• Clinical Research •

Evaluations of wavefront aberrations and corneal surface regularity in dry eye patients measured with OPD Scan III

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Abstract

● **AIM:** To compare the wavefront aberrations and corneal surface regularity between dry eye (DE) patients and normal subjects and assess its diagnostic performance for DE measured with OPD Scan-III.

● **METHODS:** Fifty right eyes of 50 DE patients and 31 right eyes of normal subjects were included. The examinations for ocular surface including logarithm of the minimum angle of resolution best-corrected distance visual acuity (logMAR BCVA) the ocular surface disease index (OSDI), tear film break-up time (TBUT) and corneal fluorescein staining (CFS). OPD Scan-III was used to measure anterior corneal aberrations including total corneal aberrations, high order aberration (HOA), coma, trefoil, spherical aberration (SA), standard deviation of corneal power (SDP), surface regularity index (SRI) and surface asymmetry index (SAI). Statistical analysis were assessed with nonparametric tests and Spearman's correlations. All parameters were also analyzed for sensitivity, specificity, and receiver operating characteristics (ROC) curves.

● **RESULTS:** Wavefront aberrations parameters including total corneal aberrations, HOA, coma, trefoil, and SA in DE group were significantly higher than those in normal group (P<0.001). Corneal surface regularity parameters including SRI and SAI in DE group were significantly higher than both in normal group (P<0.05). All the wavefront aberrations parameters had significant correlations with ocular surface parameters (P<0.05). The logMAR BCVA had positive correlations with SAI and SRI (all P<0.001). CFS scores had positive correlations with SAI and SRI (all P<0.001). All the wavefront aberrations parameters showed good diagnosis sensitivity and specificity, however, the corneal regularity parameters showed only good specificity but poor sensitivity. The cut-off value selected for trefoil in diagnosis DE showed the highest area under the curve (AUC, 0.921) values as compared to the other parameters with sensitivity of 0.955 and specificity of 0.867.

● **CONCLUSION:** Wavefront aberrations and corneal surface regularity are increased in DE patients and also correlated with ocular surface parameters. Wavefront aberrations parameters have potential to be indicators to diagnosis and monitor DE.

● **KEYWORDS:** dry eye; wavefront aberration; corneal surface regularity; OPD Scan III

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INTRODUCTION

Dry eye (DE) is gradually considered as a public health problem and one of the most frequent reasons for seeking eye care[1]. According to the Dry Eye Work Shop II (DEWS II) report in 2017, DE is defined as a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles[2]. The ocular surface including tear film which serves as the first refractive surface of the eye and is an important element in preserving visual quality[3]. Also, corneal fluorescein staining (CFS) is a common sign in DE patients which lead to the corneal surface irregularity and might have effects on the visual quality[4].

Visual disturbance is also a common ocular symptom of DE patients and several studies evaluating the visual disturbance of DE patients based on the tear film instability and corneal surface irregularity[5-6]. Studies concluded that DE patients have larger wavefront aberration values than normal patients[7-8]. It have been demonstrated that there are increased

high order aberration (HOA) in patients with DE and artificial tears could improve the visual quality[9-11]. However, in the clinical, there still lack of methods to describe or quantify the visual quality of DE patients and few study focus on the diagnostic performance of wavefront aberrations for DE. Quantification visual quality of the eye has been of increasing interest for purposes of aiding in the diagnosis of DE. There are multiple aberrometers to measure wavefront aberrations based on variety of principles such as ray tracing, Hartmann-Shack, Tscherning and automatic retinoscopy[12]. An effective and meaningful measurement for wavefront aberrations evaluations in DE patients is urgently needed[13]. Studies also showed that the indices of corneal surface regularity such as surface regularity index (SRI) and surface asymmetry index (SAI) could be used as objective diagnostic method for DE as well as for evaluating the severity of this disease[14-15].

OPD Scan III (Nidek, Tokyo, Japan) is a multifunctional and comprehensive device which could not only measures the shape and curvature of the cornea but also evaluate the wavefront aberrations at the same time[16]. In this study, we compared the cornea surface regularity and wavefront aberrations of DE patients to the normal people using OPD Scan III and aimed to evaluate the application of OPD Scan III in diagnosis and monitor DE.

SUBJECTS AND METHODS

Ethical Approval This study was conducted in accordance to the tenets of the Declaration of Helsinki and informed written consent was obtained from each subjects.

We enrolled 50 right eyes of 50 DE patients and 31 right eyes of 31 normal subjects from clinic of Peking University Third Hospital. Patients were diagnosed as DE according to the criteria provided by the DEWS[17]: 1) the ocular surface disease index (OSDI) >13; 2) tear film break-up time (TBUT) ≤5s or 5s<TBUT≤10s with positive CFS. The exclusion criteria are as follows: subjects if they were under the age of 18 or over the age of 65; high myopia; a history of ocular surgery; any type of corneal scarring such as dystrophies or infections or any other ocular disease might have effects on the visual quality.

Questionnaire and Clinical Evaluation All subjects underwent a complete evaluation of the ocular surface. Subjective ocular symptoms of patients were evaluated by the OSDI questionnaire. Logarithm of the minimum angle of resolution best-corrected distance visual acuity (logMAR BCVA) of all the subjects was registered. Measurement of TBUT and CFS was facilitated by viewing with a blue exciter filter after instilling fluorescein sodium ophthalmic strip (Liaoning Meizilin Pharmaceutical Co., Ltd., China)[18]. The fluorescein strip was moistened by a drop of saline, shaken once to remove excess fluid, and applied to the inferior bulbar conjunctiva. The subjects were instructed to blink several times over 10s to ensure adequate mixing of the dye. After blinking, the subjects were examined, and the interval between blinking and the appearance of the first dark spot in the fluorescein-stained tear layer was recorded. Three separate readings were obtained for right eye, and the results were averaged. The intensity of CFS was graded according to the National Eye Institute method that divides the cornea into five zones (central, temporal, nasal, superior, and inferior). Each zone was assigned a staining score 0-3 (0 dots, 0; 1-20 dots, 1; >20 dots without confluent staining, 2; and confluent staining, 3), and the total score of all five zones was calculated, ranging 0-15[19].

The examinations by OPD Scan III aberrometer (NIDEK Co. Ltd., Gamagori, Japan) was performed in a dark room. OPD Scan III is a multifunctional device which projects Placido ring images onto the cornea for topographic measurements. The reflected image is captured with a camera, and image analysis is done to determine the shape of the cornea. The device is also capable of wavefront aberration analysis using Zernike polynomials[20]. In our study, it was used to measure anterior corneal aberrations over 4 mm analytical zones, including total corneal aberration, HOA, coma aberration, trefoil aberration and spherical aberration (SA). The corneal surface shape parameters including standard deviation of corneal power (SDP), SRI and SAI were attained.

Statistical Analysis Statistical analysis was performed with SPSS 22.0 software (SPSS, Inc., Chicago, IL, USA). All descriptive statistics were given as the mean±SD. Differences of gender among groups were tested using Chi-square test. Nonparametric tests were used for comparing data between DE group and normal control group. An evaluation was made of the linear relationship between the parameters of OPD Scan III and the results of ocular surface evaluations including OSDI, TBUT, logMAR BCVA, and CFS scores. This was performed by using Spearman's correlation test. A P value less than 0.05 was considered statistically significant. To diagnose DE parameters of OPD Scan III, sensitivity, specificity, and cut-off values of measurement were determined using receiver operating characteristic (ROC) analysis.

RESULTS

In this study, we enrolled 50 eyes of 50 DE patients (mean age 41.02±13.37y) and 31 eyes of 31 normal subjects (mean age 45.94±15.03y). The demographic data and results of ocular surface parameters are presented in Table 1. Age and gender of each group were matched (P=0.455 and P=0.220). The comparison results showed that logMAR BCVA in DE group significantly worse than in normal group (P=0.002). Also the results showed that OSDI scores of patients in DE group were significantly higher than in normal group (P<0.001) and TUBT of patients in DE group were significantly shorter than in normal group (P<0.001).

Table 1 Demographic and ocular surface characteristics of study subjects in DE and normal groups mean±SD

Characteristics	DE	Normal	*P*
Numbers of patients (*n*)	50	31	/
Gender (M/F)	14/36	5/26	0.220
Age (y)	41.02±13.37	45.94±15.03	0.455
logMAR BCVA	0.099±0.126	0.005±0.021	0.002
OSDI scores	39.73±15.00	6.41±3.59	<0.001
TBUT (s)	4.50±2.67	11.13±3.91	<0.001
CFS scores	8.46±4.79	0	/

DE: Dry eye; logMAR BCVA: Logarithm of the minimum angle of resolution best-corrected distance visual acuity; OSDI: Ocular surface disease index; TBUT: Tear film break-up time; CFS: Cornea fluorescent staining.

Table 2 Comparisons of OPD Scan III parameters including wavefront aberrations and corneal surface regularity parameters of study subjects in DE and normal groups

Parameters	DE	Normal	*P*
Total corneal aberrations	1.81±1.50	0.82±0.92	<0.001
Corneal HOA	0.49±0.50	0.35±0.89	<0.001
Corneal coma	0.27±0.32	0.05±0.09	<0.001
Corneal trefoil	0.22±0.37	0.04±0.04	<0.001
SA	0.22±0.15	0.05±0.09	<0.001
SDP	1.16±0.42	1.07±0.27	0.493
SRI	0.55±0.33	0.41±0.25	0.049
SAI	0.49±0.25	0.38±0.15	0.001

All data are expressed as mean±SD. DE: Dry eye; HOA: High-order aberration; SA: Spherical aberrations; SDP: Standard deviation of corneal power; SRI: Surface regularity index; SAI: Surface asymmetry index.

The comparisons of OPD Scan III parameters between two groups were showed in Table 2. Wavefront aberrations including total corneal aberrations, HOA, coma, trefoil, and SA in DE group were all significantly higher than in normal group (P<0.001). Corneal surface regularity parameters including SRI and SAI in DE group were both significantly higher than in normal group (P<0.05). No differences was found in SDP in DE group and normal group (P=0.493).

The correlations between the OPD Scan III parameters and ocular surface parameters including OSDI scores, logMAR BCVA, TBUT, and CFS scores were evaluated in all the subjects and the results were showed in Table 3. It showed that OSDI scores had strong positive correlations with total corneal aberrations, HOA, coma and trefoil and had a small positive correlation with SAI (all P<0.05). The logMAR BCVA had a high positive correlation with SAI (P<0.001) and positive medium correlations with total corneal aberrations, HOA, coma, trefoil and SRI (all P<0.001). Small positive correlations were showed between logMAR BCVA and SA and SDP (all P<0.05). Besides, TBUT had a strong negative correlation with coma, trefoil and SA (P<0.001) and moderate negative correlations with total corneal aberrations and HOA (both P<0.05). Interestingly, TBUT showed no correlations with corneal surface regularity parameters such as SDP and SRI and only a small negative correlation was found between TBUT and SAI. CFS scores had large positive correlations with all wavefront aberrations parameters including total corneal aberrations, HOA, coma, trefoil, and SA. Besides, CFS scores had medium positive correlations with SAI and SRI and had a small positive correlation with SDP (P=0.007).

The diagnostic performance of all the parameters of OPD Scan III was determined. The best cut-off value was calculated for each parameter; data were then summarized for sensitivity, specificity and area under the curve (AUC) from the ROC

Table 3 Correlation analysis between ocular surface parameters and OPD Scan III parameters including wavefront aberrations and corneal surface regularity parameters

Parameters	OSDI scores	logMAR BCVA	TBUT	CFS scores
Total corneal aberrations				
r	0.541	0.351	-0.419	0.630
P	<0.001	0.001	<0.001	<0.001
Corneal HOAs				
r	0.415	0.350	-0.376	0.555
P	0.001	0.001	0.001	<0.001
Corneal coma				
r	0.601	0.493	-0.539	0.659
P	<0.001	<0.001	<0.001	<0.001
Corneal trefoil				
r	0.554	0.444	-0.555	0.706
P	<0.001	<0.001	<0.001	<0.001
SA				
r	0.527	0.252	-0.504	0.533
P	<0.001	0.023	<0.001	<0.001
SDP				
r	0.123	0.271	-0.118	0.298
P	0.275	0.014	0.295	0.007
SRI				
r	0.155	0.414	-0.168	0.468
P	0.167	<0.001	0.134	<0.001
SAI				
r	0.244	0.605	-0.259	0.397
P	0.028	<0.001	0.019	<0.001

HOA: High-order aberration; SA: Spherical aberrations; SDP: Standard deviation of corneal power; SRI: Surface regularity index; SAI: Surface asymmetry index; logMAR BCVA: Logarithm of the minimum angle of resolution best-corrected distance visual acuity; OSDI: Ocular surface disease index; TBUT: Tear film break-up time; CFS: Cornea fluorescent staining. The *r* and *P* values were determined with Spearman's correlation coefficient. Correlation coefficient grading: Small correlation strength 0.10 to 0.29; medium correlation strength 0.30 to 0.49; large correlation strength 0.50 to 1.00.

Table 4 Diagnostic performance of OPD Scan III parameters including wavefront aberrations and corneal surface regularity parameters for DE patients

Parameters	AUC	Cut-off value	Sensitivity	1-specificity	Specificty	Sensitivity-(1-specificity)
Total corneal aberrations	0.853	0.816	0.864	0.133	0.867	0.731
Corneal HOA	0.799	0.306	0.682	0.1	0.9	0.582
Corneal coma	0.908	0.086	0.841	0.1	0.9	0.741
Corneal trefoil	0.921	0.051	0.955	0.133	0.867	0.822
SA	0.883	0.082	0.773	0.1	0.9	0.673
SDP	0.554	1.38	0.271	0.1	0.9	0.173
SRI	0.628	0.665	0.318	0.067	0.933	0.251
SAI	0.669	0.445	0.455	0.133	0.867	0.322

AUC: Area under the curve; HOA: High-order aberration; SA: Spherical aberrations; SDP: Standard deviation of corneal power; SRI: Surface regularity index; SAI: Surface asymmetry index.

curve analysis which were showed in Table 4. All the wavefront aberrations parameters including total corneal aberrations, HOAs, coma, trefoil, and SA showed good diagnosis sensitivity and specificity, however, the corneal regularity parameters including SDP, SAI and SRI showed only good specificity but poor sensitivity. The cut-off value selected for trefoil in diagnosis DE showed the highest AUC values (AUC=0.921) as compared to the other parameters with sensitivity of 0.955 and specificity of 0.867 (Figure 1).

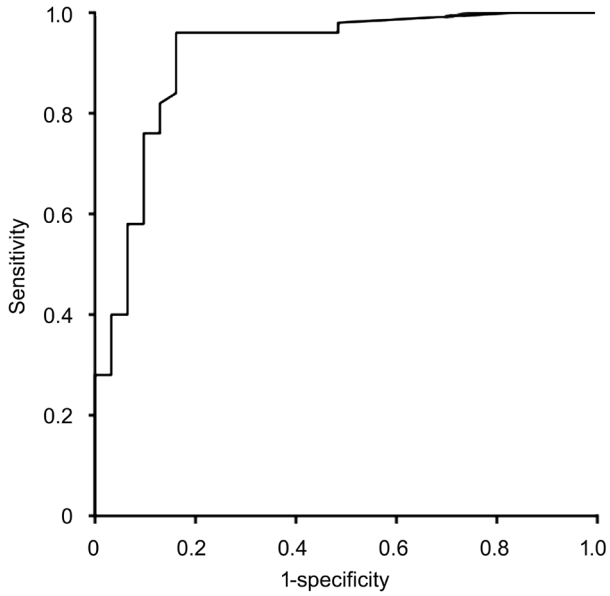

Figure 1 ROC graph analysis delineating the combined sensitivity and specificity of the trefoil using the OPD Scan III.

DISCUSSION

DE is characterized by symptoms of ocular dryness and discomfort, which can affect the visual performance. We conducted the present study to assess changes of visual quality especially wavefront aberrations and corneal surface regularity in DE patients measured with OPD Scan III. The comparisons between DE patients and normal subjects were performed and we also investigated the correlations between wavefront aberration parameters, corneal surface regularity parameters and ocular surface parameters respectively.

Visual disturbance is a main symptom of DE patients and common visual complaints associated with DE include fluctuating vision with blinking, blurred vision, glare and eye fatigue[21-22]. In our study, logMAR BCVA was significantly higher in DE group than normal group. Besides, the logMAR BCVA positively correlated to all the wavefront aberration parameters and corneal surface regularity parameters such as SAI which confirmed that the main courses of visual disturbance in DE patients could be tear film instability and ocular surface damage[23]. Visual acuity measurements have become the hallmark of visual function. Unfortunately, these conventional assessments do not detect all aspects of degraded visual function[24]. Therefore, we also assess the wavefront aberrations aiming to evaluate visual quality.

In our study, the wavefront aberrations parameters measured with OPD Scan III including total corneal aberrations, HOAs, coma, trefoil and SA in DE group were all significantly higher than in normal group and also the wavefront aberrations correlated well with ocular surface parameters. Wavefront aberrations parameters especially trefoil have good sensitivity and specificity to diagnosis DE. Among then, TBUT had a high negative correlation with coma, trefoil and SA and moderate negative correlations with total corneal aberrations and HOAs. It suggested that the stability of tear film plays an important role in the condition of visual quality. TBUT is represented the tear film stability and previous study showed changes in vertical coma and SA after blinking are associated with the changes in tear menisci and TBUT[25]. Change in wavefront aberrations created by tear-film breakup contributes to the reduction in retinal image quality[26-27].

The SRI and SAI measured by corneal topography have been shown to be significantly worse in patients with DE than in normal subjects[28]. The results of our study were consistent with previous study. CFS scores had positive correlations with

SAI and SRI. In clinical practice, fluorescein dye is frequently used for ocular staining, and DE commonly appears as positive CFS which showed corneal surface irregularity in these areas and associated with SRI and SAI.

According to the study, tear film instability and ocular surface damage are thought to be main courses of visual disturbance which resulted in the increased wavefront aberrations and corneal surface irregularity[23]. However, few study focused on evaluating both wavefront aberrations and corneal surface irregularity in DE patients. Visual disturbance is common symptoms in DE patients though, no measurement was used to evaluate the visual function of DE patients in clinical. OPD Scan III is a multifunctional device that measures the shape and curvature of the cornea and wavefront aberrations which could provide more comprehensive evaluations for DE patients. Our study demonstrated that the wavefront aberrations parameters measured by OPD Scan III had a good diagnostic performance for DE[29].

There are some limitations in current study. The sample size is still small and further larger sample study is needed in the future. In our study, we have not grade severity of the DE patients because of the lack of severe patients.

In conclusion, the wavefront aberrations and corneal surface irregularity are increased in DE patients. The OPD Scan III might have potential to be a new measurement to diagnosis DE and monitor the treatment of DE.

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