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RESEARCH



Higher order aberrations according to spherical, and astigmatic refractive errors in children

Rubén Molina^a, Beatriz Redondo^{id a,b}, Carolina Ortiz^a, Jesús Vera^{a,b}, José A Díaz^a and Raimundo Jiménez^{id a}

^aDepartment of Optics, University of Granada, Granada, Spain; ^bNew England College of Optometry, Boston, Massachusetts

ABSTRACT

Clinical relevance: The results of this study present novel insights into the impact of spherical and astigmatic refractive errors on overall, corneal and internal aberrations and may provide a clear understanding of the emmetropisation process and the development of visual function.

Background: This study aimed to assess the association between overall, corneal and internal higher-order aberrations and the spherical and astigmatic components (magnitude and angle) of refractive error in a large sample of children.

Methods: A total of 311 children aged 7 – 8 years old were classified based on spherical equivalent refraction (myopic, emmetropic and hyperopic); magnitude of astigmatism (none, low and moderate); and angle of astigmatism (with-the-rule, against-the-rule and oblique). Refractive error and overall, corneal and internal higher-order aberrations were measured using the OPD-Scan III workstation.

Results: Regarding spherical equivalent refraction, myopic eyes had greater root mean square (RMS) overall higher-order values, total spherical, tetrafoil and secondary astigmatism aberrations, and internal higher-order, total spherical and tetrafoil aberrations in comparison to emmetropic eyes. The magnitude of astigmatism was positively associated with all overall RMS aberrations and with internal higher order, coma, total coma, total spherical and tetrafoil aberrations. Eyes with with-the-rule astigmatism showed higher RMS values of coma and total coma compared to eyes with against-the-rule and oblique astigmatism.

Conclusions: Higher-order aberrations are dependent on the spherical as well as astigmatic components of refractive error. These findings enhance the current understanding of the emmetropisation process and visual function development.

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Emmetropization; ocular aberrations; retinal image quality; visual development

Introduction

The process of emmetropisation and the development of visual function are influenced by a combination of many factors, including genetic and environmental elements.^{1–3} Among these factors, the quality of the retinal image plays a key role in the process of emmetropisation and visual development.^{4,5} Low-order aberrations (i.e., defocus and astigmatism) are responsible for approximately 90% of retinal image quality.⁶ Nevertheless, these optical aberrations can be easily corrected using contact lenses, spectacles or refractive surgery, allowing for satisfactory visual performance in terms of visual acuity.⁷ In contrast, higher-order aberrations (HOAs) cannot be easily compensated for (e.g., using adaptive optics systems, phase plates and customised refractive surgery)⁸ and have detrimental effects on visual quality and development.^{9,10}

Total ocular aberrations occur on anterior and posterior corneal surfaces and the crystalline lens, with internal aberrations being a combination of the posterior corneal surface and crystalline lens aberrations and corneal aberrations originating from the anterior corneal surface.¹¹ Evidence suggests that internal aberrations arising from the crystalline lens and the posterior surface of the cornea partially compensate for anterior corneal surface aberrations, with this compensation being particularly apparent in young subjects.¹² Changes in the crystalline lens could play a role in determining retinal image quality.¹³ The crystalline lens suffers progressive thinning and flattening with age, and

these changes become increasingly pronounced until the age of approximately 10 years.^{14,15} Technological advancements in internal aberrometry have enabled the separate assessment of the roles of corneal and internal surfaces at a high level of repeatability.¹⁶

The number and type of HOAs may influence eye growth and the development of refractive errors, making this possible association particularly significant during childhood.¹⁷ There are claims that unusually low or excessive HOA levels may provide the necessary directional cue for eye growth.¹⁸ Previous studies have reported that corneal and internal aberrations may contribute to the development of refractive errors in children and young adults.^{11,19–22} In this regard, findings are inconclusive, with some studies reporting great ocular aberrations in hyperopic eyes,¹¹ while other authors have observed many aberrations in myopic eyes.²⁰ Additionally, previous investigations have found no differences in optical aberrations based on spherical refractive errors.^{23–25} Although various researchers have assessed the link between HOAs and spherical refractive errors in children,^{19–22} an investigation of the relationship between HOAs and astigmatic refractive errors in children has yielded inconclusive results.^{26–28}

To address the aforementioned limitations, the main objectives of the current study were to (i) determine whether total (overall), corneal and internal HOAs are affected by refractive error spherical components and (ii) explore the impact of the amount (absence of astigmatism, low

astigmatism and moderate astigmatism) and the angle (with-the-rule [WTR], against-the-rule and oblique astigmatism) of astigmatism on overall, corneal and internal HOAs in a large sample of children. The results of this study may help extend an understanding of the impact of HOAs on eye growth, a process that is partially determined by early visual experience.^{18,29} Furthermore, these results could have applications in enhancing optical corrections to manage the onset and progression of myopia.

Methods

Participants

Based on the effect size calculated by Thapa et al.,¹⁹ for HOAs in different refractive error groups (effect size between emmetropic and low-hyperopic children was 0.33), an *a priori* sample size calculation was performed using GPower 3.1 software.³⁰ This analysis assumed an alpha of 0.05 and a power of 0.95. Furthermore, a between-subjects analysis of variance was employed, indicating that 180 eyes were required for this study. A total of 319 children aged 7–8 years old (mean age \pm standard deviation = 7.1 ± 0.2 years) were recruited from 5 elementary schools in Granada (Spain). All the children were free of ocular pathologies, and prior ocular surgery had not been performed on them. To ensure these inclusion criteria, all the children underwent an optometric examination that included a slit lamp and direct ophthalmoscopy examination as well as an analysis of the accommodative response and amplitude to detect any functional problems affecting the accommodative system. The accommodative response and amplitude were evaluated using the monocular estimated method and push-up method, respectively. Due to recording errors or difficulties with data collection, 8 of the 319 right eyes that were measured were omitted from further analysis, leaving 311 eyes for further examination. All parents or legal guardians signed a parental consent form. Additionally, children consented to participate in this study, which adhered to the Declaration of Helsinki and was approved by the Institutional Review Board of the University of Granada.

Classification of spherical and astigmatic components

All the right eyes included in the study were categorised according to spherical equivalent refraction (spherical component + astigmatic component/2) as myopic (spherical equivalent refraction ≤ 0.5 D), emmetropic (spherical equivalent refraction > 0.50 D and < 1.00 D) and hyperopic (spherical equivalent refraction ≥ 1.00 D). All eyes were classified as having no astigmatic errors (< 0.25 D), low astigmatism (≥ 0.25 D and < 1 D) or moderate astigmatism (≥ 1.00 D). Furthermore, based on the angle of astigmatism, eyes with astigmatism were categorised as having WTR astigmatism (negative cylinder axis $\geq 150^\circ$ and $\leq 30^\circ$), against-the-rule astigmatism (negative cylinder axis $\geq 60^\circ$ and $\leq 120^\circ$) and oblique astigmatism (negative cylinder axis $> 30^\circ$ and $< 60^\circ$ and $> 120^\circ$ and $< 150^\circ$).³¹ Table 1 shows the distribution of eyes according to the spherical equivalent refraction, the magnitude of astigmatic errors and the astigmatism angle.

HOA assessment

OPD-Scan III (Nidek Inc., Tokyo, Japan) is a five-in-one true refractive workstation that combines a topographer, wavefront aberrometer, keratometer and pupillometer. To assess ocular refraction, this device uses scanning retinoscopy/sciascopy, based on the time difference captured by photodetectors due to the refraction of the eye, to calculate spherical errors, cylindrical errors and their respective axes. Regarding wavefront aberration analysis, OPD-Scan III uses Zernike polynomials based on the conversion of the refractive power map and provides three types of data: overall, corneal and internal aberrations of the eye. In addition, this device can be used with both mesopic and photopic pupils, and the analysis of the pupil area can be performed manually within the 3.0 to 9.0 mm range.³² OPD-Scan 3 computes the average value of the three measurements automatically taken by this instrument, and several studies have attested its high level of accuracy, repeatability and reproducibility.^{16,33,34} OPD-Scan III was used to obtain refractive error and HOA measurements. HOA measurements were obtained under similar conditions of space and illumination (mesopic lighting conditions

Table 1. Distribution of eyes according to the spherical equivalent refraction, magnitude of astigmatic error, as well as astigmatism angle.

		n	Age (years) (mean \pm SD)	SER (D) (mean \pm SD)	Astigmatism (D) (mean \pm SD)	Axes ($^\circ$) (mean \pm SD)
Myopia	SER ≤ -0.5 D Range (-12 to -0.5 D)	108 (34.73%)	7.06 \pm 0.23	-1.78 \pm 1.81	-0.50 \pm 0.50	65.83 \pm 62.00
Emmetropia	SER > -0.50 D and < 1.00 D Range (-0.38 to 0.88 D)	182 (58.52%)	7.05 \pm 0.23	0.14 \pm 0.33	-0.27 \pm 0.27	62.80 \pm 61.57
Hyperopia	SER ≥ 1.00 D Range (1.00 to 3.88 D)	21 (6.75%)	7.09 \pm 0.30	1.93 \pm 0.83	-0.93 \pm 0.99	89.23 \pm 62.08
Without Astigmatism	ARE < -0.25 D Range (0.00 D to 0.00 D)	89 (28.61%)	7.04 \pm 0.21	-0.22 \pm 0.72	–	–
Low astigmatism	ARE ≥ 0.25 D and < 1.00 D Range (-0.25 to -0.75 D)	190 (61.09%)	7.06 \pm 0.23	-0.30 \pm 1.33	-0.39 \pm 0.18	97.04 \pm 50.97
Moderate astigmatism	ARE ≥ 1.00 D Range (-1.00 to -3.75 D)	32 (10.29%)	7.09 \pm 0.30	-1.58 \pm 3.24	-1.48 \pm 0.64	61.78 \pm 63.66
With-the-rule astigmatism	axes $\geq 150^\circ$ and $\leq 30^\circ$ Range (1 to 28° and 151 to 179°)	84 (37.84%)	7.06 \pm 0.24	-0.75 \pm 2.25	-0.66 \pm 0.54	11.02 \pm 7.57 166.32 \pm 7.97
Against-the-rule astigmatism	axes $\geq 60^\circ$ and $\leq 120^\circ$ Range (60 to 120°)	86 (38.74%)	7.09 \pm 0.29	-0.32 \pm 1.45	-0.49 \pm 0.49	92.33 \pm 16.30
Oblique astigmatism	axes $< 150^\circ$ and $> 120^\circ$ Range (122 to 148°) axes $< 60^\circ$ and $> 30^\circ$ Range (32 to 59°)	52 (23.42%)	7.02 \pm 0.14	-0.32 \pm 1.39	-0.48 \pm 0.30	135.67 \pm 7.64 44.00 \pm 9.53

n = number of participants; SER = spherical equivalent refraction; SD = standard deviation; ARE = Astigmatic refractive error

ranging from 17 to 25 lux, as measured in the corneal plane using an Illuminance metre, namely, T-10, Konica Minolta Inc., Tokyo, Japan) without using cycloplegia.

Before each measurement, children were comfortably seated, and their chins and foreheads were placed on corresponding supports. The combination of wavefront aberrometry and corneal topography, calculated through the capture of Placido ring images, enables differentiation between aberrations caused by the anterior surface of the eye (corneal aberrations) and internal ocular media (internal aberrations). OPD scan III software calculates internal aberrations from corneal topography and overall ocular aberration data. Each participant had their seat height adjusted and their head and chin positioned correctly. The children were then instructed to look at the internal target of the instrument (a balloon) and blink a number of times before each acquisition. One measurement was taken per eye, with additional measurements done in case the map was incomplete or errors were found. In line with the standards of the Optical Society of America and the American National Standards Institute, all aberrations were expressed as Zernike coefficients up to the eighth-order aberrations.³⁵ Third-order to eighth-order HOAs were measured across a naturally dilated pupil. To control the influence of pupil size on ocular aberrations, total, internal and corneal aberrations were scaled to 5 mm based on the equivalent expressions proposed by Díaz et al.,³⁶ and the assumption that the 5 mm pupil is concentric with the natural pupil (the eyes included in this study had a pupil size ranging from 4 to 8.25 mm). These values were analysed using root-mean-square (RMS) values (μm). Overall, internal and corneal aberrations were separately considered to determine the influence of the cornea and crystalline lens.

The RMS values of total HOAs (square root of the sum of the coefficients squared of all HOAs from third- to eighth-orders), coma (square root of the sum of the squared coefficients of C_3^{-1} and C_3^1), total coma (square root of the sum of the squared coefficients of C_3^{-1} , C_3^1 , C_5^{-1} , C_5^1 , C_7^{-1} and C_7^1), trefoil (square root of the sum of the squared coefficients of C_3^{-3} and C_3^3), spherical (square root of the sum of the squared coefficients of C_4^0), total spherical (square root of the sum of the squared coefficients of C_4^0 , C_6^0 and C_8^0), tetrafoil (square root of the sum of the squared coefficients of C_4^{-4} and C_4^4) and secondary astigmatism aberrations (square root of the sum of the squared coefficients of C_4^{-2} and C_4^2) were obtained. The 3rd- and 4th-order Zernike coefficients were also considered, as these are the HOAs that most influence optical quality.³⁷

Statistical analyses

First, the normal distribution of the data (Shapiro – Wilk test) and the homogeneity of variances (Levene's test; $p > .05$) was confirmed. To assess the influence of the spherical components of refractive errors (myopic, emmetropic and hyperopic), the amount of astigmatism (absence of astigmatism, low astigmatism and moderate astigmatism) and the type of astigmatism (WTR astigmatism, against-the-rule astigmatism and oblique astigmatism) as between-participant factors on overall, internal and corneal values of the various RMSs and principal aberrations were evaluated. Multivariate analyses of variance (MANOVAs) on the different RMSs and on the principal Zernike coefficients (3rd and 4th order) were performed. Cohen's d effect size (d) and eta squared (η^2) were used to

determine the magnitude of the differences for the T-test and F-test, respectively. Post hoc analyses were corrected using the Holm procedure, and the level of statistical significance was set at 0.05.

Results

In line with previous studies, for a pupil of 5 mm, an RMS value of approximately $0.1 \mu\text{m}$ was considered clinically significant.^{38,39}

Table 2 displays the averages and standard deviations of total, internal and corneal RMS values of the different aberrations assessed in this study and Supplemental Digital Content 1, 2 and 3 illustrate the different Zernike coefficients used in each experimental group for the spherical refractive errors and the amount and angle of astigmatism, respectively.

The statistical analyses of the different RMS and principal Zernike coefficients are presented in Table 3.

Differences according to spherical refractive errors

As shown in Table 3, there were statistically significant differences in the spherical refractive errors for the overall aberrations.

Post hoc analyses revealed that the myopic group had greater internal tetrafoil RMS values compared to the emmetropic and hyperopic groups (corrected p -value < 0.001 and $d = 0.87$ in both groups) (Figure 1). A comparison between myopic and emmetropic eyes revealed greater overall HOA (corrected p -value = 0.003 and $d = 0.41$), overall total spherical (corrected p -value < 0.001 and $d = 0.43$), overall tetrafoil (corrected p -value = 0.002 and $d = 0.42$), overall secondary astigmatism (corrected p -value = .02 and $d = 0.33$), internal HOA (corrected p -value = 0.005 and $d = 0.39$) and internal total spherical aberration RMS values (corrected p -value = 0.015 and $d = 0.36$) only for the myopic group compared to the emmetropic group (Figure 1).

Additionally, a comparison of the hyperopic group with the emmetropic and myopic groups revealed a statistical significance in overall C_3^{-1} (corrected p -values = 0.013 and 0.007, while d 's = 0.63 and 0.73, respectively) and C_3^3 (corrected p -values = 0.012 and 0.040, while d 's = 0.67 and 0.56, respectively) and internal C_3^{-1} (corrected p -values = 0.020 and 0.004, while d 's = 0.60 and 0.78, respectively), and hyperopia with emmetropia in internal C_3^3 (corrected p -value = 0.011, while $d = 0.67$). Myopia was statistically significant with the rest of the group in overall and internal C_4^{-4} (overall C_4^{-4} , myopia vs emmetropia corrected p -value < 0.001 , $d = 0.71$; vs hyperopia corrected p -value = 0.001 and $d = 0.83$ and internal C_4^{-4} ; myopia vs emmetropia corrected p -value < 0.001 and $d = 0.71$; vs hyperopia corrected p -value < 0.001 and $d = 1.05$).

Differences according to the amount of astigmatism

Table 3 also shows the statistical effect obtained as a function of the amount of astigmatism for each of the aberrations measured.

Regarding overall aberrations, post hoc analyses revealed higher RMS values of HOAs, coma, total coma, spherical, total spherical and tetrafoil aberrations for the group with moderate astigmatism compared to the groups with low astigmatism (corrected p -value $< .001$ and $d = 1.03$; corrected p -value

Table 2. Descriptive values (mean \pm standard deviation) for the different RMSs assessed.

RMS (μm)	Myopia	Emmetropia	Hyperopia	Without astigmatism	Low astigmatism	Moderate astigmatism	WTR	Oblique	ATR
Overall									
High Order	0.25 \pm 0.12	0.21 \pm 0.08	0.23 \pm 0.10	0.21 \pm 0.09	0.22 \pm 0.08	0.32 \pm 0.15	0.23 \pm 0.10	0.24 \pm 0.10	0.24 \pm 0.10
Coma	0.13 \pm 0.08	0.12 \pm 0.07	0.15 \pm 0.09	0.12 \pm 0.07	0.12 \pm 0.07	0.17 \pm 0.10	0.12 \pm 0.07	0.13 \pm 0.08	0.12 \pm 0.08
Total Coma	0.13 \pm 0.08	0.12 \pm 0.07	0.15 \pm 0.09	0.12 \pm 0.07	0.12 \pm 0.07	0.17 \pm 0.10	0.13 \pm 0.07	0.14 \pm 0.08	0.12 \pm 0.08
Trefoil	0.12 \pm 0.07	0.12 \pm 0.08	0.11 \pm 0.07	0.10 \pm 0.06	0.12 \pm 0.07	0.14 \pm 0.08	0.13 \pm 0.08	0.12 \pm 0.07	0.13 \pm 0.08
Spherical	0.02 \pm 0.02	0.02 \pm 0.01	0.02 \pm 0.02	0.02 \pm 0.01	0.02 \pm 0.02	0.03 \pm 0.03	0.02 \pm 0.03	0.02 \pm 0.02	0.02 \pm 0.02
Total Spherical	0.03 \pm 0.03	0.02 \pm 0.02	0.03 \pm 0.01	0.02 \pm 0.02	0.03 \pm 0.02	0.05 \pm 0.05	0.03 \pm 0.03	0.03 \pm 0.02	0.03 \pm 0.02
Tetrafoil	0.09 \pm 0.08	0.07 \pm 0.04	0.07 \pm 0.04	0.07 \pm 0.05	0.07 \pm 0.04	0.13 \pm 0.12	0.08 \pm 0.06	0.10 \pm 0.06	0.08 \pm 0.06
Sec. Astigmatism	0.06 \pm 0.06	0.04 \pm 0.02	0.05 \pm 0.03	0.05 \pm 0.06	0.05 \pm 0.03	0.07 \pm 0.05	0.05 \pm 0.04	0.05 \pm 0.04	0.05 \pm 0.03
Internal									
High Order	0.28 \pm 0.13	0.23 \pm 0.12	0.26 \pm 0.12	0.24 \pm 0.13	0.24 \pm 0.11	0.33 \pm 0.15	0.26 \pm 0.13	0.25 \pm 0.11	0.25 \pm 0.11
Coma	0.13 \pm 0.07	0.12 \pm 0.06	0.14 \pm 0.08	0.13 \pm 0.06	0.12 \pm 0.06	0.15 \pm 0.10	0.13 \pm 0.07	0.13 \pm 0.06	0.12 \pm 0.07
Total Coma	0.14 \pm 0.07	0.13 \pm 0.06	0.15 \pm 0.08	0.13 \pm 0.06	0.13 \pm 0.06	0.16 \pm 0.10	0.13 \pm 0.07	0.13 \pm 0.07	0.13 \pm 0.07
Trefoil	0.12 \pm 0.07	0.11 \pm 0.09	0.12 \pm 0.10	0.10 \pm 0.09	0.11 \pm 0.08	0.14 \pm 0.07	0.12 \pm 0.08	0.11 \pm 0.09	0.12 \pm 0.09
Spherical	0.03 \pm 0.03	0.02 \pm 0.02	0.03 \pm 0.04	0.02 \pm 0.03	0.02 \pm 0.02	0.03 \pm 0.03	0.03 \pm 0.03	0.02 \pm 0.02	0.03 \pm 0.03
Total Spherical	0.04 \pm 0.03	0.03 \pm 0.03	0.04 \pm 0.04	0.03 \pm 0.03	0.03 \pm 0.02	0.05 \pm 0.04	0.03 \pm 0.03	0.03 \pm 0.03	0.04 \pm 0.03
Tetrafoil	0.15 \pm 0.08	0.10 \pm 0.05	0.08 \pm 0.03	0.11 \pm 0.06	0.11 \pm 0.05	0.16 \pm 0.12	0.11 \pm 0.08	0.12 \pm 0.06	0.11 \pm 0.07
Sec. Astigmatism	0.06 \pm 0.06	0.05 \pm 0.05	0.06 \pm 0.04	0.06 \pm 0.06	0.05 \pm 0.05	0.07 \pm 0.06	0.06 \pm 0.06	0.05 \pm 0.04	0.05 \pm 0.04
Corneal									
High Order	0.22 \pm 0.07	0.23 \pm 0.11	0.24 \pm 0.10	0.23 \pm 0.12	0.23 \pm 0.09	0.23 \pm 0.07	0.24 \pm 0.10	0.22 \pm 0.08	0.22 \pm 0.08
Coma	0.12 \pm 0.06	0.13 \pm 0.07	0.12 \pm 0.07	0.12 \pm 0.07	0.12 \pm 0.06	0.14 \pm 0.07	0.14 \pm 0.07	0.11 \pm 0.06	0.11 \pm 0.06
Total Coma	0.12 \pm 0.06	0.13 \pm 0.07	0.13 \pm 0.07	0.13 \pm 0.07	0.12 \pm 0.06	0.15 \pm 0.07	0.14 \pm 0.07	0.12 \pm 0.06	0.11 \pm 0.06
Trefoil	0.11 \pm 0.07	0.11 \pm 0.09	0.12 \pm 0.10	0.11 \pm 0.10	0.11 \pm 0.08	0.10 \pm 0.05	0.12 \pm 0.08	0.11 \pm 0.08	0.10 \pm 0.07
Spherical	0.02 \pm 0.02	0.02 \pm 0.02	0.02 \pm 0.03	0.02 \pm 0.03	0.01 \pm 0.02	0.02 \pm 0.02	0.01 \pm 0.01	0.02 \pm 0.02	0.02 \pm 0.02
Total Spherical	0.02 \pm 0.02	0.02 \pm 0.02	0.03 \pm 0.03	0.02 \pm 0.03	0.02 \pm 0.02	0.02 \pm 0.02	0.02 \pm 0.02	0.02 \pm 0.02	0.02 \pm 0.02
Tetrafoil	0.11 \pm 0.04	0.11 \pm 0.05	0.10 \pm 0.03	0.11 \pm 0.05	0.11 \pm 0.04	0.10 \pm 0.04	0.11 \pm 0.04	0.10 \pm 0.04	0.12 \pm 0.05
Sec. Astigmatism	0.05 \pm 0.04	0.05 \pm 0.04	0.05 \pm 0.04	0.05 \pm 0.03	0.05 \pm 0.04	0.06 \pm 0.05	0.06 \pm 0.06	0.04 \pm 0.03	0.05 \pm 0.03

RMS root means square, Sec. Secondary, WTR with-the-rule astigmatism, ATR against-the-rule astigmatism, all values are shown in μm .

Table 3. Statistical analysis according to the spherical refractive error, amount of astigmatism and angle of astigmatism.

RMSs	MANOVAs								
	Spherical refractive error			Amount of astigmatism.			Angle of astigmatism		
	Approx. F	Trace pillai	p	Approx. F	Trace pillai	p	Approx. F	Trace pillai	p
High Order	3.79	0.07	0.001*	6.52	0.12	<0.001*	0.65	0.02	0.694
Coma	1.56	0.03	0.156	2.67	0.05	0.015*	1.96	0.05	0.069
Total Coma	1.64	0.03	0.133	2.91	0.06	0.008*	1.85	0.05	0.087
Trefoil	0.32	0.01	0.927	2.50	0.05	0.021*	0.76	0.02	0.599
Spherical	1.69	0.03	0.122	2.65	0.05	0.015*	0.60	0.02	0.730
Total Spherical	3.27	0.06	0.004*	5.04	0.09	<0.001*	0.40	0.01	0.880
Tetrafoil	9.94	0.18	<0.001*	8.25	0.15	<0.001*	2.02	0.05	0.062
Sec. Astigmatism	1.27	0.02	0.271	1,843	0.04	0.088	1.02	0.03	0.414
Principal Zernike coefficients (3rd and 4th order)									
C_3^{-1}	2.78	0.05	0.011*	1.42	0.03	0.203	2.51	0.07	0.021*
C_3^1	0.36	0.01	0.902	0.394	0.01	0.883	1.15	0.03	0.331
C_3^{-3}	1.38	0.03	0.221	2.07	0.04	0.055	1.20	0.03	0.303
C_3^3	1.87	0.04	0.084	0.88	0.02	0.508	1.78	0.05	0.102
C_4^0	1.85	0.04	0.087	2.69	0.05	0.014*	0.22	0.06	0.970
C_4^{-4}	7.90	0.14	<0.001*	2.04	0.04	0.058	1.43	0.04	0.202
C_4^4	1.01	0.02	0.421	1.03	0.02	0.403	0.65	0.02	0.692
C_4^{-2}	1.13	0.02	0.342	1.72	0.03	0.115	3.27	0.09	0.004*
C_4^2	0.70	0.01	0.654	1.37	0.03	0.226	1.76	0.05	0.105

Sec. Secondary, *statistically significant differences among groups.

= 0.002 and $d = 0.66$; corrected p -value = 0.001 and $d = 0.70$; corrected p -value = 0.014 and $d = 0.47$; corrected p -value < 0.001 and $d = 0.76$; and corrected p -value < 0.001 and $d = 1.01$, respectively) and without astigmatism (corrected p -value < 0.001 and $d = 1.02$; corrected p -value = 0.002 and $d = 0.61$; corrected p -value = 0.001 and $d = 0.65$; corrected p -value < 0.001 and $d = 0.68$; corrected p -value < 0.001 and $d = 0.87$; corrected p -value < 0.001 and $d = 0.94$, respectively) (Figure 2). In addition, eyes with moderate and low astigmatism have greater trefoil RMS values than eyes without astigmatism (corrected p -value = 0.012 and $d = 0.63$; corrected p -value = 0.043 and $d = 0.30$, respectively) (Figure 2). The

group with moderate astigmatism had a greater secondary astigmatism RMS value than the group with low astigmatism (corrected p -value = 0.01 and $d = 0.70$) (Figure 2).

In comparing moderate and low astigmatism, there is statistical significance in overall C_3^{-3} and C_4^{-4} (corrected p -value = 0.003 and $d = 0.63$ and corrected p -value = 0.032 and $d = 0.49$) and moderate in the without-astigmatism group in overall C_3^{-3} and C_4^2 (corrected p -value = 0.004 and $d = 0.65$ and corrected p -value = 0.049 and $d = 0.50$).

For internal aberrations, post hoc analyses revealed that eyes with moderate astigmatism had higher RMS values of HOAs and total coma and total spherical and tetrafoil

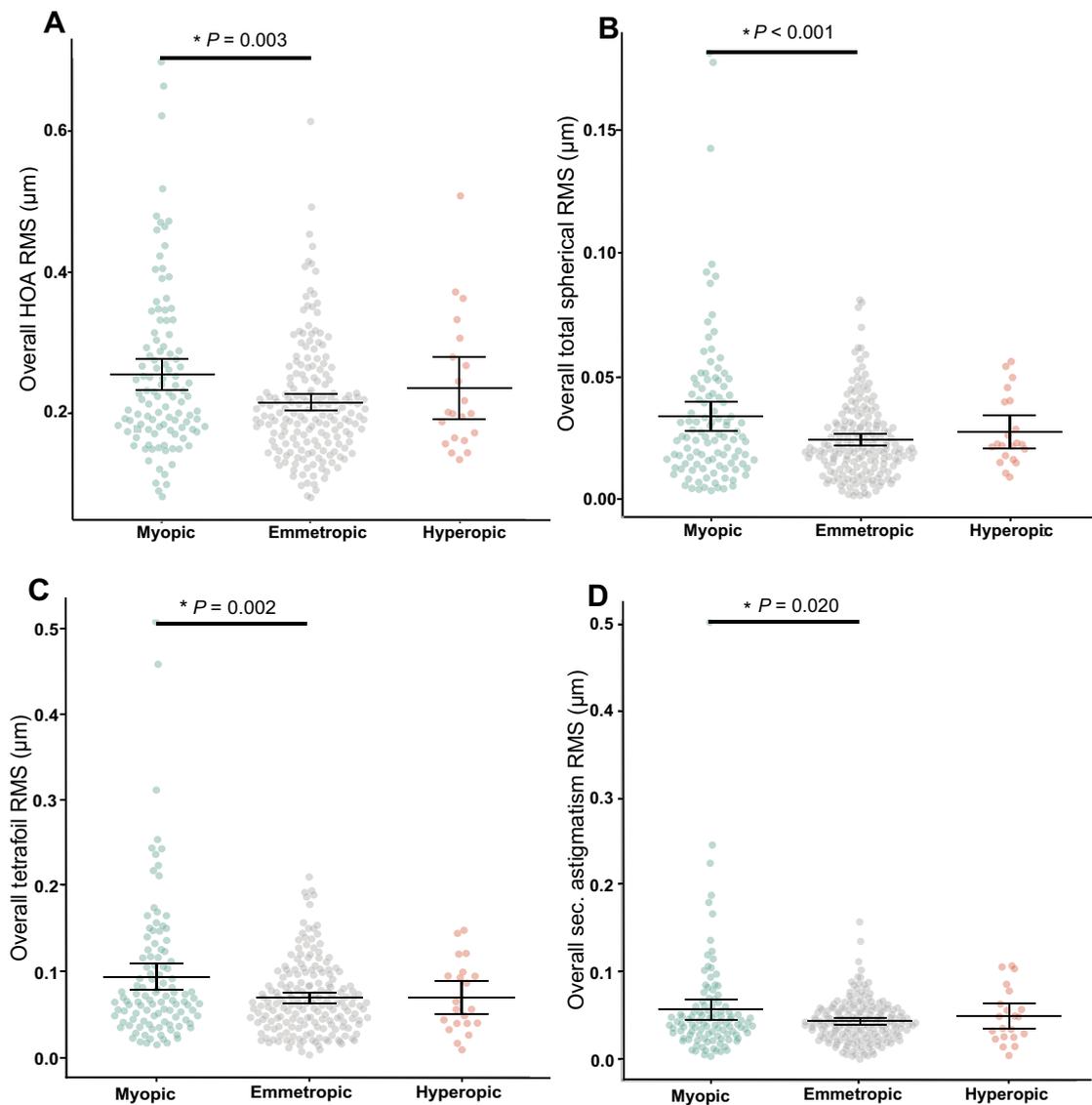


Figure 1. Scatterplot of RMS values of overall higher-order aberrations (panel A), total spherical (panel B), tetrafoil (panel C), secondary astigmatism (panel D), internal higher-order aberrations (panel E), total spherical (panel F), and tetrafoil aberrations (panel E) according to the spherical refractive errors. The central horizontal line indicates the mean value, and the whiskers represent the 95% confidence intervals. Myopic group: spherical equivalent refraction ≤ -0.5 D; emmetropic group: spherical equivalent refraction > -0.50 D and < 1.00 D; hyperopic group: spherical equivalent refraction ≥ 1.00 D; RMS = root-mean-square.

aberrations than had eyes without astigmatism (corrected p -value < 0.001 and $d = 0.64$; corrected p -value = 0.044 and $d = 0.43$; corrected p -value < 0.001 and $d = 0.64$; corrected p -value = 0.001 and $d = 0.56$, respectively) and low astigmatism (corrected p -value < 0.001 and $d = 0.80$; corrected p -value = 0.008 and $d = 0.57$; corrected p -value < 0.001 and $d = 0.75$); and corrected p -value < 0.001 and $d = 0.79$, respectively (Figure 3). In addition, eyes with moderate astigmatism had a greater coma RMS value than eyes with low astigmatism (corrected p -value = 0.015 and $d = 0.52$) (Figure 3).

The corneal C_4^0 is statistically significant in comparing moderate astigmatism with the rest of groups (vs low astigmatism corrected p -value = 0.003 and $d = 0.61$; vs without astigmatism corrected p -value = 0.001 and $d = 0.74$), while the corneal C_3^{-1} was only statistically significant when comparing the high astigmatism with low astigmatism (corrected p -value = 0.031 and $d = 0.49$) and C_4^{-2} when comparing the high astigmatism with the without-astigmatism group (corrected p -value = 0.047 and $d = 0.50$).

Differences according to the angle of astigmatism

Table 3 shows the differences observed in the analysis of corneal aberrations based on the influence of the astigmatism angle. Post hoc analyses revealed that the WTR astigmatism group had greater coma and total coma RMS values than the against-the-rule group (corrected p -values = 0.007 and 0.01; d 's = 0.46 and 0.45, respectively) and oblique astigmatism (corrected p -values = 0.045 and 0.042; d 's = 0.39 and 0.39 each) (Figure 4). Post hoc analysis revealed no statistically significant difference for the tetrafoil RMS value (corrected p -value > 0.05 for all comparisons).

Finally, when comparing the against-the-rule astigmatism group with the WTR group, statistical significance was observed in overall C_3^{-1} , C_3^3 and C_4^{-2} (corrected p -values = 0.022, 0.026 and 0.001; d 's = 0.39, 0.41 and 0.55, respectively), in internal C_3^3 and C_4^{-2} (corrected p -values = 0.026 and 0.011; d 's = 0.41 and 0.45, respectively) and corneal C_3^{-1} (corrected p -value = 0.005 and $d = 0.49$). The against-the-rule group was only statistically significant when

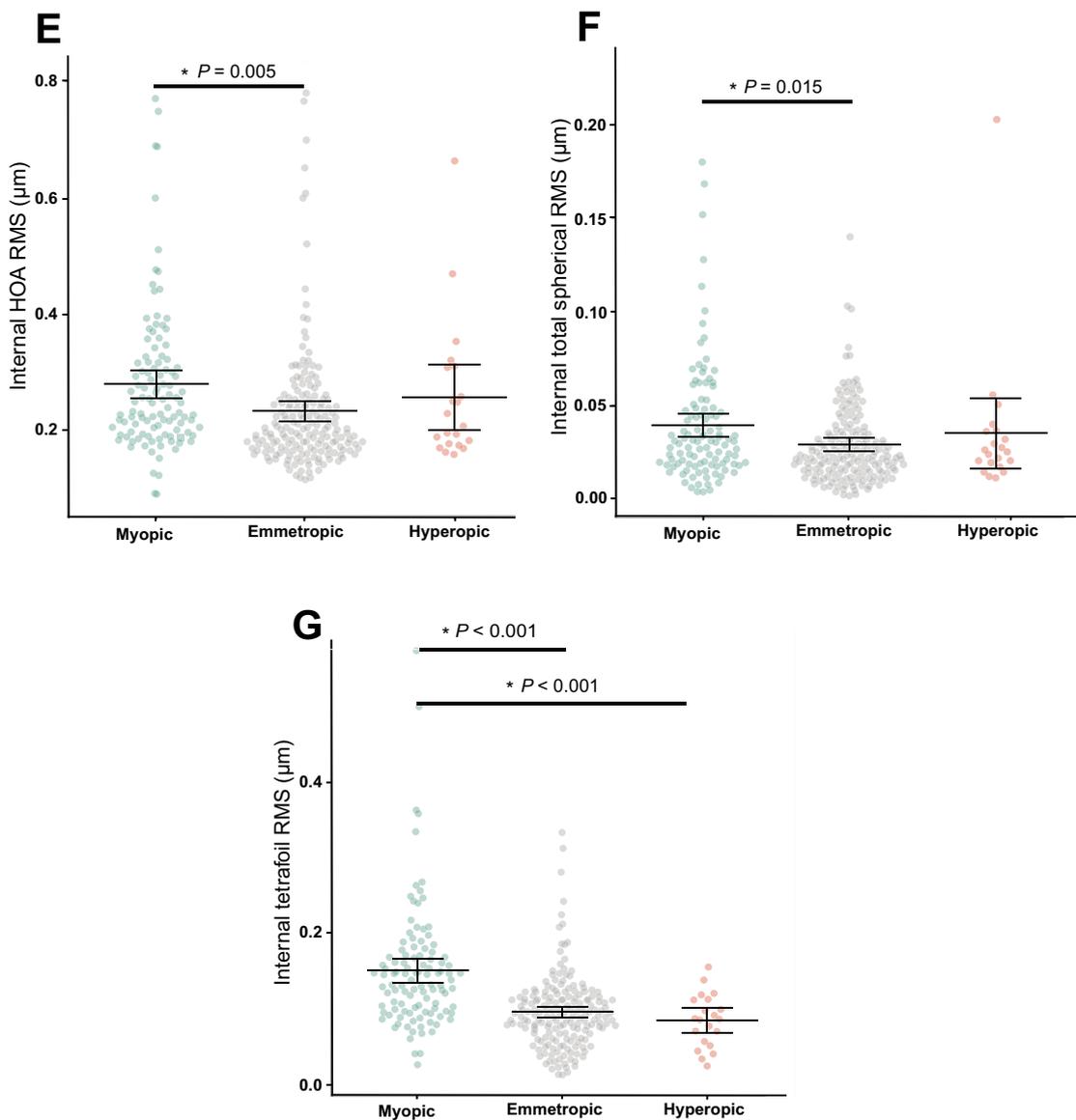


Figure 1. (Continued).

compared to the oblique group in the overall C_3^{-1} (corrected p -value = 0.016 and $d = 0.50$).

Discussion

The purpose of the current study was to evaluate the impact of the spherical and astigmatic components of refractive errors on overall, corneal and internal HOAs in children. Regarding the spherical component, this research revealed that myopic eyes had greater overall and internal values than emmetropic and hyperopic eyes in the oblique tetrafoil, which was reflected in the tetrafoil RMS values. Regarding HOA and total spherical RMS values, the myopic eyes also had higher overall and internal RMS values. Furthermore, concerning the amount of the astigmatic component, although statistical significance was only found for the overall Zernike coefficients C_3^{-3} , C_4^{-4} and C_4^2 and corneal C_3^{-1} and C_4^0 , the overall RMS values of HOAs, coma, total coma, spherical, total spherical, tetrafoil aberrations and internal HOAs were higher for the group with moderate astigmatism than for the groups of children without astigmatism and with low astigmatism. Overall secondary astigmatism and internal coma

RMS values were only positively associated when compared to low astigmatism, while the overall tetrafoil had higher values when compared to both eyes with moderate astigmatism and low astigmatism and eyes without astigmatism. Finally, in relation to the angle of astigmatism, the significant values found for overall and corneal C_3^{-1} seem to influence eyes with WTR astigmatism, which had higher values of corneal coma and total coma RMS values compared to eyes with against-the-rule and oblique astigmatism. Consequently, these results show that HOAs depend on the amount and type of refractive errors, including spherical and astigmatic components. However, it should be noted that the large sample size used in this study allows for the detection of small changes as statistically significant. Therefore, the differences found in this study should be interpreted accordingly. Future research is required to determine the clinical significance of the current results.

Regarding the spherical refractive component, differences were found in values of overall and internal HOAs between myopic and emmetropic children, which is consistent with the findings of several studies conducted on paediatric populations.^{11,20,21} Previous investigations have hypothesised

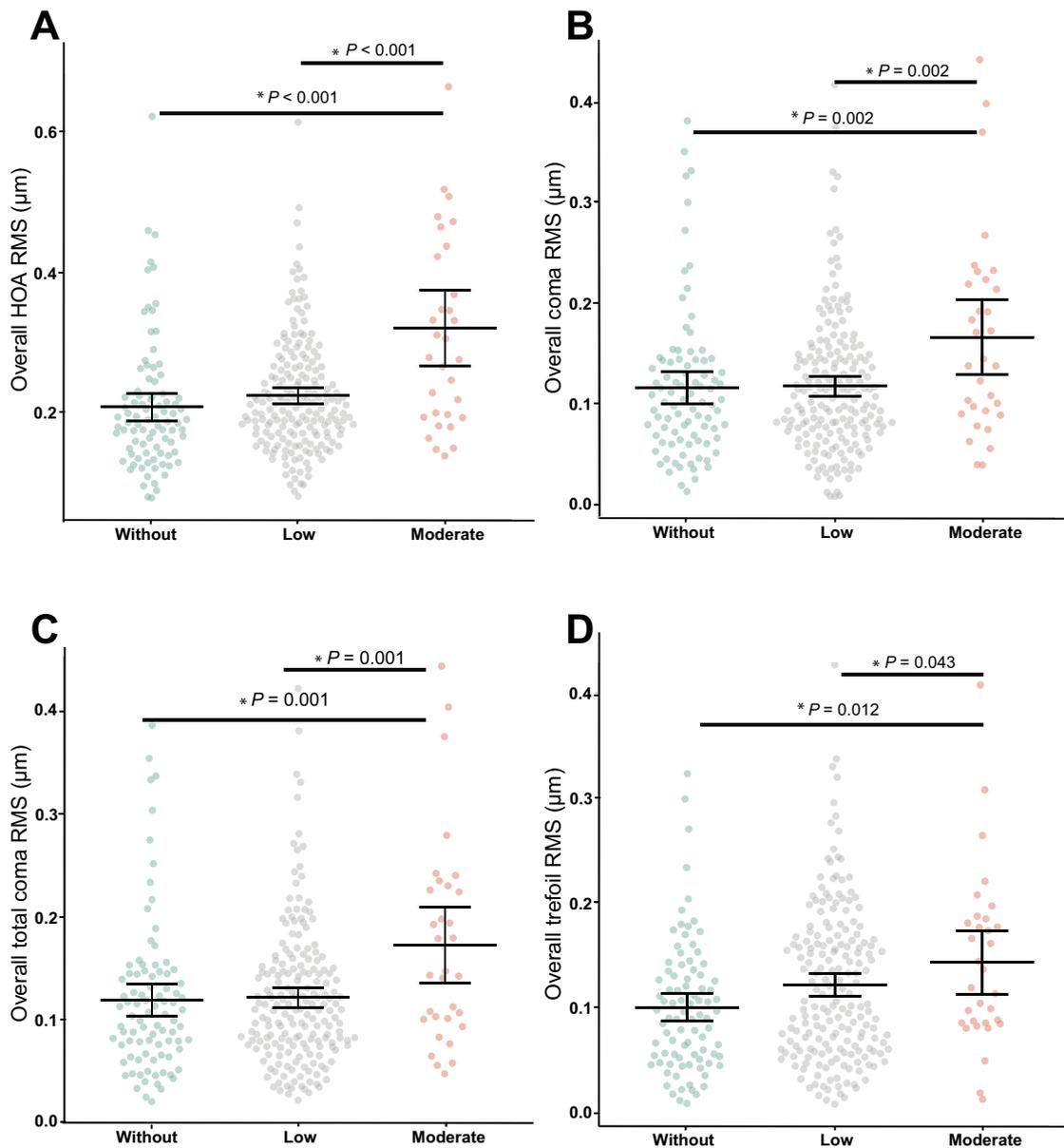


Figure 2. Scatterplot of RMS values of overall higher-order aberrations (panel A), coma (panel B), total coma (panel C), trefoil (panel D), spherical (panel E), total spherical (panel F), tetrafoil (panel G), and secondary astigmatism aberrations (panel H) according to the amount of astigmatism. The central horizontal line indicates the mean value, and the whiskers represent the 95% confidence intervals. Without: astigmatism lower than 0.25 D; low: astigmatism greater or equal to 0.25 and lower than 1 D; moderate: astigmatism greater or equal to 1 D. HOAs = total higher-order aberrations; RMS = root-mean-square.

that internal HOAs may influence refractive error development,¹¹ and the present data indicate that the crystalline lens plays a role in the differences in HOAs between refractive error groups, with Zernike coefficients C_3^{-1} , C_3^3 and especially C_4^{-4} contributing the most.

Similar to the findings by Philip et al.,¹¹ this investigation found that a large sample of adolescent myopic eyes had higher RMS values of internal total spherical aberrations compared to the rest of the eyes. In addition, there were no significant differences between groups in corneal RMS values or in the values of the Zernike coefficient C_4^0 or its RMS. However, there were differences in the RMS values of total spherical aberrations, indicating that the differences between the sixth-order and eighth-order spherical aberrations increased. There is agreement between this study and the studies by Kirwan et al., and He et al.,^{20,21} who observed that young adults with myopic eyes had higher RMS values of

HOAs than emmetropic eyes. It should be noted that the optical quality of the eye of a child eye is suboptimal compared to that of a young adult, potentially due to the development of the optical structures of the eye.⁴⁰

Previous studies have suggested that the increase in aberrations with age may be caused by alterations in the optical characteristics of the crystalline lens.^{17,41} Moreover, due to the differences observed in internal HOAs across different refractive error groups, it would be of interest to explore, using optical systems based on swept-source optical coherence tomography,^{42,43} whether there is an association between internal HOAs and the anatomical and optical characteristics of the crystalline lens in children with different refractive error ranges and types. On the other hand, optical strategies for myopia control (e.g. orthokeratology or multifocal lenses) have been shown to reduce image quality^{44,45} despite being highly effective in slowing myopia

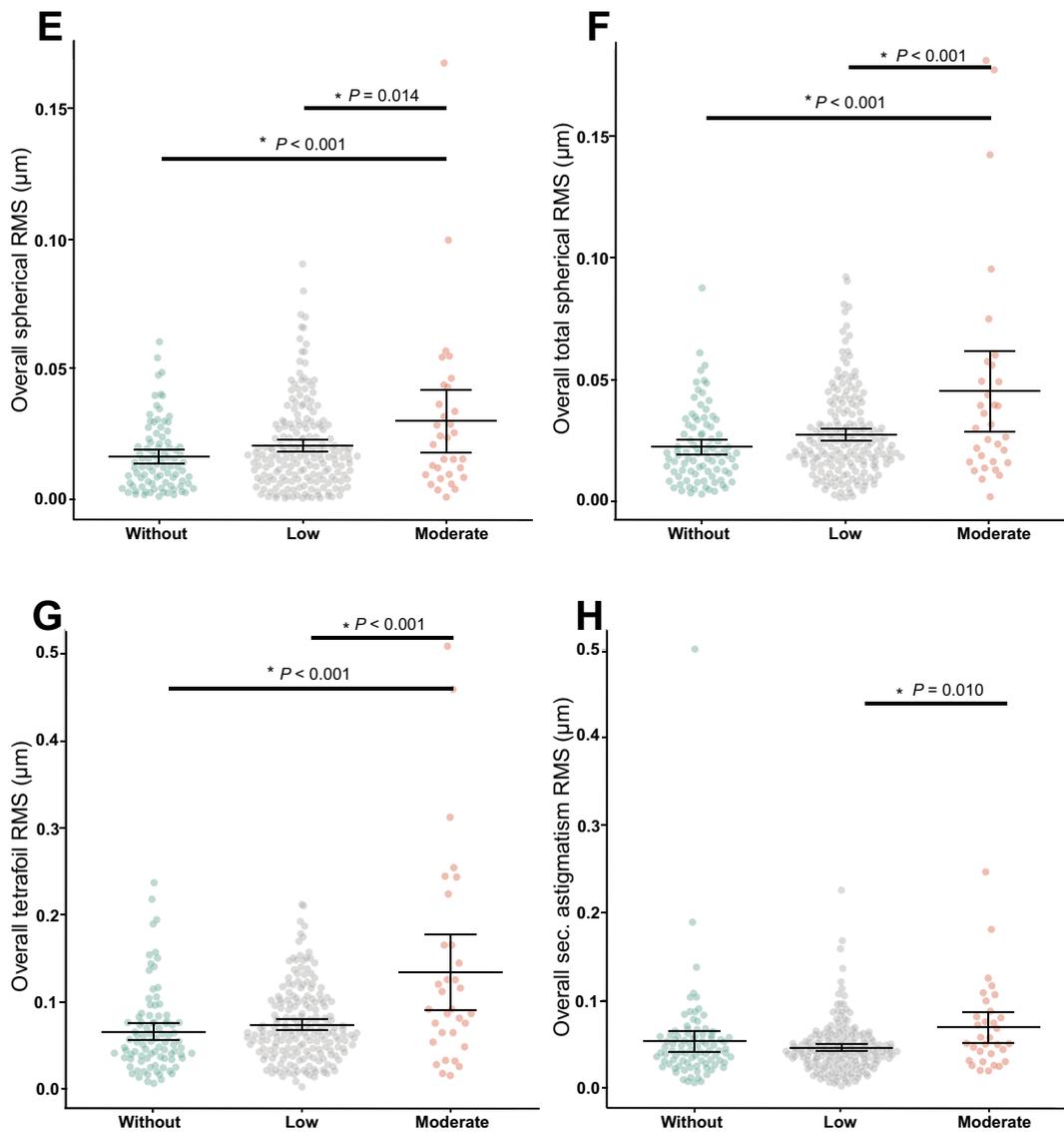


Figure 2. (Continued).

progression.⁴⁶ As recently reported by Hughes et al.,¹⁷ further longitudinal studies are required to determine the link between HOAs and myopia control strategies in refractive error development and eye growth.

This investigation also explored the impact of the amount of astigmatism on HOAs. A trend of great HOAs in eyes with high astigmatism has been observed, similar to previous research findings.^{27,28,47} Significant results for RMS values of internal HOAs, coma, total coma and total spherical and tetrafoil aberrations were observed although significant Zernike coefficients were not found in the main internal aberrations. However, since there is a thinning and flattening of the crystalline lens^{14,15} during childhood until the age of approximately 10 years, the current observations among children aged 7–8 years old cannot be extrapolated to other age groups. To date, no studies have assessed the effect of the amount of astigmatism on internal HOAs in children. Previous investigations conducted on adults have suggested that age-related changes in the optical characteristics of the crystalline lens may be responsible for the increase in aberrations with age.^{41,48} Nevertheless, third-order to seventh-order

aberrations fit a quadratic model as a function of age, showing a progressive decrease until the fourth decade of life and then a progressive increase with age.⁴⁰ Based on the accumulated scientific evidence, it is plausible that HOAs are involved in the emmetropisation process and that the differences observed in this study may be reduced in adolescents and young adults.

There is limited evidence about the impact of the type of astigmatism on HOAs, with age-related changes in the optical characteristics of the crystalline lens being suggested as the reason for variations in the number of aberrations.^{13,41} This investigation found that although there is statistical significance in the overall Zernike coefficients C_3^{-1} , C_3^3 and C_4^{-2} ; internal C_3^3 and C_4^{-2} ; and corneal C_3^{-1} , only WTR astigmatism is associated with high values of corneal coma, total coma and tetrafoil aberrations compared to all other astigmatism types. However, these results may be associated with a greater negative cylinder in the WTR group compared to other groups (Table 1). Papamastorakis et al.,⁴⁹ reported that second-order aberrations, such as total oblique astigmatism, and third-order aberrations, such as horizontal and

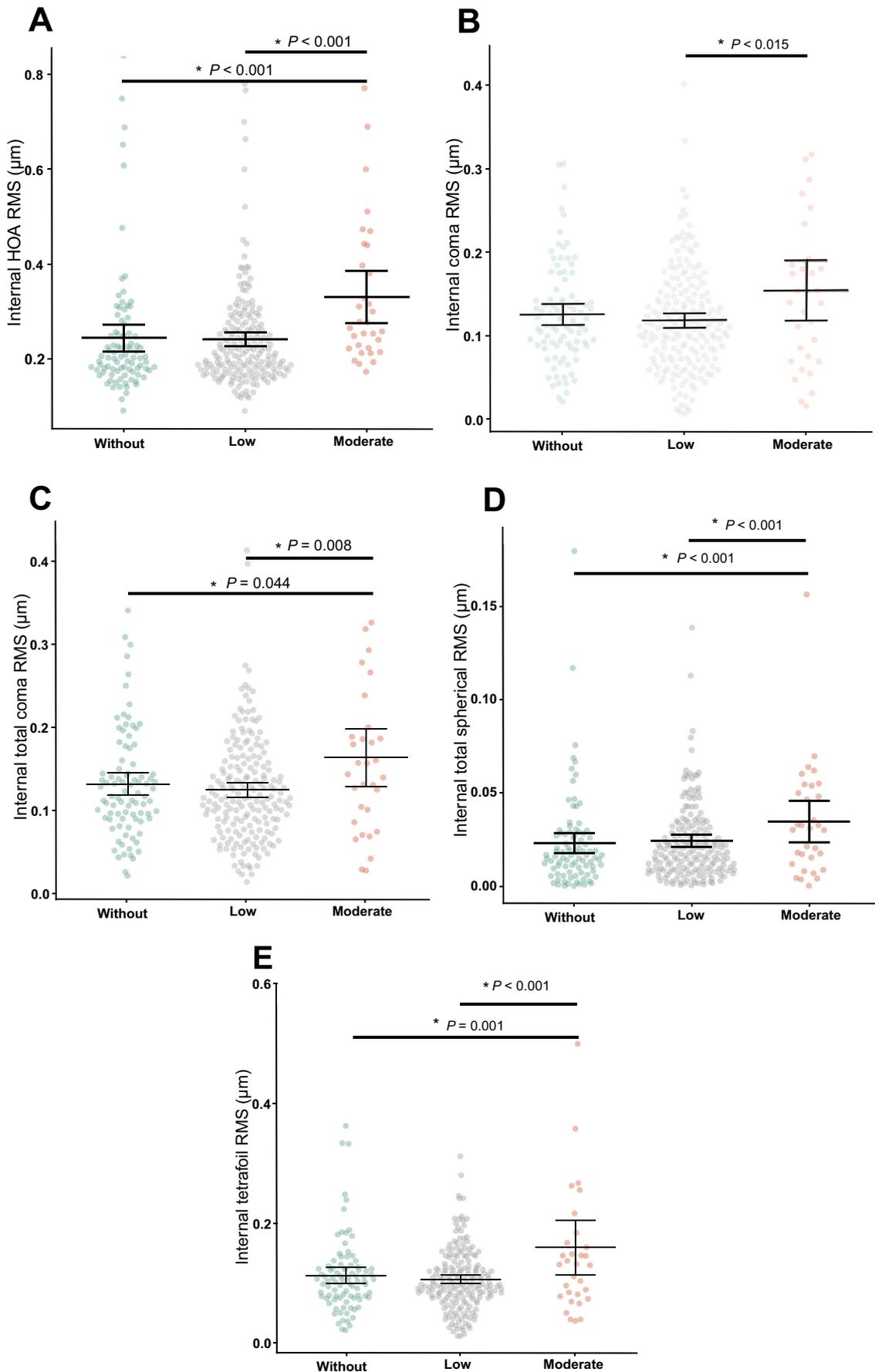


Figure 3. Scatterplot of RMS values of internal higher-order aberrations (panel A), coma (panel B), total coma (panel C), total spherical (panel D), and tetrafoil aberrations (panel E) according to the amount of astigmatism. The central horizontal line indicates the mean value, and the whiskers represent the 95% confidence intervals. Without: astigmatism lower than 0.25 D; low: astigmatism greater or equal to 0.25 and lower than 1 D; moderate: astigmatism greater or equal to 1 D. HOA = total higher-order aberrations; RMS = root-mean-square.

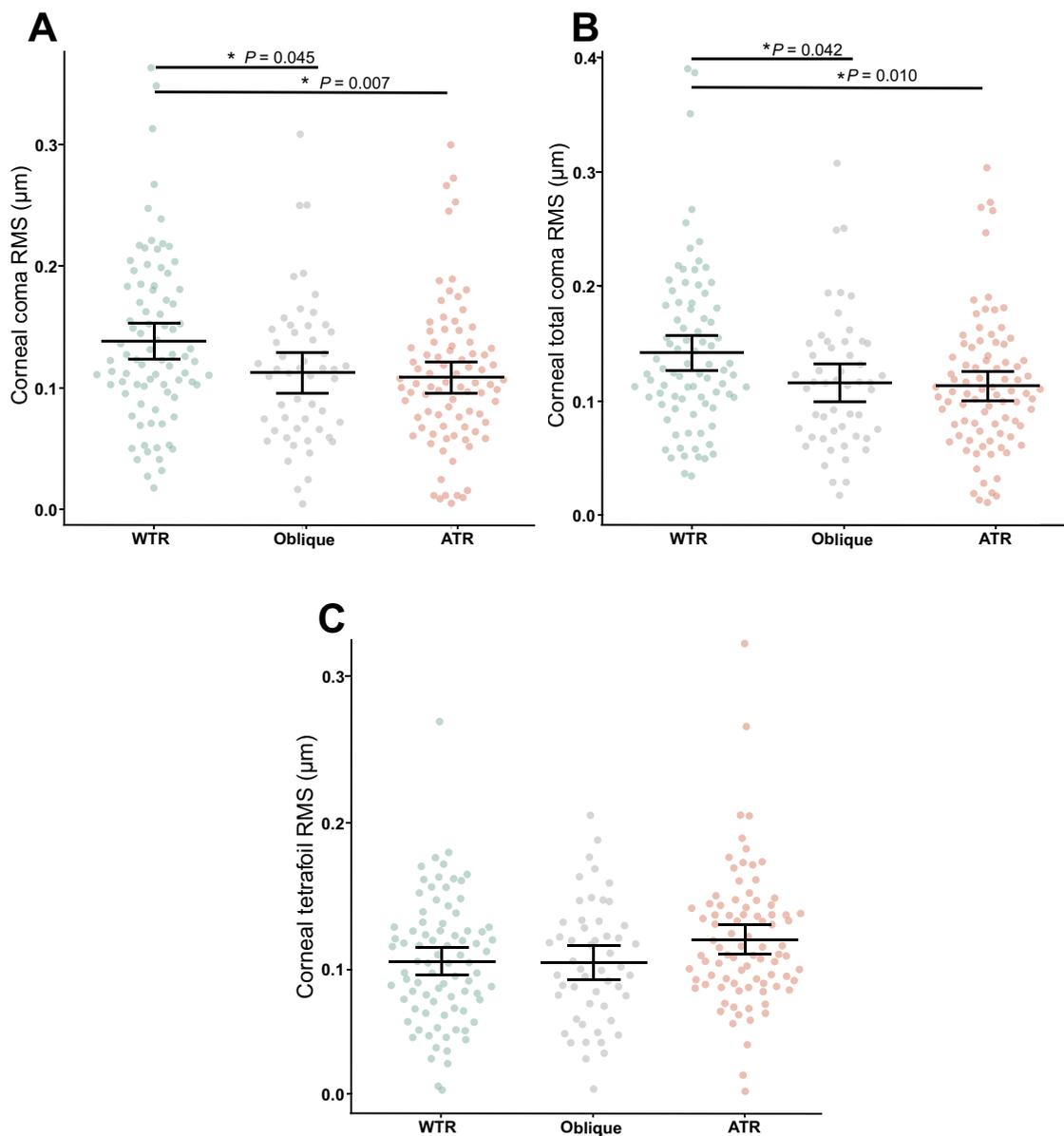


Figure 4. Scatterplot of RMS values of corneal coma (panel A), total coma (panel B), and tetrafoil (panel C) aberrations according to the type of astigmatism. The central horizontal line indicates the mean value, and the whiskers represent the 95% confidence intervals. RMS = root-mean-square; WTR: with-the-rule astigmatism; oblique: oblique astigmatism; ATR: against-the-rule astigmatism.

vertical coma, were modulated as a function of age in a population of primary and secondary school children (10–15 years). There are claims that HOAs could play a role in the process of emmetropisation¹⁷ and are partially associated with spherical and astigmatic refractive errors (amount and angle). Optometrists should consider all of these factors when prescribing optical corrections to ensure an appropriate clinical decision. Future studies are required to determine the importance of HOA compensation for emmetropisation and visual development, especially in children with significant oblique astigmatism.

This study aimed to determine the role of spherical and astigmatic components of refractive errors on overall, corneal and internal HOAs. However, the limitations of this study must be acknowledged. First, to minimise changes in optical aberrations as a function of age, the age range of the experimental sample was greatly limited (7–8 years); therefore, these results must be cautiously interpreted. Second, previous papers have suggested that changes in aberrations are mediated by changes in the crystalline^{13,41} rather than

corneal characteristics.^{50,51} Longitudinal studies assessing the changes in optical aberrations and different eye structures (e.g. swept-source segment optical coherence tomography system) would allow for the clarification of this association.

Third, in this study, internal aberrations were identified through indirect measurement using the OPD-Scan III system, with an assumption made that the anterior corneal surface contributes 75% and the lens and posterior corneal surface contribute 25% to the total refractive power of the eye, respectively. Consequently, it should also be considered that internal aberrations should be correlated with the corneal and total aberrations. However, there could be greater correlations if the RMS is composed of a great amount of noise in one of the corneal aberrations or in the total aberrations. Therefore, the measurements obtained for internal RMS should be taken with caution since this percentage is an estimate and may vary between eyes. Furthermore, in this study, measurement was only done once – in line with the manual of the instrument, potentially leading to bias due to noise. The noise would affect the RMS value and could also be

higher in one group than in another, and these factors could be one reason why differences in RMS values were found between groups. In this sense, future studies should develop data collection protocols that minimise the bias caused by various noise sources in ocular aberrations.

Fourth, several factors, such as the instrument used for aberration assessment, the ethnicity of the children (all were Caucasians in this study)²⁴ or the criteria used for refractive error classification, may limit the generalisability of the current results. Fifth, RMS wavefront error may not be the best predictor of the image quality of a patient.⁵² Zernike modes can interact and affect retinal image quality.⁵³ Therefore, future studies using different metrics and specific aberrations would be valuable.

Sixth, when comparing influential astigmatism in different groups, it was observed that the emmetropic group had more statistically significant values compared to the myopic and hypermetropic groups (corrected *p-values* <.001 and = 0.002; *d's* = 0.63 and 1.63, respectively). This result can be considered logical since the group of emmetropic children with spherical equivalent values between >-0.50 D and <1.00 D usually do not have astigmatism, and if they do, it is usually mild. This characteristic is uncommon among myopic and hyperopic individuals. On the other hand, for comparison by type of astigmatism, although there was no statistically significant difference between groups (corrected *p-values* = 0.108, 0.057 and 1.000; *d's* = 0.38, 0.33 and 0.01, when comparing oblique vs WTR, against-the-rule vs WTR and oblique vs against-the-rule, respectively), the means were slightly higher in the WTR astigmatism group (Table 1). However, this result could have influenced the outcome of the aberrations obtained in these groups and should be controlled in future studies. Seventh, the current findings must be cautiously interpreted since no cycloplegic agent was used and there is clinical evidence that aberrometry results obtained under cycloplegia differ from those obtained without cycloplegia.^{54–56} Lastly, believe it is important to evaluate the long-term effects of using various techniques for correcting HOAs on visual development and emmetropisation.^{57–59}

Conclusions

The findings of this study suggest a relationship between HOAs and the spherical and astigmatic components of refractive errors. Regarding spherical errors, myopic eyes had higher RMS values of overall and internal HOAs as well as total spherical and tetrafoil aberrations than emmetropic eyes. High amounts of astigmatism are positively linked to HOAs, and WTR astigmatism is associated with higher corneal coma and total coma RMS values than all other types of astigmatism. The present findings shed light on the impact of spherical and astigmatic refractive errors on overall, corneal and internal aberrations and may aid in the understanding of emmetropisation and the development of visual function.

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ORCID

Beatriz Redondo  <http://orcid.org/0000-0003-4571-873X>

Raimundo Jiménez  <http://orcid.org/0000-0002-8036-2532>

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