The Effect of Ocular Surface Regularity on Contrast Sensitivity and Straylight in Dry Eye

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PURPOSE. To investigate the association between visual function and ocular surface regularity in dry eye.

METHODS. We enrolled 52 eyes of 52 dry eye patients (34 dry eyes with superficial punctate keratopathy [SPK] in the central corneal region [central SPK] and 18 dry eyes without central SPK) and 20 eyes of 20 normal control subjects. All eyes had a best-corrected distance visual acuity better than 20/20. We measured two indices of contrast sensitivity function under photopic conditions: contrast sensitivity and letter contrast sensitivity. The area under the log contrast sensitivity function (AULCSF) was calculated from the obtained contrast sensitivity data. Straylight was quantified using a straylight meter.

RESULTS. Dry eyes with central SPK had significantly decreased contrast sensitivity function, including AULCSF and letter contrast sensitivity than those without central SPK and normal eyes ($P < 0.05$ for each). While the straylight values in both dry eye groups did not differ, straylight values were greater than those in normal eyes ($P < 0.05$ for both). In dry eye, the AULCSF and letter contrast sensitivity negatively correlated with the central SPK score ($R = -0.485$, $P < 0.001$, and $R = -0.541$, $P < 0.001$, respectively).

CONCLUSIONS. In dry eye, reduced contrast sensitivity in part results from central SPK overlying the optical zone and the increased straylight results from tear film instability rather than central SPK.

Keywords: dry eye, contrast sensitivity, straylight

Currently, dry eye is defined as a multifactorial disease of the tears and ocular surface that may cause visual disturbance.[1] The ocular surface including the tear film maintains ocular comfort of the eye and provides a smooth refractive surface allowing good-quality vision. Particularly, surface regularity of the central part of the cornea overlying the entrance pupil is important in term of visual function. In clinical practice, fluorescein dye is frequently used for ocular staining, and dry eye commonly appears as interpalpebral or inferior superficial punctate keratopathy (SPK), showing surface irregularity in these areas.

Since most dry eye patients except for advanced or severe cases achieve a good best-corrected visual acuity even with vision-related subjective symptoms,[2,3] degraded visual function is difficult to detect using conventional visual acuity measurements. With recent developments in the techniques and devices in ophthalmologic clinical practice, several studies have investigated visual function in dry eye patients using different methods. These include contrast sensitivity measurement as well as quantitative optical sampling methods such as measurements of corneal topographic data or wavefront aberrations. A few studies have reported the effect of SPK in the central corneal region (central SPK) of dry eye on visual function.[4–6] The severity of central SPK correlated with corneal topographic indices such as the surface regularity index and the surface asymmetry index.[4] According to the studies using wavefront sensors, dry eyes with central SPK have greater ocular higher-order aberrations than dry eyes without central SPK.[5,6]

Contrast sensitivity function measurement is well accepted as a sensitive method to assess visual performance in various clinical situations. Since any irregularity in the ocular media can decrease contrast sensitivity,[7] it is reasonable to hypothesize that unstable tear film over the irregular ocular surface in dry eye would be related to a reduction in contrast sensitivity function. Recently, straylight measurement has been used as an objective way to evaluate quality of vision.[8] Straylight is known to be a cause of disability glare[9–11] and corneal pathologic conditions may produce increased straylight.[12] Decreased contrast sensitivity[13–15] and increased straylight[16,17] in dry eye has been reported; however, little is known about the effects of ocular surface regularity in the central corneal region on contrast sensitivity and straylight.

In this study, we explored the relationship between visual function and ocular surface regularity in dry eye by evaluating contrast sensitivity function and straylight quantitatively.

METHODS

This was a prospective case-control study, which was approved by the institutional review board of Osaka University Hospital

and Tsukuba University Hospital, and the study adhered to the tenets of the Declaration of Helsinki. All patients provided informed consent after receiving an explanation of the nature and possible consequences of the study.

Patient Population

We enrolled 52 eyes of 52 dry eye patients (mean age 50.8 ± 8.6 years; 34 eyes in 34 patients with Sjögren syndrome and 18 eyes of 18 patients with keratoconjunctivitis sicca). The diagnostic criteria for dry eye[18] were as follows: (1) presence of dry eye–related ocular symptoms; (2) abnormal tear production (Schirmer's test value at 5 minutes of ≤5 mm) or abnormal tear film stability (tear break-up time [BUT] ≤5 seconds); (3) corneal/conjunctival epithelial damage (fluorescein staining score ≥3/9 in accordance with the van Bijsterveld score[19]). The exclusion criteria were as follows: history of ocular surgeries, temporal or permanent punctal occlusion, contact lens wear, meibomian gland dysfunction, and any type of corneal scarring such as dystrophies or infections. We used the data set of healthy subjects whose straylight data were previously reported.[16] We used 20 eyes of 20 age-matched healthy subjects with no ocular pathology except any refractive errors as a control group. In both dry eye and normal groups, all eyes had a best-corrected distance visual acuity better than 20/20.

Examination Protocol

Examinations were sequentially performed as follows: All patients were questioned regarding the absence or presence of 12 subjective ocular symptoms (ocular fatigue, dryness, uncomfortable sensation, foreign body sensation, ocular pain, blurred vision, sensitivity to bright light, itching, heavy sensation, discharge, excess tearing, and redness). Then, clinical measurements were performed in the following order: (1) visual function measurement (measurement of contrast sensitivity and straylight); (2) assessment of BUT and ocular surface staining using fluorescein dye; and (3) Schirmer's test. All the measurements were taken between 10:00 AM and 2:00 PM in a room where the temperature (20°–25°C) and humidity (30%–40%) were controlled.

Visual Function Measurements

To evaluate contrast sensitivity function under photopic conditions, we used two contrast sensitivity charts (CSV-1000; Vector Vision Co., Greenville, OH, USA): CSV-1000E sine wave grating chart for contrast sensitivity and CSV-1000RN contrast sensitivity chart for letter contrast sensitivity. All patients were evaluated monocularly under best spectacle correction at a viewing distance of 2.5 m. The luminance of the chart background was automatically calibrated to 85 cd/m². The principles and technique of these charts have been described previously.[20-22]

The CSV-1000E chart consists of four rows and eight columns of circular patches. Each row represents a different spatial frequency (3, 6, 12, and 18 cyc/deg), and each frequency includes eight different levels of contrast. Each column represents a grating patch, and a blank patch. The patient was instructed to indicate whether the grating appears in the top or bottom patch for each column. The contrast level of the last correct response was recorded as the contrast threshold in logarithmic scale. The area under the log contrast sensitivity function (AULCSF) was calculated, in accordance with the method described previously.[23]

The CSV-1000RN chart comprises 24 letter optotypes, each of the same size and low spatial frequency (2.4 cyc/deg). There are eight contrast levels (10.0%, 7.09%, 5.03%, 3.57%, 2.53%, 1.79%, 1.27%, and 0.90%) and each contrast level includes three different letters. Measurements started in sequence from the highest to the lowest contrast level. The total number of accurately identified letters was recorded.

Measurement of straylight was performed using a straylight meter (C-Quant; Oculus GmbH, Wetzlar, Germany). This measurement was based on the compensation comparison method. The principles and procedures involved in the use of straylight meter have been described elsewhere.[8,12,24,25] In brief, the center of the test field was divided into two halves and was surrounded by a flickering ring, which served as a source of straylight. When the compensation light was presented to one-half, the other half did not receive any compensation light. This flickering straylight was compared to a comparison field. The patient was instructed to choose the side that flickered more intensely. The amount of straylight was expressed as the logarithm of straylight parameters (log [s]). At each measurement, we confirmed that the measurements were reliable, based on a reliability parameter, defined as the expected standard deviation, and a quality parameter.[25]

Ocular Surface Examinations

Fluorescein dye was used to assess ocular staining and BUT. A sterile fluorescein strip was moistened using nonpreserved saline, shaken once to remove excess fluid, and applied to the inferior bulbar conjunctiva. The subjects were instructed to blink several times for a few seconds to ensure adequate mixing of the dye. Three BUT measurements were made using a metronome and the mean was calculated. Fluorescein corneal staining was evaluated according to the National Eye Institute/Industry Workshop method that divides the cornea into five regions.[26] Each region was given a staining score from 0 to 3, and the total score of all five regions was then calculated. Fluorescein conjunctival staining was scored from 0 to 3 using a blue-free barrier filter.[27] As with the corneal score, total score for the conjunctiva staining was obtained. The 5-minute Schirmer's test using sterile strips was performed without anesthesia. Based on the presence of central SPK, dry eye patients were divided into two groups, dry eye with or without central SPK.

Statistical Analysis

All statistical analyses were conducted using analytical software (SigmaPlot, version 12.0 for Windows; Systat Software, Inc., San Jose, CA, USA). Comparisons of the clinical parameters between the two dry eye groups were performed using the Wilcoxon rank-sum test. To compare contrast sensitivity and straylight data among the three groups, a Kruskal–Wallis 1-way ANOVA on ranks with Dunnett's correction for multiple comparisons was used. Correlations were assessed with Spearman's rank-correlation coefficient. Values of $P < 0.05$ were considered statistically significant.

RESULTS

The demographic and clinical data of the two dry eye groups and the normal eye group are summarized in Table 1.

As presented in Figure 1, contrast sensitivity at all four spatial frequencies was significantly reduced in dry eyes with central SPK compared to normal eyes ($P < 0.05$ for each). At spatial frequencies of 3, 12, and 18 cyc/deg, the contrast sensitivity of dry eyes with central SPK were significantly lower than those of dry eyes without central SPK ($P < 0.05$ for each). We found that the AULCSF calculated from these data was

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Table 1. Demographic and Clinical Data of the Three Study Groups

Parameter	Normal Eyes,* $n = 20$	Dry Eyes Without Central SPK, $n = 18$	Dry Eyes With Central SPK, $n = 34$	P Value†
Age, y	51.9 ± 7.2	53.4 ± 6.8	49.6 ± 9.1	0.531
Schirmer's test, mm	21.6 ± 7.2	2.7 ± 3.0	2.2 ± 3.7	0.287
BUT, s	7.9 ± 1.2	2.2 ± 0.8	1.6 ± 0.9	0.044
Corneal staining score	0.0 ± 0.0	2.9 ± 2.2	6.7 ± 3.5	<0.001
Conjunctival staining score	0.2 ± 0.4	3.4 ± 2.0	4.6 ± 1.6	0.221

Data are expressed as the mean ± SD.
* Data from normal eyes are from Koh et al.[16]
† Values of *P* for comparisons between dry eye with and without central SPK.

significantly lower in dry eyes with central SPK than normal and dry eyes without central SPK ($P < 0.05$ for both; Table 2). The letter contrast sensitivity of dry eyes with central SPK was significantly reduced, compared to dry eyes without central SPK and normal eyes ($P < 0.05$ for both; Table 2).

Straylight was significantly higher in both dry eye groups with and without central SPK, although there was no significant difference between these groups (Table 2).

The correlations between the central SPK score and visual function data in dry eyes are presented in Figure 2. Significant negative correlations were observed between the central SPK score and AULCSF ($R = -0.485$, $P < 0.001$). The central SPK score also showed a significant negative correlation with letter contrast sensitivity ($R = -0.541$, $P < 0.001$). However, no significant correlation was observed between the central SPK score and straylight ($R = 0.045$, $P = 0.747$).

DISCUSSION

The current study revealed significantly higher straylight in dry eyes with and without central SPK and significantly reduced contrast sensitivity function in dry eyes with central SPK, compared to those in normal eyes. In dry eye, the severity of central SPK correlated with contrast sensitivity function.

Contrast sensitivity function is reported to correlate with abilities associated to quality of life.[28,29] The decreased contrast sensitivity of dry eye in our results was consistent with that in previous reports.[13–15] While Rolando et al.[13] found

FIGURE 1. Contrast sensitivity at four specific frequencies in normal and dry eyes. *$P < 0.05$ (dry eyes with central SPK versus normal eyes). #$P < 0.05$ (dry eyes with central SPK versus dry eyes without central SPK).

lower contrast sensitivity in both dry eyes with and without SPK, Huang et al.[14] reported that dry eyes with SPK had significantly lower contrast sensitivity than dry eyes without SPK. Although the location of SPK in the cornea was not described in these reports, our results were consistent with theirs,[14] suggesting the influence of surface irregularities of the central cornea on contrast sensitivity in dry eye.

In the current study, letter contrast sensitivity was also evaluated. The utility of this chart has been previously reported.[30,31] Since this chart uses the same size numbers, it is easy for the patients and suitable for non-English speaking patients. Moreover, this chart is capable of detecting subtle visual deteriorations compared to the conventional chart, owing to the greater setting area of the low contrast. Our results showed a significant reduction of letter contrast sensitivity in dry eye with central SPK compared to dry eye without central SPK, which may suggest the utility of letter contrast sensitivity measurements in detecting subtle visual alterations in patients with dry eye. Previously, contrast sensitivity after instillation of antiglaucoma eye drops was evaluated using the same letter contrast sensitivity chart used in this study.[22] A future study investigating the effect of artificial eye drops or dry eye drops using letter contrast sensitivity measurement would be interesting to explore the tear film behavior in dry eye, which has been previously studied using conventional contrast sensitivity measurements.[14,15,32,33]

Straylight was higher in both dry eye groups compared to normal eyes, and there were no significant differences between the two dry eye groups. Further, there was no relationship between central SPK and straylight. Recently, van de Wouw et al.[17] reported straylight values in patients with severe keratoconjunctivitis sicca using the same straylight meter utilized in our study. According to that study, increased straylight values were observed in patients with keratocon-
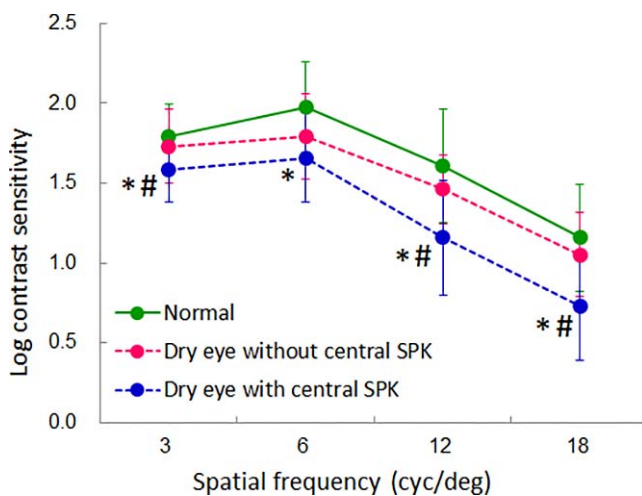
Table 2. Visual Function Data

Visual Function	Normal Eyes, $n = 20$	Dry Eyes Without Central SPK, $n = 18$	Dry Eyes With Central SPK, $n = 34$
AULCSF	1.35 ± 0.11 (1.31–1.43)	1.24 ± 0.16 (1.17–1.34)	1.08 ± 0.19*† (0.99–1.22)
Letter contrast sensitivity (no. of letters)	19.2 ± 2.7 (18.0–21.8)	16.7 ± 3.0 (15.0–18.0)	14.4 ± 1.9*† (13.0–15.0)
Straylight values log, s	1.07 ± 0.14 (0.95–1.19)	1.24 ± 0.20* (1.16–1.29)	1.26 ± 0.21* (1.08–1.43)

Data are expressed as mean ± SD (interquartile range).
* $P < 0.05$ versus normal eyes.
† $P < 0.05$ versus dry eyes without central SPK.
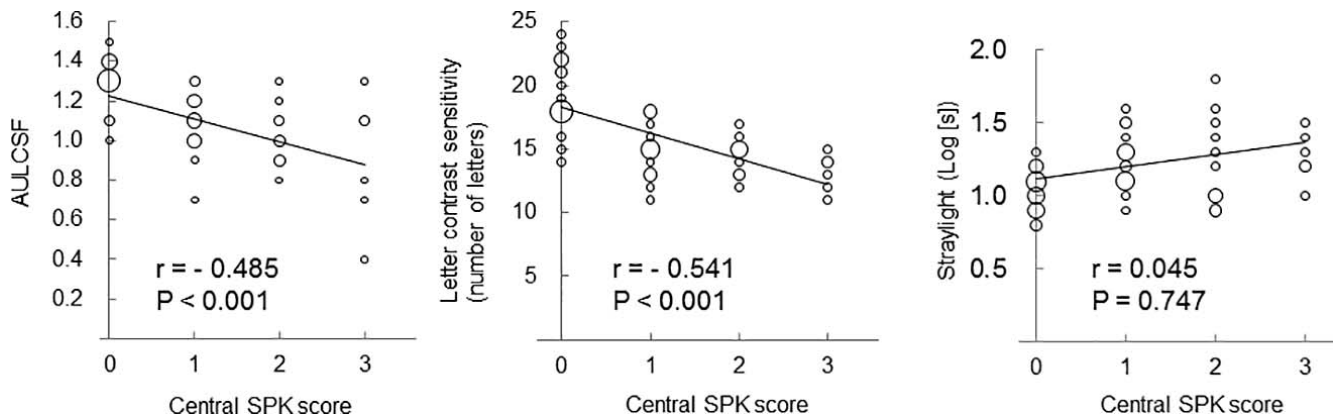
FIGURE 2. Correlations between SPK in the central corneal region (central SPK) score and contrast sensitivity function and straylight. **(A)** The area under the log contrast sensitivity function correlated negatively with central SPK ($R = -0.485$, $P < 0.001$). **(B)** Significant negative correlations were found between the central SPK score and letter contrast sensitivity ($R = -0.541$, $P < 0.001$). **(C)** No significant correlation was observed between central SPK score and straylight.

junctivitis sicca and this increase was not correlated to the amount of corneal epithelial damage graded with the van Bijsterveld's scoring system,[19] which is consistent with both our previous[16] and current studies. We make the following speculation for the lack of correlation between straylight and central SPK. Straylight is reported to be sensitive to epithelial changes in corneal microstructure[34] and it is difficult to relate clinically visible corneal changes to straylight.[34,35] Increased straylight values in subjects with hydrogel soft contact lenses have been reported,[36,37] while soft contact lens wear did not influence straylight values.[35] Although the water content of lenses used in these studies was not described, it is possible that the changes in hydration or wettability of the prelens tear film may influence the straylight values. The prelens tear film on the soft contact lens is close to the precorneal tear film on the cornea in terms of maintaining the surface wettability. Therefore, the increased straylight in dry eye may be mostly attributed to the changes in hydration in the tear film over the corneal epithelium, than the clinically visible changes in epithelium as SPK. As previously described,[16] the techniques used to measure straylight may be partially responsible for the lack of a correlation between straylight and central SPK in dry eye. Although subjects can blink freely during the straylight measurement, measurements may require the subjects to maintain their gaze for some time, which may disrupt the tear film layer, leading to increased changes in hydration of the ocular surface in dry eye. Further investigation is needed to clarify the relationship between straylight and the ocular surface, including tear film or SPK.

A significant correlation between the central SPK score and contrast sensitivity function was shown in the current study. Several studies have demonstrated the relationship between SPK and visual function in dry eye.[4–6,14] On the other hand, as discussed above, there is no relationship between SPK and straylight in dry eye. Although there are differences in the diagnostic criteria for dry eye and measurement techniques among the studies, these findings imply that the use of appropriate methods should be considered in detecting the decreased visual function that may result from corneal surface irregularities in dry eye. Based on the current study and previous findings, the differences detected by visual function tests and associated factors of ocular surface regularity in dry eye may be as follows. The effect of the tear film instability can be predicted by straylight measurements, and influences from the corneal surface irregularity in the central corneal region can be detected by the contrast sensitivity measurements.

However, considering that complex factors are found in a few dry eye cases, we do not believe that this is applicable to all cases. Nevertheless, it might be useful to investigate the factors associated with ocular surface regularity and visual function in other ocular surface diseases. The relationship between contrast sensitivity and straylight in eyes with ocular surface diseases has not been fully clarified. As the next step, the correlation of contrast sensitivity and straylight in eyes with ocular surface diseases including corneal epithelial disorders needs to be investigated.

There are a few limitations in the current study. The relationship between subjective symptoms and visual function was not assessed. Since ocular discomfort or subtle visual disturbances may be the motivation for dry eye patients to visit clinics, investigations on the correlation between subjective symptoms and visual function are needed, and a study addressing this issue is underway. In our study, central SPK was scored on a 0 to 3 scale; SPK scoring by area and density[38] in a large number of patients with dry eye would help to clarify the potential influence of SPK in the degradation of contrast sensitivity in dry eye and to validate SPK as a possible factor. Contrast sensitivity function was measured only under photopic conditions in the present study. Reduced mesopic visual performance of contrast sensitivity is observed in eyes after refractive surgery.[39,40] An investigation of mesopic visual performance would be helpful to understand the visual performance in the daily life of dry eye patients, because blurred vision or glare are common visual complaints among dry eye patients.

In conclusion, SPK in the central corneal zone in dry eye is likely to contribute to decreased contrast visual function and increased straylight may result from tear film stability. A significant correlation was observed between the severity of central SPK and contrast sensitivity, demonstrating that contrast sensitivity testing could detect visual disturbances associated with corneal damage overlying the optical zone.

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