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Linsong Qi

qilinsong06@163.com

Air Force Medical Center

Yao Lu
Siyuan Chen
Chen Zhao
Qi Qi
Yan Tang
Ding Ding
Zhikang Zou
Yong Liu

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Figure 1 and 6 are not available with this version.

Changes in Ocular Biometrics of Non-Myopic High School Students: A Prospective Cohort Study on Myopia Risk Factors

Running title: Ocular Biometrics Shifts Linked to Myopia Onset in Adolescents

Lu Yao[1,#], Siyuan Chen[2,#], Chen Zhao[1], Qi Qi[3], Yan Tang[4], Ding Ding[5], Zhikang Zou[6,*], Yong Liu[1,*], Linsong Qi[1,7,*]

[1]Department of Ophthalmology, Air Force Medical Center, Beijing 100142, China

[2]Department of Ophthalmology, Eastern Theater Air Force Hospital, Nanjing 210000, China

[3]Department of Physical Examination, Cadet Bureau of PLA Air Force, Beijing 100195, China

[4]Department of Ophthalmology, Western Theater Air Force Hospital, Chengdu 610000, China

[5]Department of Ophthalmology, Northern Theater Air Force Hospital, Shenyang 110092, China

[6]Department of Clinic and Research, Air Force Medical Center, Beijing 100142, China

[7]Military Medical Innovation Center, Air Force Medical University, Xi'an 710032, China

[*]Correspondence to:

Linsong Qi, Department of Ophthalmology, Air Force Medical Center, Beijing 100142, China; Military Medical Innovation Center, Air Force Medical University, Xi'an 710032, China. qilinsong06@163.com

Yong Liu, Department of Ophthalmology, Air Force Medical Center, Beijing 100142, China. eyely@126.com

ZhiKang Zou, Department of Clinic and Research, Air Force Medical Center,

30 Fucheng Road, Beijing 100142, China. zouzhikang1979@126.com

#Co-first authors: Lu Yao and Siyuan Chen

Abstract

Background. To characterize pre-myopia ocular biometric signatures and identify actionable early predictive biomarkers for myopia onset in non-myopic senior high school adolescents.

Methods. This 30-month prospective cohort study enrolled 325 14–16-year-old students with baseline spherical equivalent refraction (SER) between 0 D and + 2.00 D. Comprehensive ophthalmic assessments including SER, axial length (AL), anterior chamber depth (ACD), lens thickness (LT), and central corneal thickness (CCT) were performed at baseline in September 2020, with follow-up evaluations scheduled at 15 and 30 months to track longitudinal changes in refractive status, biometric parameters, and new myopia incidence.

Results. The 15-month cumulative new-onset myopia rate was 7.57%, rising to 16.84% at 30 months. Participants who later developed myopia

(final SER $\leqslant -0.5$ D) presented significantly lower baseline SER, longer AL, deeper ACD, higher AL/CR (corneal radius) ratio, and thinner LT than the non-myopic subgroups (all $P < 0.05$). This group also exhibited more rapid refractive deterioration and axial elongation across both follow-up visits. ROC analysis identified optimal baseline predictive thresholds for myopia onset: AL/CR at 2.99, ACD at 3.76 mm, and LT at 3.58 mm. Longitudinal cutoffs were also validated: 0–15 month AL elongation > 0.10 mm and AL/CR increment > 0.01, plus 15–30 month AL elongation > 0.07 mm and AL/CR increment > 0.01, all demonstrated strong predictive power.

Conclusions. For adolescents approaching emmetropization stability, dynamic biometric shifts including accelerated axial elongation, anterior chamber deepening, lens thinning, and elevated AL/CR are robust early biomarkers for incident myopia, supporting targeted pre-myopia intervention.

Keywords. myopia, adolescent, Axial length, AL/CR ratio, baseline SER,

ocular biometric parameters

Introduction

Myopia has rapidly escalated into a major global public health crisis over the past decades(1). High myopia, or pathological myopia, can lead to permanent visual impairment and even blindness, imposing heavy economic and care burdens on individuals and families(2). China faces an exceptionally severe myopia epidemic: data released by the Chinese Health Commission in 2022 showed that the overall myopia rate among children and adolescents reached 53.6%, and regional studies have reported that myopia affects 67.3% of Grade 7 students and 83.2% of university students in central China(3). Although national authorities including the Ministry of Education have issued targeted implementation plans to promote myopia prevention and control across the country(4), a large number of school-aged children and adolescents still develop new-onset myopia every year(5).

Against this backdrop, the Chinese Ministry of Education, in collaboration with the Air Force, launched the Teenager Aviation School (TASAF) across 15 cities in China. The Air Force Teenager Aviation School recruits strictly selected non-myopic 14-16 year old male freshmen, who share highly consistent living conditions, academic workload and standardized myopia prevention management during senior high school. However, previous studies still recorded persistently high new myopia incidence in this group, which severely limits their access to visual-demanding occupations such as aviation and aerospace(6, 7).

Ocular biometric parameters have been widely proven to be closely associated with the incidence and progression of myopia(8). Existing research has confirmed that changes in indicators including axial length (AL)(9), central corneal thickness (CCT)(10), axial length/corneal curvature radius ratio (AL/CR ratio)(11), and lens thickness (LT)(12) can indicate the occurrence and development of myopia at an early stage, and are recognized as potential biomarkers for evaluating the refractive status

of children and adolescents(13-16). However, current relevant research is mostly focused on school-age children, and there is a notable lack of targeted cohort studies focusing on 15-18 year old senior high school adolescents, a critical transition period when emmetropization stabilizes and myopia onset risk still remains.

To fill this research gap, we conducted a 30-month prospective cohort investigation on students from TASAF, with systematic monitoring of spherical equivalent refraction (SER) and ocular biometric parameters. The core objective of this study is to identify the changing patterns of ocular biological parameters related to myopia onset in non-myopic senior high school students, screen out ocular biomarkers that can early predict the impending myopia onset in adolescents, and provide evidence-based data support for the early detection and intervention of myopia incidence.

Methods

Study design and subjects

A total of 325 male adolescents aged 14-16 (15.4 ± 0.6) years from

TASAF were randomly selected. These students underwent baseline assessments including SER (calculated as spherical degree + 1/2 cylinder degree), AL, ACD, LT, and CCT in September 2020, followed by subsequent follow-ups in December 2021 and March 2023(Figure 1). SER≤ - 0.5 diopter (D) indicated myopia. Annual losses to follow-up may be attributed to factors such as poor academic performance, the emergence of systemic or ocular diseases, and other causes. The study followed the principles of the Declaration of Helsinki. Ethical approval for the study was obtained from the Air Force Medical Center. Written informed consents were obtained from the students and their parents or legal guardians.

Inclusion criteria: 1. without a history of ocular surgery, ocular trauma, or an ocular disease that affected the vision; 2. slit-lamp microscopy revealed no obvious pathological changes such as lens and vitreous opacity; 3. without receiving myopia prevention and control treatments, such as low-dose atropine eye drops (concentration 0.01%), orthokeratology lenses,

myopia control spectacles, or corneal refractive surgery; 4. SER between -0.25 D and +2.00 D in both eyes, cylinder≤0.50D, uncorrected visual acuity ≥ 20/20 in both eyes.

Exclusion criteria: with a history of endocrine disorders, immune-mediated diseases, or other systemic conditions that may affect the eye.

Computerized optometry

Before computerized optometry was performed, pupils of both eyes were dilated using 0.5% tropicamide-phenylephrine ophthalmic solution (Mydrin-P, Santen, Japan) every 5 min for 4 times. Computerized optometry was determined by computerized autorefractor (KR-8900, Topcon, Japan) after 20 min when the fourth drop was instilled. Three consecutive measurements were obtained from both eyes of each student, and the averages were recorded.

Ocular biometric parameters measurements

Measurements of ocular biometric parameters (CCT, ACD, LT, AL, WTW, PS, corneal curvature (keratometry readings: K1 and K2), and AL/CR

ratios) were performed with an ocular biometry system (OA-2000, TOMEY, Japan). Measurements were performed under natural illumination and the mean of three measurements was taken as the final measurement value.

Statistical analysis

All statistical analyses were performed using SPSS 24.0 software (IBM Corp., Armonk, NY, USA). All measurement data was presented as the mean ± standard deviation ($\bar{x} \pm s$). The comparisons between groups were made using analysis of variance (one-way ANOVA). Tukey method was conducted for pairwise comparisons. Pearson correlation analysis was performed between K1, K2, AL, ACD, LT, CCT, PS, WTW, AL/CR and SER. Fisher's exact test was employed to compare the distribution across different refractive error subgroups. Receiver operating characteristic (ROC) curve analysis was utilized to evaluate the predictive role of various indicators for myopia. Data from the right eyes were included for statistical analysis.The significance level was set at $P < 0.05$.

Results

The change of SER and ocular biometric parametersof the students

The data from the remaining 291 students were included in the statistical analysis after excluding all students lost to follow-up. From baseline to the 30-month follow-up, SER showed a progressive decrease ($P < 0.05$, Figure 2A) while AL and the AL/CR ratio exhibited a progressive increase ($P < 0.05$, Figure 2B and 2F). ACD at both follow-up was significantly deeper than at baseline ($P < 0.05$, Figure 2C). LT and CCT at baseline and the second follow-up was significantly thicker compared to the first follow-up ($P < 0.05$, Figure 2D and 2E) .

The total SER change over a 30-month period was -0.18 ± 0.03 D. The SER change was -0.08 ± 0.02 D in the first year and -0.10 ± 0.03 D in the second year. The total AL change was 0.14 ± 0.01 mm. The AL change was 0.07 ± 0.01 mm in the first year and 0.06 ± 0.01 mm in the second year.

Correlation of SER and ocular biometric parameters

At the end of the 30-month follow-up, final SER was positively correlated with baseline SER (r = 0.2287, P = 0.0000) and LT (r = 0.1835, P =0.0017), but negatively correlated with baseline AL (r = -0.1725, P =0.0032), ACD (r = -0.2506, P =0.0000), and AL/CR ratio (r = -0.31, P =0.0010) (Figure 3). Furthermore, the final SER is negatively correlated with the changes in AL ($\triangle_1 r$ = -0.4137, P = 0.0000; $\triangle_2 r$ = -0.4466, P =0.0000; $\triangle_3 r$ = -0.5438, P = 0.0000) (Figure 4A-C) and AL/CR ratio ($\triangle_1 r$ = -0.3272, P = 0.0000; $\triangle_2 r$ = -0.3346, P =0.0000; $\triangle_3 r$ = -0.4763, P = 0.0000) (Figure 4D-F) for the 0~15-month, 15~30-month and 0~30months follow-ups.

Comparative analysis of SER and ocular biometric parameters of different final SER subgroups

Students were stratified into four subgroups based on the SER at 30-month follow-up: ≤ - 0.5 D (n = 35), >-0.5 D to≤0 D (n = 78), > 0 D to ≤+0.5 D (n = 111) and ＞+0.5 D (n = 67). Comparative analyses were performed on SER and ocular biometric parameters across subgroups at

baseline and during follow-ups. There was a statistically significant difference in baseline SER between the subgroup with SER > -0.5 D to $\leqslant$ 0 D and the subgroup with SER > + 0.5 D ($P < 0.05$)(Figure 5A). There was a statistically significant difference in baseline AL between the subgroup with SER > 0 D to $\leqslant$ + 0.5 D and the subgroup with SER > + 0.5 D ($P < 0.05$). At the 30-months follow-up, the AL in the subgroup with SER > + 0.5 D was significantly shorter than that in the other three subgroups($P < 0.05$) (Figure 5B).

At baseline, ACD in both the subgroup with SER $\leqslant$ - 0.5 D and the subgroup with SER > - 0.5 D to $\leqslant$ 0 D was significantly greater than that in the subgroup with SER > + 0.5 D. At the 30-months follow-up, ACD in these two subgroups remained significantly higher than in the other two subgroups, while the subgroup with SER > 0 D to $\leqslant$ + 0.5 D also exhibited a significantly greater depth compared to the group with SER > + 0.5 D (P < 0.05) (Figure 5C).

At both baseline and the 30-months follow-up, LT in the the subgroup

with SER ≤ - 0.5 D and the subgroup with SER > - 0.5 D to ≤ 0 D was significantly thinner than that in the subgroup with SER > + 0.5 D ($P < 0.05$) (Figure 5D).

The AL/CR in the SER ≤ -0.5D subgroup was significantly higher than that in both the subgroup with SER > 0 D to ≤ + 0.5 D and the subgroup with SER > + 0.5 D subgroup at baseline and during the 30-months follow-up ($P < 0.05$). The AL/CR ratio in the > + 0.5 D subgroup was the lowest among all groups at both baseline and the 30-months follow-up ($P < 0.05$) (Figure 5E).

The total 30-month change in SER was -0.99±0.40 D in the subgroup with final SER ≤ - 0.5 D, - 0.47±0.29 D in the subgroup with final SER > - 0.5 D to ≤ 0 D, - 0.05±0.35 D in the subgroup with final SER > 0 D to ≤ + 0.5 D subgroup, and + 0.38 ± 0.41 D in the subgroup with final SER > + 0.5 D (Figure 6A). Students in the subgroup with final SER ≤ - 0.5 D exhibited significantly greater SER changes during both the 0 ~ 15-months and 15 ~ 30-months follow-up ($P < 0.05$). They also

demonstrated the largest AL changes compared to other subgroups for the 0 ~ 15-months follow-up ($P < 0.05$)(Figure 6B). Furthermore, this subgroup showed relatively large changes in AL/CR ratio over the two follow-up ($P < 0.05$), with the change for the 0~15-months follow-up being significantly higher than that in the other subgroups ($P < 0.05$)(Figure 6E). For this subgroup, the change in ACD was significantly greater only than that in the SER > + 0.5 D subgroup($P < 0.05$)(Figure 6C). No statistically significant differences in LT changes were observed across all subgroups($P > 0.05$)(Figure 6D). Changes in ocular biometric parameters were relatively modest in the other three subgroups (Figure 6).

The predictive role of ocular biological parameters in the onset of myopia

The role of different parameters in predicting myopia was validated using the ROC curve. The baseline AL/CR ratio, ACD, and LT demonstrated significant predictive value for myopia ($P < 0.05$), with corresponding area under the ROC curve (AUC) values of 0.65, 0.63, and 0.60. Baseline

SER and AL did not show statistical significance in terms of myopia prediction (Table 1). The changes in AL and AL/CR during the two follow-up periods demonstrated significant predictive value for myopia ($P < 0.05$) (Table 1).

Discussion

Building on our prior multiple long-term cohort studies conducted in TASAF, we have previously identified SER, outdoor exposure time and near-work intensity as the three major factors associated with myopia onset and myopic shift in adolescents(6, 17). However, none of these earlier serial studies systematically analyzed the dynamic patterns of ocular biometric parameters specifically among non-myopic adolescents. Against this research gap, the present 30-month prospective follow-up study enrolled 291 non-myopic senior high school students aged 14–16 years. The final cumulative myopia incidence was 16.28%, with a total 30-month SER myopic shift of only -0.18 ± 0.03 D. Both core metrics demonstrated lower values than those documented in historical cohorts of

comparable adolescent populations(6, 7), a difference that can be largely explained by the stricter inclusion criteria adopted here: we refined the baseline SER eligibility range from the previous -0.25 D ⩽ SER ⩽ +2.0 D to 0 D ⩽ SER ⩽ +2.0 D, thereby excluding participants who were already pre-myopic at baseline. Notably, a substantial proportion of participants still developed incident myopia over the 30-month follow-up, confirming that targeted early risk stratification and pre-myopic intervention strategies for this specific adolescent population carry critical public health and clinical significance.

Ocular biometric parameters(18)serve as the foundational metrics for constructing adolescent refractive profiles and implementing myopia prevention and control strategies. In our prior population-based cross-sectional study(17)encompassing 7514 adolescents aged 15–19 years, we systematically demonstrated that statistically significant age-dependent differences in ocular biometric parameters persist throughout the pre-myopic phase, and myopic shift is significantly correlated with

changes in AL and AL/CR. This 30-month continuous prospective cohort study, conducted in a homogenized senior high school student population, represents the first systematic characterization of the dynamic patterns of ocular biometric changes preceding myopia onset among non-myopic high school students. Our findings confirm that baseline AL, ACD, LT, AL/CR ratio, and their respective longitudinal changes throughout follow-up are all significantly associated with both the magnitude of myopic shift and the risk of incident myopia.

Axial length is a critical metric in clinical refractive surveillance for myopia. Multiple prior cohort studies have confirmed that abnormal, rapid axial elongation can be detected as early as 1 year before myopia onset(19). While the findings of the present study are fully consistent with this established conclusion, we further demonstrate that significant abnormal AL growth initiates at least 15 months prior to myopia development. Through ROC curve analysis, we further verified that AL elongation exceeding 0.1 mm at the 15-month follow-up visit serves as a

strong predictive factor for incident myopia, with an AUC of 0.79. This finding suggests that intensified follow-up protocols and personalized intervention strategies should be initiated for senior high school students who exhibit AL growth greater than 0.1 mm within the first 15 months of surveillance.

Epidemiologically validated(20), age-stratified AL thresholds for Chinese children and adolescents have been validated, delineating high-risk cutoffs of 23.92 mm for the 13–15-year age group and 24.42 mm for the 16–18-year age group. Exceeding these population-specific thresholds is associated with a 4.41-fold elevated risk for myopia onset relative to the general adolescent population. In our cohort, the mean baseline AL of the incident myopia subgroup (23.93 mm) demonstrated high concordance with this population-validated threshold. These results substantiate the clinical utility of this population-derived AL threshold in our study population, indicating that non-myopic students whose baseline AL reaches or surpasses this cutoff should be identified as high-priority

candidates for intensified myopia prevention strategies during routine follow-up.

Previous studies(21) have demonstrated that the AL/CR ratio exhibits significantly stronger correlation with SER than AL. In the present study, the baseline AL/CR ratio demonstrated moderate predictive utility for myopia onset, achieving an AUC of 0.65. This relatively modest performance is likely attributable to the restricted SER distribution within our highly selected cohort. The widely accepted critical threshold for incident myopia is an AL/CR ratio > 3.0(22), whereas the optimal baseline AL/CR cutoff identified in our study was 2.99. This slight discrepancy may be attributed to our cohort's greater baseline hyperopic reserve and more stable overall refractive profile. Notably, the longitudinal change in AL/CR ratio during follow-up demonstrated superior predictive performance compared to the static baseline value. Specifically, the change in AL/CR over the 0–15 month follow-up period achieved an AUC of 0.77, indicating that dynamic annual monitoring of the AL/CR

ratio provides superior clinical warning value compared to a single baseline measurement. Consistent with the trend observed for axial length, individuals who developed myopia exhibited a rapid abnormal elevation in AL/CR at least 15 months before myopia onset. The predictive performance of individual ocular biometrics in this cohort remains suboptimal, underscoring the need for future studies to integrate multi-dimensional biometric and environmental exposure data into a combined model to improve the accuracy of early myopia risk stratification.

A significant negative correlation was confirmed(23) between ACD and SER, consistent with prior established findings. The high myopia-risk subgroup presented with a deeper baseline anterior chamber, which underwent further deepening concomitant with subsequent axial elongation. This pattern is consistent with the physiological mechanism of global ocular expansion during myopic progression. Current evidence(24) regarding the association between ACD and myopia severity remains inconsistent, with some studies(25) suggesting a stronger

association in high myopia and others reporting no significant differences. As our study population did not include participants with moderate or high myopia, we could not contribute further evidence to resolve this ongoing debate.

In addition to axial elongation and anterior chamber deepening, dynamic alterations in LT constitute a fundamental compensatory mechanism in refractive regulation. The compensatory thinning of the lens in response to axial growth reduces lenticular refractive power, partially counteracting the induced myopic shift. Clinical myopia occurs when axial elongation exceeds this compensatory limit(26). While our study found no significant inter-subgroup differences in LT changes across follow-ups, a trend of initial lens thinning followed by recovery thickening was noted. Future investigations integrating direct lenticular power measurements are warranted to elucidate this compensatory mechanism in greater depth.

This study has several limitations. First, the final analytic sample size is relatively limited. Second, the follow-up period was subject to a relatively

high attrition rate. Nevertheless, a comparison of baseline characteristics between participants who completed the study and those lost to follow-up revealed no statistically significant differences in SER or ocular biometric parameters, thereby reducing concerns regarding selection bias. Third, the study cohort consisted exclusively of male participants, which restricts the generalizability of the findings. Future studies should enroll participants of both sexes and from diverse geographic regions to further validate and extend these findings.

In conclusion, this study is the first to systematically characterize the dynamic ocular biometric changes associated with incident myopia in adolescents approaching emmetropization stability. By identifying specific thresholds for axial elongation, anterior chamber deepening, lens thinning, and AL/CR elevation that signal impending myopia onset, it provides a timely evidence base for developing targeted early screening and prevention strategies in high school populations.

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Declarations

- Ethics approval and consent to participate

The study followed the principles of the Declaration of Helsinki. Ethical approval for the study was obtained from the Air Force Medical Center. Written informed consents were obtained from the students and their parents or legal guardians.

- Consent for publication

We confirm that this manuscript has not been published previously and is not under consideration for publication elsewhere. We approve its submission to your journal and agree to its potential publication in the journal, should it be accepted after peer review.

- Availability of data and materials

We agree to make the data and materials supporting the findings of this study available in accordance with the journal's data sharing policy. The datasets during and/or analyzed during the current study are available from the corresponding author on reasonable request.

- Competing interests

The authors declare that they have no competing interests.

- Funding

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- Authors' contributions

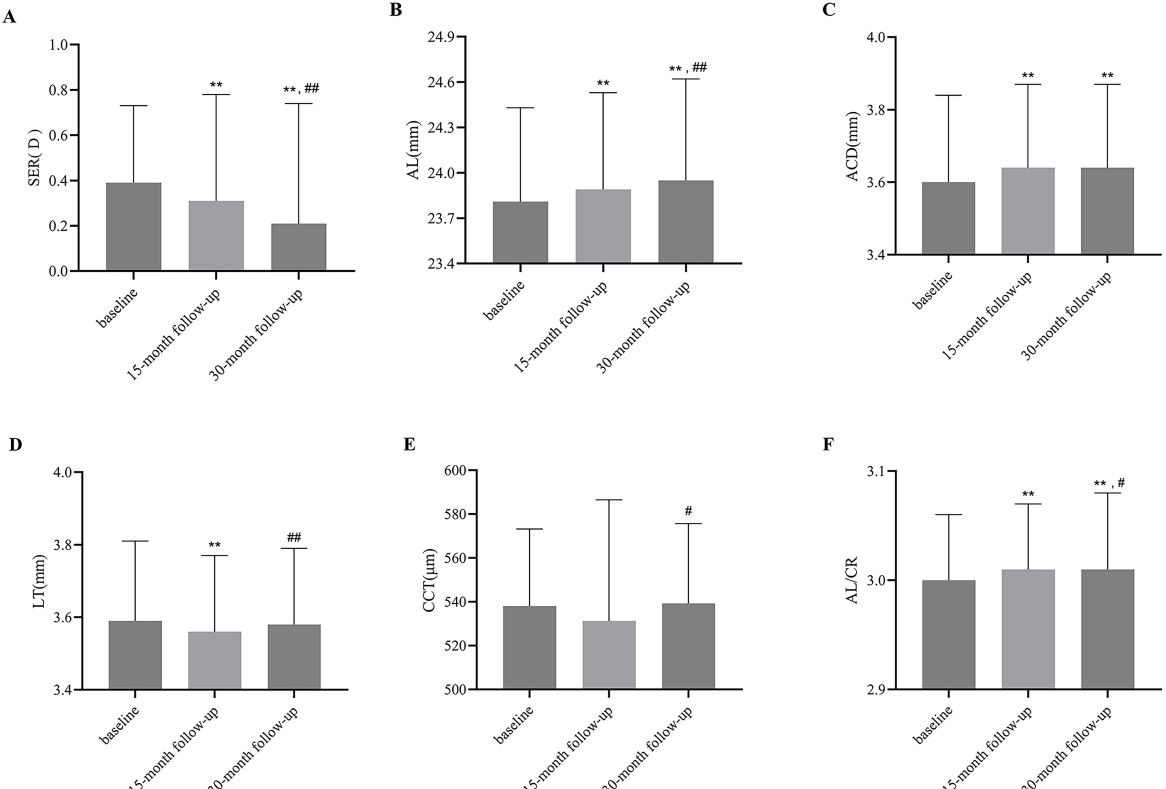
Lu Yao also contributed to the study conception and design and helped analyze the data and draft the article. Siyuan Chen contributed to the study conception and design and helped acquire and analyse the data and draft the article. Chen Zhao, Qi Qi, Yan Tang, Ding Ding helped with data acquisition and analyse the data. Yong Liu and Zhikang Zou helped with study conception and design, data analysis and interpretation. Linsong Qi oversaw all aspects of the study and participated in study conception and design, data analysis and interpretation, and critical revision of the manuscript for intellectual content. All the authors have read and approved the final manuscript. Lu Yao and Siyuan Chen equally contributed to this work.

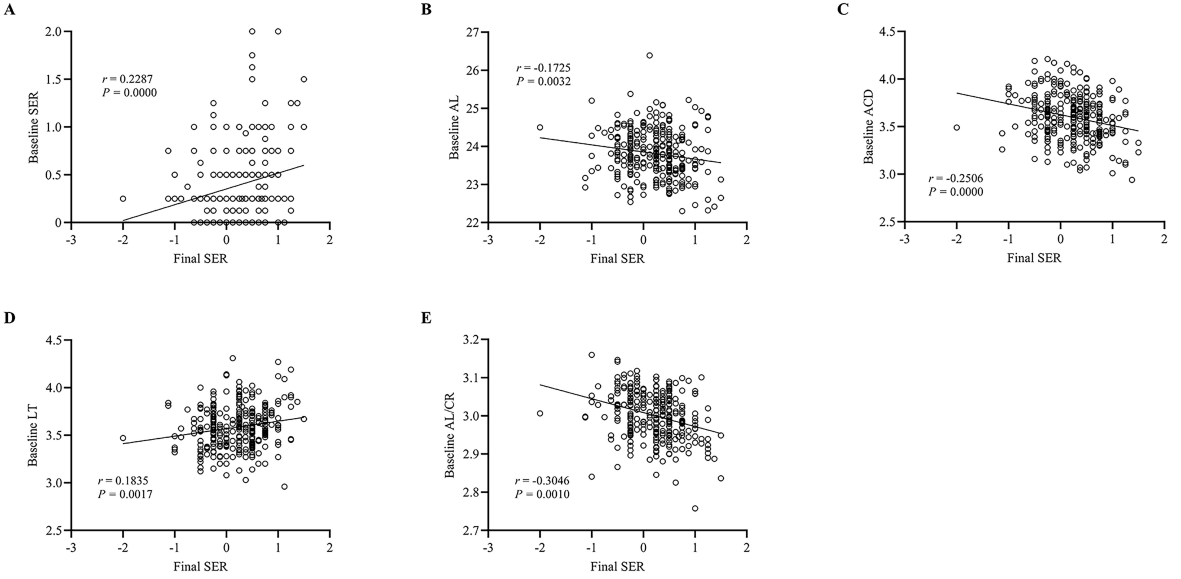
- Acknowledgements

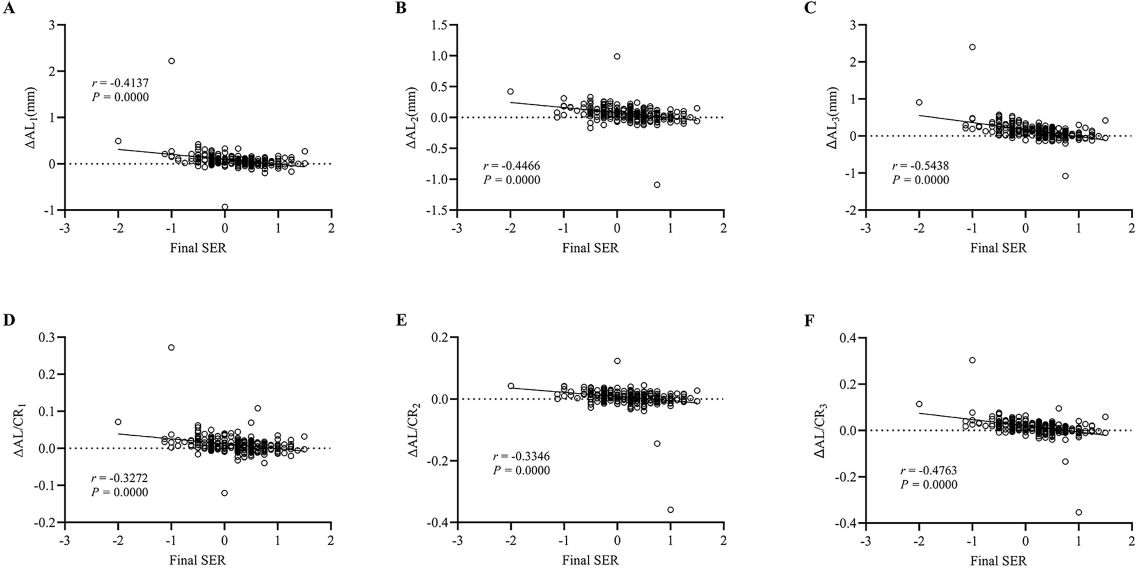
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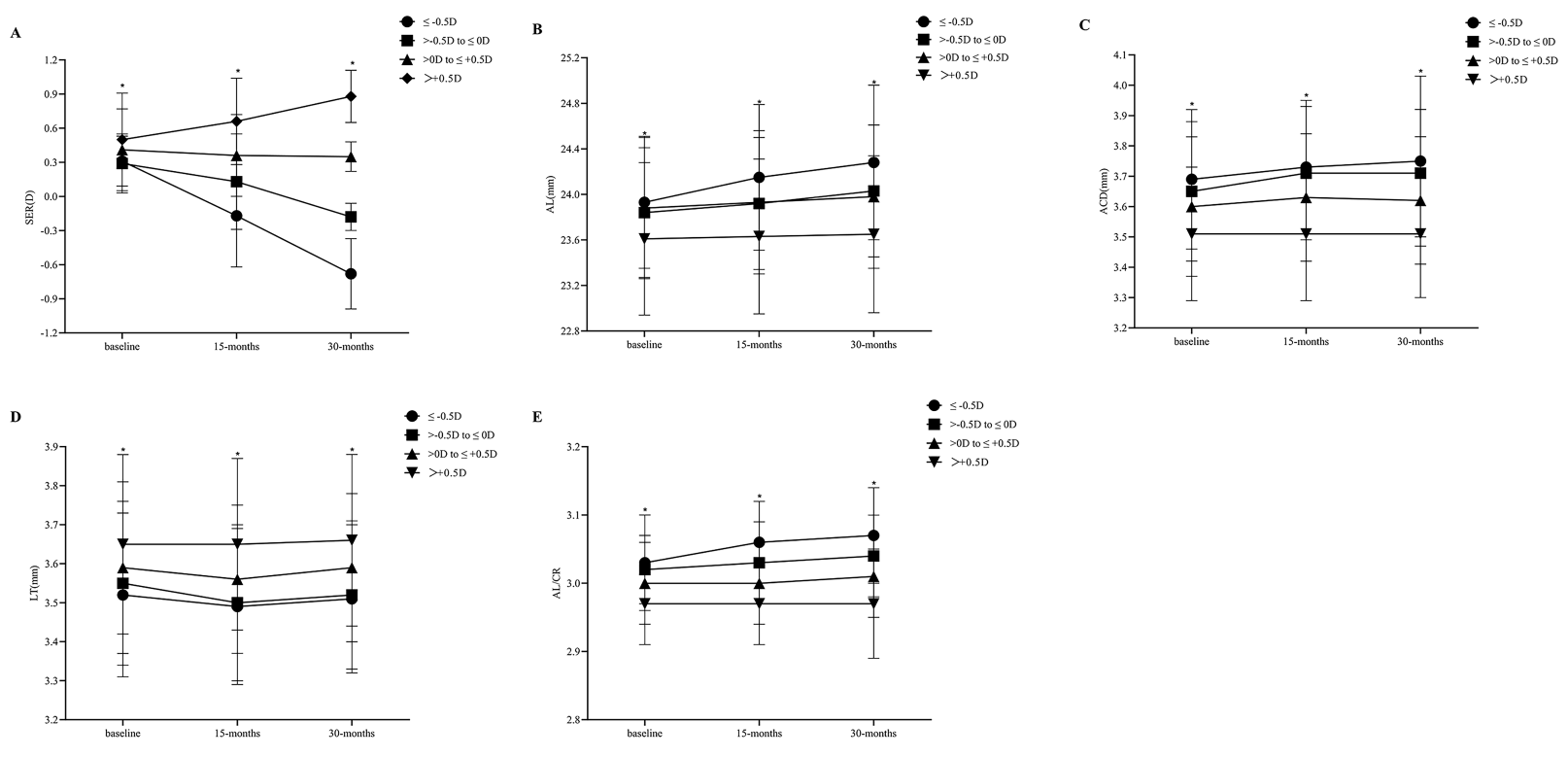
Table 1. The predictive capacity of ocular biometric parameters for myopia onset

	Cutoff	Sensitivity	Specificity	Youden	AUC（95% CI）	*P*
Baseline AL/CR	2.99	0.86	0.45	0.31	0.65 (0.55, 0.75)	0.004
Baseline ACD	3.76	0.51	0.77	0.29	0.63 (0.53, 0.73)	0.012
Baseline LT	3.58	0.54	0.69	0.23	0.60 (0.50, 0.70)	0.049
△AL for 0~15m visit	0.10	0.66	0.80	0.45	0.79 (0.70, 0.87)	<0.001
△AL for 15~30m visit	0.07	0.77	0.60	0.36	0.73 (0.63, 0.82)	<0.001
△AL/CR for 0~15m visit	0.01	0.83	0.59	0.42	0.77 (0.68, 0.85)	<0.001
△AL/CR for 15~30m visit	0.01	0.66	0.69	0.34	0.69 (0.59, 0.79)	<0.001


A
SER(D)
1.0
0.8
0.6
0.4
0.2
0.0
**
**, ##
baseline
15-month follow-up
30-month follow-up
B
AL(mm)
24.9
24.6
24.3
24.0
23.7
23.4
**
**, ##
baseline
15-month follow-up
30-month follow-up
C
ACD(mm)
4.0
3.8
3.6
3.4
**
**
baseline
15-month follow-up
30-month follow-up
D
LT(mm)
4.0
3.8
3.6
3.4
**
##
baseline
15-month follow-up
30-month follow-up
E
CCT(μm)
600
580
560
540
520
500
#
baseline
15-month follow-up
30-month follow-up
F
AL/CR
3.1
3.0
2.9
**
**, #
baseline
15-month follow-up
30-month follow-up


A
Baseline SER
Final SER
r = 0.2287
P = 0.0000
B
Baseline AL
Final SER
r = -0.1725
P = 0.0032
C
Baseline ACD
Final SER
r = -0.2506
P = 0.0000
D
Baseline LT
Final SER
r = 0.1835
P = 0.0017
E
Baseline AL/CR
Final SER
r = -0.3046
P = 0.0010


A
ΔAL1(mm)
r = -0.4137
P = 0.0000
Final SER
B
ΔAL2(mm)
r = -0.4466
P = 0.0000
Final SER
C
ΔAL3(mm)
r = -0.5438
P = 0.0000
Final SER
D
ΔAL/CR1
r = -0.3272
P = 0.0000
Final SER
E
ΔAL/CR2
r = -0.3346
P = 0.0000
Final SER
F
ΔAL/CR3
r = -0.4763
P = 0.0000
Final SER


A
≤ -0.5D
>-0.5D to ≤ 0D
>0D to ≤ +0.5D
>+0.5D
SER(D)
1.2
0.9
0.6
0.3
0.0
-0.3
-0.6
-0.9
-1.2
baseline
15-months
30-months
B
≤ -0.5D
>-0.5D to ≤ 0D
>0D to ≤ +0.5D
>+0.5D
AL(mm)
25.2
24.8
24.4
24.0
23.6
23.2
22.8
baseline
15-months
30-months
C
≤ -0.5D
>-0.5D to ≤ 0D
>0D to ≤ +0.5D
>+0.5D
ACD(mm)
4.1
4.0
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
baseline
15-months
30-months
D
≤ -0.5D
>-0.5D to ≤ 0D
>0D to ≤ +0.5D
>+0.5D
LT(mm)
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
baseline
15-months
30-months
E
≤ -0.5D
>-0.5D to ≤ 0D
>0D to ≤ +0.5D
>+0.5D
AL/CR
3.2
3.1
3.0
2.9
2.8
baseline
15-months
30-months