Impact of Astigmatism on Axial Elongation in School-Age Children: A Five-Year Population-Based Study in Tianjin, China

Dong Liang,[1] Bei Du,[2] Tsz-Wing Leung,[1,3,4] Zhuzhu Liu,[2] Qiang Su,[2] Nan Jin,[2] Ziyu Zhang,[2] Mingguang He,[1,3,4] Hua Yan,[5–8] Ruihua Wei,[2] and Chea-Su Kee[1,3,4]

[1]School of Optometry, Hong Kong Polytechnic University, Hong Kong
[2]Tianjin Key Laboratory of Retinal Functions and Diseases, Tianjin Branch of National Clinical Research, Center for Ocular Disease, Eye Institute and School of Optometry, Tianjin Medical University Eye Hospital, Tianjin, China
[3]Research Centre for SHARP Vision (RCSV), Hong Kong Polytechnic University, Hong Kong
[4]Centre for Eye and Vision Research (CEVR), Hong Kong
[5]Department of Ophthalmology, Tianjin Medical University General Hospital, Tianjin, China
[6]Tianjin Key Laboratory of Ocular Trauma, Tianjin, China
[7]Ministry of Education International Joint Laboratory of Ocular Diseases, Tianjin, China
[8]Tianjin Institute of Eye Health and Eye Diseases, Tianjin, China

Correspondence: Chea-Su Kee, School of Optometry, Hong Kong Polytechnic University, 11 Yuk Choi Rd., Kowloon, Hong Kong; c.kee@polyu.edu.hk.
Ruihua Wei, Eye Institute and School of Optometry, Tianjin Medical University Eye Hospital, 251 Fukang Rd., Nankai District, Tianjin 300384, China; rwei@tmu.edu.cn.
Hua Yan, Department of Ophthalmology, Tianjin Medical University General Hospital, 154 Anshan Rd., Heping District, Tianjin 300052, China; zyyyanhua@tmu.edu.cn.

DL and BD contributed equally to the work presented here and should therefore be regarded as equivalent authors.

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Purpose. To investigate the progression rates of axial length (AXL) among school-age children with baseline astigmatism and spherical ametropia.

Methods. Annual vision screenings were conducted at seven schools in Tianjin, China, from 2018 to 2022. Ocular biometry and non-cycloplegic autorefraction were collected. Children 5 to 16 years old without any myopia interventions were included and categorized by their baseline astigmatism magnitude (control, low, or high) and axis orientation (with the rule [WTR], against the rule [ATR], or oblique). Additionally, children were classified by baseline spherical ametropia (compound hyperopic, compound myopic, or other). Annual AXL progression rates of right eyes were calculated using regression models and compared across different types of astigmatism and spherical ametropia.

Results. A total of 10,732 Chinese children (baseline age, 9.26 ± 2.42 years; follow-up duration, 2.63 ± 1.01 years) were included and divided into a younger cohort (age < 11 years; $n = 7880$) and an older cohort (age ≥ 11 years; $n = 2852$). Across both age groups and all astigmatism magnitudes, ATR astigmatism exhibited the most rapid AXL progression, followed by oblique and WTR astigmatism. Two-way ANCOVA of the combined cohort revealed that both high-magnitude and ATR astigmatism were significantly associated with AXL progression ($P \leq 0.018$). However, the impact of astigmatism on AXL progression varied depending on baseline spherical ametropia, as high-magnitude and ATR astigmatism increased AXL progression in compound myopic eyes but decreased progression in compound hyperopic eyes.

Conclusions. Both baseline magnitude and axis orientation of astigmatism are significantly associated with axial elongation in children. However, these associations may vary with spherical ametropia, with differential patterns being observed between compound hyperopic and myopic eyes.

Keywords: astigmatism, axial length, emmetropization, refractive error, myopia

Astigmatism, one of the most prevalent refractive errors globally, affects an estimated 14.9% of children and a significant 40.4% of adults.[1] Astigmatism can be classified into three categories based on the axis orientation of the principal power meridians: with the rule (WTR), against the rule (ATR), or oblique (OBL). Despite the prevailing uncertainty surrounding the etiology of astigmatism,[2] its clinical relevance is well documented. Notably, significant astigmatism during early childhood is associated with various ocular and visual disorders, such as amblyopia,[3] strabismus,[4] abnormal retinal electrophysiology,[5] and decreased cognitive or behavioral performance.[6–8]

Astigmatism, which frequently coexists with myopia, has been linked to myopia development.[2,9] It is hypothesized that astigmatism could serve as an optical visual cue, guiding the process of emmetropization by integrating optical

signals from the two principal meridians.[10,11] Conversely, the optical blur resulting from astigmatism could also disrupt the normal emmetropization process, leading to myopia development similar to the effects of form deprivation.[12,13] This hypothesis is supported by animal studies[14–18] showing that early imposition of astigmatism using a cylindrical lens can alter the course of emmetropization. In human studies, a higher magnitude of astigmatism[12,13,19,20] or ATR astigmatism[13,21,22] during early childhood has been associated with an increased likelihood of developing myopia or an accelerated progression of myopia. Furthermore, astigmatism has been linked to ocular structural changes, including chorioretinal thickness[23,24] and vascular density.[25] Collectively, these pieces of evidence underscore the potential role of astigmatism in influencing eye growth.

Although existing studies have investigated the association between astigmatism and refractive development,[12,13,19–22] a substantial research gap persists concerning the impact of early astigmatism on ocular axial elongation. Furthermore, existing studies, which are often limited by their small sample sizes, have reported controversial conclusions, underscoring the need for a larger scale study to elucidate these relationships more comprehensively. Moreover, the interaction between astigmatism and spherical ametropia (i.e., hyperopic vs. mixed vs. myopic astigmatism) and its effect on eye growth remains largely unexplored. To address these research gaps, we conducted a 5-year study on a large cohort of school-age children in Tianjin, China. Our study aimed to estimate and compare the progression rates of axial length (AXL) among children with different baseline astigmatism and spherical ametropia. This research marks a critical step toward a more comprehensive understanding of the role of astigmatism in emmetropization. The insights gained from this study promise to be instrumental in formulating personalized management and intervention strategies for pediatric refractive errors.

Methods

This longitudinal cohort study was conducted through annual vision screenings at seven primary and secondary schools in Tianjin, China, from 2018 to 2022. The screenings were carried out between September and December each year, targeting students from grades 1 to 12. However, the COVID-19 pandemic interrupted the screening process in 2020 and 2022, leading to incomplete data collection for these 2 years. The numbers of participants each year were as follows: 12,683 in 2018, 13,583 in 2019, 5466 in 2020, 16,026 in 2021, and 5438 in 2022.

Measures and Outcomes

Vision screenings were performed by trained optometrists and ophthalmologists. AXL was measured using a Lenstar 900 biometer (Haag-Streit, Koeniz, Switzerland), with three consecutive recordings averaged for accuracy. For non-cycloplegic autorefraction, the Spot Vision Screener (Welch Allyn, Skaneateles Falls, NY, USA) was utilized from 2018 to 2020, and the KR-800 autorefractor (Topcon, Tokyo, Japan) was employed in 2021 and 2022. This change was prompted by the integration of our project into a broader citywide vision screening initiative, requiring standardized equipment. Three consecutive readings of autorefraction were obtained and averaged for each eye, and those with discrepancies over 0.50 diopter (D) in either spherical or cylindrical power were discarded and remeasured. Both biometers and autorefractors were calibrated before each screening session. Because data were acquired through non-cycloplegic measurement, the progression of AXL (an ocular biometric parameter less affected by ocular accommodation) was used as the primary outcome measure, with spherical equivalent refraction (SER) progression serving as a reference.

Due to the high correlations in AXL, SER, and astigmatism between right and left eyes (Pearson's correlation range, 0.88–0.97; all $P < 0.001$), only data from the right eyes were used for subsequent analyses. Individual annual progression rates for AXL and SER were calculated by fitting linear regressions to the longitudinal data for each eye. Missing data, attributed to COVID-19 disruptions, were not imputed to avoid introducing potential biases due to improperly addressing the complex patterns inherent in longitudinal data. To evaluate the effect of astigmatism on eye growth, mean AXL and SER progression rates were compared among groups categorized by the magnitude and axis orientation of baseline astigmatism:

- Astigmatism magnitude
  - None (controls), cylindrical power > -0.50 D
  - Low, cylindrical power from >-1.50 D to ≤ -0.50 D
  - High, cylindrical power ≤ -1.50 D
- Axis orientation (for astigmatic eyes)
  - WTR, cylindrical axes between 0° and 30° or 150° and 180°
  - ATR, cylindrical axes between 60° and 120°
  - OBL, cylindrical axes between 31° and 59° or 121° and 149°

In addition, subcohort analyses were conducted to investigate the impact of astigmatism within different spherical ametropia subtypes and sex groups. Spherical ametropia was categorized by baseline spherical powers along two principal meridians (with 0 D serving as the reference):

- Spherical ametropia
  - Compound hyperopic, both principal meridians >0.50 D
  - Compound myopic, both principal meridians ≤ -0.75 D
  - Other ametropic/emmetropic, at least one meridian from >-0.75 D to ≤ 0.50 D

Acknowledging the potential influence of active accommodation on spherical ametropia measurements obtained through non-cycloplegic autorefraction in children,[26] this study adopted a more conservative criterion for ametropia definition.

Study Population

This study included Chinese children 5 to 16 years old at the time of examination who had at least two annual vision screening records available for longitudinal analysis. Children who reported a history of contact lens wear, orthokeratology, or any form of myopia control interventions were excluded. Additionally, to maintain consistency in assessing the effect of axis orientation of astigmatism on eye

growth, children who demonstrated a change in the types of axis orientation during the follow-up period were excluded (Supplementary Fig. S1). To account for potential age-related differences in eye growth rates,[27,28] the study population was stratified into two age cohorts for further analyses: a younger cohort (5 to 10 years old at baseline) and an older cohort (11 to 15 years old at baseline).

This study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Tianjin Medical University Eye Hospital and The Hong Kong Polytechnic University (HSEARS20230210006). Written informed consent was obtained from the parents or legal guardians of all participating children before the vision screenings.

Statistical Analysis

Statistical analyses were performed using SPSS Statistics 27.0 (IBM, Chicago, IL, USA) and R 4.0 (R Foundation for Statistical Computing, Vienna, Austria). Data are presented as mean ± standard deviation (SD), 95% confidential interval (CI), or median (interquartile range), unless specified otherwise. To test the effect of baseline astigmatism on eye growth, a two-way analysis of covariance (ANCOVA) with Bonferroni's post hoc comparisons (factor 1, astigmatism magnitude; factor 2, astigmatism axis orientation) were employed to compare the AXL progression rates among the astigmatism groups, adjusted for baseline age, sex, follow-up duration, and baseline AXL as covariates. If a significant two-way interaction effect between two factors was found, their simple main effects on AXL progression were reported; otherwise, their main effects were reported. Partial eta-squared (η^2) was calculated to indicate the effect size in ANCOVA tests: small effect, $\eta^2 = 0.01$ to 0.06; medium effect, $\eta^2 = 0.06$ to 0.14; and large effect, $\eta^2 > 0.14$.[29] A two-tailed $P < 0.05$ was considered statistically significant for all statistical tests.

Results

Baseline and Follow-Up Characteristics

Longitudinal data from 10,732 children, comprised of a total of 35,672 records, were analyzed. The younger cohort ($n = 7880$) had a mean baseline age of 8.14 ± 1.39 years, with a mean follow-up period of 2.74 ± 0.98 years. The older cohort ($n = 2852$) had a mean baseline age of 12.73 ± 1.09 years and a mean follow-up period of 2.34 ± 1.04 years. At baseline, 4800 eyes (44.7%) in the combined cohort had no astigmatism and served as the control group, 5057 eyes (47.1%) exhibited low astigmatism, and 875 eyes (8.2%) had high astigmatism. Among the astigmatic eyes, 4789 (80.9%) were classified as WTR, 654 (11.0%) as ATR, and 489 (8.2%) as OBL astigmatism. Regarding baseline spherical ametropia, 612 eyes (5.7%) exhibited compound hyperopia, 1477 (13.8%) exhibited compound myopia, and 8643 (80.5%) were categorized as other ametropia/emmetropia (Supplementary Table S1).

The Table summarizes the demographic and biometric characteristics at baseline and follow-up visits. The mean baseline AXL and SER were 23.23 ± 1.01 mm and –0.07 ± 1.05 D for the younger cohort and 24.30 ± 1.19 mm and –1.69 ± 1.98 D for the older cohort, respectively. Over the follow-up period, the mean AXL and SER progression rates were 0.28 ± 0.39 mm/year and –0.39 ± 0.51 D/year for the younger cohort, and 0.31 ± 0.41 mm/year and –0.38 ± 0.57 D/year for the older cohort, indicating a prevailing trend toward axial elongation and myopia development. In contrast, changes in astigmatism over time were minimal, with mean progression rates of 0.05 ± 0.25 D/year and –0.01 ± 0.37 D/year for the younger and older cohorts, respectively, suggesting that astigmatism remained relatively stable throughout the follow-up period. Supplementary Table S2 provides a more detailed demographic and biometric characteristics across different astigmatism groups at baseline. No significant differences were observed among the groups

Table. Demographic and Biometric Characteristics at Baseline and Follow-Up of Study Population

Demographic	Combined Cohort	Age Cohorts*	
		Younger	Older
Participants, *n*	10,732	7880	2852
Baseline age (y), mean ± SD	9.36 ± 2.42	8.14 ± 1.39	12.73 ± 1.09
Follow-up duration (y), mean ± SD	2.63 ± 1.01	2.74 ± 0.98	2.34 ± 1.04
Gender, *n* (%)			
Boys	5706 (53.2)	4137 (52.5)	1569 (55.0)
Girls	5026 (46.8)	3743 (47.5)	1283 (45.0)
Education at baseline, *n* (%)			
Primary schools	8946 (83.4)	7880 (100)	1066 (37.4)
Secondary schools	1786 (16.6)	0	1786 (62.6)
School type at baseline, *n* (%)			
Local schools	6238 (58.1)	4505 (57.2)	1733 (60.8)
International schools	4494 (41.9)	3375 (42.8)	1119 (39.2)
Biometry at baseline, mean ± SD			
Axial length (mm)	23.51 ± 1.15	23.23 ± 1.01	24.30 ± 1.19
Spherical equivalent (D)	−0.50 ± 1.54	−0.07 ± 1.05	−1.69 ± 1.98
Refractive astigmatism (D)	−0.71 ± 0.62	−0.67 ± 0.59	−0.82 ± 0.66
Biometry at follow-up, mean ± SD			
Axial length (mm/y)	0.29 ± 0.50	0.28 ± 0.44	0.31 ± 0.46
Spherical equivalent (D/y)	−0.38 ± 0.55	−0.39 ± 0.51	−0.38 ± 0.57
Refractive astigmatism (D/y)	0.03 ± 0.28	0.05 ± 0.25	−0.01 ± 0.34

* The full study cohort was divided into a younger cohort (5 to 10 years old) and an older cohort (11 to 15 years old) at baseline.

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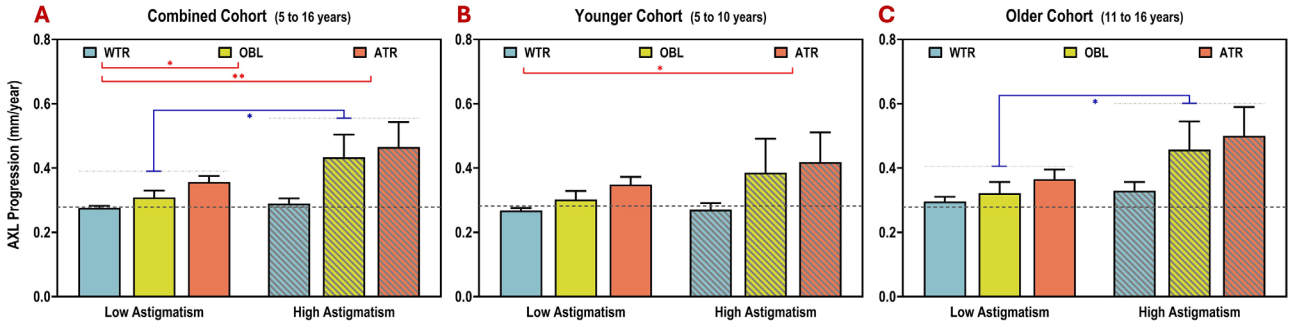

Figure 1. AXL progression rates across different types of astigmatism in combined, younger, and older cohorts. The figure shows the progression rates of AXL stratified by astigmatism magnitude and axis orientation in the (**A**) combined cohort, (**B**) younger cohort, and (**C**) older cohort. The *dotted line* represents controls. *Blue*, *yellow*, and *red bars* represent WTR, OBL, and ATR astigmatism, respectively. *Solid bars* indicate low astigmatism, and *striped bars* denote high astigmatism. *Error bars* represent standard errors. Statistical significance was determined by two-way ANCOVAs with Bonferroni's post hoc tests after adjustment for baseline age, sex, follow-up duration, and baseline AXL. *$P < 0.05$, **$P < 0.01$. *Blue asterisks* indicate comparisons between low and high astigmatism subgroups; *red asterisks* highlight differences between the axis orientation subgroups.

regarding baseline age, sex, follow-up duration, or ocular biometric measures (all $P \geq 0.10$).

Impact of Astigmatism on Axial Elongation

The mean AXL progression rates across different astigmatism groups in the combined, younger, and older cohorts are presented in Figure 1. Two-way ANCOVA revealed no significant interaction effect between the baseline magnitude and axis orientation of astigmatism on AXL progression in any cohort (all $P \geq 0.224$) while controlling for baseline age, sex, follow-up duration, and baseline AXL. Therefore, an analysis of the main effects for astigmatism magnitude and axis orientation was performed, revealing two key findings.

First, axial elongation varied significantly with the axis orientation of astigmatism in the combined cohort ($P < 0.001$, $\eta^2 = 0.037$) and the younger cohort ($P = 0.031$, $\eta^2 = 0.024$), demonstrating a marginal significance in the older cohort ($P = 0.050$, $\eta^2 = 0.043$). Post hoc analyses of the combined cohort revealed significantly faster axial elongation in eyes with ATR (0.415 mm/year; $P = 0.008$) and OBL astigmatism (0.373 mm/year; $P = 0.049$) compared to WTR astigmatism (0.285 mm/year). However, no significant difference was observed between ATR and OBL astigmatism ($P > 0.999$). A similar trend, as depicted in Figure 1, was observed in both the younger and older cohorts. In the younger cohort, only the difference between WTR (0.271 mm/year) and ATR (0.398 mm/year) reached statistical significance ($P = 0.045$). Neither the comparison between WTR and OBL (0.351 mm/year) nor the comparison between ATR and OBL was statistically significant ($P \geq 0.614$). In the older cohort, post hoc comparisons did not reveal any statistically significant differences, likely due to the smaller sample size (WTR, 0.314 mm/year; OBL, 0.389 mm/year; ATR, 0.439 mm/year; all $P \geq 0.164$).

Second, the magnitude of baseline astigmatism was significantly associated with axial elongation. In the combined cohort, eyes with high astigmatism (0.399 mm/year) exhibited significantly faster axial elongation compared to those with low astigmatism (0.316 mm/year; $P = 0.018$, $\eta^2 = 0.015$). A similar trend was observed in the older cohort (low astigmatism, 0.324 mm/year; high astigmatism, 0.427 mm/year; $P = 0.039$, $\eta^2 = 0.036$). However, this difference did not reach statistical significance in the younger cohort (low astigmatism, 0.309 mm/year; high astigmatism, 0.364 mm/year; $P = 0.302$).

In addition to axial elongation, SER progression rates were analyzed across astigmatism groups (Supplementary Fig. S2). Consistent with the AXL progression findings, both baseline magnitude and axis orientation of astigmatism had significant main effects on SER progression in the combined and older cohorts (all $P \leq 0.017$; $\eta^2 = 0.029$ to 0.150) while controlling for baseline age, sex, follow-up duration, and baseline SER. Similarly, high-magnitude and ATR astigmatism exhibited more myopic SER progression compared to low-magnitude and WTR astigmatism.

Impact of Astigmatism Across Spherical Ametropia and Sex

The impact of astigmatism on AXL progression was examined within subcohorts by baseline spherical ametropia subtypes (compound hyperopia, compound myopia, or other ametropia/emmetropia) and by sex (female or male). However, due to the limited number of compound hyperopic eyes with high OBL astigmatism ($n = 1$) or high ATR astigmatism ($n = 0$) (see Supplementary Table S1 for details), our subcohort analyses specifically compared AXL progression across different magnitudes of astigmatism within the WTR orientation (i.e., controls vs. low WTR vs. high WTR) and across different axis orientations in those with low magnitude of astigmatism (i.e., low WTR vs. low OBL vs. low ATR) in different spherical ametropia and sex subcohorts. This approach was employed to ensure the validity of our statistical analysis, considering the small sample size in some subgroups.

Impact of Magnitude of Astigmatism Across Spherical Ametropia Subtypes. Figure 2 illustrates the AXL progression rates among control eyes and those with low and high WTR astigmatism, stratified by the baseline spherical ametropia subtypes: compound hyperopia, compound myopia, and other ametropia/emmetropia. A significant interaction between astigmatism magnitude and spherical ametropia subtypes was observed in the combined cohort ($P = 0.001$, $\eta^2 = 0.027$) and the younger cohort ($P = 0.036$, $\eta^2 = 0.025$), indicating that the effect of astigmatism on AXL progression differed depending on the baseline

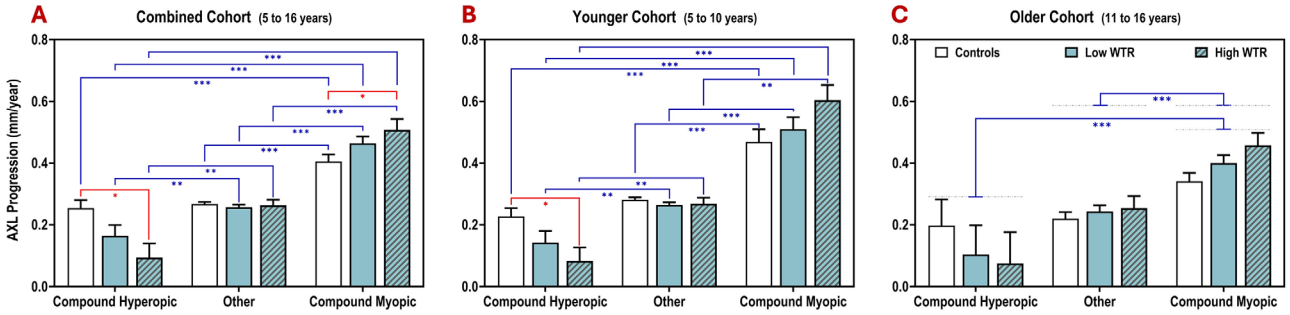

Figure 2. AXL progression rates across different magnitudes of WTR astigmatism and spherical ametropia. The figure shows the effect of the magnitude of WTR astigmatism on AXL progression across different spherical ametropia in the (**A**) combined cohort, (**B**) younger cohort, and (**C**) older cohort. *White*, *solid blue*, and *striped blue bars* represent the control, low, and high WTR astigmatism groups, respectively. *Error bars* represent standard errors. Statistical significance was determined by two-way ANCOVAs with Bonferroni's post hoc tests after adjustment for baseline age, sex, follow-up duration, and baseline AXL. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$. *Blue asterisks* indicate comparisons between spherical ametropia subtypes; *red asterisks* highlight differences between the astigmatism magnitude subgroups.

refractive state. This interaction was not significant in the older cohort ($P = 0.319$).

As shown in Figure 2A, within the combined cohort, AXL progression was significantly associated with the magnitude of baseline astigmatism in both compound hyperopic eyes ($P = 0.017$, $\eta^2 = 0.016$) and compound myopic eyes ($P = 0.007$, $\eta^2 = 0.014$), but with opposite effects. In the compound hyperopic group, high WTR astigmatism (0.097 mm/year) exhibited significantly reduced AXL progression compared to non-astigmatic control eyes (0.254 mm/year; $P = 0.013$). Conversely, in the compound myopic group, high WTR astigmatism (0.508 mm/year) showed significantly increased AXL progression compared to control eyes (0.405 mm/year; $P = 0.024$).

A similar bidirectional trend was observed in the younger cohort (Fig. 2B), with astigmatism magnitude significantly associated with AXL progression in compound hyperopic eyes ($P = 0.012$, $\eta^2 = 0.015$). Consistent with the combined cohort, high WTR astigmatism (0.085 mm/year) in the younger group showed significantly less AXL progression compared to the control eyes (0.227 mm/year; $P = 0.027$). Although a similar trend of increased AXL progression with higher WTR astigmatism was also observed in compound myopic eyes, this difference did not reach statistical significance (controls, 0.469 mm/year; low WTR, 0.508 mm/year; high WTR, 0.600 mm/year; $P = 0.293$). The older cohort (Fig. 2C) exhibited a similar bidirectional pattern, but the interaction between baseline astigmatism magnitude and spherical ametropia subtypes was not statistically significant.

Consistent with the AXL progression findings, the impact of astigmatism magnitude on SER progression rates was also modulated by baseline spherical ametropia subtypes. Higher WTR astigmatism was consistently associated with less myopic SER progression in compound hyperopic eyes but significantly greater myopic progression in compound myopic eyes and other ametropic/emmetropic group (Supplementary Figs. S3A–S3C).

To further quantify the effect of spherical ametropia magnitude on AXL progression and its potential interaction with astigmatism magnitude, the compound myopic subcohort, in which astigmatism magnitude demonstrated a significant effect on AXL progression, was further stratified into low myopic (both meridians ≤ -0.75 D but not both meridians ≤ -3.00 D) and medium myopic (both meridians ≤ -3.00 D) groups. The analysis of the compound hyperopic subcohort was not conducted due to the limited sample size. As shown in Supplementary Figures S4A to S4C, a significant main effect of myopia magnitude was observed, with individuals classified as low myopic showing less AXL progression than those classified as medium myopic in both the combined cohort (0.326 vs. 0.400 mm/year; $P < 0.001$) and the older cohort (0.303 vs. 0.397 mm/year; $P < 0.001$). This difference was not observed in the younger cohort (0.382 vs. 0.409 mm/year; $P = 0.488$). However, the interaction between myopia magnitude and astigmatism magnitude was not statistically significant in the combined, younger, or older cohorts (all $P \geq 0.498$).

Impact of Axis Orientation of Astigmatism Across Spherical Ametropia Subtypes. Figure 3 illustrates the AXL progression rates across the low WTR, low OBL, and low ATR astigmatism groups, stratified by baseline spherical ametropia subtypes. Although a trend toward faster axial elongation in eyes with ATR and OBL astigmatism compared to WTR astigmatism was observed, particularly in the compound myopic and other ametropic/emmetropic groups, the interaction between astigmatism axis orientation and spherical ametropia on AXL progression was not statistically significant in the combined, younger, or older cohorts (all $P \geq 0.348$). Additionally, no significant main effect of axis orientation of astigmatism was found (all $P \geq 0.606$), potentially due to reduced sample sizes. A similar effect of axis orientation of astigmatism on SER progression was also observed (Supplementary Figs. S3D–S3F).

Impact of Astigmatism Across Sex. The AXL progression rates across different astigmatism and sex groups are shown in Supplementary Figure S5. No significant interaction effect was found between sex and either astigmatism magnitude or axis orientation on AXL progression in any of the age cohorts (all $P \geq 0.588$). However, a significant main effect of sex on AXL progression was observed. When stratifying participants by WTR astigmatism magnitude (i.e., controls, low WTR, or high WTR), males showed faster AXL progression than females in both the combined cohort (0.306 vs. 0.253 mm/year; $P < 0.001$) and the younger cohort (0.309 vs. 0.231 mm/year; $P < 0.001$), but not in the older cohort (0.299 vs. 0.298 mm/year; $P = 0.968$) (Supplementary Figs. S5A–S5C). Similarly, when stratifying by axis orientation of astigmatism (i.e., low WTR, low OBL, or low ATR), males in the younger cohort showed faster

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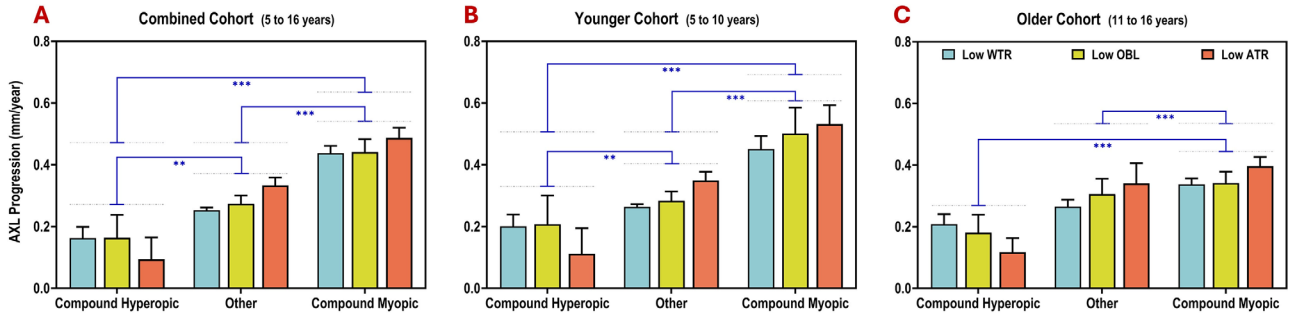

Figure 3. AXL progression rates across different axis orientations of low astigmatism and spherical ametropia. The figure shows the effect of the axis orientation of low astigmatism on AXL progression across different spherical ametropia in the (**A**) combined cohort, (**B**) younger cohort, and (**C**) older cohort. *Blue*, *yellow*, and *red bars* represent low WTR, oblique OBL, and ATR astigmatism, respectively. *Error bars* represent standard errors. Statistical significance was determined by two-way ANCOVAs with Bonferroni's post hoc tests after adjustment for baseline age, sex, follow-up duration, baseline AXL, and astigmatism magnitude. $^{**}P < 0.01$, $^{***}P < 0.001$. *Blue asterisks* indicate comparisons between spherical ametropia subtypes.

AXL progression than females (0.340 vs. 0.281 mm/year; $P = 0.023$), but this difference was not statistically significant in the combined cohort (0.328 vs. 0.299 mm/year; $P = 0.163$) or the older cohort (0.316 vs. 0.315 mm/year, $P = 0.543$) (Supplementary Figs. S5D–S5F).

The impact of astigmatism on SER progression across sex groups is presented in Supplementary Figure S6. Similar to the AXL progression findings, a significant difference in SER progression between males and females was observed in the combined and younger cohorts ($P \leq 0.002$), but not in the older cohort ($P = 0.302$), when stratifying by WTR astigmatism magnitude. No significant difference was found when stratifying by the axis orientation of low astigmatism (all $P \geq 0.584$).

Discussion

In this 5-year study of 10,732 Chinese school-age children, we explored the relationship between baseline astigmatism with axial elongation and myopia development. Our comprehensive analysis yielded two significant findings. First, baseline astigmatism was significantly associated with eye growth. Children with high-magnitude and ATR astigmatism experienced greater axial elongation. Second, the association between baseline astigmatism and axial elongation varied with baseline spherical ametropia. Specifically, higher astigmatism was linked to increased axial elongation in compound myopic eyes but decreased progression in compound hyperopic eyes. Moreover, greater axial elongation in ATR compared to WTR astigmatism was observed in the compound myopic and other ametropic/emmetropic groups, but not in compound hyperopic eyes. These findings underscore the significant and complex role of astigmatism in eye growth.

Our study, distinguished by its large sample size and longitudinal design, offers a novel insight into how baseline astigmatism influences changes in axial length—the primary ocular biometry associated with myopia progression. Our findings suggest that both magnitude and the axis orientation of baseline astigmatism were associated with axial elongation in the combined cohort, with similar patterns observed in both younger and older subcohorts (Fig. 1). Specifically, eyes with ATR astigmatism exhibited the greatest axial elongation, followed by OBL and then WTR astigmatism. In addition, a higher magnitude of astigmatism was associated with greater AXL progression compared to lower magnitude.

To the best of our knowledge, only one previous study involving 108 Chinese preschoolers (ages 2–6 years) documented increased axial growth with higher astigmatism.[19] However, that study did not observe a significant difference in AXL progression between WTR and ATR astigmatism,[19] which contrasts with our findings. This discrepancy could be due to the small sample size of their study cohort, particularly for children with ATR astigmatism ($n = 9$).[19] Furthermore, most eyes in that study likely had hyperopic astigmatism, with a mean SER of 0.89 D.[19] It is noteworthy that, in our study, increased AXL progression associated with ATR astigmatism was specifically identified in compound myopic or other ametropic/emmetropic eyes, but not in compound hyperopic eyes (Fig. 3). Our study is the first, to our knowledge, to demonstrate a significant longitudinal association between astigmatism axis orientation and axial elongation in school-age children.

Although the impact of astigmatism on axial elongation is largely underexplored, its effect on refractive development has been extensively documented. For example, previous studies have linked infantile astigmatism to increased progression of refractive myopia during infancy[12] and a higher likelihood of developing myopia at school age.[13,30] Additionally, higher baseline astigmatism in young children has been associated with a more pronounced myopic shift[19] and a steeper SER progression slope over the follow-up period.[20] These findings are supported by our observations on AXL progression, further emphasizing the significant role of astigmatism and its magnitude in eye growth.

Regarding the impact of astigmatism axis orientation, previous studies have also reported findings consistent with our results, where ATR astigmatism in infants and children was more likely to lead to subsequent myopia[13,21] or greater myopic progression.[22] This is further supported by morphological analyses of the posterior eyeball which have revealed significant differences in chorioretinal structure between WTR and ATR astigmatism.[23,24] These structural variations suggest a potential role for the axis orientation of astigmatism in development of the posterior eyeball.

However, although our findings align with the above-mentioned studies, it is noteworthy that other research has not established a significant association between astigmatism—in terms of neither magnitude[31–33] nor

axis orientation[19,34–36]—and myopia development. These discrepancies may arise from methodological differences, such as variations in sample sizes, definitions of astigmatism, and age ranges of participants, factors known to affect the relationship between astigmatism and myopia development.[34,35] For example, astigmatism magnitude had a significant main effect on axial elongation in our study; therefore, using different definition criteria for astigmatism could lead to varying results. Similarly, axial elongation showed slight differences between younger and older cohorts, with the impact of baseline astigmatism appearing more pronounced in older ages (Fig. 1). Notably, our study observed consistent patterns of associations between baseline astigmatism (both magnitude and axis orientation) and axial elongation across both younger and older ages (Fig. 1), although some effects were not statistically significant, potentially due to reduced sample sizes. As the largest longitudinal study to date, our research encompasses a broad spectrum of participant ages (i.e., 5–16 years) and astigmatism characteristics (i.e., varying magnitudes and axes), allowing for a more representative and comprehensive evaluation of the role of astigmatism in eye growth.

In addition to baseline astigmatism, previous studies have reported that baseline spherical ametropia can also influence emmetropization[37–39] and myopia development.[40–42] Such findings suggest that the impact of astigmatism on myopia development could be confounded by children's spherical ametropia. This complexity is further highlighted by studies showing that different types of astigmatism, such as mixed, simple, or compound astigmatism, can affect myopia progression in distinct ways. For example, mixed astigmatism does not exhibit significant myopia progression until it evolves into simple or compound myopic astigmatism.[43] Additionally, infants with hyperopic WTR or myopic ATR astigmatism are prone to develop greater myopia during childhood.[44] Our subcohort analysis also revealed that higher magnitude astigmatism increased AXL progression in compound myopic eyes but decreased in compound hyperopic eyes across both younger and older ages (Fig. 2). Similarly, greater AXL progression in ATR compared to WTR astigmatism was observed only in the compound myopic and other ametropic/emmetropic eyes (Fig. 3). These differential impacts underscore the importance of considering the baseline spherical ametropia when examining the effects of astigmatism on emmetropization and myopia development. Our study is the first, to our knowledge, to explore how these complex interactions affect axial elongation and myopia development during school age.

Our study contributes to the understanding of the impact of astigmatism magnitude on the emmetropization process. Previous research in monkeys[14,16] and chicks[17,18] has shown that imposing astigmatism can alter the course of emmetropization, with the end points directed toward either the circle of least confusion or the least hyperopic focal plane associated with the imposed astigmatism.[45] In our subcohort analyses, compound hyperopic eyes with higher astigmatism showed significantly reduced axial elongation compared to those with lower astigmatism (Fig. 2), suggesting that the eye growth was directed toward the least hyperopic focal plane. In humans, myopic eyes, which are more prolate in shape,[46–49] tend to have relative peripheral hyperopic defocus,[50,51] whereas hyperopic eyes are more oblate and show relatively peripheral myopic defocus.[52] These peripheral defocus could potentially serve as a signal to regulate myopia development,[53] even when the fovea image is in focus with optical correction. Therefore, in hyperopic eyes, higher astigmatism would bring the least hyperopic focal plane closer to the retina in the periphery compared to those with lower astigmatism, probably leading to reduced myopic progression and axial elongation. This observation aligns with findings from our recent chick study,[18] where hyperopic astigmatic blur with higher astigmatism magnitude resulted in lower myopic error compared to similar hyperopic astigmatic blur with lower astigmatism magnitude.

Although the defocus mechanism explained above provides some insight, it does not fully explain the increased axial elongation in our compound myopic astigmatic eyes (Fig. 2). This could be due to several factors. For example, myopic eyes tend to have larger accommodative lag[54,55] and higher ocular aberrations[56,57] than emmetropic and hyperopic eyes. These deficiencies could impose a higher magnitude of hyperopic defocus and degrade the quality of the retinal image,[58] thereby complicating the effect of astigmatism on eye growth. Furthermore, the sensitivity of the focusing mechanism is reduced in myopic eyes,[59,60] making it more challenging for the myopic retina to determine the level of defocus. The chronic blur caused by significant astigmatism could further diminish the ability of the retina to regulate emmetropization,[9,13] potentially confounding the endpoint for emmetropization.

Our study found that ATR astigmatism was associated with greater axial elongation than WTR in compound myopic and other ametropic/emmetropic eyes (Fig. 3). This finding suggests that horizontally oriented visual signals might be more potent in promoting axial elongation. Previous studies have reported varying effects of WTR and ATR astigmatism on refractive[13,21,22] and structural changes of the eyes,[23,24,61] but the underlying mechanism is still unclear. One possible explanation is the orientation selectivity of the retinal and neural processing pathways. For example, the retinal circuits and cells of many vertebrates, such as ganglion and amacrine cells,[62] respond more robustly to stimuli that align with their preferred orientation.[63,64] Given that relative hyperopic defocus predominantly occurs along the horizontal meridian,[65] eyes with myopic ATR astigmatism (where the most hyperopic focal line is horizontally orientated) would receive stronger stimuli for axial elongation compared to myopic-WTR astigmatism. Supporting this hypothesis, studies in cat have shown that more neurons[66,67] or larger areas of the cortical surface[68] are tuned to horizontal than to vertical stimuli. This suggests that horizontally oriented stimuli may play a critical role in directing eye growth. However, this hypothesis does not explain the insignificant but decreased axial elongation in hyperopic ATR astigmatism compared to hyperopic WTR astigmatism (Fig. 3), possibly caused by some astigmatism-related ocular biometric factors, such as compensated corneal astigmatism, which could confound axial elongation.

This study has some limitations. First, employing non-cycloplegic autorefraction using two different instruments in vision screenings might introduce biases in SER measurements. Studies in Chinese school-age children have reported a mean myopic shift ranging from –0.17 to –0.49 D with the same model of instruments.[69–71] For example, Mu et al.[71] reported a mean difference in SER between cycloplegic retinoscopy and non-cycloplegic Spot autorefraction of –0.49 ± 0.78 D, with 95% limits of agreement ranging from –2.96 to +1.06 D. To address this, we adopted a more conservative criterion for myopia definition (i.e.,

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both principal meridians ≤ –0.75 D), and primarily focused on AXL progression rather than SER progression. The measurements of astigmatism and axial length are less influenced by non-cycloplegic examinations,[72,73] reinforcing the credibility of our findings. Although these strategies minimize the influence of non-cycloplegic measurements, the potential for overestimating myopia and underestimating hyperopia cannot be entirely eliminated. Therefore, caution is warranted when interpreting findings related to SER. Second, without records of habitual spectacle prescriptions, this observational study cannot quantify the precise retinal image blur resulting from astigmatism during the follow-up period. Consequently, the observed AXL progression may stem from varying degrees of uncorrected astigmatism. Even with full optical correction, the relatively higher off-axis astigmatism in lenses with higher cylindrical power[74] may also contribute to the progression. Future studies that control for optical corrections are essential to validate our proposed mechanism. Third, our study had a limited sample size of high OBL or high ATR astigmatism, which may affect the robustness of our conclusions. This imbalanced distribution of astigmatism types may have limited our statistical power to detect a potential interaction effect between astigmatism magnitude and axis orientation on axial elongation. Future analyses with more balanced samples across different astigmatism and spherical ametropia are therefore required to fully explore these potential interactions. Despite these limitations, the strength of our study lies in its novel findings with a large sample size, thus offering the potential to guide future research in this field.

In conclusion, this 5-year large-scale cohort study of 10,732 Chinese school-age children has revealed that baseline magnitude and axis orientation of astigmatism are significantly associated with axial elongation. However, these associations may vary depending on the baseline spherical ametropia. Specifically, high-magnitude and ATR astigmatism can be linked to increased axial elongation in compound myopic eyes, but with decreased progression in compound hyperopic eyes. These findings not only suggest the significant role of early astigmatism in eye growth but also provide valuable insights for developing personalized management and interventions for pediatric refractive errors.

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