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CLINICAL STUDY

The relationship between clinical signs and dry eye symptoms

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Abstract

Purpose   To evaluate (i) the relationship between traditional and new clinical tests (lid-wiper epitheliopathy (LWE), lid-parallel conjunctival folds (LIPCOF)) and dry eye symptoms in non-contact lens wearers, and (ii) that a combination of these tests can improve predictive ability for the development of dry eye symptoms.
Methods   Tear meniscus height (TMH), non-invasive break-up time (NIBUT), ocular hyperaemia, LIPCOF, phenol red thread test (PRTT), corneal and conjunctival staining, and LWE grades were observed in a cohort of 47 healthy, non-lens wearers (male = 17, female = 30, median age = 35 years, range = 19–70). Symptoms were assessed using the Ocular Surface Disease Index (OSDI).
Results   LWE was significantly correlated to both temporal and nasal LIPCOF ($0.537 < r < 0.607$, $P < 0.05$). LIPCOF and LWE were significantly correlated to NIBUT and PRTT ($r > -0.248$, $P < 0.001$). Significant correlations were found between NIBUT and TMH ($r = 0.461$, $P = 0.001$) and PRTT ($r = 0.640$, $P < 0.001$). OSDI scores were significant correlated to NIBUT, TMH, PRTT, LIPCOF, and LWE ($r > |0.31|$; $P < 0.05$). Significant discriminators of OSDI +/− were NIBUT (area under the receiver operative characteristic curve (AUC) = 0.895), TMH (0.715), PRTT (0.781), LIPCOF (temporal/nasal/Sum 0.748/0.828/0.816), and LWE (0.749). Best predictive ability was achieved by combining NIBUT with nasal LIPCOF (AUC = 0.944).
Conclusions   The individual tests NIBUT, TMH, PRTT, LIPCOF, and LWE were significantly, but moderately, related to OSDI scores. The strongest relationship appeared by combining NIBUT with nasal LIPCOF.
Eye (2011) **25**, 502–510; doi:10.1038/eye.2010.228; published online 21 January 2011

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Introduction

Many patients suffer from ocular-related symptoms, such as stinging, burning, itching, light sensitivity, and blurry vision,[1–5] which limit the quality of life, as well as occupational productivity.[6,7] Correlations between these symptoms and individual clinical dry eye tests, like meibomian gland assessment, tear meniscus height (TMH) measurement, tear break-up time, phenol red thread test, Schirmer test, ocular staining, and ocular hyperaemia, are frequently poor.[8–11]

A combination of tests might improve analysis of dry eye,[9,12–14] but there is no agreement on which combination provides the best results.[11,12] New clinical tests, such as lid-wiper epitheliopathy (LWE)[15] and lid-parallel conjunctival folds (LIPCOF),[13,16–19] show promising predictive ability for dry eye. Combining the clinical grading of temporal and nasal LIPCOF to produce a new score (named LIPCOF Sum) has shown useful predictive ability for dry eye symptoms in experienced soft contact lens wearers,[19] as well as in naive contact lens wearers.[13] The benefit of this test combination in examining a healthy non-contact lens wearing population is unknown.

LWE is a clinically observable alteration in the epithelium of the lid wiper, which is that portion of the marginal conjunctival epithelium of the upper eyelid that wipes the ocular surface during blinking. In patients with dry eye, the tear film is thought to be insufficient to separate the ocular surface and lid wiper.[15] Because of this deficiency, the lid wiper is subjected to trauma during blinking, as a result of the continual rubbing of the narrow surface area of lid wiper tissue against the corneal surface.[15,18–20]

LIPCOF are sub-clinical folds in the temporal and nasal lower quadrants of the bulbar conjunctiva, parallel to the lower lid margin, easily observable by slit-lamp biomicroscope

(Figure 1).[13,16–19] Bulbar conjunctival folds were first described by Hughes *et al*[21] and named conjunctivochalasis and they have been reported in severe dry eye patients.[22–36] LIPCOF might represent the first mild stages of conjunctivochalasis and thus share the same aetiology. Several causes of bulbar conjunctival folds are hypothesised: conjunctival 'looseness' as a result of inflammatory processes,[23,27,36] a decrease of elastic fibres,[27,36] aging,[25,27] or lymphatic dilation by mechanical forces between the lower lid and conjunctiva that gradually interferes with lymphatic flow.[31] Increased friction in blinking might follow from insufficient mucins, or an altered composition of the resident mucins at the ocular surface.[17–19]

Whilst LWE has been reported to be predictive of dry eye symptoms in non-lens wearers and contact-lens wearers,[15] it is not known how LIPCOF relates to symptoms in healthy non-contact lens wearers. An appraisal of these signs may form an important part of any assessment amongst the general population. This study aimed to (i) analyse the relationships between the results of clinical tests and ocular signs, as well as symptoms, and (ii) evaluate the usefulness of such clinical tests in detecting the early stages of dry eye in healthy non-contact lens wearers.

Materials and methods

Forty-seven healthy, non-lens wearers (male $= 17$, female $= 30$, median age$_{all} = 35$ years, range$_{all} = 19–70$ (median age$_{male} = 34.6$ years, median age $_{female} = 36.3$)) who had never worn contact lenses previously were selected from volunteers attending the optometry practice of Horst Riede GmbH, Weinheim, Germany for a routine eye exam. The tear film characteristics and ocular
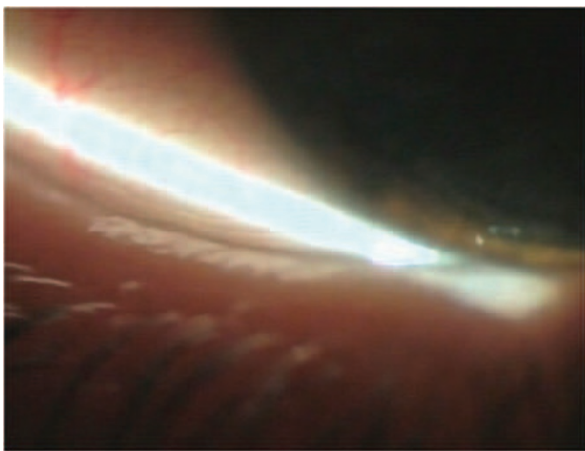

Figure 1 Two parallel conjunctival folds at the temporal quadrant of the eye (LIPCOF grade 2).

surface of the eyes were evaluated during a single clinical session and subjects asked to complete the Ocular Surface Disease Index (OSDI) questionnaire. Symptoms were masked for the observer, as well as the result of slit-lamp microscope evaluation for the subjects. All measures were conducted on the right eye only.

Inclusion and exclusion criteria

Subjects were excluded if they had Sjögren's syndrome, rheumatoid arthritis, diabetes, recent ocular infections, hay fever, any history of ocular surgery, use of any medication or eye drops known to affect the ocular surface, worn contact lenses or had contact lens experiences, or were pregnant. All procedures were conducted in accordance with the Declaration of Helsinki (1983), and approval for the study was given by the Cardiff School of Optometry and Vision Sciences Ethics Committee. All subjects gave written informed consent before participating in the study.

Techniques

Tear meniscus height
TMH was measured by a slit-lamp microscope (with a graticule in 0.05 mm units) at the centre of the lower lid margin. The slit was positioned horizontal to the lower lid with indirect illumination, to exclude invasive triggers like glaring or heating. Three consecutive readings were evaluated and the median noted.

Non-invasive break-up time (NIBUT)
NIBUT was determined non-invasively using a TearScope Plus (Keeler Ltd., Windsor, UK) with a fine grid insert.[37] NIBUT was the time measured, in seconds, between the full opening of the eyelids after a complete blink and the first break in the tear film (using the included stop-watch of the TearScope Plus). Three consecutive readings were evaluated and the median noted.

Ocular hyperaemia
Limbal and bulbar hyperaemia of the horizontal segment of the ocular surface was evaluated by slit-lamp microscope using $12 \times$ magnification and classified using the CCLRU grading scale (University of New South Wales, Sydney, Australia),[38–40] interpolated in 0.1 increments.

Lid-parallel conjunctival folds
LIPCOF was evaluated in the area perpendicular to the temporal and nasal limbus on the bulbar conjunctiva above the lower lid (temporal and nasal LIPCOF,

respectively) with a slit-lamp microscope using 18–24 × magnification as necessary,[13,17–19] and classified using the optimised grading scale (Table 1).[13,17–19] A further combined LIPCOF score (LIPCOF Sum) was calculated by adding together the nasal LIPCOF grade and temporal LIPCOF grade.[19] Care was taken to differentiate between parallel, permanent conjunctival folds (LIPCOF) and disrupted micro-folds.[13,17–19,41–45]

Phenol red thread test (PRTT)
Subjects were asked to keep their eyes open (blinking gently, if necessary) for 15 s while a phenol red-impregnated cotton thread (Zone-Quick; Menicon Co. Ltd., Nagoya, Japan) was placed in the lower conjunctival sac. This test is based on the Hamano cotton thread test measuring tear volume in the lower meniscus sac.[46] Since the PRTT can effectively differentiate between aqueous deficient and non-aqueous deficient dry eye[47] it was used in this study as a surrogate of the Schirmer test I, being less invasive.

Corneal and conjunctival staining
Conjunctival and corneal staining were assessed by applying 1% lissamine green and 2% fluorescein, and classified into four grades, interpolated in 0.1 increments (CCLRU grading scale).[38–40] The fluorescein grading scale was used for both measures in the absence of a published recommendation for lissamine green staining.

Lid-wiper epitheliopathy (LWE)
LWE was made visible using a combination of instilled 1% lissamine green and 2% fluorescein, and evaluated for the upper lid. A second instillation of both dyes was carried out after 5 min.[48] LWE was observed using a slit-lamp microscope with 18 × magnification, classified according to Korb et al.[15,20] Care was to taken to differentiate between the fluorescein and lissamine staining associated with Marx's line and that from staining of the lid wiper.[15,20]

Ocular Surface Disease Index
Each subject's symptoms were evaluated after objective observation by a validated German translation of the

Table 1 Optimised grading scale of LIPCOF[13,18,19]

	LIPCOF grade
No conjunctival folds	0
One permanent and clear parallel fold	1
Two permanent and clear parallel folds, (normally < 0.2 mm)	2
More than two permanent and clear parallel folds, (normally > 0.2 mm)	3

Abbreviation: LIPCOF, lid-parallel conjunctival fold.

OSDI questionnaire.[49] Total OSDI scores were calculated as recommended by Schiffman et al:[3]

$$OSDI = \frac{\text{sum of scores} \times 25}{\text{number of questions answered}}$$

Statistical analyses
Data were examined for normality by Kolmogorov–Smirnov test and appropriate statistical tests used. Correlations between tear film tests were evaluated by Pearson correlation or Spearman rank, if variables were parametric or non-parametric, respectively; differences were evaluated using Mann–Whitney U-test. Best test combination was calculated by logistic regression analyses (forward: likelihood ratio (LR)). Discrimination and predictive ability of test/test combinations were analysed by receiver operative characteristic curve (ROC). The data were analysed using SPSS 16.0 (SPSS Inc., Chicago, IL, USA) and BiAS 8.4.2 (Epsilon Verlag, Frankfurt, Germany).

Results
Significant correlations were observed between the clinical measures NIBUT, PRTT, LIPCOF, LWE, bulbar hyperaemia, and age ($-0.364 < r < 0.454$; $P < 0.034$; Table 2), but the effect of gender was not significant with any clinical measure (U-test, $P > 0.05$). Both temporal and nasal LIPCOF were significantly correlated to bulbar hyperaemia ($0.293 < r < 0.492$, $P < 0.023$), while only temporal LIPCOF was related to limbal hyperaemia ($r = 0.288$, $P = 0.025$). LWE was significantly correlated to both temporal and nasal LIPCOF ($0.537 < r < 0.607$, $P < 0.001$). NIBUT and PRTT were significantly negatively correlated to LIPCOF and LWE ($-0.479 < r < -0.248$, $P < 0.05$). Only NIBUT was significantly negatively correlated to bulbar hyperaemia (Pearson, $r = -0.492$, $P = 0.018$). NIBUT was significantly correlated to PRTT ($r = 0.640$, $P < 0.001$) and TMH (Spearman rank, $r = 0.461$, $P = 0.001$).

The tear film tests NIBUT, TMH, and PRTT, as well the ocular signs LIPCOF (temporal, nasal, Sum) and LWE, were significantly correlated to OSDI scores ($-0.591 < r < 0.586$; $P < 0.019$; Table 3, Figures 2 and 3).

Subjects were grouped by the OSDI score into 20 OSDI + and 27 OSDI− by a cut-off value of 15 (ref. 3) and the ability of the tests to discriminate between OSDI + (median OSDI score = 4.2) and OSDI− (median OSDI score 18.8) was evaluated by ROC. The tear film tests NIBUT, TMH, and PRTT were significant discriminators between groups, as well as the ocular signs LIPCOF (temporal, nasal, Sum) and LWE ($P < 0.01$; Tables 4 and 5). NIBUT was the best discriminator of the set of

Table 2 Correlations between tests of only the right eye, (r-value)

	Age	TMH	NIBUT	Temporal LIPCOF	Nasal LIPCOF	Bulbar hyperaemia	Limbal hyperaemia	PRTT	Corneal staining	Conjunctival staining	LWE
TMH	−0.145										
NIBUT	**−0.364***	**0.461***									
Temporal LIPCOF	**0.284**	0.046	**−0.359***								
Nasal LIPCOF	**0.454***	−0.149	**−0.479***	**0.592***							
Bulbar hyperaemia	**0.360***	−0.004	**−0.307***	**0.492***	**0.293**						
Limbal hyperaemia	0.047	0.044	−0.101	**0.288**	0.028	**0.673**					
PRTT	**−0.437***	**0.375***	**0.640***	−0.248	**−0.402**	−0.255	0.012				
Corneal staining	−0.188	−0.018	−0.043	0.002	0.063	−0.006	0.161	−0.075			
Conjunctival staining	−0.049	0.048	0.041	0.043	−0.163	−0.038	−0.108	0.110	−0.080		
LWE	**0.340***	−0.146	**−0.419***	**0.537***	**0.607***	**0.275**	−0.068	**−0.390**	0.058	0.163	

Abbreviations: LIPCOF, lid-parallel conjunctival fold; LWE, lid-wiper epitheliopathy; NIBUT, non-invasive break-up time; PRTT, phenol red thread test; TMH, tear meniscus height.
*Significant after Bonferroni adjustment.
Correlation coefficients in bold indicate significance levels were $0.001 < P > 0.042$.

Table 3 Correlations between tests and symptoms

	OSDI score	
	r	P
TMH	−0.450	0.001*
NIBUT	−0.591	<0.001*
Temporal LIPCOF	0.305	0.019
Nasal LIPCOF	0.586	<0.001*
LIPCOF Sum	0.427	0.001*
PRTT	−0.407	0.002*
Bulbar hyperaemia	0.229	0.061
Limbal hyperaemia	0.046	0.379
Corneal staining	0.012	0.469
Conjunctival staining	0.060	0.344
LWE	0.453	0.001*

Abbreviations: LIPCOF, lid-parallel conjunctival fold; LWE, lid-wiper epitheliopathy; NIBUT, non-invasive break-up time; PRTT, phenol red thread test; OSDI, Ocular Surface Disease Index; TMH, tear meniscus height.
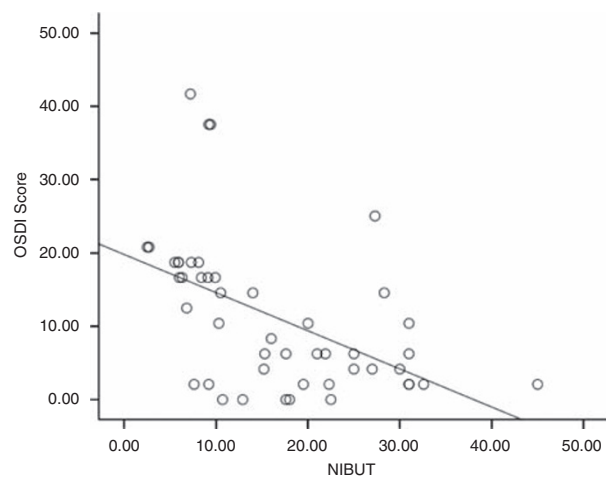*Significant after Bonferroni adjustment.

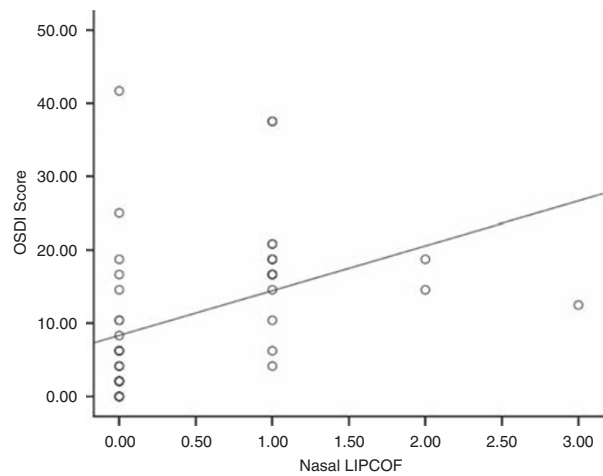**Figure 3** Nasal LIPCOF was significantly correlated to OSDI scores.

Figure 2 NIBUT was significantly correlated to OSDI scores.

tear film tests with an area under the ROC (AUC) of 0.895 and nasal LIPCOF was the best discriminator of the ocular signs (AUC = 0.828). A combination of NIBUT and nasal LIPCOF resulted in an improved predictive ability (AUC = 0.94; Figure 4).

$$OSDI + / - = -0.227 \times NIBUT + 2.841 \times nasal\,LIPCOF + 1.816$$

This test combination, here named Dry Eye Test Combination (DTC), was significantly correlated to OSDI scores (Pearson, $r = 0.558$, $P < 0.001$) (Figure 5). The power calculation of the completed study resulted in a power of >0.92.

Table 4 Area under the ROC (AUC), P-value (P), 95% confidence interval of AUC, threshold (TH), sensitivity, and specificity

	AUC	P	95% Confidence interval		TH	Sensitivity	Specificity
TMH	0.715	0.013	0.565	0.865	0.2 (ref. 66)	0.65	0.65
NIBUT	0.895	<0.001	0.791	1.000	10.0 (ref. 65)	0.80	0.93
Temporal LIPCOF	0.748	0.004	0.603	0.893	2 (ref. 19)	0.60	0.81
Nasal LIPCOF	0.828	<0.001	0.698	0.957	1 (ref. 19)	0.73	0.91
LIPCOF Sum	0.816	<0.001	0.687	0.945	2 (ref. 19)	0.70	0.81
Bulbar hyperaemia	0.664	0.057	0.501	0.827	2.35[a]	—	—
Limbal hyperaemia	0.509	0.914	0.341	0.678	2.05[a]	—	—
PRTT	0.781	0.001	0.642	0.919	10 (ref. 70)	0.25	0.93
Corneal staining	0.519	0.830	0.349	0.688	0.1[a]	—	—
Conjunctival staining	0.506	0.949	0.337	0.674	1.0[a]	—	—
LWE	0.749	0.004	0.597	0.901	1 (ref. 19)	0.48	0.96
Dry eye test combination	0.944	<0.001	0.865	1.024	−0.19[a]	0.90	0.89

Abbreviations: LIPCOF, lid-parallel conjunctival fold; LWE, lid-wiper epitheliopathy; NIBUT, non-invasive break-up time; PRTT, phenol red thread test; TMH, tear meniscus height.
[a]Thresholds derived from this data set.

Table 5 Median scores, interquartiles of the significant discriminators of OSDI +/−

	Normal		Dry eye	
	Median	Interquartiles	Median	Interquartiles
TMH	0.20	0.20–0.30	0.18	0.10–0.20
NIBUT	21.00	15.30–30.00	7.70	5.93–9.78
PRTT	22.00	16.00–23.00	10.00	14.5–17.75
Temporal LIPCOF	1.00	0.00–1.00	2.00	1.0–2.0
Nasal LIPCOF	0.00	0.00–0.00	1.00	0.25–1.00
LIPCOF Sum	1.00	0.00–2.00	3.00	2.00–3.00
LWE	0.00	0.00–0.00	0.75	0.00–2.00

Abbreviation: LIPCOF, lid-parallel conjunctival fold; LWE, lid-wiper epitheliopathy; NIBUT, non-invasive break-up time; PRTT, phenol red thread test; OSDI, Ocular Surface Disease Index; TMH, tear meniscus height.
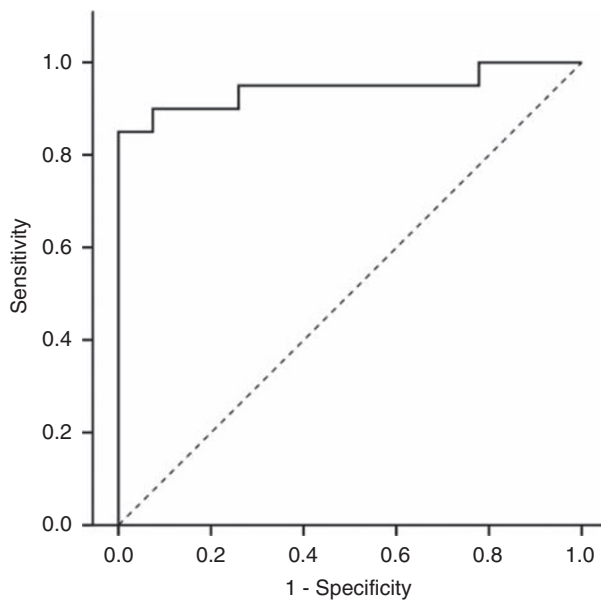

Figure 5 NIBUT combined with nasal LIPCOF was significantly correlated to OSDI scores.

Figure 4 Discrimination of dry eye symptoms by a combination of NIBUT and nasal LIPCOF.

Discussion

The subjects in this sample of a cohort of non-contact lens wearers presented with ocular signs within a relatively normal range (Table 6). The evaluated low LWE grades (77% ⩽1) are comparable to values reported by Korb et al,[15] where 82% of the subjects presented with LWE grade ⩽1. The bulbar hyperaemia median score (CCLRU 2.3) and limbal hyperaemia median scores (CCLRU 2.0) were slightly higher than published norms, but within normal confidence limits.[39,50] Median ocular staining of this cohort was at a normal level.[38,51,52] For LIPCOF, this is the first time that median scores have been reported in non-contact lens wearers (1/0/1 (temporal/nasal/Sum)), which is less than that reported in experienced soft contact lens wearers (2/0/2).[17,19] Interestingly, while the prevalence of dry eye is known to be increased in elderly women,[53,54] no gender bias was found in the tests

Table 6 Median scores, interquartiles and range (min–max) of clinical tests

	Median	Inter-quartiles	Mini-mum	Maxi-mum
TMH	0.20	0.15–0.30	0.05	0.40
NIBUT	15.20	8.10–25.00	2.50	45.00
PRTT	18.00	12.00–22.00	7.00	30.00
Temporal LIPCOF	1.00	0.00–2.00	0.00	3.00
Nasal LIPCOF	0.00	0.00–1.00	0.00	3.00
LIPCOF Sum	1.00	0.00–3.00	0.00	5.00
Bulbar hypereamia	2.30	1.80–2.80	1.20	3.20
Limbal hypereamia	2.00	1.80–2.80	1.00	3.60
Corneal staining	0.00	0.00–0.00	0.00	1.74
Conjunctival staining	0.00	0.00–0.00	0.00	3.00
LWE	0.00	0.00–0.50	0.00	3.00
OSDI score	8.33	2.08–16.67	0.00	41.67

Abbreviations: LIPCOF, lid-parallel conjunctival fold; LWE, lid-wiper epitheliopathy; NIBUT, non-invasive break-up time; PRTT, phenol red thread test; OSDI, Ocular Surface Disease Index; TMH, tear meniscus height.

in this study. This may be due to the mild nature of the dry eye symptoms reported by this subject cohort.

Both temporal and nasal LIPCOF were significantly correlated to LWE, as well as to ocular hyperaemia, whereas nasal LIPCOF was able to do so for bulbar hyperaemia only. In addition, LWE and LIPCOF were significantly correlated to tear film stability and tear volume. These findings reflect the hypothesised mechanical origin of LIPCOF and LWE.[15,17–19] In LWE, squamous cells are visible at the lid wiper, which is in contact with the bulbar conjunctiva where the tear film is insufficient[15] and/or reduced mucin quantity exists.[17,18] Squamous epithelial cells are a feature of tissues that experience frequent rubbing,[15] and their presence in the particular region of the lid wiper[55] infers that this area of the marginal conjunctiva is intimately and mechanically associated with the surfaces of the oculus bulbi.

Tear film volume is reported to be an important contributor to a stable tear film,[47,56–59] and in this study the positive correlations observed between NIBUT and both TMH and PRTT strengthens this theory. Mainstone et al[58] reported a significant negative correlation between tear volume and staining, whereas others found none.[57,60] No significant correlations were found between tear volume and ocular surface staining in this study. However, this might be due to the severity of the dry eye groups in the other studies. The frequency of dry eye symptoms in the cohort observed in this study was measured by use of the OSDI, a 12-item patient-reported outcome questionnaire designed to quantify ocular disability due to dry eye disease. Subjects evaluated in this study represent mild-to-moderate dry eye rather than severe dry eye.[61,62]

No correlations between dry eye symptoms and conjunctival and corneal staining, as well as bulbar and limbal hyperaemia, were observed in this cohort of marginal dry eye patients. These findings are in accordance with current literature, where the poor relationships between ocular signs and dry eye symptoms are criticised.[8–11,19] However, the use of a composite index might have shown a stronger relationship between staining and dry eye severity, as reported by Sullivan et al.[63] The classic tests TMH, NIBUT, and PRTT, as well as the new LIPCOF (nasal and temporal) and LWE tests were significant correlated to dry eye symptoms (Table 2), although these correlations varied in their strengths. The relationship between LWE and dry eye symptoms investigated in this study confirms the findings of Korb et al,[15] where LWE was reported to correlate to symptoms as determined by the total Standard Patient Evaluation of Eye Dryness (SPEED) score. LIPCOF has been shown to relate to dry eye symptoms in experienced contact lens wearers[19] as well as naive contact lens wearers,[13] and this study strengthens the usefulness of LIPCOF in non-contact lens wearers as well.

The predictive ability of the evaluated tests to distinguish between those subjects classified as having dry eye (OSDI score $\geqslant 15$, OSDI $+$) and those classified as non-dry eye (OSDI$-$) was analysed by ROC. In a ROC curve, the true positive rate (sensitivity) is plotted as a function of the false positive rate (1-specificity) for different cut-off points of a parameter. The resulting AUC is a measure of how well a parameter can distinguish between two diagnostic groups (OSDI $+$ / OSDI$-$). In addition to the AUC, the corresponding P-value indicates if the AUC is significant larger than an AUC of 0.5 (no discrimination). If the P-value is lower than 0.05 then it can be concluded that the AUC is significantly different from 0.5 and, therefore, there is evidence that the test has an ability to distinguish between the two subject groups. Classification of AUC is reported as: 0.5 indicates no discrimination, between 0.7 and 0.8 indicates acceptable discrimination, >0.8 indicates excellent discrimination and >0.9 outstanding discrimination.[64] According to this classification, NIBUT, nasal LIPCOF, and LIPCOF Sum were excellent discriminators, and TMH, PRTT, temporal LIPCOF, and LWE were acceptable discriminators. These results are not surprising, since NIBUT,[13,65] TMH,[58,66] PRTT,[46,47] LIPCOF,[13,16,18,19] and LWE[15,18,19] are accepted tests in dry eye assessment. Even though bulbar hyperaemia approached significance ($P = 0.055$), its AUC was too small to be a predictive discriminator. All other tests were not able to discriminate between symptomatics and asymptomatics (OSDI $+$ /$-$). This is in accordance with clinical experience and the published

literature, where ocular signs like conjunctival and corneal staining or ocular hyperaemia are found to have a poor ability to detect dry eye in mild to moderate cases.[2,9,10,14,57,67,68]

Using a combination of tests has been recommended to improve the predictive ability for dry eye.[9,12–14,63] However, there is no agreement on which tests should be combined and, to our knowledge, it was unknown before this study whether LWE and LIPCOF would be able to help such a combination of tests in non-contact lens wearers. Since a combination of LIPCOF Sum and NIBUT showed an improved predictive ability for later contact lens related dry eye symptoms in naive contact lens wearers,[13] a comparable combination appeared to be obvious in non-contact lens wearers. The best test combination was calculated by logistic regression analysis (forward: LR), where each variable was automatically added until best predictive ability of OSDI +/− was achieved. This analysis resulted in a formula, combining NIBUT with nasal LIPCOF, which gave an outstanding[64] discrimination of OSDI +/−.

It is somewhat surprising that temporal LIPCOF was excluded by this analysis. Previous work demonstrated an association between temporal LIPCOF and an objective SICCA score in dry eye patients[16] and prior findings of our group have indicated the usefulness of both nasal LIPCOF and temporal LIPCOF as notable tests in lens wearers.[13,18,19] Höh et al[16] reported significantly increased temporal LIPCOF grades in dry eye patients, although no relationship between nasal LIPCOF and dry eye was found in their study. However, in this study, we classified LIPCOF using an optimised grading scale,[13,17–19] rather than the 'LIPCOF score' published by Höh et al,[16] which evaluated the height of the set of folds in comparison to the tear meniscus height.[16,69] Previous findings of our group suggested an improvement of the predictive ability of LIPCOF using a new classification,[13,17] where the LIPCOF score is not derived from the height of the folds, but from the number of lid-parallel conjunctival folds that accumulate one above the other.[17]

This optimised LIPCOF score enhanced the evaluation of both temporal and nasal LIPCOF, but nasal LIPCOF performed better than temporal LIPCOF and even LIPCOF Sum. Even though the correlations between LIPCOF (temporal, nasal, Sum) and OSDI scores were moderate only, LIPCOF was a good discriminator between normal and mild dry eyes, especially nasal LIPCOF. The results suggest the importance of preferentially evaluating nasal LIPCOF—not only temporal LIPCOF[16]—in dry eye assessment in clinical practice. A combination of nasal LIPCOF and NIBUT might be useful as a quick screening test to detect mild dry eye patients in clinical practice.

Conclusions

To our knowledge, this is the first time that the relationships between single dry eye tests and LIPCOF (temporal, nasal, Sum), as well as the ability of LIPCOF to detect dry eye symptoms, analysed by a validated dry eye questionnaire, have been evaluated in a cohort of normal non-contact lens wearers. LIPCOF and LWE were related, as was found in contact lens wearers in a prior investigation,[18,19] and also related to tear film stability and volume. The tear film tests NIBUT, TMH, and PRTT, as well as the ocular signs LIPCOF and LWE, were significantly increased in symptomatics. The most predictive single tests were NIBUT, nasal LIPCOF, and LIPCOF Sum. A combination of NIBUT and nasal LIPCOF (here named Dry Eye Test Combination (DTC)), showed the best predictive ability of dry eye symptoms in this cohort of non-contact lens wearers. These findings underline the importance of evaluating NIBUT and nasal LIPCOF in the daily clinical routine, even in apparently healthy subjects, to detect mild to moderate dry eye.

Summary

What was known before
- Relations between nasal and temporal lid-parallel conjunctival folds and dry eye symptoms in contact lens wear.

What this study adds
- Relations between nasal and temporal lid-parallel conjunctival folds and dry eye symptoms in non-contact lens wearers. Their predictive ability of dry eye symptoms. Best test combination useful as screening test to detect mild dry eye patients in clinical practice.

Conflict of interest

The authors declare no conflict of interest.

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