



THE EFFECT OF PALPEBRAL FISSURE HEIGHT IN PRIMARY GAZE POSITION ON TEAR FILM STABILITY

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SUMMARY – This study aimed to investigate the effect of palpebral fissure height in primary gaze position in healthy individuals on tear film stability. In this cross-sectional study, 120 subjects (60 male and female each) were enrolled and divided according to age into two groups, i.e., group 1 (aged 18-50 years) and group 2 (aged 51 and older). Palpebral fissure height on both eyes was measured in primary gaze position with a clear plastic ruler held in a central vertical position between the upper and lower lid margin, and the standard tear break-up time (TBUT) test was performed to evaluate tear film stability. Palpebral fissure height was significantly higher in younger than older subjects in all measurements on both eyes ($p < 0.001$), and TBUT was shorter in older than in younger subjects. In all subjects included in the study, palpebral fissure height was not related to TBUT ($p = 0.589$). However, analyzing the two age groups separately, a significant negative correlation was found between the palpebral fissure height and TBUT in both groups of younger ($p < 0.001$) and older ($p = 0.009$) subjects. In conclusion, an enlarged exposed ocular surface due to higher palpebral fissure height in healthy individual's primary gaze position negatively affects tear film stability expressed by TBUT.

Key words: Palpebral fissure height; Tear break-up time test; Healthy individuals

Introduction

Tear film stability plays an important role in ocular health. Moreover, a stable precorneal tear film protects and moisturizes the cornea and provides a primary refracting surface for optimal optical quality¹. One of the core mechanisms of dry eye disease (DED), according to the Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) II Report, as well as a Consensus Report by the Asia Dry Eye Society (ADES), is instability of the tear film^{2,3}. It was a basis for a new diagnosis and treatment concept for dry

eye, termed as tear film-oriented diagnosis and therapy (TFOD and TFOT) in Japan and Asia³. The new definition of dry eye proposed by the TFOS DEWS II emphasizes the loss of tear film homeostasis as a dry eye main characteristic. Also, ocular surface and tear component deficiencies can contribute to a loss of tear film homeostasis, in addition to many factors that include eyelid and blink abnormalities^{1,4}. TFOS DEWS II Pathophysiology Report highlighted tear hyperosmolarity induced by evaporation, tear instability, and inflammatory response as part of a vicious circle, described as a common pathway for all forms of DED⁴. It is known that tear hyperosmolarity arises due to excessive evaporation from the exposed ocular surface and consequent thinning of the tear film^{5,6}. Since hyperosmolarity and tear film instability correlate positively with each other⁶, it is clear that an enlarged ex-

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posed ocular surface alters eye desiccation. Palpebral fissure height in primary gaze position determines the eye-opening and exposure to external conditions. Hence, it can be considered as an intrinsic risk factor for developing DED⁶⁻⁸. Palpebral fissure height is a factor that correlates positively with exposed ocular surface⁷. Accordingly, an enlarged exposed ocular surface accelerates evaporation and negatively affects tear film stability. Enlarged exposed ocular surface and palpebral fissure height due to proptosis is a well-known risk factor for ocular surface damage and development of DED among patients with endocrine exophthalmos^{9,10}. The main functions of tear film are its stability and prevention of ocular surface desiccation¹¹. Traditionally, the most frequently used tear film stability test in everyday clinical practice is the fluorescence tear break-up time (TBUT) test^{12,13}. According to the DEWS Report 2007, TBUT is defined as the interval between the last complete blink and the first appearance of a dry spot or disruption in the tear film. An unstable tear film is characterized by short TBUT⁶.

Since an enlarged exposed ocular surface negatively affects tear film stability and alters eye desiccation, it is presumed that a higher dimension of palpebral fissure height among healthy individuals may influence the development of tear instability and DED. Therefore, this study aimed to investigate the impact of palpebral fissure height in primary gaze position in healthy individuals on tear film stability.

Patients and Methods

This cross-sectional study was performed in the Department of Ophthalmology, Zagreb University Hospital Center in Zagreb, following the Declaration of Helsinki and approved by the Hospital Ethics Committee. The subjects included in the study received both written and oral information about the study and signed written informed consent.

A total of 120 adult subjects consecutively attending the Outpatient Ophthalmology Department for standard eye examination during two months were enrolled in the study. Subjects with ophthalmic pathology (ocular trauma, acute ocular inflammation, glaucoma, previous eye or lid operations, reconstructive and plastic surgical procedures, orbit and lid pathology such as orbital cellulitis, blepharitis and lid tumors, anophthalmos and known or suspected dysthyroid orbitopathy) or other conditions and disorders that could influence tear film stability (thyroid pathology, diabetes, facial

abnormalities, facial paresis) were excluded from the study.

First, palpebral fissure height was measured in all subjects in primary gaze position with a clear plastic ruler held as close to the eye as possible. Central vertical distance between the upper and lower lid margin was measured. Three consecutive measurements on both eyes were performed by the same examiner. Nunes *et al.*¹⁴ compared different measuring palpebral fissure methods and found no statistically significant difference between the manual and digital measurements. Hence, manual measurement with a plastic ruler is as reliable as digital and was performed in this study. After that, TBUT was measured during slit-lamp examination under cobalt blue illumination. For TBUT test, one drop of 1% fluorescein sodium was applied to the inferior fornix of both eyes. The subjects were asked to blink at least three times naturally and keep their eyes open while looking straight ahead, and time interval between the last blink and appearance of the first dry spot of tear film was measured with a digital stopwatch. The same examiner performed three consecutive measurements of TBUT on both eyes.

Statistical analysis was performed by Statistica software package version 13.3 (TIBCO Inc., USA). The normality of data distribution was tested by Kolmogorov-Smirnov test and homogeneity of variance by Leven test. Results of descriptive analyses were expressed as mean \pm standard deviation (SD) for continuous data and numbers for categorical data. Differences in distributions of continuous data were evaluated by parametric tests since the assumption of homogeneity of variance for tested variables was met. The t-test was used to test differences between independent variables, and the repeated measures ANOVA test was used to test differences between dependent variables. Differences in distributions of categorical data were assessed by the χ^2 -test. Pearson's correlation test was used to assess the strength of associations. The level of statistical significance was set at $p < 0.05$.

Results

This study included 120 subjects (60 male and 60 female), mean age 46.51 ± 18.38 years. According to age, subjects were divided into two groups, i.e., group 1 (subjects aged 18–50 years) and group 2 (subjects aged 51 and older). Descriptive statistics of basic characteristics of subjects included in the study are presented in Table 1. The mean age of group 1 and group 2 subjects

Table 1. Basic characteristics of subjects divided into two groups according to age

	Group 1 (n=60)	Group 2 (n=60)	t ^a χ^b	p
Age (years)*	30.97±9.24	62.05±10.23	-17.468 ^a	<0.001^a
Gender (m/f)**	30/30	30/30	0.000 ^b	1.000 ^b

*mean ± standard deviation; **numbers; ^at-test df = 118; ^b χ^2 -test df = 1

Table 2. Mean age of male and female subjects divided into two age groups

	Males (n=60)	Females (n=60)	t	p
Group 1 Age (years)	28.47±8.00	33.47±9.82	-2.160	0.035
Group 2 Age (years)	58.63±9.88	65.47±9.54	-2.725	0.008

mean ± standard deviation; t-test df = 58

Table 3. Palpebral fissure height on the first, second and third measurement on the right and left eye in subjects divided into two groups according to age

	Group 1 (n=60)	Group 2 (n=60)	t ^a	p ^a
Palpebral fissure height on the right eye 1 st measurement (mm)	10.94±0.91	9.26±1.08	9.248 ^a	<0.001^a
Palpebral fissure height on the right eye 2 nd measurement (mm)	10.95±0.88	9.28±1.11	9.133 ^a	<0.001^a
Palpebral fissure height on the right eye 3 rd measurement (mm)	10.90±0.87	9.28±1.06	9.086 ^a	<0.001^a
Palpebral fissure height on the left eye 1 st measurement (mm)	10.94±0.88	9.26±1.07	9.430 ^a	<0.001^a
Palpebral fissure height on the left eye 2 nd measurement (mm)	10.91±0.88	9.28±1.06	9.192 ^a	<0.001^a
Palpebral fissure height on the left eye 3 rd measurement (mm)	10.93±0.90	9.28±1.06	9.203 ^a	<0.001^a
F ^b	1.261 ^b	1.634 ^b		
p ^b	0.291 ^b	0.156 ^b		

mean ± standard deviation; ^at-test df = 118; ^brepeated measures ANOVA test df = 6

Table 4. Mean value of all six measurements of palpebral fissure height on both eyes in subjects divided into two groups according to age

	Group 1 (n=60)	Group 2 (n=60)	t	p
Palpebral fissure height on both eyes (mm) (N=360)	10.93±0.88	9.27±1.07	22.727	<0.001

mean ± standard deviation; t-test df = 118

Table 5. Tear film break-up time (TBUT) on the first, second and third measurements on the right and left eye in subjects divided into two groups according to age

	Group 1 (n=60)	Group 2 (n=60)	t ^a	p ^a
TBUT on the right eye 1 st measurement (s)	9.78±4.92	8.43±3.63	1.762 ^a	0.072 ^a
TBUT on the right eye 2 nd measurement (s)	9.93±4.81	8.17±3.57	2.415 ^a	0.017^a
TBUT on the right eye 3 rd measurement (s)	9.88±4.81	8.28±3.65	2.179 ^a	0.031^a
TBUT on the left eye 1 st measurement (s)	9.95±4.95	8.58±3.29	1.779 ^a	0.078 ^a
TBUT on the left eye 2 nd measurement (s)	9.78±4.75	8.33±3.21	1.959 ^a	0.052 ^a
TBUT on the left eye 3 rd measurement (s)	9.85±4.87	8.62±3.26	1.629 ^a	0.106 ^a
F ^b	0.247 ^b	0.823 ^b		
p ^b	0.958 ^b	0.557 ^b		

mean ± standard deviation; ^at-test df = 118; ^brepeated measures ANOVA df = 6

Table 6. Mean value of all six measurements of tear film break-up time (TBUT) on both eyes in subjects divided into two groups according to age

	Group 1 (n=60)	Group 2 (n=60)	t	p
TBUT on both eyes (s) (N=360)	9.87±4.82	8.34±3.42	4.903	<0.001

mean ± standard deviation; at-test df = 118

Table 7. Correlation between mean values of palpebral fissure height and tear break-up time (TBUT) on both eyes in subjects divided into two groups according to age

		Palpebral fissure height on both eyes	
		Group 1	Group 2
TBUT on both eyes	r	-0.232	-0.137
	t	-4.511	-2.625
	p	<0.001	0.009

Pearson's correlation test

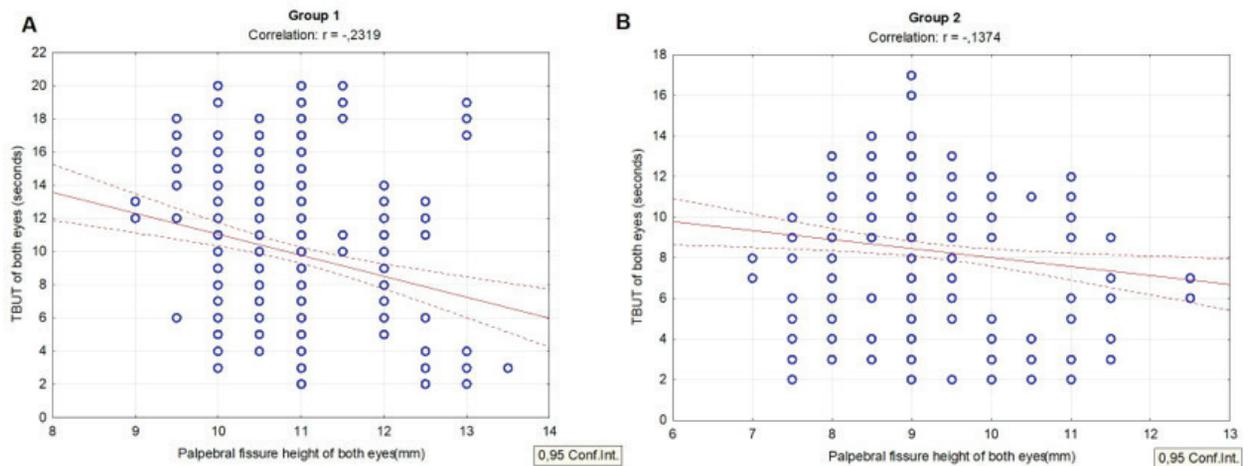


Fig. 1. Correlation between palpebral fissure height and tear break-up time (TBUT) on both eyes in subjects divided into group 1 (A) and group 2 (B) according to age.

was 30.97 ± 9.24 and 62.05 ± 10.23 years, respectively. The groups did not differ by gender. In both groups, the number of males and females was identical (Table 1) and females were significantly older than males (Table 2).

Palpebral fissure height was significantly higher in younger (group 1) than older subjects (group 2) on all three measurements on both eyes ($p < 0.001$), with no differences within the examined groups ($p > 0.05$) (Table 3). The mean palpebral fissure height was 10.93 ± 0.88 (range 9–13.5) mm in younger subjects and 9.27 ± 1.07 (range 7–12.5) mm in older subjects (Table 4).

The values of TBUT were shorter in older (group 2) than in younger subjects (group 1) on all three measurements on both eyes, but only differences on the second and third measurements on the right eye between the groups were statistically significant ($p = 0.017$ and $p = 0.031$, respectively), with no differences within the examined groups ($p > 0.05$) (Table 5).

Since there was no significant difference within the examined age groups among the three measurements of palpebral fissure height and TBUT on the right and left eyes (Tables 4 and 6), the mean values (mean \pm SD) of all six measurements of palpebral fissure height and TBUT on both eyes were used in further statistical analysis.

The palpebral fissure height in all subjects included in the study was not related to TBUT ($r = -0.020$, $p = 0.589$). However, after dividing study subjects into

groups according to age, a statistically significant negative correlation was found between the palpebral fissure height and TBUT both in younger ($p < 0.001$) and older ($p = 0.009$) subjects (Table 7, Fig. 1).

Discussion

Increased palpebral fissure height is recognized as an essential risk factor for the development of tear film instability and ocular surface damage among patients with dysthyroid orbitopathy^{7,15,16}. Moreover, palpebral fissure height in these patients correlates positively with higher tear evaporation rate, increased tear film osmolarity, and significantly lower values of TBUT compared to healthy subjects^{9,10,17,18}. Since the pathology of dry eye has been well investigated among patients with dysthyroid orbitopathy, one of the proposed mechanisms is proptosis and upper eyelid retraction, which is highlighted as a factor that leads to ocular surface exposure to environmental conditions and desiccation^{9,10}. It is estimated that palpebral fissure height correlates positively with exposed corneal surface causing acceleration of tear film evaporation with consequential tear film hyperosmolarity and instability^{7,19}. Several studies found lower values of TBUT in patients with thyroid pathology and increased palpebral fissure height compared to healthy individuals^{17,18,20–22}.

Pansell *et al.*²³ investigated the effect of palpebral fissure height in different vertical gaze positions and exposed ocular surface on tear film stability by

measuring TBUT in 23 healthy young subjects. They found shorter TBUT values in up-gaze with enlarged palpebral fissure height and extended TBUT in down-gaze with decreased palpebral fissure height. So far, no published paper was found about the association and effect of palpebral fissure height in primary gaze position in healthy subjects on tear film stability in the same age group. According to different studies, the average functional values of eyelids and dimensions of periocular structures differ according to age, sex, and race²⁴⁻²⁶. Changes in the eyelid vertical dimensions seem to be more pronounced after 45 years of age, with a decrease of values²⁷. Therefore, the subjects in the present study were divided into two age groups. The mean palpebral fissure height in this study was 10.93 ± 0.88 (range 9-13.5) mm in younger subjects and 9.27 ± 1.07 (range 7-12.5) mm in older subjects. Younger subjects had a significantly higher palpebral fissure height on both eyes than older subjects ($p < 0.001$), which corresponds to other results reported in the literature²⁶⁻²⁸.

The fluorescence TBUT test is, together with Schirmer test and patient history, one of the most widely used and preferred clinical tests for DED diagnosis in routine clinical practice¹³. According to many studies, the proposed cut-off for dry eye diagnosis is less than 10 seconds (s)^{8,29}, while Abelson *et al.*³⁰ recommended a cut-off of ≤ 5 s with a mean TBUT 7.1 s. The sensitivity and specificity of the TBUT test are 72.2% and 61.6%, respectively³¹. Instillation of fluorescence might affect the accuracy of measurements. However, Paugh *et al.*³² found that a TBUT test with liquid NaFl has excellent diagnostic accuracy compared to standard and modified fluorescein strips. Moreover, they suggested a cut point of 5.3 to 6.0 s for optimum test sensitivity and specificity. In this study, TBUT values of all three measurements on both eyes were shorter in older subjects than those in younger subjects. However, only the second and third measurement values on the right eye were significantly different ($p < 0.05$) between the groups. The same pattern has already been reported in a previous study³³. This can be explained by the fact that tear film stability can be affected by fluorescein³⁴. Hence, the DEWS II Diagnostic Methodology report suggests three natural blinks for the test and three consecutive measurements³⁵. According to Johnson *et al.*³⁶, accurate estimation of TBUT requires more recordings, unless breakup time is very short. Since the

second and third measurements showed a significant difference, TBUT can be considered reliable and accurate. A combined analysis of all six measurements on both eyes in the present study showed a significant difference in TBUT values between age groups. The younger subjects had significantly longer TBUT values than older subjects (9.87 ± 4.82 s *vs.* 8.34 ± 3.42 s, $p < 0.001$) (Table 6). Ayaki *et al.*³⁷ also found the association between age and shorter TBUT values among 704 consecutive patients visiting general eye clinics and complaining of ocular discomfort.

Finally, no relation was found between palpebral fissure height and tear film stability expressed by TBUT in all subjects included in this study. However, after dividing the subjects into age groups, a significant negative association between the palpebral fissure height and TBUT values was found in both groups, with more noticeable results in younger ($p < 0.001$) than older ($p = 0.009$) subjects. Since the age causes involuntional eyelid changes, especially pronounced after 45 years of age, all younger subjects included in this study had a higher palpebral fissure height than older subjects, and those with much higher dimensions in each group consequently had a larger exposed ocular surface with shorter TBUT values.

This study had some potential limitations. First, its single hospital-based design and relatively small study sample limited the ability to generalize and reliably replicate the results to the entire healthy population. Second, only one clinical test, the TBUT test, was used to determine tear film stability. However, this was the first study investigating the impact of palpebral fissure height in primary gaze position in healthy individuals on tear film stability. Therefore, to validate this study results, additional investigations using other clinical signs of tear film stability and dry eye symptoms should be performed.

Conclusion

This study showed that an enlarged exposed ocular surface due to higher palpebral fissure height in healthy individuals' primary gaze position negatively affected tear film stability and altered eye desiccation in both age groups. In the future, further studies are needed to investigate differences in other clinical signs of tear film instability and dry eye symptoms between age and gender groups in correlation with palpebral fissure height.

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Sažetak

UTJECAJ VISINE VJEĐNOG RASPORKA U PRIMARNOM POLOŽAJU POGLEDA NA STABILNOST SUZNOG FILMA

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Cilj ovog istraživanja bio je ispitati utjecaj visine vjeđnog rasporka u primarnom položaju pogleda kod zdravih osoba na stabilnost suznog filma. U ovo presječno istraživanje bilo je uključeno 120 ispitanika (60 muškaraca i 60 žena) i prema životnoj dobi podijeljeno u dvije ispitivane skupine: 1. skupina (u dobi od 18-50 godina) i 2. skupina (u dobi od 51 i više godina). Visina vjeđnog rasporka na oba oka mjerena je u primarnom položaju pogleda prozirnim plastičnim ravnalom koje se držalo u središnjoj okomitoj liniji između ruba gornje i ruba donje vjeđe, a standardni test pucanja suznog filma (*tear break-up time*, TBUT) primijenjen je za procjenu stabilnosti suznog filma. Visina vjeđnog rasporka bila je u svim mjerenjima na oba oka značajno veća u mlađih nego u starijih ispitanika ($p < 0,001$), a TBUT je bio kraći u starijih nego u mlađih ispitanika. U svih ispitanika uključenih u istraživanje visina vjeđnog rasporka nije bila povezana s TBUT-om ($p = 0,589$). No, analizirajući dvije dobne skupine odvojeno utvrđena je značajna negativna povezanost između visine vjeđnog rasporka i TBUT-a u obje skupine, u mlađih ($p < 0,001$) i starijih ($p = 0,009$) ispitanika. U zaključku, povećana izložena očna površina zbog veće visine vjeđnog rasporka u primarnom položaju pogleda u zdravih osoba negativno utječe na stabilnost suznog filma izraženu TBUT-om.

Ključne riječi: Visina vjeđnog rasporka; Test pucanja suznog filma; Zdrave osobe