




Characteristics of the Ocular Surface in Myopic Child Candidates of Orthokeratology Lens Wear

Yuanfang Yang · Qinghui Wu · Wei Pan · Longbo Wen ·
Zhiwei Luo · Haoran Wu · Guangyao Ran · Zhikuan Yang ·
Xiaoning Li 

Received: June 2, 2023 / Accepted: August 9, 2023 / Published online: September 4, 2023
© The Author(s) 2023, corrected publication 2023

ABSTRACT

Introduction: The purpose of this study was to investigate the characteristics of objective ocular surface parameters using non-invasive objective instruments in children with myopia who are candidates for orthokeratology lens wear.

Y. Yang · G. Ran · Z. Yang
Aier School of Ophthalmology, Central South University, Changsha 410015, China

Q. Wu · Z. Yang · X. Li (✉)
Changsha Aier Eye Hospital, Changsha 410015, China
e-mail: lixiaoning@aierchina.com

X. Li
Aier College of Ophthalmology & Optometry, Hubei University of Science and Technology, Xianning 437000, China

Y. Yang · W. Pan · L. Wen · Z. Luo · H. Wu ·
G. Ran · Z. Yang · X. Li
Aier Institute of Optometry and Vision Science, Changsha 410015, China

Y. Yang · Z. Yang · X. Li
Hunan Province Optometry Engineering and Technology Research Center, Changsha 410015, China

Y. Yang · Z. Yang · X. Li
Hunan Province International Cooperation Base for Optometry Science and Technology, Changsha 410015, China

Methods: Children with myopia who are candidates for orthokeratology lens wear were retrospectively investigated. The subjects were divided into three age groups. The Keratograph 5M and LipiView interferometry were used to assess non-invasive tear meniscus height (TMH), non-invasive tear film break-up time (NIBUT), conjunctival hyperemia redness score (RS), meibomian gland loss (MGL) score, lipid layer thickness (LLT), and blink pattern analysis, including the number of partial blinks (PB) and total blinks (TB), as well as the partial blink rate (PBR).

Results: A total of 1119 children with myopia (2070 eyes) aged 7–18 years were selected. The mean TMH, NIBUT, and LLT of the subjects was 0.21 mm, 12.45 s, and 65.28 nm, respectively. The mean RS and upper and lower MGL scores were 0.64, 1.00, and 1.06, respectively. The mean PB, TB, and PBR was 5.13, 6.46, and 0.81, respectively. Age was significantly correlated to all ocular surface parameters ($p = 0.00$), except for PB. NIBUT and LLT did not differ between male participants and female participants (all $p > 0.05$). TMH, RS, and upper and lower MGL were significantly higher in male participants than in female participants (all $p < 0.01$). In addition, NIBUT was positively associated with TMH ($r = 0.13$, $p = 0.00$) and LLT ($r = 0.28$, $p = 0.00$). Both upper and lower MGL were positively correlated with TMH, PB, and TB (all $p = 0.00$), whereas upper MGL was negatively correlated with NIBUT and LLT (all $p < 0.05$).

TB was negatively correlated with NIBUT and LLT (all $p = 0.00$). PB had no relation with TMH, NIBUT, and LLT (all $p > 0.05$). In addition, PBR was positively correlated with NIBUT and LLT (all $p = 0.00$) but not with TMH, RS, or MGL (all $p > 0.05$). Overall, 57.00% had a TMH ≤ 0.2 mm, 43.20% had a NIBUT ≤ 10 s, 48.10% had an LLT ≤ 60 nm, and 88.10% had a PBR > 0.4 .

Conclusions: Child orthokeratology candidates have enhanced tear secretion and increased meibomian gland deficiency with aging. In addition, the adult dry eye diagnostic criteria may apply to orthokeratology candidates aged 12–18 years but should be lower for younger candidates. Given the proportion of abnormal risk, it is necessary to assess tear film status and blink pattern by reliable and feasible objective examination before fitting orthokeratology.

Keywords: Orthokeratology; Ocular surface; Tear film; Lipid layer; Meibomian gland loss; Blink pattern

Key Summary Points

Orthokeratology wearing is a challenge to ocular surface homeostasis, which can impact the safety of myopia control. Ocular surface characteristics in children, including tear film function, have not been investigated as extensively as in adults.

The non-invasive objective ocular surface examination with correlated indicators is reliable, providing an important guide for the safety of orthokeratology fitting. Thus, we investigated the characteristics of ocular surface objective parameters among children with myopia who are candidates for orthokeratology lens wear, exploring the proportion of children with myopia with dry eye risk in different pediatric populations.

This study enrolled and analyzed the objective ocular surface characteristics of 1119 children with myopia aged 7–18 years who were orthokeratology candidates without a contact-lens-wearing history.

Our final analysis revealed that child orthokeratology candidates have enhanced tear secretion and increased meibomian gland deficiency with aging.

The adult dry eye diagnostic criteria may apply to orthokeratology candidates aged 12–18 years but should be lower for younger candidates. In consideration of the proportion of abnormal risk, it is necessary to assess tear film status and blink pattern by reliable and feasible objective examination before fitting orthokeratology.

INTRODUCTION

Children's ocular surfaces are increasingly exposed to climate change, pollution, screen time, and myopia treatments such as atropine, multifocal soft contact lenses, and orthokeratology (OrthoK) [1–8]. The current study revealed a high prevalence of contact lens wear related to clinically diagnosed and severe symptoms of dry eye disease [9]. The use of OrthoK is regarded as an effective and safe approach for myopia control and has been well-documented in previous studies [10–12]. However, there are concerns that wearing OrthoK might induce a characteristic spatial disturbance in the stability of the tear film [6]. Assessment of children's ocular surface has not received sufficient attention in the past; even the diagnostic criteria for children are based on adult criteria. Contact lens wear has become a challenge to ocular surface homeostasis, which

can also impact the safety of myopia control. Thus, it is necessary to master the ocular surface condition of children before wearing OrthoK.

Numerous previous studies have found an increase in dry eye prevalence with age [13, 14] at varying levels of severity according to gender [15, 16], while some studies did not find a significant association [17–19]. Meanwhile, Rojas-Carabali et al. reported that healthy children had at least one abnormal ocular surface result and 33.33% had a dry eye disease diagnosis, according to the Tear Film and Ocular Surface Society Dry Eye Workshop (TFOS DEWS II) [20, 21]. DEWS II offers a mechanism for recognizing dry eye in the adult population. However, ocular surface characteristics in children, including tear film function, have not been investigated as extensively as in adults. There is limited evidence in the literature as to the association between age, sex, and ocular surface status. Ocular surface health in children may be adversely affected by similar ocular, systemic, and environmental factors as in adults. Thus, the importance of evaluating tear film in adolescents is high.

Understanding tear film and meibomian gland function in children enhances our ability to diagnose variation from normal parameters in dry eye and ocular surface disease, as most of the recommended values are based on adult study results. There is also a lack of information regarding ocular surface features in adolescents. This study aimed to summarize ocular surface features in children with myopia who are candidates for orthokeratology lens wear and to explore the proportion of children with myopia with dry eye risk in different pediatric populations. Meanwhile, we also explored the interaction of ocular surface indicators in maintaining tear film homeostasis in children as well as the criteria for ocular surface abnormalities before orthokeratology fitting. This study provides a basis to compare ocular surface test results with other groups of children.

METHODS

This cross-sectional retrospective study was conducted in a single-center setting, at the Changsha Aier Eye Hospital in Changsha, Hunan, China. This study was conducted following the Declaration of Helsinki and approved by the Institutional Ethics Committee of Changsha Aier Eye Hospital (approval number: KYPJ002). As the study was retrospective, informed consent was not required by the ethics committee.

Subjects

A total of 1119 myopic children who were candidates for orthokeratology lens wear were consecutively recruited at the Changsha Aier Eye Hospital from May 2021 to December 2021. We collected their ocular surface examinations before wearing orthokeratology. The inclusion criteria were as follows: (1) aged 7–18 years; (2) myopia ≤ -0.50 diopter (D), and with astigmatism of up to 2.0 D, with keratometry values between 40.0 D and 45.0 D; (3) best-corrected visual acuity of no worse than 20/25 and normal intraocular pressure; (4) children with myopia who meet the criteria for the orthokeratology prescription and no corneal staining with fluorescein; (5) no history of orthokeratology or soft lens wear; and (6) Keratograph 5 M Testing and LipiView Interferometry were performed. Participants were excluded if they had pathological changes of the lid margin or cornea, uvea, or retina; had other systemic diseases that may influence the ocular surface; or had a history of contact lens wear, other ocular treatments, or surgeries.

Keratograph 5M Testing

The Keratograph 5M (Oculus GmbH, Wetzlar, Germany) was used to obtain non-invasive tear meniscus height (TMH), average non-invasive tear film break-up time (NIBUT), conjunctival hyperemia redness score (RS), and meibomian gland loss (MGL) score, as described previously

[22, 23]. Meibomian gland loss was graded as 0 (no loss of meibomian glands), 1 (dropout of $< 1/3$ of total meibomian glands), 2 (dropout of one-third to two-thirds of total meibomian glands), and 3 (dropout of $> 2/3$ of total meibomian glands), as proposed by Arita et al. [24] Two skilled physicians scored the patient's meibomian gland test and they were trained consistently to ensure the accuracy of the patient's test results.

LipiView Interferometry

The LipiView Interferometry (Johnson & Johnson Inc., New Brunswick, NJ) was used to obtain average lipid layer thickness (LLT) and blink pattern analysis such as partial blink rate (PBR), number of partial blinks (PB), and number of total blinks (TB). A 20 s video was captured to document the interference pattern of the tear film for each eye. The LLT deriving from the image was calculated as interferometric color units (ICU), where 1 ICU reflects approximately 1 nm [25]. The maximum LLT value was limited to 100 nm. The number of total/partial blinks in 20 s was measured using the LipiView Interferometer. The number of total blinks was the sum of partial and complete blinks. The partial blink rate was the number of partial blinks / number of total blinks $\times 100\%$ [26].

Definition

Positive signs of aqueous deficiency and lipid deficiency were defined as present in one or both eyes with a TMH ≤ 0.2 mm, BUT ≤ 10 s, LLT ≤ 60 nm, or the existence of PBR > 0.4 [21, 27].

Statistical Analyses

All the subjects received examinations of both eyes. All statistical analyses were performed with SPSS Statistics software (version 26.0; SPSS Inc., Chicago, IL, USA). Data are presented as mean \pm standard deviation (SD) or n (%). The normality of variables data was assessed using the Shapiro–Wilk test. Age differences, spherical equivalent (SE), and ocular surface parameters

among the three age groups were examined through a one-way analysis of variance (ANOVA) and post hoc analysis with Bonferroni correction. The comparison between gender of the ocular surface parameters used the independent samples t -test. The differences in gender and positive clinical sign rates of aqueous deficiency or lipid deficiency were examined using chi-squared tests. Correlations between variables were analyzed by Pearson and Spearman correlation. All tests were two-tailed, and $p < 0.05$ was considered significant.

RESULTS

A total of 1119 children with myopia without OrthoK wear history (2070 eyes) aged between 7 and 18 years were enrolled in the study. The demographics and ocular surface parameters are summarized in Table 1. The subjects were divided into three age groups on the basis of approximate Chinese school grade level, as follows: 7–11 years (group 1, elementary school age), 12–14 years (group 2, middle school age), and 15–18 years (group 3, high school age). The mean age and spherical equivalent (SE) were 11.26 years and -2.76 D; a significant difference in age, gender, and SE among the three age groups was observed (all $p = 0.00$).

The mean TMH, NIBUT, and LLT of the subjects was 0.21 ± 0.06 mm, 12.45 ± 6.58 s, and 65.28 ± 24.57 nm, respectively. The mean RS and MGL score (upper and lower) were 0.64 ± 0.30 , 1.00 ± 0.43 , and 1.06 ± 0.50 , respectively. The mean PB, TB, and PBR was 5.13 ± 3.50 , 6.46 ± 3.82 , and 0.81 ± 0.27 , respectively (Table 1). Among the three groups, TMH, NIBUT, LLT, RS, MGL score, and PBR were significantly lower in the younger age groups (all $p = 0.00$). The PB was similar among the three age groups ($p = 0.09$). Moreover, the younger age groups (group 1 and group 2) had significantly more TB than group 3 ($p = 0.00$) (Fig. 1).

Except for PB, as presented in Table 2, age was significantly positively correlated to TMH, NIBUT, RS, MGL (upper and lower), LLT, and PBR (all $p = 0.00$). In contrast, negative correlations were observed in TB ($p = 0.00$). Also

Table 1 Demographics and ocular surface parameters among three age groups

	Group 1 (7–11 years)	Group 2 (12–14 years)	Group 3 (15–18 years)	Overall study sample	<i>p</i>	Post hoc significance
<i>N</i> (eyes)	1216	610	244	2070		
Age (years)	9.49 ± 1.20	12.96 ± 0.80	15.86 ± 0.98	11.26 ± 2.52	0.00**	
Gender					0.00**	
Female (%)	62.80%	28.30%	8.90%			
Male (%)	54.40%	30.70%	14.80%			
SE	−2.50 ± 1.33	−3.08 ± 1.69	−3.25 ± 1.68	−2.76 ± 1.52	0.00**	
TMH (mm)	0.19 ± 0.06	0.22 ± 0.06	0.24 ± 0.07	0.21 ± 0.06	0.00**	1 < 2 < 3
NIBUT (s)	11.73 ± 6.54	13.08 ± 6.49	14.52 ± 6.45	12.45 ± 6.58	0.00**	1 < 2 < 3
RS	0.62 ± 0.29	0.64 ± 0.28	0.72 ± 0.31	0.64 ± 0.30	0.00**	1 = 2 < 3
MGL						
Upper	0.97 ± 0.42	1.04 ± 0.41	1.06 ± 0.48	1.00 ± 0.43	0.00**	1 < 2 = 3
Lower	1.02 ± 0.48	1.10 ± 0.52	1.13 ± 0.46	1.06 ± 0.50	0.00**	1 < 2 = 3
LLT (nm)	63.37 ± 24.61	66.17 ± 24.10	72.44 ± 24.24	65.28 ± 24.57	0.00**	1 = 2 < 3
PBR	0.79 ± 0.28	0.83 ± 0.26	0.89 ± 0.21	0.81 ± 0.27	0.00**	1 < 2 < 3
PB	5.12 ± 3.46	5.32 ± 3.54	4.69 ± 3.55	5.13 ± 3.50	0.09	1 = 2 = 3
TB	6.60 ± 3.73	6.53 ± 3.87	5.45 ± 3.98	6.46 ± 3.82	0.00**	1 = 2 > 3

SE spherical equivalent, *TMH* tear meniscus height, *NIBUT* non-invasive tear film break-up time, *RS* conjunctival hyperemia redness score, *MGL* meibomian gland loss score, *LLT* lipid layer thickness, *PBR* partial blink rate, *PB* number of partial blinks, *TB* number of total blinks

Group 1 (1), Group 2 (2), Group 3 (3)

Data are presented as mean ± standard deviation. ***p* < 0.01

presented in Table 3, NIBUT and LLT did not differ between male participants and female participants (all *p* > 0.05). TMH, RS, and MGL (upper and lower) were significantly higher in male participants than in female participants; PBR, PB, and TB were significantly higher in female participants than in male participants (all *p* < 0.01).

Both NIBUT and LLT were positively correlated with TMH (all *p* = 0.00). In addition, NIBUT was positively correlated with LLT (*p* = 0.00), as shown in Fig. 2. In addition, both upper and lower MGL was positively correlated with TMH, PB, and TB (all *p* = 0.00), and upper MGL was negatively correlated with NIBUT and LLT (all *p* < 0.05). Neither NIBUT nor LLT was

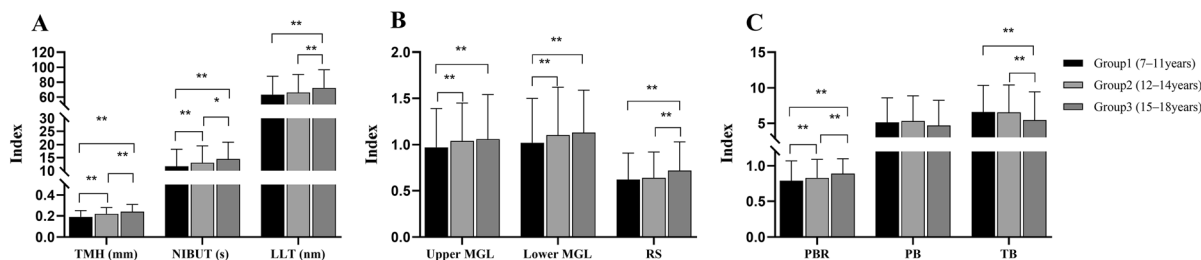


Fig. 1 Characteristics of the ocular surface in three age groups. Bar graph showing the average **A** tear meniscus height (TMH), non-invasive tear film break-up time (NIBUT), and lipid layer thickness (LLT); **B** meibomian

gland loss (MGL) score (upper, lower) and conjunctival hyperemia redness score (RS); and **C** partial blink rate (PBR), number of partial blinks (PB), and number of total blinks (TB) in three age groups. * $p < 0.05$, ** $p < 0.01$

correlated with lower MGL, as presented in Table 2. TB was negatively correlated with NIBUT and LLT (all $p = 0.00$) (Fig. 2), while PB had no relation with TMH, NIBUT, and LLT (all $p > 0.05$). Additionally, PBR was positively correlated with NIBUT and LLT (all $p = 0.00$) but not with TMH, RS, or MGL (all $p > 0.05$).

Table 4 lists the demographic features of this population and the prevalence of subjects having clinical signs of aqueous deficiency or lipid deficiency. From a total of 2070 eyes, 57.00% had a TMH ≤ 0.2 mm; 43.20% had a NIBUT ≤ 10 s; 48.10% had an LLT ≤ 60 nm; and 88.10% had a PBR > 0.4 . Among the three age groups, there were significant differences in TMH ≤ 0.2 mm, BUT ≤ 10 s, LLT ≤ 60 nm, and PBR > 0.4 (all $p = 0.00$). We noted that the abnormal rates of TMH ≤ 0.2 mm and PBR > 0.4 were significantly higher in female participants than in male participants (all $p < 0.05$). No significant difference was noted in the prevalence of NIBUT ≤ 10 s and LLT ≤ 60 nm between male participants and female participants (all $p > 0.05$).

DISCUSSION

The Keratograph 5M [28] and LipiView interferometry [29], which can accurately and non-invasively determine the objective parameters of the ocular surface, even for children with low compliance, are available and reliable. The non-invasive objective ocular surface examination with correlated indicators is reliable, providing an important guide for the safety of

orthokeratology fitting. Thus, we investigated the characteristics of ocular surface objective parameters among children with myopia who are candidates for orthokeratology lens wear, exploring the proportion of children with myopia with dry eye risk in different pediatric populations. Meanwhile, we also explored the interaction of ocular surface indicators in maintaining tear film homeostasis in children and providing a basis to compare ocular surface test results with other groups of children.

The mean TMH of 0.21 mm in this study aligns with previous studies reporting on children [20, 30] and adults [22]. Moreover, the NIBUT of 12.45 s aligns with other studies in children [20, 30, 31], and is higher than 10.40 s in the adult study [22]. In keeping with the TMH and NIBUT increase with age in our study, tear secretion is thought to be maximal around age 10–20 years [32] and then decrease as reported [33–35]. However, we noticed that the mean values of TMH in participants of this study aged 7–11 years were lower than the adults' diagnosed threshold values of dry eye. Similar to previous studies with healthy children and adults [5, 36–38], the mean value of LLT in the present study was 65.28 nm, less than adults with dry eyes [38]. LLT and PBR increased with age, consistent with the study of Weng and Li [39, 40]. In this study, PBR increased with aging, which may be due to a decrease in TB as a result of increased near work, such as smartphone use and study time, with aging. As Chidi-Egboka et al. suggested, smartphone use in children results in dry eye

Table 2 Associations between age and ocular surface parameters

	Age		TMH		NIBUT		LLT		PBR		PB		TB	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
TMH	0.29	0.00**	1.00		0.13	0.00**	0.09	0.00**	0.03	0.29	−0.02	0.35	−0.05	0.04*
NIBUT	0.16	0.00**	0.13	0.00**	1.00		0.28	0.00**	0.15	0.00**	−0.01	0.65	−0.10	0.00**
RS	0.10	0.00**	0.02	0.31	−0.05	0.05*	−0.03	0.19	−0.01	0.58	−0.03	0.18	−0.04	0.07
MGL upper	0.11	0.00**	0.18	0.00**	−0.05	0.03*	−0.05	0.02*	0.01	0.80	0.08	0.00**	0.08	0.00**
MGL lower	0.10	0.00**	0.19	0.00**	−0.04	0.09	−0.03	0.14	0.01	0.74	0.08	0.00**	0.08	0.00**
LLT	0.11	0.00**	0.09	0.00**	0.28	0.00**	1.00		0.16	0.00**	−0.02	0.31	−0.12	0.00**
PBR	0.11	0.00**	0.03	0.29	0.15	0.00**	0.16	0.00**	1.00		0.39	0.00**	−0.12	0.00**
PB	−0.04	0.07	−0.02	0.35	−0.01	0.65	−0.02	0.31	0.39	0.00**	1.00		0.81	0.00**
TB	−0.09	0.00**	−0.05	0.04*	−0.10	0.00**	−0.12	0.00**	−0.12	0.00**	0.81	0.00**	1.00	

TMH tear meniscus height, NIBUT non-invasive tear film break-up time, RS conjunctival hyperemia redness score, MGL meibomian gland loss score, LLT lipid layer thickness, PBR partial blink rate, PB number of partial blinks, TB number of total blinks
 −1 ≤ *r* ≤ 1. **p* < 0.05, ***p* < 0.01

symptoms and immediately sustained slowing of blinking [41]. In this study, PB was unchanged, then PBR increased. We found MGL increased with age in agreement with Arita R et al., and there was a significant positive correlation between age and the lid margin abnormality score in populations aged 0–80 years [24]. Because the meibomian gland has been described to be morphologically complete at birth [42], we hypothesize that increased lacrimal gland function with age may instead aggravate the blockage of the meibomian glands and cause the deficiency. Our results showed that tear secretion increased with age from 7 years to 18 years. The ocular surface values of orthokeratology candidates aged 12–18 years were comparable to or better than those of adults, but those of the younger children were not. Ozdemir et al. revealed that tear function declined, especially the tear film break-up time values with advancing age, from age 20–86 years [43]. With aging, children have enhanced tear secretion with increased meibomian gland deficiency.

In our study, both NIBUT and LLT were negatively correlated with TB; and they were positively correlated with PBR. Blink pattern could be considered as an additive measure for abnormal ocular surface assessment [44]. As indicated in Jie et al.’s findings, PB may lead to less squeezing of the meibomian glands by the

orbicularis muscle, resulting in less effective meibum secretion [39]. Proper blinking is essential for tear film homeostasis and may serve as a compensatory mechanism. Similar to contact lens wearers who report dry eye symptoms, they appear likely to also benefit from improved blink efficiency [45]. In the present study, PB was not significantly correlated with tear film parameters in OrthoK candidates. Instead, TB showed a negative correlation with tear film parameters. On the basis of this study, we can speculate that the decrease in total blinks causes a decrease in the squeezing of the lid gland, combined with an increase in LLT and impaired lipid drainage in adolescents, thus leading to an increase in MGL. This would also explain the positive correlation found between MGL and TMH in our study—precisely, the enhanced tear secretion of aqueous and lipid functions with increasing age in childhood and the poor lipid drainage due to environmental pollution or electronics use. Lee et al. found no significant differences in PBR and upper meiboscores between non-lens wearers with OrthoK wearers; however, OrthoK wearers showed increased LLT and higher meiboscores of lower eyelids [5]. LLT thickening induced by OrthoK wear may be related to a negative feedback mechanism. On the basis of the various correlations among the ocular surface parameters, we speculated that enhanced lacrimal secretion

Table 3 Ocular surface parameters between gender

N	TMH	NIBUT	RS	Upper MGL	Lower MGL	LLT	PBR	PB	TB	
Male	1005	0.21 ± 0.07	12.56 ± 6.65	0.69 ± 0.29	1.04 ± 0.45	1.10 ± 0.51	64.43 ± 25.26	0.79 ± 0.29	4.70 ± 3.20	6.16 ± 3.60
Female	1065	0.20 ± 0.06	12.35 ± 6.52	0.60 ± 0.29	0.96 ± 0.40	1.02 ± 0.48	66.08 ± 23.89	0.84 ± 0.26	5.54 ± 3.70	6.73 ± 3.99
<i>t</i>	3.73	0.73	6.84	4.35	3.40	-1.50	-3.23	-5.28	-3.92	
<i>p</i>	0.00**	0.47	0.00**	0.00**	0.00**	0.13	0.00**	0.00**	0.00**	

TMH tear meniscus height, NIBUT non-invasive tear film break-up time, RS conjunctival hyperemia redness score, MGL meibomian gland loss score, LLT lipid layer thickness, PBR partial blink rate, PB number of partial blinks, TB number of total blinks

Data are presented as mean ± standard deviation

***p* < 0.01

and a more stable tear film in OrthoK candidates may in turn somehow lead to a reduced blink frequency. Ocular surface parameters interacted with each other and blink pattern are related to tear film stability.

Cut-off values of TMH ≤ 0.2 mm, BUT ≤ 10 s, LLT ≤ 60 nm, or the existence of PBR > 0.4 are recommended for the diagnosis of the clinical signs of aqueous deficiency and lipid deficiency, measured using the Keratograph 5 M and LipiView Interferometry [27]. The prevalence of dry eye by symptoms and signs was 13.55%, and that of dry eye by symptoms alone was 31.40% in Chinese people aged 5–89 years [46]. We found 57% and 43.2% of children tended to have inadequate tear volume and tear stability, respectively; moreover, 48% of children tended to have thinner lipid layer thickness, and 88% of children had higher abnormal blink rates. Moreover, these abnormality rates decreased significantly with aging. Gender did not affect the abnormality rates of NIBUT and LLT. Female participants had higher abnormalities in both TMH and PBR than male participants. At the same time, we consider that the dry eye diagnostic criteria may not be appropriate for younger children, leading to a higher rate than actual values. Still, the abnormal risk rates in children are of concern. Children with dry eye may have fewer symptoms and complain of more symptoms than adults with similar severity of dry eye conditions [47]. In addition, children's dry eye subjective symptoms of complaints may not be reliable and may mismatch with objective clinical signs, in which case objective examination would be more reliable. Given the accurate and non-invasive ocular surface instruments, objective examinations can serve as important indicators for dry eye risk before fitting orthokeratology. Meanwhile, we consider that age should be taken into account when assessing dry eye risk in OrthoK candidates, and adult criteria can be applied aged 12 years and older. For children 11 years and younger, however, the existing diagnostic criteria should be lowered due to their lacrimal gland function development.

The study provided a data basis for ocular surface parameters in children with myopia. Liu

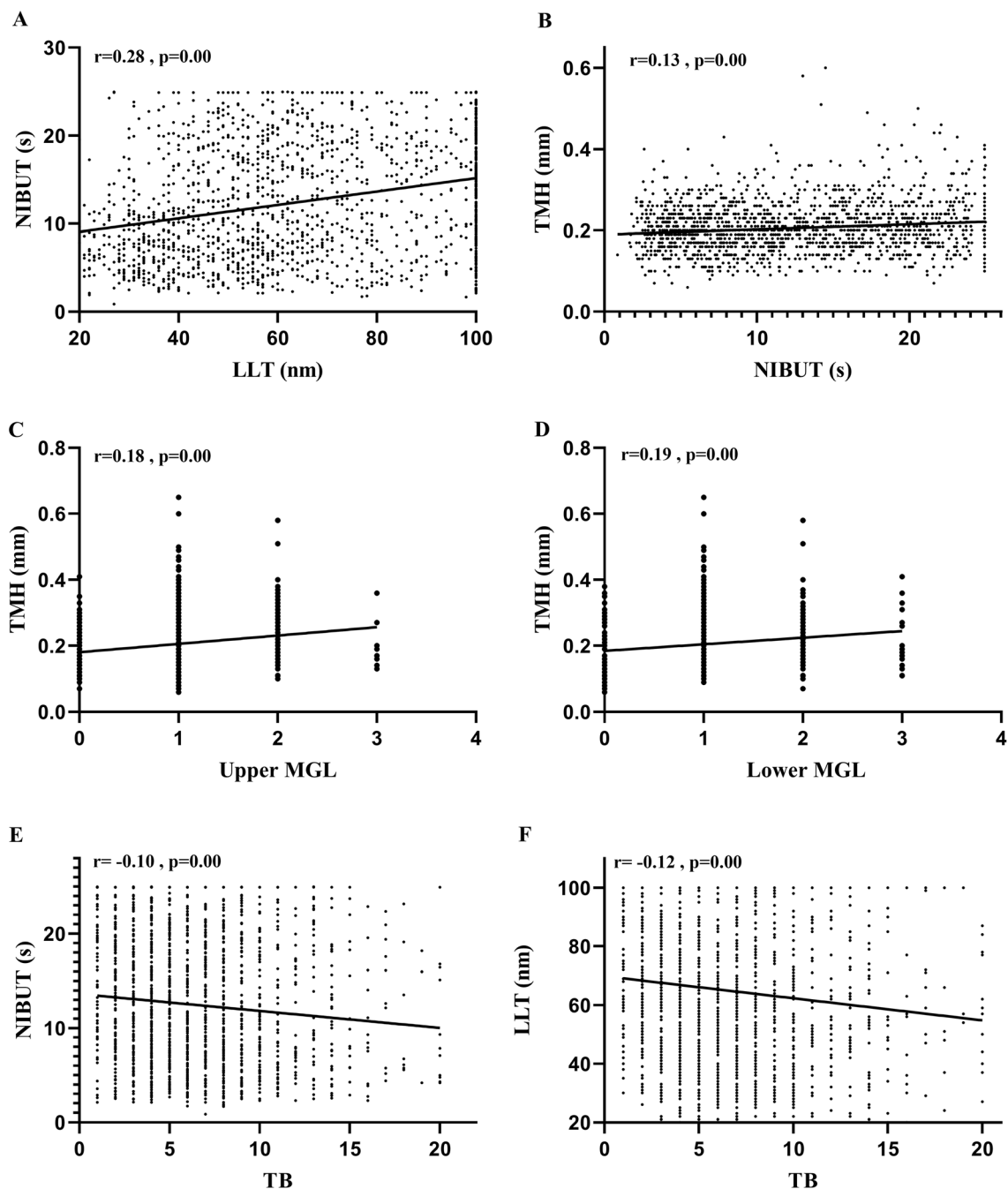


Fig. 2 Correlation analyses between non-invasive tear film break-up time (NIBUT), tear meniscus height (TMH), lipid layer thickness (LLT), meibomian gland loss (MGL),

and number of total blinks (TB). **A** NIBUT and LLT; **B** TMH and NIBUT; **C** TMH and upper MGL; **D** TMH and lower MGL; **E** NIBUT and TB; **F** LLT and TB

et al. reported that dry eye in children has been underestimated or over-treated [48], with treatment consisting of artificial tear eye drops, autologous serum eyedrops, and environmental

recommendations that had applied to children [49, 50]. Most studies focused on children with dry eye associated with a number of congenital and autoimmune issues. With increased

Table 4 Clinical signs of aqueous deficiency and lipid deficiency by age and gender

<i>N</i> (%)	Age group			<i>p</i>	Gender		<i>p</i>	Total All
	Group 1	Group 2	Group 3		Male	Female		
TMH ≤ 0.2 mm	793 (65.30%)	301 (49.30%)	85 (34.80%)	0.00**	541 (53.90%)	638 (59.90%)	0.00**	1179 (57.00%)
NIBUT ≤ 10 s	555 (48.40%)	224 (38.50%)	64 (28.70%)	0.00**	402 (42.40%)	441 (44.00%)	0.49	843 (43.20%)
LLT ≤ 60 nm	586 (50.90%)	278 (46.30%)	90 (38.80%)	0.00**	476 (49.30%)	478 (46.90%)	0.28	965 (48.10%)
PBR > 0.4	946 (86.00%)	521 (89.80%)	189 (95.00%)	0.00**	774 (86.20%)	882 (89.90%)	0.01*	1656 (88.10%)

TMH tear meniscus height, NIBUT non-invasive tear film break-up time, LLT lipid layer thickness, PBR partial blink rate
p* < 0.05, *p* < 0.01

electronics and eye burden, dry eye in children without any systemic disease increased. Tear-related visual function parameters were correlated with ocular discomfort [51]. Moreover, OrthoK separates the tear film into the pre- and post-lens. OrthoK use can reduce tear film break-up time and tear stability; moreover, corneal epithelial damage may cause shorter BUT [52]. When the tear volume is not sufficient, this friction between the contact lens and the ocular surface may cause the presence of foreign bodies, dryness, and discomfort sensations [53]. Positive correlations were observed among NIBUT, LLT, and TMH in this study, consistent with tear film homeostasis. As the total lipid layer increases, tear evaporation decreases, and then tear volume increases, which in turn prolongs tear film break-up time. It is more important to evaluate the ocular surface before fitting orthokeratology in adolescents to ensure the safety of wearing. Hence, a thorough OrthoK pre-fitting evaluation should focus on these critical parameters, especially TMH and NIBUT, to assess the risk as well as to establish a targeted treatment plan.

This study was retrospective, and we could not control for certain confounding factors, including the participants' environment and electronic screen use time. We also did not obtain subjective ocular surface symptoms in these children with myopia. Future work may build on the foundations established in this

study to explore further prospective observations to clarify conflicting points and confirm the causal relationship between OrthoK lens use and changes in tear film homeostasis.

CONCLUSIONS

Child orthokeratology candidates have enhanced tear secretion and increased meibomian gland deficiency with aging. The adult dry eye diagnostic criteria may apply to orthokeratology candidates aged 12–18 years, but should be lower for younger candidates. In consideration of the proportion of abnormal risk, it is necessary to assess tear film status and blink pattern by reliable and feasible objective examination before fitting orthokeratology.

Author Contributions. All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by Yuanfang Yang, Qinghui Wu, Wei Pan, Longbo Wen, Zhiwei Luo, Haoran Wu, Guangyao Ran, Zhikuan Yang, and Xiaoning Li. The first draft of the manuscript was written by Xiaoning Li, Yuanfang Yang, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding. This study was supported by the Science Research Foundation of Aier Eye Hospital Group (Grant No.AF2003D7) and the Natural Science Foundation of Hunan Province (Grant No. 2022JJ40002 and 2021JJ40004). The journal's Rapid Service Fees were funded by the authors.

Data Availability. The datasets generated during and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest. Yuanfang Yang, Qinghui Wu, Wei Pan, Longbo Wen, Zhiwei Luo, Haoran Wu, Guangyao Ran, Zhikuan Yang, and Xiaoning Li have nothing to disclose.

Ethical approval. This study was conducted following the Declaration of Helsinki and approved by the Institutional Ethics Committee of Changsha Aier Eye Hospital (approval number: KYPJ002). As the study was retrospective, informed consent was not required by the ethics committee.

Open Access. This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

REFERENCES

1. Zhang Y, Chen H, Wu X. Prevalence and risk factors associated with dry eye syndrome among senior high school students in a county of Shandong Province, China. *Ophthalmic Epidemiol.* 2012;19(4):226–30.
2. Zhang X, et al. Dry eye management: targeting the ocular surface microenvironment. *Int J Mol Sci.* 2017;18(7):1398.
3. Elhusseiny AM, et al. Relationship between screen time and dry eye symptoms in pediatric population during the COVID-19 pandemic. *Ocul Surf.* 2021;22:117–9.
4. Song YY, et al. Atropine in ameliorating the progression of myopia in children with mild to moderate myopia: a meta-analysis of controlled clinical trials. *J Ocul Pharmacol Ther.* 2011;27(4):361–8.
5. Lee J, et al. Evaluation of the meibomian glands using the tear interferometer wearing orthokeratology lenses. *BMC Ophthalmol.* 2022;22(1):133.
6. Cho WH, et al. Analysis of tear film spatial instability for pediatric myopia under treatment. *Sci Rep.* 2020;10(1):14789.
7. Xu L, et al. Comparison between heated eye mask and intense pulsed light treatment for contact lens-related dry eye. *Photobiomodul Photomed Laser Surg.* 2022;40(3):189–97.
8. Uchino M, et al. Prevalence of dry eye disease and its risk factors in visual display terminal users: the Osaka study. *Am J Ophthalmol.* 2013;156(4):759–66.
9. Uchino M, et al. Japan Ministry of Health study on prevalence of dry eye disease among Japanese high school students. *Am J Ophthalmol.* 2008;146(6):925–9.
10. Si JK, et al. Orthokeratology for myopia control: a meta-analysis. *Optom Vis Sci.* 2015;92(3):252–7.
11. Bullimore MA, Johnson LA. Overnight orthokeratology. *Cont Lens Anterior Eye.* 2020;43(4):322–32.
12. Fan L, et al. Clinical study of orthokeratology in young myopic adolescents. *Int Contact Lens Clin.* 1999;26(5):113–6.
13. Onwubiko SN, et al. Dry eye disease: prevalence, distribution and determinants in a hospital-based population. *Cont Lens Anterior Eye.* 2014;37(3):157–61.

14. Tellefsen Nøland S, et al. Sex and age differences in symptoms and signs of dry eye disease in a Norwegian cohort of patients. *Ocul Surf.* 2021;19:68–73.
15. Vehof J, et al. Prevalence and risk factors of dry eye in 79,866 participants of the population-based Lifelines cohort study in the Netherlands. *Ocul Surf.* 2021;19:83–93.
16. Dana R, et al. Estimated prevalence and incidence of dry eye disease based on coding analysis of a large, all-age United States health care system. *Am J Ophthalmol.* 2019;202:47–54.
17. Wang X, et al. Evaluation of dry eye and meibomian gland dysfunction in teenagers with myopia through noninvasive keratograph. *J Ophthalmol.* 2016;2016:6761206.
18. Doughty MJ. Further assessment of gender- and blink pattern-related differences in the spontaneous eyeblink activity in primary gaze in young adult humans. *Optom Vis Sci.* 2002;79(7):439–47.
19. Lavezzo MM, et al. Eye blink in newborn and pre-school-age children. *Acta Ophthalmol.* 2008;86(3):275–8.
20. Rojas-Carabali W, et al. High prevalence of abnormal ocular surface tests in a healthy pediatric population. *Clin Ophthalmol.* 2020;14:3427–38.
21. Willcox MDP, et al. TFOS DEWS II tear film report. *Ocul Surf.* 2017;15(3):366–403.
22. Tian L, et al. Repeatability and reproducibility of noninvasive keratograph 5M measurements in patients with dry eye disease. *J Ophthalmol.* 2016;2016:8013621.
23. Blackie CA, et al. The relationship between dry eye symptoms and lipid layer thickness. *Cornea.* 2009;28(7):789–94.
24. Arita R, et al. Noncontact infrared meibography to document age-related changes of the meibomian glands in a normal population. *Ophthalmology.* 2008;115(5):911–5.
25. Finis D, et al. Evaluation of lipid layer thickness measurement of the tear film as a diagnostic tool for Meibomian gland dysfunction. *Cornea.* 2013;32(12):1549–53.
26. Chang SW, Wu WL. Association between dry eye parameters depends on tear components. *J Clin Med.* 2022;11(11):3056.
27. Wolffsohn JS, et al. TFOS DEWS II Diagnostic Methodology report. *Ocul Surf.* 2017;15(3):539–74.
28. García-Marqués JV, et al. Repeatability of non-invasive Keratograph break-up time measurements obtained using oculus Keratograph 5M. *Int Ophthalmol.* 2021;41(7):2473–83.
29. Lee JM, et al. Ocular surface analysis: a comparison between the LipiView(®) II and IDRA(®). *Eur J Ophthalmol.* 2021;31(5):2300–6.
30. Tichenor AA, et al. Tear film and meibomian gland characteristics in adolescents. *Cornea.* 2019;38(12):1475–82.
31. Nichols JJ, et al. Evaluation of tear film interference patterns and measures of tear break-up time. *Optom Vis Sci.* 2002;79(6):363–9.
32. Norn MS. Tear secretion in normal eyes. Estimated by a new method: the lacrimal streak dilution test. *Acta Ophthalmol (Copenh).* 1965;43(4):567–73.
33. Cho P, Yap M. Schirmer test. I. A review. *Optom Vis Sci.* 1993;70(2):152–6.
34. Stapleton F, et al. TFOS DEWS II epidemiology report. *Ocul Surf.* 2017;15(3):334–65.
35. Chidi-Egboka NC, et al. The ocular surface in children: a review of current knowledge and meta-analysis of tear film stability and tear secretion in children. *Ocul Surf.* 2019;17(1):28–39.
36. Yu H, et al. Orthokeratology lens wear for 2 years in children did not alter tear film lipid thickness by non-invasive interferometry. *Front Med (Lausanne).* 2022;9: 821106.
37. Zhao Y, et al. The significance of meibomian gland changes in asymptomatic children. *Ocul Surf.* 2018;16(3):301–5.
38. Jung JW, et al. Analysis of factors associated with the tear film lipid layer thickness in normal eyes and patients with dry eye syndrome. *Invest Ophthalmol Vis Sci.* 2016;57(10):4076–83.
39. Weng HY, et al. Characteristics of tear film lipid layer in young dry eye patients. *J Formos Med Assoc.* 2021;120(7):1478–84.
40. Li J, et al. Assessment of tear film lipid layer thickness in patients with Meibomian gland dysfunction at different ages. *BMC Ophthalmol.* 2020;20(1):394.
41. Chidi-Egboka NC, Jalbert I, Golebiowski B. Smartphone gaming induces dry eye symptoms and reduces blinking in school-aged children. *Eye (Lond).* 2023;37(7):1342–9.
42. Shirakawa R, Arita R, Amano S. Meibomian gland morphology in Japanese infants, children, and

- adults observed using a mobile pen-shaped infrared meibography device. *Am J Ophthalmol*. 2013;155(6):1099-1103.e1.
43. Ozdemir M, Temizdemir H. Age- and gender-related tear function changes in normal population. *Eye (Lond)*. 2010;24(1):79–83.
 44. Jie Y, et al. Evaluation of incomplete blinking as a measurement of dry eye disease. *Ocul Surf*. 2019;17(3):440–6.
 45. Young G, et al. A multi-centre study of lapsed contact lens wearers. *Ophthalmic Physiol Opt*. 2002;22(6):516–27.
 46. Song P, et al. Variations of dry eye disease prevalence by age, sex and geographic characteristics in China: a systematic review and meta-analysis. *J Glob Health*. 2018;8(2): 020503.
 47. Han SB, et al. Children with dry eye type conditions may report less severe symptoms than adult patients. *Graefes Arch Clin Exp Ophthalmol*. 2013;251(3):791–6.
 48. Liu ZG, Li W. Pay attention to the diagnosis and treatment of dry eye in children. *Zhonghua Yan Ke Za Zhi*. 2018;54(6):406–8.
 49. Mac Cord Medina F, et al. Management of dry eye related to systemic diseases in childhood and longterm follow-up. *Acta Ophthalmol Scand*. 2007;85(7):739–44.
 50. Kojima T, et al. The effect of autologous serum eyedrops in the treatment of severe dry eye disease: a prospective randomized case-control study. *Am J Ophthalmol*. 2005;139(2):242–6.
 51. Xie C, Wei R. Long-term changes in the ocular surface during orthokeratology lens wear and their correlations with ocular discomfort symptoms. *Cont Lens Anterior Eye*. 2023;46(1):101757.
 52. Li J, Dong P, Liu H. Effect of overnight wear orthokeratology lenses on corneal shape and tears. *Eye Contact Lens*. 2018;44(5):304–7.
 53. Kojima T. Contact lens-associated dry eye disease: recent advances worldwide and in Japan. *Invest Ophthalmol Vis Sci*. 2018;59(14):Des102-des108.