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Article

# Impact of Dry Eye Disease on Vision Quality: An Optical Quality Analysis System Study

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**Purpose:** We evaluated the relationship between ocular surface clinical tests and quality of vision in patients with dry eye disease (DED).

**Methods:** In this study, 136 eyes of 72 dry eye patients were evaluated retrospectively using the ocular surface disease index (OSDI), measurement of tear film break-up time (TBUT), the Oxford score, Van Bijsterveld score, and Schirmer I test. Quality of vision was assessed with the optical quality analysis system (OQAS) using the objective scatter index (OSI) recorded over 20 seconds without blinking. Correlations between dry eye symptoms and signs, and OSI measurements were evaluated.

**Results:** The OSI and OSI standard deviation (OSI SD) were correlated with TBUT ($r = -0.21$, $P = 0.013$ and $r = -0.18$, $P = 0.038$, respectively), Oxford score ($r = 0.31$, $P = 0.0002$ and $r = 0.18$, $P = 0.032$, respectively), and the Van Bijsterveld score ($r = 0.33$, $P = 0.0001$ and $r = 0.25$, $P = 0.003$, respectively). The OSI also was correlated with the Schirmer test ($r = -0.19$, $P = 0.025$), OSDI ($r = 0.17$, $P = 0.04$), and the ocular symptoms subscale of the OSDI ($r = 0.21$, $P = 0.01$). OSI SD was correlated with the environmental triggers subscale of the OSDI ($r = 0.21$, $P = 0.016$).

**Conclusions:** Quality of vision measured with the OQAS was correlated with dry eye symptoms and signs. The OQAS could be a useful tool to better evaluate visual function in patients with DED.

**Translational Relevance:** The OQAS provides a better understanding of patient complaints about alteration of vision quality. It might be useful to integrate this objective system in severity assessments and follow-up of DED, especially for treatment evaluations.

## Introduction

Dry eye disease (DED) is a multifactorial disease of the tears and ocular surface. It is estimated to affect approximately 5% to over 50% of the population, depending on the diagnostic criteria, sex, and age.[1,2] DED is a symptomatic disease that combines ocular surface pain or discomfort and impaired visual function,[3,4] which greatly decreases patient quality of life.[5,6]

The optical quality of the retinal image results from light passing through the ocular structures. The precorneal tear film is the first structure that influences the optical light path, and optical quality of the eye surface depends largely on its properties.[7] In DED patients, there is a deficiency in tear secretion quantity and/or quality that leads to tear film irregularities and early break-up. Consequently, it induces aberrations and scattering in the optical system and reduces retinal image quality.[8] Studies using the Hartmann-Shack wavefront sensor aberrometer showed image aberrations in DED,[9,10] but ignored the scattering effect, and, thus, may have overestimated optical quality in these patients.[11]

More recently, the optical quality analysis system (OQAS; OQAS II; Visiometrics S.L., Tarrasa, Spain), a double-pass (DP) system aberrometer, was used to evaluate the aberrations and scattering induced by the optical system and tear film during the interblink period,[12–14] showing good reproducibility.[15,16] OQAS is a noninvasive instrument that records images of a monochromatic point source after reflection on the retina and a double pass through the ocular media. It was developed to provide an objective evaluation of the optical quality of ocular structures. The tear film analysis program of OQAS records dynamic changes of the objective scatter index (OSI) values and calculates the mean value of the OSI over 20 seconds and its standard deviation (OSI SD). These changes in OSI values stem from tear film dynamic alterations, since opacity of the cornea, lens, or vitreous body does not vary over such a short period. In a previous study using OQAS on a small number of patients with DED, our group already showed decreased optical quality demonstrated by increased parameters on the OSI and its OSI SD in groups with different levels of dry eye severity compared to control subjects.[14] However, to date no clear data exist showing a direct correlation between clinical tests and objective parameters of optical quality in DED.

Therefore, we assessed the relationship between visual quality and clinical tests used to evaluate DED symptoms and signs on a larger DED population.

## Patients and Methods

### Patients

In this retrospective study, 136 eyes of 72 patients, diagnosed with DED at the Center for Clinical Investigation of the Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts (CIC INSERM 1423), Paris, France, were evaluated between February 2014 and March 2016. DED was diagnosed by the association of ocular symptoms, tear film abnormalities (tear break-up time [TBUT] $<$ 10 seconds and/or Schirmer test $<$ 10 mm) with or without ocular surface damage (corneal and conjunctival staining) according to the 2007 International Dry Eye Workshop criteria.[17] Exclusion criteria were contact lens wear within the past 3 months, best-corrected visual acuity (BCVA) $<$ 20/20, use of a topical treatment the day of examination, spherical error $>$ 6 diopters, history of ocular surgery, trauma or other ocular disease, or treatment that may have influenced the ocular surface. The study protocol followed the tenets of the Declaration of Helsinki and informed consent was obtained from all patients. Ethics committee approval was obtained from the Comité de Protection des Personnes (Ile de France V, agreement number 10793).

### Questionnaire and Clinical Examination

All patients underwent a complete analysis of the ocular surface including, in this order, the ocular surface disease index (OSDI) symptoms questionnaire, OQAS, TBUT, ocular surface fluorescein staining (grades 0–15, according to the Oxford score), lissamine green staining (0–9, according to the van Bijsterveld score), and finally a Schirmer I test.

Before clinical examination, the disease-specific OSDI questionnaire was completed by the patients. This included three subscales: ocular symptoms (OSDI-symptoms) composed of five questions, vision-related activities of daily living (OSDI-function) composed of four questions, and environmental triggers composed of three questions. The 12 items of the OSDI were graded on a scale of 0 to 4: 0, none of the time; 1, some of the time; 2, half of the time; 3, most of the time, and 4, all of the time. Each subscale (0–100) was computed, as well as an overall averaged score (0–100).[18]

Visual quality was evaluated with the OQAS, which records and analyzes double-pass retinal images of a point source. The OQAS uses a laser diode with a 780-nm wavelength. After reflection in the retina and a double pass through the ocular media, the light was recorded by a charge-coupled camera device. The DP images were acquired at best focus, corrected internally in the instrument by an optometer. Aberrations and intraocular scattering were evaluated using the OSI, defined as the ratio of the intensity at an eccentric location in the DP image and central area, representing the impact of the ocular structures on the DP image caused by aberration and scattering. In this study, serial measurements were taken just after blinking and then at 0.5-second intervals over 20 seconds, with the subject instructed to avoid blinking. The blink period was eliminated for measurement of the mean OSI (Fig. 1). Optical quality changes were acquired before any clinical ocular surface tests. The two parameters analyzed were OSI (mean value of the OSI over 20 seconds) and OSI SD.

TBUT was measured with fluorescein 0.5% (Fluoresceine Faure, single-dose 0.4 mL; Serb, Brussels, Belgium) instilled in the lower fornix. The patient was allowed to blink at a spontaneous rate, and the

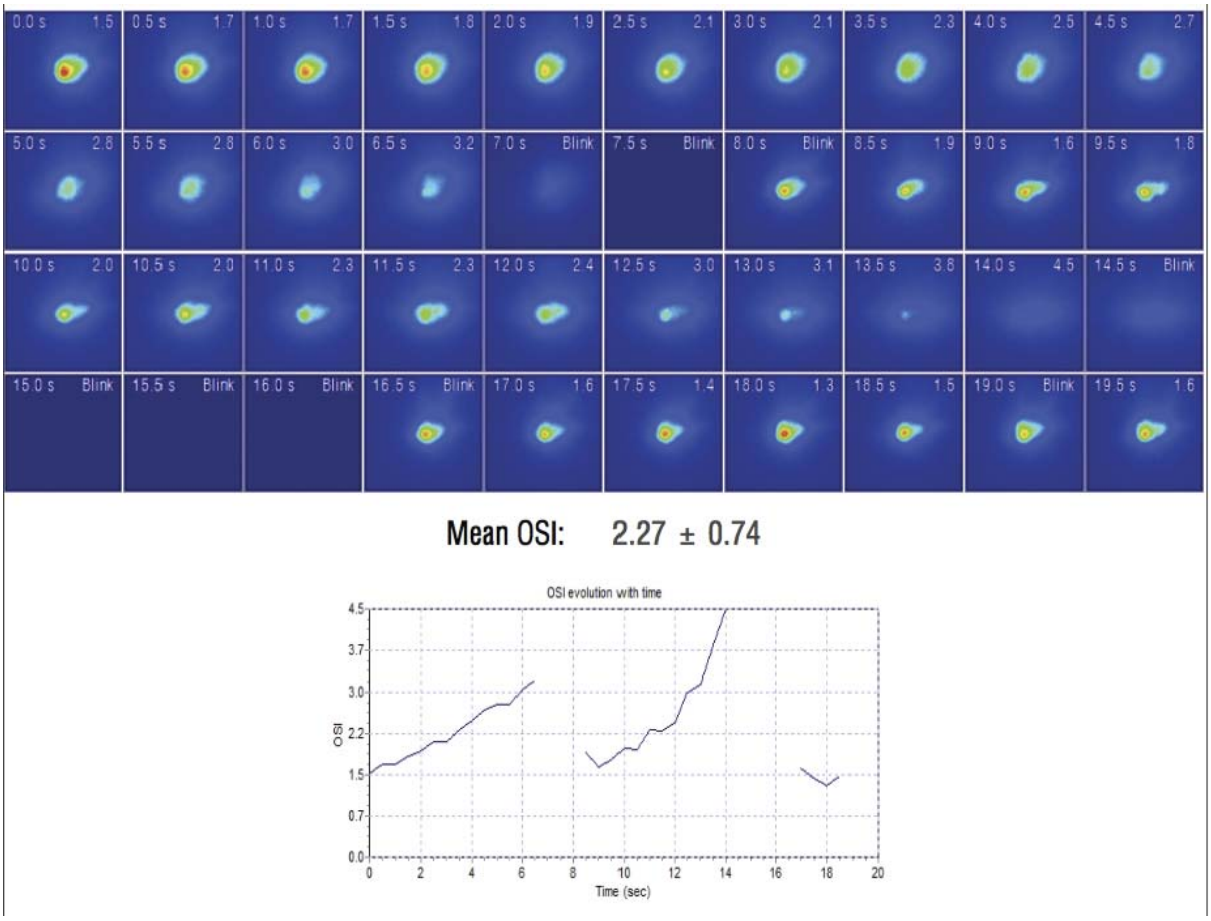


**Figure 1.** Example of tear film analysis with the OQAS. A series of 40 consecutive images was recorded. *Blank images* indicate the blinking periods. The OSI and OSI SD were calculated over a period of 20 seconds.

elapsed time from the last blink to the appearance of the first break in the continuous layer of fluorescein, as observed under cobalt blue light through a yellow filter, was measured in seconds. Ocular surface fluorescein staining was graded 0 to 5 in each of three zones (nasal conjunctival area, cornea, temporal conjunctival area), and grade 0 to 15, according to the Oxford score.

The van Bijsterveld score was measured after instillation of 1% lissamine green with ophthalmic strips (GreenGlo; Sigma Pharmaceuticals, Croydon, UK). Staining was graded on a scale of 0 to 3 in the exposed nasal and temporal bulbar conjunctiva and cornea, with a total maximum score of 9.

For the Schirmer test, the extremity of a paper strip (Schirmer-Plus Gecis, Neung-sur-Beuvron, France) was placed in the lower eyelid without anesthesia and eyes open. After 5 minutes, the filter paper was removed and the distance between the leading edge of wetness and the initial fold was measured, with the result given in mm/5 min.

## Statistical analysis

Demographic data were presented as mean ± SD. A Spearman correlation test was used to evaluate the correlation between OQAS parameters and the results of the DED tests. A $P < 0.05$ was considered statistically significant.

# Results

A total of 136 eyes of 72 patients with DED (58 females, 14 males; mean age, 49.2 ± 17.3 years; range, 16–83 years) were evaluated. Mean OSDI score was 54.5 ± 23.6 (range, 4.2–93.75), mean TBUT was 5.3 ± 2.7 (range, 0–10) seconds, and mean Schirmer I test was 14.6 ± 9.7 (range, 0–35) mm. Mean Oxford score was 1.1 ± 1.5 (range, 0–7) and mean van Bijsterveld score was 1.7 ± 2 (range, 0–8). According to the 2007 Dry Eye Workshop, the average level of dry eye severity was moderate in our

**Table 1.** Demographic Information and Clinical Test Results: Patient Demographics and Clinical Characteristics ($n = 72$ Patients, 136 Eyes)

| | Mean ± SD (range) |
|---|---|
| Gender | Males (25 eyes)/58 females (111 eyes) (23/77%) |
| Age | 49.2 ± 17.3 (16/83) |
| OSDI | |
| Overall score (0–100) | 54.5 ± 23.6 (4.2/93.75) |
| Symptoms (0–100) | 53.5 ± 23. (10/100) |
| Functions (0–100) | 45.1 ± 29.9 (0/100) |
| Environmental triggers (0–100) | 55.5 ± 33.6 (0/100) |
| TBUT, s | 5.3 ± 2.7 (0/10) |
| Oxford (0–15) | 1.1 ± 1.5 (0/7) |
| Van Bijsterveld (0–9) | 1.7 ± 2 (0/8) |
| Schirmer test, mm/5 min (0–35) | 14.6 ± 9.7 (0/35) |
| OSI (0–25) | 1.9 ± 1.55 (0.4/9.3) |
| OSI SD | 0.47 ± 0.51 (0.05/2.9) |

population. Mean OSI and OSI SD were 1.9 ± 1.55 (range, 0.4–9.3) and 0.47 ± 0.51 (range, 0.05–2.9) , respectively. Demographic and clinical data are presented in Table 1.

Concerning clinical tests, the OSDI was correlated with TBUT only ($r = -0.23$, $P = 0.02$). TBUT was correlated with other clinical tests, such as Oxford score ($r = -0.33$, $P < 0.0001$), van Bijsterveld score ($r = -0.42$, $P < 0.0001$), and the Schirmer I test ($r = 0.26$, $P = 0.002$). Oxford score correlated with van Bijsterveld score ($r = 0.73$, $P < 0.0001$) and the Schirmer I test ($r = -0.25$, $P = 0.004$). The van Bijsterveld score and Schirmer I test also were correlated ($r = -0.25$, $P = 0.004$). The results of dry eye clinical test correlations are shown in Table 2.

Considering vision quality parameters, the OSI and OSI SD were correlated with TBUT ($r = -0.21$, $P = 0.013$ and $r = -0.18$, $P = 0.038$, respectively), Oxford score ($r = 0.31$, $P = 0.0002$ and $r = 0.18$, $P = 0.032$, respectively), and van Bijsterveld score ($r = 0.33$, $P = 0.0001$ and $r = 0.25$, $P = 0.003$, respectively). The OSI also was correlated with the OSDI ($r = 0.17$, $P = 0.04$) and Schirmer test ($r = -0.19$, $P = 0.025$). There were no correlations between OSI SD and OSDI ($r = 0.12$, $P = 0.17$) and the Schirmer test ($r = -0.11$, $P = 0.192$). The results of correlations between quality of vision and clinical tests are presented in Table 3.

When analyzing the correlation between OSDI subscales and clinical tests, TBUT was correlated with all subscales: ocular symptoms, vision-related function, and environmental triggers ($r = -0.16$, $P = 0.05$; $r = -0.27$, $P = 0.002$; and $r = -0.18$, $P = 0.05$, respectively). OSI was correlated with the ocular symptoms subscale ($r = 0.21$, $P = 0.01$), but not with the vision-related function and environmental triggers subscales ($r = 0.06$, $P = 0.48$ and $r = 0.09$, $P = 0.28$, respectively). OSI SD was correlated only with the environmental triggers subscale ($r = 0.21$, $P = 0.016$), but not with ocular symptoms and vision-related function subscales ($r = 0.08$, $P = 0.35$ and $r = 0.03$, $P = 0.74$, respectively). Results of the correlations between OSDI overall score and subscales with all tests in DED patients are presented in Table 4.

**Table 2.** Correlations Between the Different Clinical Tests ($n = 136$ Eyes)

| | OSDI Score | TBUT | Oxford | Van Bijsterveld | Schirmer |
|---|---|---|---|---|---|
| OSDI score | | | | | |
| | *r* | −0.23[a] | 0.11 | 0.05 | −0.12 |
| | *P* | 0.022[a] | 0.224 | 0.562 | 0.174 |
| TBUT | | | | | |
| | *r* | | −0.33[a] | −0.42[a] | 0.26[a] |
| | *P* | | <0.0001[a] | <0.0001[a] | 0.002[a] |
| Oxford | | | | | |
| | *r* | | | 0.73[a] | −0.25[a] |
| | *P* | | | <0.0001[a] | 0.004[a] |
| Van Bijsterveld | | | | | |
| | *r* | | | | −0.25[a] |
| | *P* | | | | 0.004[a] |

[a] Signifies correlations between parameters.

**Table 3.** Correlations Between the OSI and OSI SD With the Different Clinical Tests

| | OSDI Score | BUT | Oxford | Van Bijsterveld | Schirmer | Age | Sex | OSI SD |
|---|---|---|---|---|---|---|---|---|
| OSI | | | | | | | | |
| *r* | 0.17[a] | −0.21[a] | 0.31[a] | 0.33[a] | −0.19[a] | 0.36[a] | 0.01 | 0.71[a] |
| *P* | 0.038[a] | 0.013[a] | 0.0002[a] | 0.0001[a] | 0.025[a] | <0.0001[a] | 0.91 | <0.0001[a] |
| OSI SD | | | | | | | | |
| *r* | 0.12 | −0.18[a] | 0.18[a] | 0.25[a] | −0.11 | 0.13 | −0.07 | |
| *P* | 0.167 | 0.038[a] | 0.032[a] | 0.003[a] | 0.192 | 0.126 | 0.43 | |

[a] Signifies correlations between parameters.

## Discussion

We observed a direct correlation between optical quality evaluated with OSI and OSI SD, and dry eye clinical test results and symptoms. Poor optical quality was observed in patients with DED correlated with its clinical severity. Most patients with DED have a normal BCVA; however, these patients also complain of blurred or fluctuating vision because of tear film instability and/or poor quality, and the induced aberrations and scattering.[12,13] Alterations of the optical quality of the eye in mild-to-moderate DED patients is largely underestimated by ophthalmologists. Nevertheless, DED has a real impact, altering vision quality, on patients and their quality of life and work productivity.[19,20] In clinical practice, there is a weak correlation between the different ocular surface tests and symptoms reported by patients with DED.[21,22] As the clinical tests used to evaluate dry eye in practice do not assess optical quality of the ocular surface, this may explain at least in part the absence of a correlation between symptoms and signs in these patients. Consequently, it might be useful to have a device that evaluates optical quality alterations in DED patients that can be used easily in clinical practice.

Many studies have evaluated tear film behavior and its impact on optical quality with interferometry, retroillumination,[23] videokeratoscopy,[24] Hartmann-Shack aberrometry and more recently the double-pass (OQAS) method,[12] as in our study. Improvement of these techniques has increased our knowledge on the impact of DED[11] on vision quality. In one of the first studies analyzing DED with OQAS, Benito et al.[12] showed that patients with mild dry eye had more scattering and aberrations with an increase in the intensity distribution index over time compared to control patients. The intensity distribution index was

**Table 4.** Results of Correlations Between the OSDI Overall Score and Subscales With Dry Eye Clinical Tests ($n$ = 136 Eyes)

| | TBUT | Van Bijsterveld | Oxford | Schirmer | OSI | OSI SD | Environmental Triggers | Vision-related Function | Symptoms |
|---|---|---|---|---|---|---|---|---|---|
| OSDI | | | | | | | | | |
| Overall score | | | | | | | | | |
| *r* | −0.23[a] | 0.05 | 0.1 | −0.12 | 0.18[a] | 0.12 | 0.68[a] | 0.84[a] | 0.87[a] |
| *P* | <0.0001[a] | 0.56 | 0.22 | 0.17 | 0.04[a] | 0.17 | <0.0001[a] | <0.0001[a] | <0.0001[a] |
| Symptoms | | | | | | | | | |
| *r* | −0.16[a] | −0.03 | 0.06 | −0.12 | 0.21[a] | 0.08 | 0.49[a] | 0.66[a] | |
| *P* | 0.05[a] | 0.72 | 0.45 | 0.17 | 0.01[a] | 0.35 | <0.0001[a] | <0.0001[a] | |
| Vision-related function | | | | | | | | | |
| *r* | −0.27[a] | 0.13 | 0.14 | −0.11 | 0.06 | 0.03 | 0.43[a] | | |
| *P* | 0.002[a] | 0.13 | 0.12 | 0.18 | 0.48 | 0.74 | <0.0001[a] | | |
| Environmental triggers | | | | | | | | | |
| *r* | −0.18[a] | 0.04 | −0.05 | 0.03 | 0.09 | 0.21[a] | | | |
| *P* | 0.05[a] | 0.67 | 0.55 | 0.75 | 0.28 | 0.016[a] | | | |

[a] Signifies correlations between parameters.

equivalent to OSI and corresponded to the ratio of the light intensity at an eccentric location in the image and central part. In a previous study by our group, Tan et al.[14] developed and evaluated new OSI parameters, that is the mean value of the OSI changes (ΔOSI) and mean value of the OSI SD in 56 eyes with DED and 35 control subjects. They observed that the OSI SD increased significantly with the levels of dry eye severity, a finding similar to the results of our study on 136 eyes. Similar results were observed considering the OSI SD and its correlation to the Oxford and van Bijsterveld corneal staining scores, but in the latter study we also showed a significant correlation between the OSI SD and TBUT. Furthermore, we used the OSI parameter, which was not evaluated in the study by Tan et al.,[14] and we found more correlations with this simple parameter directly given by the OQAS software without the complex calculation processes, as we did in our first study. Interestingly, OSI was correlated with all clinical tests (TBUT, Oxford score, van Bijsterveld score, and Schirmer test) as well as OSDI. To our knowledge, to date no study has observed a correlation between the OSI parameter with all clinical tests and OSDI.

It is important to analyze the OSI and OSI SD to assess optical quality in DED patients. The OSI corresponds to an estimate of the average diffusion of the eye's entire optical system over 20 seconds. Although it is correlated with dry eye severity, OSI can be influenced by the cornea, lens, vitreous, or some other cause of light scattering within the optical system, and it is correlated with age. In contrast, OSI SD is only due to tear film alterations, since opacity of the cornea, lens, or vitreous does not vary over such a short period.[25] This might explain why the OSI SD was correlated with TBUT and not with age. Surprisingly, the Schirmer 1 test was correlated with OSI but not with OSI SD. Visual quality might be more closely related to the quality of the tear film, in terms of homogeneity and regularity, than to the quantity of reflex tear secretion evaluated by the Schirmer 1 test. The correlation between OSI and the Schirmer test could be explained by the corneal alterations secondary to DED, such as epithelial keratitis or corneal irregularities. Nevertheless, this result emphasizes the poor clinical value of the Schirmer 1 test[26–28] in evaluating the extent of vision impairment in patients with DED. Indeed, the Schirmer 1 test can give opposite values depending on the type of DED, with a normal or even high value for evaporative DED, as found in meibomian gland dysfunction.[29,30]

A reduction in optical quality highly impacts quality of life, even though the BCVA is considered normal with standard charts. The OSDI questionnaire was developed to assess the vision-related health-targeted quality of life in DED patients.[18] The OSDI analyses three subscales: vision-related function, ocular symptoms, and environmental triggers. In our study, the three OSDI subscales were correlated with TBUT, but not with the other clinical tests. This result was already shown in many studies and confirmed the weak correlation between signs and symptoms in DED.[31–33] Interestingly, in our study, the OSI was correlated with OSDI score and particularly with the ocular symptoms subscale (sensitivity to light, grittiness, pain, blurred vision, and poor vision). This result suggested that tear film instability induced aberrations and scattering, and consequently fluctuating vision that is perceived by patients. However, we did not observe a correlation between OSI and the vision function-related subscale of the OSDI. Similarly, this subscale correlated the least with other clinical tests, such as TBUT, the Schirmer I test, Oxford score, and van Bijsterveld score, as demonstrated by Schiffman et al.[18] This subscale evaluating the impact of ocular surface diseases on vision-related activities of daily living might be not be sensitive for evaluation of quality of vision of patients with DED. Interestingly, the OSI SD correlated with the environmental triggers subscale of the OSDI. Environmental conditions, such as cold and dry air, affect tear film stability and function, with decreased TBUT[34] and an increased tear evaporation rate,[35] and might have a direct impact on quality of vision in patients with DED.

Some limitations, including the retrospective nature of this study, should be considered when interpreting the results. First, although significant, a low strength of correlation between OSI and OSI SD with dry eye clinical tests was observed. The variability and low reproducibility of DED clinical tests, often uncorrelated, are reported frequently in DED studies and might explain these results. The sex differences in our sample with a higher number of women compared to men also is a limitation. Nevertheless, the higher prevalence of DED in women has been reported in numerous studies.[1,2] Moreover, as there was no difference between men and women for the optical quality parameters OSI and OSI SD in our study, this might not have influenced the results.

The quality of vision alterations and symptoms probably are underestimated in patients with DED and poorly evaluated with classical clinical tests. The

high number of patients included has allowed us to evaluate the correlation between dry eye severity, the result of clinical tests, and quality of vision in patients with DED. The OQAS provides a better understanding of patient symptoms and complaints, in particular considering the alteration of vision quality, and it might be useful to integrate quality-of-vision parameters in severity assessments or treatment evaluations. It is regrettable that, in the new definition from the DEWS II, there no longer was mention of the visual impact of DED, although new tests reliably analyze this, and the impact of poor vision on quality of life now is recognized. It could be suggested that visual impairment be included again in the definition of DED to avoid under-recognition of this important aspect of the disease by general ophthalmologists, and we would encourage practitioners to consider testing it more widely with the objective methods currently available.

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