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Long-term changes in the ocular surface during orthokeratology lens wear and their correlations with ocular discomfort symptoms

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ABSTRACT

Purpose: To evaluate the changes in ocular surface parameters during orthokeratology lens wear and determine their correlations with ocular discomfort symptoms.

Methods: Fifty individuals were enrolled in this prospective pilot study. Clinical evaluation of the ocular surface included the ocular surface disease index, slit-lamp examination, Keratograph 5M, optical quality analysis system, and corneal staining. After baseline examinations, clinical tests were performed at 1 day, 1 week, 1 month, 3 months, 6 months, and 12 months after orthokeratology lens wear. Correlations between ocular discomfort symptoms and signs of ocular discomfort were evaluated.

Results: Overall ocular surface disease index score and two subscale scores (ocular symptoms and vision-related function) significantly increased at the 3-month visit ($P < 0.05$), and decreased to levels close to baseline at the12-month visit ($P > 0.05$). The basic objective scatter index and the mean tear film objective scatter index increased, peaking at 3-month visit ($P < 0.05$) and gradually decreased thereafter. The modulation transfer function cut-off significantly decreased at the 3-month visit ($P < 0.05$). During the 12-month study period, the overall ocular surface disease index score and vision-related function score were significantly and positively correlated with the basic objective scatter index and mean tear film objective scatter index ($P < 0.05$). After 1 week of lens wear, Grade 1 corneal staining increased to 16.4 %, mostly involving the central and inferior cornea.

Conclusions: Orthokeratology lens wear increased ocular discomfort symptoms and decreased the function of tear film, mainly within 3 months of lens wear. Tear-related visual function parameters were correlated with ocular discomfort. A new parameter, tear film objective scatter index, measured with the optical quality analysis system, was more sensitive in detecting the quality and stability of tear film than traditional indicators.

1. Introduction

The global prevalence of myopia is constantly rising, with 5 billion people predicted to be myopic by the year 2050 [1]. Overnight orthokeratology lens is a reverse-geometry gas-permeable rigid contact lens, which is worn during the night to reshape the anterior corneal surface leading to a temporary reduction in refractive error [2]. Although orthokeratology lens is a safe option [3,4], 30–40 % of patients reported occasional ocular discomfort after lens insertion [5]. Contact lens-related discomfort is a common problem encountered by patients and is a major reason for discontinuing lens wear [6]. The Tear Film & Ocular Surface Committee in 2013 reported that contact lens-related discomfort is strongly associated with tear film instability [7].

It is important to detect the severity of eye related symptoms when a diagnosis of dry eye is made [8]. Out of currently available questionnaires to assess dry eye symptoms, only the ocular surface disease index (OSDI) questionnaire is more often applied for children [9]. The OSDI questionnaire is a valid instrument and is used to assess the frequency of ocular discomfort [10]. The questionnaire includes three subscales related to visual quality and ocular discomfort associated with ocular pain or environmental factors [11]. Previous studies on orthokeratology lens have found occurrence of altered corneal morphology, such as flattening of the central cornea and steepening of the paracentral cornea [12,13]. Surface irregularities on the cornea may affect the distribution and fluid dynamics of the tear film [14]. Among the various methods that can evaluate tear film stability, the most common and traditional

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diagnostic test is the tear breakup time (TBUT) [15]. However, previous studies have failed to find a significant correlation between the TBUT and overall OSDI score [16,17]. This study speculated that possible reasons for previous results concerned two aspects. Firstly, the TBUT is invasive and observer-dependent, which imparts low reproducibility [18]. Secondly, the OSDI provides one score to evaluate ocular discomfort; however, the three subscales involve three different aspects including ocular discomfort associated with ocular pain or environmental factors and vision-related function. To date, no studies have demonstrated direct correlations between the traditional ocular surface parameters and subscales of the OSDI questionnaire in patients who have undergone orthokeratology lens.

The optical quality of the tear film is a parameter for evaluation of the tear film stability [19,20]. The optical quality analysis system II (OQAS II) evaluates temporal changes in the quality and stability of tear film based on a dynamic analysis of retinal images [21] with excellent repeatability [22]. In this study, one major parameter was the basic objective scatter index (OSI) provided by the OQAS, which was defined as a ratio between the integrated light in the periphery and central peak of the double-pass retinal images. Basic OSI describes the scattering index of refractive media, such as the cornea, lens, and vitreous (excluding the tear film), and it represents the impact of aberration and scattering on the retinal images. The OQAS also shows dynamic changes in OSI over 20 s and calculates the mean value and standard deviation of the 20-s OSI. The changes in 20-s OSI represent the scattering index changes of all refractive media, mainly derived from tear film dynamic alterations. A previous study found that the mean OSI significantly increased within 20 s in patients with dry eye disease [23]. Guo et al. observed that the mean tear film OSI increased, illustrating that the stability of the tear film decreased after 1 month of orthokeratology lens wear [24]. However, these studies did not consider the effects of corneal morphology on visual quality. To avoid the effects of corneal morphological changes, this study proposed a new parameter, the tear film OSI (TF-OSI), which was the difference obtained by subtracting the basic OSI from the 20-s OSI values. The mean value and standard deviation of the TF-OSI could objectively reflect changes in the quality and stability of the tear film. No clear data exists that shows a definite correlation between OSI-related parameters and the OSDI score and scores on the three subscales in patients with orthokeratology lens wear.

This study aimed to analyze the 1-year effect of orthokeratology lens wear on ocular symptoms, tear film, and vision quality in patients with myopia. Additionally, factors potentially associated with ocular discomfort in patients with orthokeratology lens wear were also explored. The results in this study could aid clinicians better understand the progress of ocular discomfort symptoms after orthokeratology lens wear and directly benefit the fitting of orthokeratology lenses.

2. Methods

2.1. Participants

This prospective study was conducted at Tianjin Medical University Eye Hospital (Tianjin, China) from June 2019 to January 2021. Written informed consent was obtained from all participants or their guardians before participation in the study. This study adhered to the Declaration of Helsinki and was approved by the Institutional Ethical Committee Review Board (2019KY(L)-01). The inclusion criteria were as follows: age, 8–14 years; myopia between −1.00 D and −5.00 D; astigmatism < 1.50 D; best corrected monocular visual acuity > 20/20; no strabismus or ocular surface diseases; and no history of surgery or contact lens wearing.

2.2. Orthokeratology lens

All orthokeratology lenses (Euclid Systems Corp., Herndon, VA, USA) were made from Boston Equalens II material (Boston, MA, USA) (Dk: 85 × 10^{-11} [cm^2/s] [mL O_2/mL•mmHg]), having a coaxial spherical 5-zone reverse geometry with a center thickness of 0.24 mm. Total lens diameter ranged from 10.6 to 10.8 mm, the back optic zone diameter was 6.2 mm, and the reverse curve width was 0.6–0.8 mm. All patients were required to wear the lenses for at least 8 h per night for 6 days a week.

2.3. Measurements

The same experienced operator conducted all measurements throughout the study. All evaluations were performed between 9 and 11 a.m. and at 2–4 h after lens removal. All patients with myopia underwent uncorrected visual acuity testing, objective optometry measured with an autorefractometer (Topcon, Tokyo, Japan) without cycloplegia, slit-lamp examination (SL-D2; Topcon), OSDI questionnaire, tear film stability assessment using Keratograph 5M (Oculus, Menlo Park, CA, USA), visual quality assessment using optical quality analysis system II (Visiometrics, Terrassa, Spain), and corneal staining using commercially available pre-packaged sterile fluorescein paper tape (Jingming New Technology Development Co. Ltd., Tianjin, China).

2.4. Ocular surface disease index (OSDI) questionnaire

The OSDI questionnaire is more often used to evaluate the severity of dry eye disease in children [9,25]. The OSDI consists of an overall score (based on 12 questions) and three subscale scores (ocular symptoms [five questions], vision-related function [four questions], and environmental triggers [three questions]). The questionnaire is graded on a scale from 0 to 4 points (0, never; 1, some of the time; 2, half of the time; 3, most of the time; and 4, all the time). The overall OSDI score was calculated using the following formula:

$$\text{OSDI} = [(\text{sum of the scores for all questions answered}) \times 100]/[(\text{total number of questions answered})/4]$$

The subscale score was calculated similarly, with only the questions answered from each subscale used to produce their own score. The questionnaire and subscale score each ranged from 0 to 100 points. A higher score indicates a more severe condition [10].

2.5. Keratography 5M

Keratography 5M may provide a simple non-invasive method of examination for dry eyes with acceptable sensitivity, specificity, and repeatability [26,27]. Participants were instructed to fixate on a central target during tear meniscus height (TMH) measurement and blink normally. Inferior tear meniscus images were captured immediately after blinking and measured using the manual cursor provided by the system. The first noninvasive tear breakup time (NITBUT-f) was automatically measured as the time between the second complete blink and the distortion of the Placido rings reflected from the pre-corneal tear film surface. The average noninvasive tear breakup time (NITBUT-av) was defined as the average time of all tear film break-up points on the central cornea within an 8-mm diameter.

2.6. Optical quality analysis system II (OQAS II)

Tests were performed monocularly in a dark room. The spherical refractive error (−8.00 to +5.00 D) was automatically corrected by the double-pass system, and astigmatism ≥0.50 D was corrected with an external cylindrical lens. Visual quality parameters, including the basic objective scatter index (OSI), total OSI, and modulation transfer function (MTF) cut-off, were recorded over a 4-mm pupil size. The basic OSI is an objective parameter that describes intraocular scattered light representing the scattering index of refractive media, such as the cornea, lens, and vitreous, excluding the tear film. A lower OSI indicates better

optical quality. This program also consisted of a 20-s examination with an OSI measurement every 0.5 s. After the measurement, the mean and standard deviation of the 20-s OSI were recorded as "mean OSI" and "SD OSI," respectively. The total OSI represents the scattering index of all refractive media, including the tear film. To explore the effects of the tear film on visual quality, this study set up a new parameter, the TF-OSI (Fig. 1). The TF-OSI was obtained by subtracting the basic OSI from total OSI. The MTF cut-off reflected the highest spatial frequency that could be identified by the eyes under the lowest contrast ratio of 1 %. A higher MTF cut-off indicated better optical quality.

2.7. Corneal fluorescein staining

Corneal staining was evaluated by instilling 30 μL of 1 % fluorescein solution into the inferior conjunctival sac using a micropipette. After three blinks, corneal fluorescein staining was assessed in each of the five regions of the cornea using a slit-lamp microscope under a cobalt blue filter. For each individual, the five corneal zones were ranked from 0 to 4 according to the degree of staining [28]. The grading criteria were as follows: Grade 0, no punctate staining; Grade 1, slightly scattered punctate staining; Grade 2, dense distribution of corneal punctate staining; Grade 3, small areas of epithelial defect; and Grade 4, large areas of epithelial defect.

2.8. Statistical analysis

Statistical analyses were performed using SPSS 22.0 (IBM Corp., Armonk, NY, USA). Only data from the right eyes were analyzed for each individual. The normality was checked using the Kolmogorov–Smirnov test. Non-normally distributed data were analyzed using the Freidman test, followed by the Dunn–Bonferroni multiple comparison post-hoc test. Post-hoc tests were conducted only when the global test results were statistically significant. This study used Spearman's correlation test to evaluate the correlations between the ocular surface questionnaire and clinical test results. All continuous variables are expressed as means ± standard deviations, and statistical significance was set at $P < 0.05$.

3. Results

The study included 50 individuals (age range, 8–14 years; female to male ratio, 24:26; mean spherical equivalent, −3.05 ± 1.29 D). Two individuals dropped out of the study because of broken contact lenses. Another two patients stopped orthokeratology lens wear due to eye discomfort. During the study period, no infectious keratitis or other serious complications occurred.

The OSDI score and scores on the three subscales (i.e., ocular symptoms, vision-related function, and environmental triggers) showed similar trends over the follow-up period (Fig. 2A). Overall OSDI score and scores on two subscales (ocular symptoms and vision-related function) changed significantly during the 12-month follow-up period ($\chi2 = 21.721$, $P = 0.001$; $\chi2 = 26.403$, $P < 0.001$; $\chi2 = 34.889$, $P < 0.001$, respectively). Compared to the baseline value, the overall OSDI score for ocular discomfort significantly increased at the 3-month visit ($P = 0.009$) and significantly decreased at the 12-month visit compared to that at 3 months ($P = 0.006$). The ocular symptom subscale score significantly increased at the 3-month visit compared to baseline ($P = 0.013$) and significantly decreased at the 6-month and 12-month visit compared to that at 3 months ($P = 0.002$ and $P = 0.009$, respectively). Compared to the baseline value, the vision-related function subscale score significantly increased at the 3-month visit ($P = 0.016$). Moreover, it significantly decreased at the 12-month visit compared to that at 3 months ($P = 0.032$). Overall OSDI score and scores on two subscales (ocular symptoms and vision-related function) gradually decreased to levels close to baseline at 12 months of lens wear (all $P > 0.05$). Finally, the environmental triggers subscale score increased at the 3-month visit compared to the baseline value and decreased at the 6-month and 12-month visit compared to that at 3 months; however, these changes were not statistically significant ($\chi2 = 5.792$, $P = 0.327$) (Table 1).

The TMH, NITBUT-f, and NITBUT-av did not change significantly over the study period ($\chi2 = 6.023$, $P = 0.421$; $\chi2 = 2.096$, $P = 0.911$; $\chi2 = 5.737$, $P = 0.453$, respectively) (Fig. 2B, Table 1).

Three OSI-related parameters (i.e., basic OSI, mean TF-OSI, and SD TF-OSI) peaked at the 3-month visit, and gradually decreased thereafter. However, the MTF cut-off showed an opposite trend (Fig. 2C). There were significant differences between the baseline values and all follow-up values for the three OSI-related parameters and MTF cut-off ($\chi2 = 98.092$, $P < 0.001$; $\chi2 = 39.567$, $P < 0.001$; $\chi2 = 24.308$, $P < 0.001$; $\chi2 = 52.519$, $P < 0.001$, respectively). Compared to baseline value, the basic OSI significantly increased at 1 day, 1 week, and at 1, 3, and 6 months of orthokeratology lens wear ($P = 0.006$, $P < 0.001$, $P < 0.001$, $P < 0.001$, $P < 0.001$, respectively). The basic OSI significantly decreased at the 12-month visit compared to those at 1 week, 1 month, and 3 months ($P < 0.001$, $P < 0.001$, and $P < 0.001$, respectively). The mean TF-OSI significantly increased at 1 day, 1 week, 1 month, 3 months, and 6 months of lens wear compared with that at baseline ($P = 0.001$, $P < 0.001$, $P < 0.001$, $P < 0.001$, and $P < 0.001$, respectively). The SD TF-OSI significantly increased at 1 day, 1 week, 1 month, and 3 months of lens wear compared to that at baseline ($P = 0.002$, $P = 0.004$, $P = 0.027$, $P = 0.001$, respectively). Compared to the baseline value, the MTF cut-off significantly decreased at 1 week, 1 month, 3 months, and 6 months of lens wear ($P < 0.001$, $P < 0.001$, $P < 0.001$, and $P = 0.002$, respectively). The MTF cut-off significantly increased at 12 months compared to that at 1 week, 1 month, and 3 months ($P = 0.006$, $P = 0.016$, and $P = 0.001$, respectively) (Table 1).

The correlations between the overall OSDI score, three subscale scores, and all ocular surface parameters in patients who underwent orthokeratology lens are presented in Table 2. During the 12-month orthokeratology lens wear, the overall OSDI score was significantly positively correlated with the basic OSI and mean TF-OSI ($r = 0.943$, $P = 0.005$ and $r = 0.943$, $P = 0.005$, respectively). There were no correlations between the overall OSDI score and other ocular parameters, such as MTH ($r = -0.314$, $P = 0.544$), NITBUT-f/av ($r = -0.143$, $P = 0.787$ and $r = 0.200$, $P = 0.704$, respectively), SD TF-OSI ($r = 0.371$, $P = 0.468$), or MTF cut-off ($r = -0.771$, $P = 0.072$). The vision-related function score was significantly positively correlated with the basic OSI ($r = 0.943$, $P = 0.005$), mean TF-OSI ($r = 1.000$, $P < 0.001$), and SD TF-OSI ($r = 0.829$, $P = 0.042$), but not with the MTH ($r = 0.143$, $P = 0.787$), NITBUT-f/av ($r = 0.086$, $P = 0.872$ and $r = 0.314$, $P = 0.544$, respectively), or MTF cut-off ($r = -0.657$, $P = 0.156$). No clear correlations were observed between the symptom subscale or environmental triggers subscale scores and all ocular surface parameters (all $P > 0.05$).

The corneal fluorescein staining results during the 12-month orthokeratology lens wear are presented in Table 3. Corneal staining was at

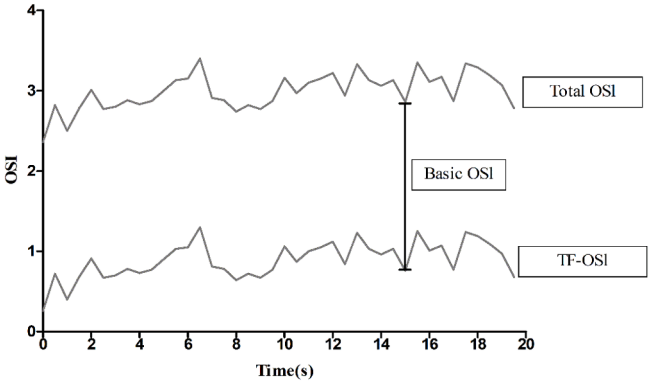

Fig. 1. Schematic representation of the computational approach of TF-OSI. OSI: objective scatter index; TF-OSI: tear film OSI.

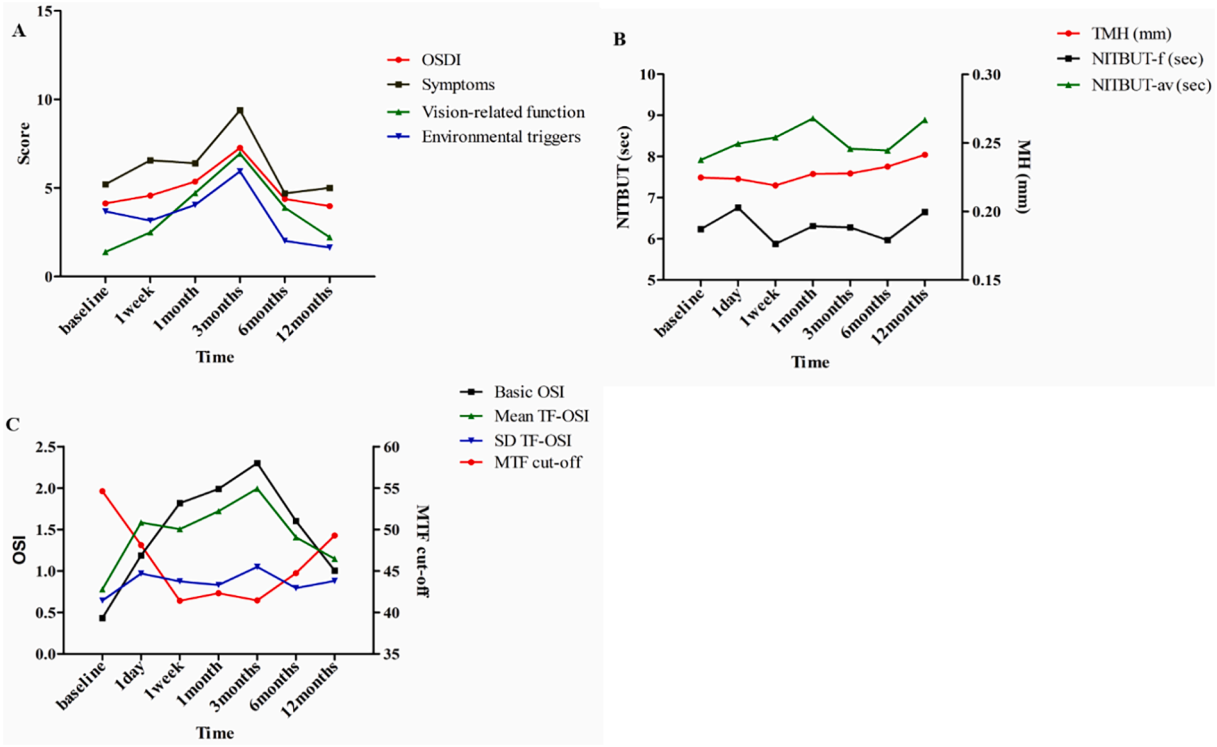

Fig. 2. Line diagram depicting baseline and temporal changes in ocular discomfort symptoms and signs of ocular discomfort. OSDI: ocular surface disease index; TMH: tear meniscus height; NITBUT-f: first noninvasive tear breakup time; NITBUT-av: average noninvasive tear breakup time; OSI: objective scatter index; TF-OSI: tear film OSI; MTF cut-off: modulation transfer function cut-off; SD, standard deviation.

Table 1
Ocular parameters (mean ± standard deviation) during 12-month orthokeratology lens wear.

	Baseline	1 day	1 week	1 month	3 months	6 months	12 months	$\chi 2$	P
OSDI									
Overall score (0–100)	4.13 ± 4.21	–	4.57 ± 4.06	5.36 ± 4.49	7.26 ± 4.52[a]	4.38 ± 4.45	3.98 ± 3.20[e]	21.721	**0.001**
Symptoms (0–100)	5.20 ± 4.88	–	6.57 ± 5.02	6.40 ± 4.37	9.39 ± 5.12[a]	4.70 ± 4.67[e]	5.00 ± 4.68[e]	26.403	< **0.001**
Vision-related function (0–100)	1.39 ± 3.84	–	2.50 ± 4.97	4.72 ± 7.16	6.94 ± 6.95[a]	3.89 ± 7.18	2.22 ± 5.76[e]	34.889	< **0.001**
Environmental triggers (0–100)	3.68 ± 6.81	–	3.16 ± 7.30	4.04 ± 8.62	5.94 ± 8.72	2.02 ± 5.42	1.64 ± 3.59	5.792	0.327
TMH (mm)	0.25 ± 0.07	0.24 ± 0.06	0.22 ± 0.03	0.23 ± 0.05	0.23 ± 0.04	0.23 ± 0.06	0.24 ± 0.06	6.023	0.421
NITBUT-f (sec)	6.24 ± 2.74	6.76 ± 3.14	5.88 ± 2.27	6.31 ± 2.65	6.28 ± 2.96	5.97 ± 2.65	6.55 ± 3.44	2.096	0.911
NITBUT-av (sec)	7.92 ± 2.94	8.31 ± 2.85	8.46 ± 2.42	8.93 ± 3.03	8.19 ± 2.70	8.15 ± 2.00	8.89 ± 2.16	5.737	0.453
Basic OSI	0.43 ± 0.35	1.19 ± 0.95[a]	1.82 ± 1.49[a]	1.99 ± 1.57[ab]	2.30 ± 2.15[ab]	1.60 ± 1.44[a]	1.00 ± 0.72[c,d,e]	98.092	< **0.001**
Mean TF-OSI	0.78 ± 1.27	1.58 ± 1.61[a]	1.50 ± 1.08[a]	1.72 ± 1.42[a]	1.99 ± 1.94[a]	1.41 ± 1.00[a]	1.15 ± 1.19	39.567	< **0.001**
SD TF-OSI	0.64 ± 0.95	0.97 ± 1.00[a]	0.87 ± 0.87[a]	0.83 ± 0.85[a]	1.05 ± 1.10[a]	0.79 ± 0.87	0.88 ± 0.93	24.308	< **0.001**
MTF cut-off	54.63 ± 7.64	48.11 ± 11.62	41.41 ± 11.87[a]	42.32 ± 11.99[a]	41.45 ± 14.10[a,b]	44.74 ± 11.51[a]	49.27 ± 9.66[c,d,e]	52.519	< **0.001**

OSDI, ocular symptoms disease index; TMH, tear meniscus heights; NITBUT-f/av, first/average noninvasive tear breakup time; OSI, objective scatter index; TF-OSI, tear film objective scatter index; MTF cut-off, modulation transfer function cut-off; SD, standard deviation.

[a] $P < 0.05$, compared to baseline.
[b] $P < 0.05$, compared to 1 day.
[c] $P < 0.05$, compared to 1 week.
[d] $P < 0.05$, compared to 1 month.
[e] $P < 0.05$, compared to 3 months.

Grade 0 at baseline in all patients. After 1 week of lens wear, Grade 1 corneal staining markedly increased to 16.4 % and was 9.1 %, 7.3 %, 9.1 %, and 12.7 % at 1, 3, 6, and 12 months, respectively. No patient had corneal staining above Grade 2. Corneal staining mostly involved the central and inferior cornea. Despite corneal staining, the patients opted to continue lens wear under careful monitoring, accompanied by antibiotics and artificial tears.

4. Discussion

4.1. Changes in the overall OSDI score and the three subscale scores during the 12-month orthokeratology lens wear

The ocular discomfort associated with orthokeratology lens wear was assessed using the OSDI, which provides a quantifiable assessment of the frequency of ocular discomfort symptoms and the impact of these symptoms on vision-related functioning. Carracedo et al. [29] found that

Table 2
Results of correlations between ocular parameters alterations and OSDI questionnaire during 12-month orthokeratology lens wear.

	Overall score (0–100)	Symptoms (0–100)	Vision-related function (0–100)	Environmental triggers (0–100)
TMH (cm)				
r	−0.314	−0.543	0.143	−0.429
P	0.544	0.266	0.787	0.397
NITBUT-f (*sec*)				
r	−0.143	−0.086	0.086	0.029
p	0.787	0.872	0.872	0.957
NITBUT-av (*sec*)				
r	0.200	0.200	0.314	−0.029
P	0.704	0.704	0.544	0.957
Basic OSI				
r	0.943	0.714	0.943	0.657
P	**0.005**	0.111	**0.005**	0.156
Mean TF-OSI				
r	0.943	0.486	1.000	0.600
P	**0.005**	0.329	< **0.001**	0.208
SD TF-OSI				
r	0.371	0.771	0.829	0.600
P	0.468	0.072	**0.042**	0.208
MTF cut-off				
r	−0.771	−0.714	−0.657	−0.371
p	0.072	0.111	0.156	0.468

OSDI, ocular symptoms disease index; TMH, tear meniscus heights; NITBUT-f/av, first/average noninvasive tear breakup time; OSI, objective scatter index; TF-OSI, tear film objective scatter index; MTF cut-off, modulation transfer function cut-off; SD, standard deviation.
Bold values signify correlations between parameters.

dryness and discomfort from orthokeratology lenses was lower than gas-permeable lenses worn daily. A possible reason is that the orthokeratology lens does not involve usage while eyes are open; thus, mechanical stimulation of the lens itself and incomplete blinking have a minor effect on ocular discomfort. However, in previous works, orthokeratology lens wear has increased dry eye symptoms [16,17],and a few patients temporarily stopped wearing orthokeratology lenses due to eye discomfort [16]. Regarding the OSDI questionnaire, this study showed more severe ocular symptoms and loss of vision-related function at 3 months, which improved at 6 months, and recovered to baseline scores at 12 months of lens wear. It is speculated that the reason for the recovery could be restored tear film stability and improved tolerance to extended wearing of contact lenses. The ocular surface of patients with orthokeratology lens wear was relatively unaffected by several environmental stimuli, such as low humidity, air conditioning, and wind.

4.2. Changes in NITBUT during the 12-month orthokeratology lens wear and their correlations with the OSDI score

The TMH and TBUT are important traditional indicators used to evaluate tear function. According to the results of this study, orthokeratology lens wear did not induce a significant change in the TMH during the 12 months of lens wear. A previous study also found that orthokeratology lens wear had little effect on basal tear secretion as measured by the Keratograph 5M [30] or Schirmer I test [17,31]. These findings suggest that orthokeratology lens wear does not result in an apparent reduction in tear volume. However, another study reported that the orthokeratology lens, as an ocular foreign body, can stimulate short term tear secretion [16]. Different studies have reported different tear film breakup time. This study did not observe a significant decrease in NITBUT-f or NITBUT-av during the 12 months of lens wear, in line with the findings of a previous study [16]. Na et al. [17] found that the TBUT measured by fluorescein was unchanged. However, orthokeratology-induced TBUT significantly decreased in a study by Li et al [31]. These discrepancies could be attributed to the different sequence and methods of examination. Invasive detection, such as by using fluorescein, may stimulate the ocular surface.

It was found that the OSDI score did not correlate well with traditional objective clinical measures, such as the TMH or NITBUT. This finding is consistent with those of previous studies that also failed to find a clear correlation between objective clinical signs and ocular symptoms [32,16,17]. Interestingly, a previous study found a weak negative Spearman correlation between NITBUT-f and OSDI in patients with dry eye disease with meibomian gland dysfunction [32]. Moreover, Wang et al. [16] reported that the OSDI score increased to their maximum after 6 months of orthokeratology lens wear, but the NITBUT-f and NITBUT-av did not substantially differ during this period. This trend was corroborated by another study [17]. The OSDI includes three subscales: ocular symptoms, vision-related function, and environmental triggers. This study did not observe a correlation between the subscales and changes in tear film break-up metrics, such as NITBUT-f and NITBUT-av, over the 12-month follow-up period. Similarly, no correlations were observed between the subscales and TMH. In conclusion, this study demonstrated that the NITBUT and TMH are not strong indicators of OSDI score.

4.3. Changes in visual quality during the 12-month orthokeratology lens wear and their correlations with the OSDI score

In normal conditions, the uncorrected visual acuity of orthokeratology-treated patients is 20/20 or better [24]. However, satisfaction with visual acuity and quality of vision is subjectively rated as not good by some patients. Therefore, a more precise assessment of optical quality alterations and their impact on vision quality is important in patients undergoing orthokeratology lens wear. The OQAS can be used to objectively assess optical quality of eyes [33] and tear film quality dynamics [21,34]. Here, the basic OSI of all patients was 0.43 ± 0.35 before lens wear, which was worse than that reported by Martínez-Roda et al. [35] (0.38 ± 0.19). However, the results of this study were still within the normal range [35]. It was found that the basic OSI significantly increased at 3 months of lens wear. This may be attributed to the fact that the central corneal thickness decreased significantly over a 3-month period and stabilized thereafter [36]. Corneal epithelial

Table 3
The grade and location of corneal staining during 12-month orthokeratology lens wear.

	baseline	1 day	1 week	1 month	3 months	6 months	12 months
Quadrant	(%)	(%)	(%)	(%)	(%)	(%)	(%)
Grade 0	100	98.2	83.6	90.9	92.7	90.9	87.3
Grade 1	0	1.8	16.4	9.1	7.3	9.1	12.7
Quadrant	(%)	(%)	(%)	(%)	(%)	(%)	(%)
Superior	0	0	0	0	0	0	0
Inferior	0	1.8	5.5	1.8	3.6	3.6	3.6
Nasal	0	0	1.8	0	0	0	0
Temporal	0	0	0	0	0	1.8	3.6
Central	0	0	9.1	7.3	3.6	3.6	5.5

damage may also be a cause of the increased OSI. In the present study, Grade 1 corneal staining was observed after 1 week of lens wear and was mostly distributed in the central and inferior cornea. This finding is consistent with observations from other studies [37,38]. Walline et al. [37] found that corneal staining was mostly located in the central and inferior cornea after orthokeratology lens wear. In a study by Mika et al. [38], Grade 1 corneal staining was the most prevalent type. Although the incidence of corneal staining seemed to be relatively high, the severity was low and did not pose a threat to the cornea. The increased irregularity of the corneal shape caused by orthokeratology lens wear may worsen corneal aberration and, consequently, the overall visual quality. The new OSI parameter, TF-OSI, can record dynamic changes in the tear film within 20 s and assist in monitoring the visual quality alterations observed in patients undergoing orthokeratology lens wear. This study found that the mean TF-OSI and SD TF-OSI tended to rise, peaking after 3 months of lens wear, and then gradually decreasing. It is speculated that this was due to an unstable tear film, because local tear film breakup causes uneven distribution of tears on the ocular surface, which results in deflection of the light entering the cornea instead of being concentrated on the retina [39]. Ocular surface damage may further aggravate tear film instability [40]. The stronger the effect of the tear film on light scattering, the larger the light spot reflected on the retina. Thus, black and white gratings were difficult to distinguish by eye, which resulted in a decreased MTF cut-off frequency in this study. In summary, unstable pre-corneal tear film and exposure of the underlying irregular corneal surface may result in increased intraocular scatter and ocular aberrations.

OSDI questions can be divided into two aspects: 1) visual function subscale score, including questions associated with visual acuity aspects that evaluate difficulties affecting daily living, such as reading or watching TV (as the participants were teenagers, there were no questions regarding possible difficulties in driving); and 2) discomfort symptom subscale score, including questions associated with ocular discomfort related to ocular pain or environmental factors [41]. In this study, the OSI was correlated with the overall OSDI score and particularly with the visual function score. This suggests that decreased visual quality, caused by orthokeratology lens, has an impact on patients' quality of life. In this study, the TF-OSI was correlated well with visual function compared to the 20-s OSI [34,39]. The new TF-OSI proposed here excluded the influence of other refractive media and simply reflected tear film scattering, which is more suitable for evaluating the tear film of patients treated with orthokeratology lenses. These findings suggested that tear film instability can result in aberrations and scattering, and consequently cause fluctuating vision in patients. TF-OSI-related parameters primarily reflect alterations in the tear film occurring in the central cornea and may be a sensitive indicator of tear film instability before significant changes appear. Alterations in vision quality could explain the absence of a direct correlation between ocular discomfort symptoms and the traditional clinical parameters of tears observed in patients treated with orthokeratology lenses.

In conclusion, subjective symptoms of discomfort and tear film-related visual function parameters were worse at 3 months of orthokeratology lens wear but were gradually restored thereafter. This study elucidated that the OSDI score and vision-related function subscale score were clearly associated with several tear-related parameters (the basic OSI, mean TF-OSI, and SD TF-OSI values). Thus, the OQAS provides a better interpretation of complaints of ocular discomfort in orthokeratology lens wear. The new parameter, TF-OSI, was more sensitive in detecting the quality and stability of the tear film compared to traditional tear film indicators (TMH, NITBUT-f, and NITBUT-av). Thus, the OQAS may be useful in tear film assessments and long-term follow-up examination of patients treated with orthokeratology lenses.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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