers and calculating the intraclass correlation coefficients (ICCs). Second, to determine the ability of the blepharo-tensiometer to detect changes in the eyelid pressures in different types of ocular surface disorders, we compared the eyelid pressure of healthy eyes with dry eyes. Third, the correlations between the eyelid pressure and the location and magnitude of fluorescein staining of the ocular surface were analyzed. Fourth, the eyelid pressure in eyes with lid-wiper epitheliopathy (LWE) was measured.

RESULTS. The ICCs ranged from 0.675 to 0.911 for the upper eyelid and 0.663 to 0.925 for the lower eyelid. The pressures of the upper and lower eyelids were significantly higher in dry eyes than in healthy eyes. The inferior ocular surface staining scores were strongly correlated with the lower eyelid pressure by multivariate analysis. The lower eyelid pressure was significantly correlated with the grade of the lower LWE.

CONCLUSIONS. The blepharo-tensiometer can obtain repeatable measurements of the eyelid pressure and can be used to evaluate the pressure of the eyelids on the ocular surface in healthy and diseased eyes. The significant correlations between the eyelid pressure and the ocular surface staining suggests that the pressure on the ocular surface probably contributes to ocular surface disorders.

Keywords: eye blinks, eyelid pressure, friction, dry eyes

Blinking and eyelid movements play important roles in the distribution of tears and in the maintenance of the integrity of the ocular surface.1,2 During blinking, the movements of the upper and lower eyelids rub the ocular surface and generate a frictional force. The degree of the frictional force is calculated by multiplying the coefficient of friction by the normal force exerted on the surface. Mathers and Lemp3 used specular microscopy to demonstrate that the frictional force induced by blinking removed cells from the corneal epithelium, and they suggested that the frictional force increased the exfoliation and thus altered the migration and turnover of the corneal epithelial cells.

Cher4 proposed a new term, “blink-related microtrauma,” for the ocular surface disorders that arise from the frictional force of the eyelids on the ocular surface or from lubrication disorders of the eyes. Superior limbic keratoconjunctivitis (SLK) is an example of this type of disorders, and it was suggested to be caused by focal friction generated between the palpebral conjunctiva and the superior limbus region of the cornea and conjunctiva during blinking.

Korb et al.5 studied the eyelid margins of the palpebral conjunctiva, which are in contact with the ocular surface, and they reported their findings in cases of epithelial disorders of the eyelid margins of the palpebral conjunctiva called lid-wiper epitheliopathy (LWE). They suggested that the friction developed between the upper eyelid margins and the cornea was the cause of LWE. Shiraishi et al.6,7 reported that LWE-like lesions were also present at the lower eyelid margin.

Since the report of Snellen in 1869,8 various methods have been used to measure the eyelid pressure but all of them had unique problems in usability and versatility.9–15 We overcame these problems by developing a device that allowed us to easily record valid and accurate eyelid pressures under stationary conditions (i.e., eyelids closed, and also under dynamic conditions, i.e., during blinking).16 This device was named a blepharo-tensiometer.

The aim of this study was to determine the ability of the blepharon-tensiometer to detect changes in the eyelid pressure in different types of ocular surface disorders. To accomplish this, we compared the eyelid pressure of healthy eyes with that in dry eyes and to that with LWE.

Materials and Methods

The protocols used in all these studies were approved by the institutional review board of the Ehime University and the University Hospital Medical Information Network Clinical Trials Registry. An informed consent for the examinations and measurements was obtained from all subjects, and the
procedures used conformed to the tenets of the Declaration of Helsinki.

**Eyelid Pressure Measurement by Blepharo-Tensiometer**

The eyelid pressure was measured with the blepharo-tensiometer that was developed in our laboratory and was described in detail in an earlier publication. Briefly, the blepharo-tensiometer consisted of a tactile pressure sensor (DigiTacts Single Point Sensors; Pressure Profile Systems, Inc., Los Angeles, CA, USA) that detects the pressure exerted by the eyelids on its surface (Fig. A). The pressure sensor was connected to a personal computer (Fig. B; Dell, Round Rock, TX, USA).

The pressures of the upper and lower eyelids were measured individually using the same sensor for each subject. To protect the cornea, a sterile disposable soft contact lens was placed on the cornea after the eye was anesthetized with topical 0.4% oxybuprocaine. The pressure sensor with the protective polyurethane cap was inserted between the soft contact lens and the inner surface of the eyelid. The eyelid pressure was measured while the eyes were closed. Reprinted with permission from Sakai E, Shiraishi A, Yamaguchi M, Ohta K, Ohashi Y. Blepharo-tensiometer: new eyelid pressure measurement system using tactile pressure sensor. *Eye Contact Lens*. 2012;38:326–330. Available at: https://journals.lww.com/claojournal/Abstract/2012/09000/Blepharo_Tensiometer___New_Eyelid_Pressure.12.aspx.

**Repeatability of Blepharo-Tensiometer**

To determine the test-retest reliability of the blepharo-tensiometer, the pressures of the upper and lower eyelids were measured on 3 separate days from both eyes of 12 healthy volunteers. The intraclass correlation coefficients (ICCs) were calculated.

**Effect of Age on Eyelid Pressure**

It is well known that the eyelids lose their elasticity with increasing age and the lids droop. This suggests that the eyelid pressure on the ocular surface should decrease with increasing age. To confirm that the blepharo-tensiometer does measure the eyelid pressures, we examined the eyelid pressure in healthy individuals of different ages. To accomplish this, 34 right eyes of 34 healthy volunteers consisting of 14 men and 20 women were studied. Their average age was 51.7 ± 17.6 years with a range from 20 to 85 years. The eyelid pressures were measured with the blepharo-tensiometer, and the effect of age on the eyelid pressure was determined statistically.

**Alterations of Eyelid Pressure in Dry Eyes**

The eyelid pressures of 130 eyes of 65 patients diagnosed with dry eye patients were compared with those of 58 eyes of 31 healthy controls. Dry eye was diagnosed according to the 2006 revised Japanese Dry Eye Diagnostic Criteria. The dry eye group (D group) consisted of 13 men and 52 women whose mean age was 58.7 ± 15.0 (mean ± SD) years. The healthy control group (N group) consisted of 14 men and 17 women whose mean age was 51.1 ± 17.3 (±SD) years. All subjects had a preliminary eye examination to confirm that they did not have any other eye diseases, history of ocular surgery, or eye trauma.
TABLE 1. Grading of the Lid Wiper Epitheliopathy

<table>
<thead>
<tr>
<th>Horizontal Staining Score*</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10% of the length of eyelid</td>
<td>0</td>
</tr>
<tr>
<td>10% ≤ 25% of the length of eyelid</td>
<td>1</td>
</tr>
<tr>
<td>25% ≤ 50% of the length of eyelid</td>
<td>2</td>
</tr>
<tr>
<td>≥50% of the length of eyelid</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sagittal Staining Score†</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25% of the width of lid wiper</td>
<td>0</td>
</tr>
<tr>
<td>25% ≤ 50% of the width of lid wiper</td>
<td>1</td>
</tr>
<tr>
<td>50% ≤ 75% of the width of lid wiper</td>
<td>2</td>
</tr>
<tr>
<td>≥75% of the width of lid wiper</td>
<td>3</td>
</tr>
</tbody>
</table>

Grading of LWE

<table>
<thead>
<tr>
<th>Average of horizontal and sagittal staining scores</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>0.5–1.0</td>
<td>1</td>
</tr>
<tr>
<td>1.5–2.0</td>
<td>2</td>
</tr>
<tr>
<td>2.5–3.0</td>
<td>3</td>
</tr>
</tbody>
</table>


* The horizontal length of the staining extends from the inner canthus to the lateral canthus.† The sagittal width of staining extends from just proximal to the line of Marx’s line to the subtarsal fold.

Effect of Lid-Wiper Epitheliopathy (LWE) on Eyelid Pressure

These experiments were performed on 79 eyes of 43 healthy non-contact lens wearers (24 men and 19 women, mean age ± SD, 23.6 ± 1.9 years). All subjects had a preliminary eye examination to confirm that they did not have any eye disease, history of ocular surgery, or eye trauma. The incidence and degree of LWE was determined by the lissamine green staining method. The grade of the LWEs along the upper and lower eyelid margins was determined after applying 5 µL of 2% lissamine green vital dye. The grading of the LWE of each eyelid was determined by the horizontal length and sagittal width of the lissamine green staining as was done by Korb et al. with some modification (Table 1; Fig. 2). The grading of the LWE was made with careful examination to differentiate the thin line of the vital dye staining of the mucocutaneous junction denoting Marx’s line. The grade of LWE was evaluated 30 seconds after the installation of the lissamine green.

Evaluation of Other Factors Used to Assess Ocular Surface

We calculated the correlations between the eyelid pressures and the location and scores of ocular surface staining and other factors used to assess the integrity of the ocular surface. These factors included the Schirmer I test scores (mm), fluorescein tear film break-up time (BUT; mean of 3 measurements), meibomian gland dysfunction (MGD; grade 0–3), tear meniscus height (TMH; low/medium/high), one-way measurement at the center of lower eyelid using a slit-lamp and eyepiece graticule, superior conjunctivochalasis (grade 0–3), inferior conjunctivochalasis (grade 0–3), superior or inferior lid-wiper epitheliopathy (LWE; grade 0–3), eyelid folds (1 fold/2 folds, at upper eyelid margin), and eyelid ptosis (present/absent, at upper eyelid) (Table 2).

Statistical Analyses

All data are presented as the means ± SD. Statistical analyses were performed with Student’s t-tests, ICC, and regression analyses. The Steel-Dwass multiple comparison tests were used to compare the average eyelid pressure for each of the four grades of LWEs. A P < 0.05 was considered statistically significant. All analyses were performed with JMP for Windows, Version 7 (SAS Institute, Cary, NC, USA).

RESULTS

Repeatability of Blepharo-Tensiometer

The ICC ranged from 0.884 to 0.911 for the right upper eyelids (day 1: 20.42 ± 6.08, day 2: 20.25 ± 7.02, day 3: 20.90 ± 7.05 [average eyelid pressure of each day ± SD, mm Hg]) and 0.675 to 0.865 for the left upper eyelids (day 1: 20.84 ± 5.36, day 2:...
The mean eyelid pressure was 16.95 ± 6.08 mm Hg for the upper eyelid and 16.11 ± 7.27 mm Hg for the lower lid. The eyelid pressure decreased with increasing age. The coefficient of correlation of the eyelid pressure was negatively and significantly correlated with age for both the upper (r = 0.740; P < 0.0001; Fig. 4a) and lower eyelid pressures (r = 0.570; P = 0.000432; Fig. 4B).

Eyelid Pressure in Normal Eyes and Dry Eyes

The mean eyelid pressure for the normal eyes (N) group was 16.25 ± 6.18 mm Hg for the upper lid and 16.39 ± 6.82 mm Hg for the lower lid. For the dry eyes (D) group, the mean eyelid pressure was 20.23 ± 5.73 mm Hg for the upper lid and 19.55 ± 6.58 mm Hg for the lower lids. The pressures for both eyelids were significantly higher in the D group than in the N group (Table 3; upper P < 0.0001, lower P = 0.0040). When the eyelid pressures were compared by age, no significant difference was observed between ages younger than 39 years and 40 to 49 years in the N and D groups. However, the eyelid pressures were significantly higher in the D group than the N group.
group for the older ages, especially ages of 50 to 59 years (Table 3; upper \( P = 0.0068 \), lower \( P = 0.0127 \)) and 60 to 69 years (Table 2; upper \( P = 0.0007 \), lower \( P = 0.0230 \)). In the N group, all the eyelid pressures decreased with increasing age, and this trend was not observed in the D group, where the values for each age group were not significantly different. However, no significant difference was observed between N and D groups in the lower eyelid pressure for ages over 70 years (Table 3).

**Eyelid Pressure in Eyes With Lid-Wiper Epitheliopathy (LWE)**

An upper LWE was detected in 24 of 79 eyes (30.4%), and the mean grade was 0.53 ± 0.10 (±SEM). For the lower LWE, the incidence was 41 of 79 eyes (51.9%), and the mean grade was 1.08 ± 0.13. Both the incidence and grade of the lower LWE were significantly higher than that of the upper LWE (\( P < 0.001 \)).

The average eyelid pressure of the upper eyelid in those subjects showing LWE was 23.0 ± 1.1 mm Hg, and no significant difference was detected in the eyelid pressure for any grade of upper LWE. The average eyelid pressure of the lower eyelid was 21.7 ± 1.0 mm Hg, and the eyelid pressure in eyes with grade 3 lower LWE (27.9 ± 2.8 mm Hg) was significantly higher than that of eyes with grade 0 lower LWE (19.7 ± 1.3 mm Hg, \( P < 0.05 \), Fig. 5).

### Table 3. Eyelid Pressure in Healthy and Dry Eyes by Age

<table>
<thead>
<tr>
<th>Age</th>
<th>Upper eyelid pressure, mm Hg</th>
<th>Lower eyelid pressure, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>D</td>
</tr>
<tr>
<td>6</td>
<td>21.36 ± 5.03</td>
<td>18.86 ± 5.77</td>
</tr>
<tr>
<td>40-49</td>
<td>21.22 ± 4.20</td>
<td>19.38 ± 5.93</td>
</tr>
<tr>
<td>50-59</td>
<td>14.14 ± 3.95</td>
<td>19.25 ± 5.24</td>
</tr>
<tr>
<td>60-69</td>
<td>11.22 ± 5.95</td>
<td>21.05 ± 5.95</td>
</tr>
<tr>
<td>70+</td>
<td>11.54 ± 3.08</td>
<td>20.28 ± 6.73</td>
</tr>
<tr>
<td>Total</td>
<td>16.25 ± 6.18</td>
<td>20.23 ± 5.73</td>
</tr>
</tbody>
</table>


* A regression analysis by age.
† Values between dry and healthy eyes.

**Evaluations of Other Factors Used to Assess Integrity of Ocular Surface**

We calculated the correlations between the location and scores of the ocular surface staining and other factors used to assess the integrity of the ocular surface. The ocular surface staining score in each region is shown in Table 4. The correlations between the ocular surface staining score and the eyelid pressure of each region are shown in Table 5.

The ocular surface staining score of the inferior cornea (KFS-I) and inferior conjunctiva (CFS-I) were correlated with the higher pressures of the lower eyelid (\( r = 0.19, P = 0.0307 \); \( r = 0.20, P = 0.0252 \), respectively). The correlations between the upper and lower eyelid pressure and the staining scores for the superior and middle cornea and the intrapalpebral conjunctiva were not significant (Table 5). The Schirmer I test scores were significantly correlated with the CFS-T and CFS-N scores (\( r = 0.21, P = 0.0224 \); \( r = 0.25, P = 0.0068 \), respectively), and the BUT values were significantly correlated with the CFS-S (\( r = 0.22, P = 0.0131 \); \( r = 0.27, P = 0.0018 \), respectively), and the CFS-I (\( r = 0.25, P = 0.0043 \)) values. The MGD values were correlated with the CFS-S, CFS-I, and CFS-N scores (\( r = 0.30, r = 0.19, r = 0.21, r = 0.20, r = 0.19 \); and \( P = 0.0012, P = 0.0445, P = 0.0251, P = 0.0263, P = 0.0371 \), respectively). The superior conjunctivochalasis values were correlated with the CFS-S (\( r = 0.36, P < 0.0001 \), Table 5).

To determine how the eyelid pressures were correlated with other factors that measure the ocular surface integrity, we performed multivariate analyses. The results are summarized in

![Figure 5](https://example.com/figure5.png)

**Figure 5.** Prevalence and grade of LWE and eyelid pressure. The prevalence of upper LWE was 30.4%, and the mean grade was 0.53 ± 0.10 (±SEM). For lower LWE, the prevalence was 51.9%, and the mean grade was 1.08 ± 0.13 (±SEM). The average eyelid pressure of upper eyelid was 23.0 ± 1.1 mm Hg (±SEM), and no significant difference was detected in the eyelid pressure between any grade of upper LWE. The average eyelid pressure of the lower eyelid was 21.7 ± 1.0 mm Hg, and the eyelid pressure in eyes with grade 3 of lower LWE was 27.9 ± 2.8 mm Hg (±SEM), which is significantly higher than that of eyes with grade 0 of lower-LWE at 19.7 ± 1.3 mm Hg (\( P < 0.05 \)). Reprinted with permission from Yamamoto Y, Shiraishi A, Sakane Y, Ohta K, Yamaguchi M, Ohashi Y. Involvement of eyelid pressure in lid-wiper epitheliopathy. *Curr Eye Res*. 2016;41:171-178.
The analyses showed that the ocular surface staining scores of KFS-I were strongly correlated with the Schirmer I test and MGD. The ocular surface staining scores of the CFS-T were also strongly correlated with the location of the fluorescein ocular surface staining and the eyelid pressure. Our results indicated that the upper and lower eyelid pressures were weakly correlated with the superior and inferior ocular surface disorders, but when multiregression analyses were performed, the correlation between the lower eyelid pressure and the staining scores of the inferior cornea and conjunctiva was found to be significant. We also found that the increased lower eyelid pressure was significantly higher in eyes with grade 3 lower LWE than in eyes with grade 0 lower LWE. Based on these findings, the inferior ocular surface disorders, including the lower LWE, may be affected by the lower eyelid pressure.

Kessing used a radiographic method to show that the filling of the space between the upper palpebral and bulbar conjunctiva with a contrast medium was different from that of the lower space. The upper space was shown to be distributed relatively evenly from the conjunctival fornix to the eyelid margin, whereas the lower space was relatively unevenly distributed, with a large space near the fornix close to the lid margin, and no space where the palpebral conjunctiva adhered closely to the bulbar surface. The difference from the upper and lower space might affect the relationship between the eyelid pressure and the location of the fluorescein ocular surface staining and the eyelid pressure. Our results indicated that the upper and lower eyelid pressures were weakly correlated with the superior and inferior ocular surface disorders, but when multiregression analyses were performed, the correlation between the lower eyelid pressure and the staining scores of the inferior cornea and conjunctiva was found to be significant.

The results showed that the eyelid pressure decreased significantly with increasing age for both the upper and lower eyelids. We also found that the eyelid pressure was significantly higher in dry eyes than in healthy eyes especially in patients older than 50 years of age. However, these findings do not provide any evidence on whether the higher eyelid pressure was due to the dry eye conditions, or if the higher eyelid pressure in dry eye patients exacerbated the dry eye symptoms. Future studies will be designed to answer this question.

We then asked whether there were any ocular surface disorders caused by an increase in the eyelid pressure, and if there were, which part of the ocular surface would be affected by the eyelid pressure? To try to answer this question, we determined whether significant correlations existed between the location of the fluorescein ocular surface staining and the eyelid pressure. We then asked whether there were any ocular surface disorders caused by an increase in the eyelid pressure, and if there were, which part of the ocular surface would be affected by the eyelid pressure? To try to answer this question, we determined whether significant correlations existed between the location of the fluorescein ocular surface staining and the eyelid pressure. Our results indicated that the upper and lower eyelid pressures were weakly correlated with the superior and inferior ocular surface disorders, but when multiregression analyses were performed, the correlation between the lower eyelid pressure and the staining scores of the inferior cornea and conjunctiva was found to be significant. We also found that the increased lower eyelid pressure was significantly higher in eyes with grade 3 lower LWE than in eyes with grade 0 lower LWE. Based on these findings, the inferior ocular surface disorders, including the lower LWE, may be affected by the lower eyelid pressure.

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eyelid pressures and the appearance ratio of the upper and lower LWE. Thus, the upper and lower eyelids may exert different degrees of frictional force during blinking. Consequently, a high-eye lid pressure and the anatomy of the lower eyelid may be risk factors for lower LWE. On the other hand, no significant difference was found between the upper eyelid pressure and the grade of the upper LWE. The cause of these findings could not be determined definitively but they are most likely due to the different locations of the movements of eyelids. The lower LWE generally occurs at the nasal margin of the palpebral conjunctiva near the lower punctum. This area corresponds to where the eyelid moves against the surface of the bulbar conjunctiva. For the upper LWE, the movement is in the region of the middle of the upper eyelid, which moves over a smooth corneal surface. The results of the multiregression analyses showed that the staining score of the intrapalpebral conjunctiva was significantly correlated with the Schirmer I test scores followed by the BUT scores. The staining scores of the upper and lower areas of the ocular surface which are usually covered by the eyelids. The staining scores of the superior conjunctiva and cornea were strongly correlated with the superior conjunctivochalasis. These results are in good agreement with earlier studies that reported reduction in the superior conjunctivochalasis.

We studied the effects of the eyelid pressure on the LWE and other ocular surface disorders, which is only one factor in the contents or writing of the manuscript. The Dry Eye Society, Tokyo, Japan. The Dry Eye Society had no role in the publication of the manuscript. Disclosure: M. Yamaguchi, None; A. Shiraishi, None

**References**


