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Pediatric Ophthalmology & Strabismus

Refractive Associations With Whole Eye Movement Distance and Time Among Chinese University Students: A Corvis ST Study

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Received: August 9, 2023
Accepted: November 8, 2023
Published: December 12, 2023

Keywords: eye movement; axial length; refractive status; university students; corvis ST

Citation: Li DL, Qin Y, Zheng YJ, Yin ZJ, Li YZ, Ma R, Liang G, Pan CW. Refractive associations with whole eye movement distance and time among chinese university students: A corvis ST study. Transl Vis Sci Technol. 2023;12(12):13, https://doi.org/10.1167/tvst.12.12.13

Purpose: Eye movement has been frequently studied in clinical conditions, but the association with myopia has been less explored, especially in population-based samples. The purpose of this study was to assess the associations of eye movement measured by the Corvis ST with refractive status in healthy university students.

Methods: A total of 1640 healthy students were included in the study (19.0 ± 0.9 years). Eye movement parameters (whole eye movement [WEM]; whole eye movement time [WEMT]) were measured by the Corvis ST. Spherical equivalent (SE) was measured using an autorefractor without cycloplegia. IOL Master was used to assess axial length (AL).

Results: AL was negatively correlated with WEM and WEMT ($r_{WEM} = -0.28$, $r_{WEMT} = -0.08$), and SE was positively correlated with WEM and WEMT ($r_{WEM} = 0.21$, $r_{WEMT} = 0.14$). For the risk of high myopia, breakpoint analysis and restricted cubic spline model showed that the knots of the significant steep downward trend of WEM and WEMT were 0.27 mm and 20.4 ms, respectively. The piecewise linear regression model revealed a significant correlation between AL, SE, and WEM when the value of WEM was below 0.27 mm. Additionally, when WEMT exceeded 20.4 ms, a significant decrease in AL and an increase in SE were observed with increasing WEMT.

Conclusions: A larger distance and longer duration of eye movement were correlated with a lower degree of myopia and shorter AL, and there was a threshold effect.

Translational Relevance: The findings might aid in understanding the pathogenesis of myopia and provide a theoretical foundation for clinical diagnosis and prediction.

Introduction

Myopia, the most common refractive error, is becoming increasingly prevalent worldwide, with a notably high incidence in East and Southeast Asia.[1,2] Approximately 10% to 20% of myopic patients will develop high myopia, which can lead to complications of irreversible vision loss, including myopic macular degeneration, retinal detachment, and so on.[3] Myopia and high myopia are primarily characterized by excessive elongation of the eye.[4] In recent years, corneal visualization technology (Corvis ST; Oculus, Wetzlar, Germany) has been used to quantitatively evaluate the biomechanical properties of the cornea, eyeball, and constant components, facilitating the study of relevant biomechanics.

Corvis ST is a non-contact device that provides much information about the biomechanics of the cornea. Whole eye movement (WEM) and whole eye movement time (WEMT) are indicators that reflect eye movement in the measurement and represent the overall force profile of the cornea, eyeball, and constant components. When the air is released, the eyeball itself moves back slightly, and when the cornea returns to its original contour, the eyeball moves forward again. Slight but noticeable movement of the entire eye can be found during the measurement.[5] Hwang et al.[6] proposed that eye displacement can be used to quantify the biomechanical parameters of orbital soft tissue behind the eye, including changes in ocular fat and extraocular muscles. WEM has some important relationships with clinical factors. It has been used as an index for detecting keratoconus and has also been applied in glaucoma research.[7–10] In a small clinical sample study, longer axial length (AL) was associated with smaller WEM,[11] but investigations in normal populations were lacking. The existing explanation for the relationship between AL and global eye movement is mainly eyeball compliance.[12–14] The studies suggested that eyes with longer AL generally exhibit greater compliance of the eyeball, resulting in lower ocular rigidity. During the jetting process, the eyeball is more prone to deformation rather than posterior displacement, leading to a lower WEM.[6,15,16]

WEM and WEMT are relatively new parameters, and few studies have addressed their epidemiological association with AL and refractive status, especially in healthy populations. In the few studies to date, WEM has only been briefly correlated with AL as an indicator of corneal biomechanics, and the sample size is small.[10,11,17,18] Data on eye movement and refractive parameters in normal populations are lacking, and possible nonlinear associations have not been explored. Therefore this study aimed to explore the linear and nonlinear associations between eye movements and refractive parameters in Chinese university students and to provide a basis for exploring the mechanism of myopia.

Methods

Study Population

The study comes from the Dali University Student Eye Health Study, a school population study conducted in Yunnan province in southwestern China. The purpose of this study was to identify exposures and risk factors for common eye diseases among college students. The study design and detailed protocol have been described elsewhere.[19–23] Before the investigation, informed consent was obtained from each participant before enrollment. All freshmen of Dali University participated in this questionnaire survey and eye examination in 2021. People with ocular lesions unrelated to myopia (keratoconus, acute infection, etc.) were excluded. A total of 2014 students completed the questionnaire and vision test, with a response rate of 74.7%. In addition, 369 participants with a history of corneal refractive surgery and five participants without eye movement parameters were excluded, leaving 1640 participants for the current analysis. There were no differences in age or sex between subjects and nonsubjects ($P > 0.05$). The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Affiliated Hospital of Yunnan University (February 22, 2021; approval number 2021040).

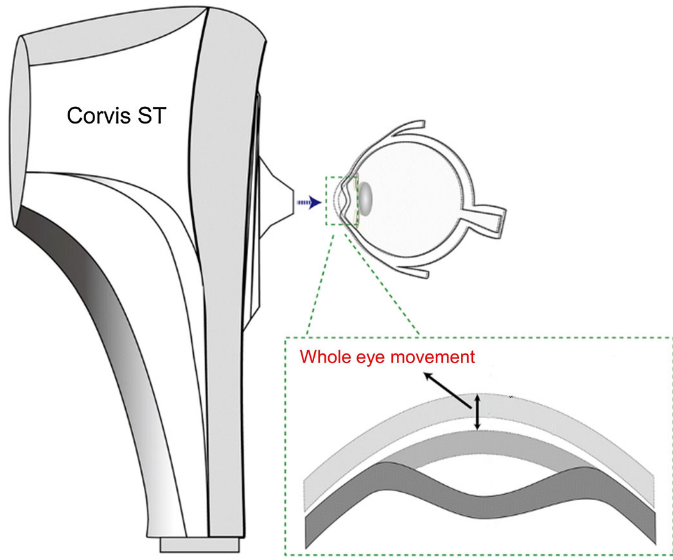

Figure 1. Schematic diagram of whole eye movement by Corvis ST.

Eye Examination

The WEM and WEMT were measured by the Corneal Dynamic Graph Flow Analyzer (Corvis ST; Oculus). This is a device that uses a noncontact tonometer, Scheimpflug geometry, and an ultra-high-speed camera to measure intraocular pressure and various corneal biomechanical parameters. When the Corvis ST jets, a slight but noticeable movement of the entire eye can be observed during the deformation to recovery of the cornea, as shown in Figure 1. During the examination, the participant placed the lower jaw in the mandibular drag and the forehead against the frontal rest; the examination eye was open and flat in front of them, gazing at the red dot in the screen of the red-dot instrument; and the measurer operated the joystick to align the cornea to automatically identify the parameter. Only the reliable measurements that were identified as "OK" by the Corvis ST monitor were selected.

The refractive status was measured using an autorefractor (KR800; Topcon Optical Company, Tokyo, Japan) without cycloplegia. Spherical equivalent (SE) was calculated as the sum of spherical and one-half of the cylindrical. Myopia was defined as an SE less than −0.5 diopter (D), and high myopia was defined as an SE less than −6.0 D. For refractive measurement, the first five valid readings are used and averaged with vector methods to give a single estimate of refractive error. For spherical and cylinder components, all five readings should be at most 0.50 D apart. AL was measured using the IOL Master (Zeiss Meditec, Dublin, CA, USA). The AL measurement was conducted three times, and then the average value was obtained. These eye examinations were carried out by professional ophthalmologists.

Covariate Variables

Sociodemographic characteristics, including age and sex (men or women), were recorded using a self-administered questionnaire. Weight and height were measured by trained school nurses using standard procedures. The weight on the digital scale is accurate to 0.1 kg, and the height on the scale is accurate to 0.1 cm. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared (kg/m^2).

Statistical Analyses

Because of the strong correlation between the biometric parameters of the left and right eyes (Pearson correlation coefficient > 0.90), only the right eye was analyzed at present. Pearson's correlation coefficient was used to test the relationship between WEM and WEMT age, SE, and AL. The *t* tests were used to identify differences in systemic factors and ocular parameters between men and women. Linear regression models were used to examine the associations between WEM and WEMT SE and AL. Considering that the association of eye movements with refractive parameters might be nonlinear, we explored the associations using the restricted cubic spline model and breakpoint analysis. In restricted cubic spline analysis, the independent variable is divided into intervals and a cubic polynomial function is used to fit the data within each interval. Breakpoint analysis describes the change in the dependent variable relative to the independent variable by fitting multiple segments.

All analyses were performed using SPSS 23.0 software (SPSS Inc., Chicago, IL) and R software version 4.2.3. A P value < 0.05 was considered statistically significant.

Results

A total of 1640 students (510 men and 1130 women) aged 15.7 to 24.4 years were enrolled, with a mean age of 19.0 ± 0.9 years. Basic and ocular characteristics, as well as sex differences, are shown in Table 1. The mean AL and SE of the overall population were 24.84 mm and −3.70 D. The mean WEM and WEMT were 0.21 mm and 20.89 ms, respectively. Men tended to have greater weight, height and BMI, lower myopia, longer AL, greater WEM, and longer WEMT than women (all $P < 0.05$, Table 1).

The scatter plots of WEM, WEMT and age, AL, and SE are shown in Figure 2. The values of both WEM and WEMT increased with increasing age ($r_{WEM} = 0.07$, $r_{WEMT} = 0.08$, both $P < 0.05$; Figs. 2A, 2B).

Table 1. Characteristics and Gender Differences of the Included Participants in the Study

Characteristic	Total (n = 1640, Mean ± SD)	Men (n = 510, Mean ± SD)	Women (n = 1130, Mean ± SD)	*P*
Age, year	19.01 ± 0.93	19.06 ± 0.87	18.98 ± 0.95	0.12
Body weight, kg	56.50 ± 11.45	63.89 ± 12.64	53.16 ± 9.09	<0.001
Body height, cm	164.48 ± 8.38	173.08 ± 6.72	160.59 ± 5.75	<0.001
BMI, kg/m^2	20.80 ± 3.36	21.27 ± 3.69	20.59 ± 3.17	<0.001
AL, mm	24.84 ± 1.17	25.24 ± 1.22	24.66 ± 1.10	<0.001
SE, D	−3.70 ± 2.37	−3.47 ± 2.49	−3.80 ± 2.31	0.01
WEM, mm	0.21 ± 0.05	0.22 ± 0.05	0.21 ± 0.04	0.04
WEMT, ms	20.89 ± 0.59	21.00 ± 0.59	20.84 ± 0.59	<0.001

SD, standard deviation.

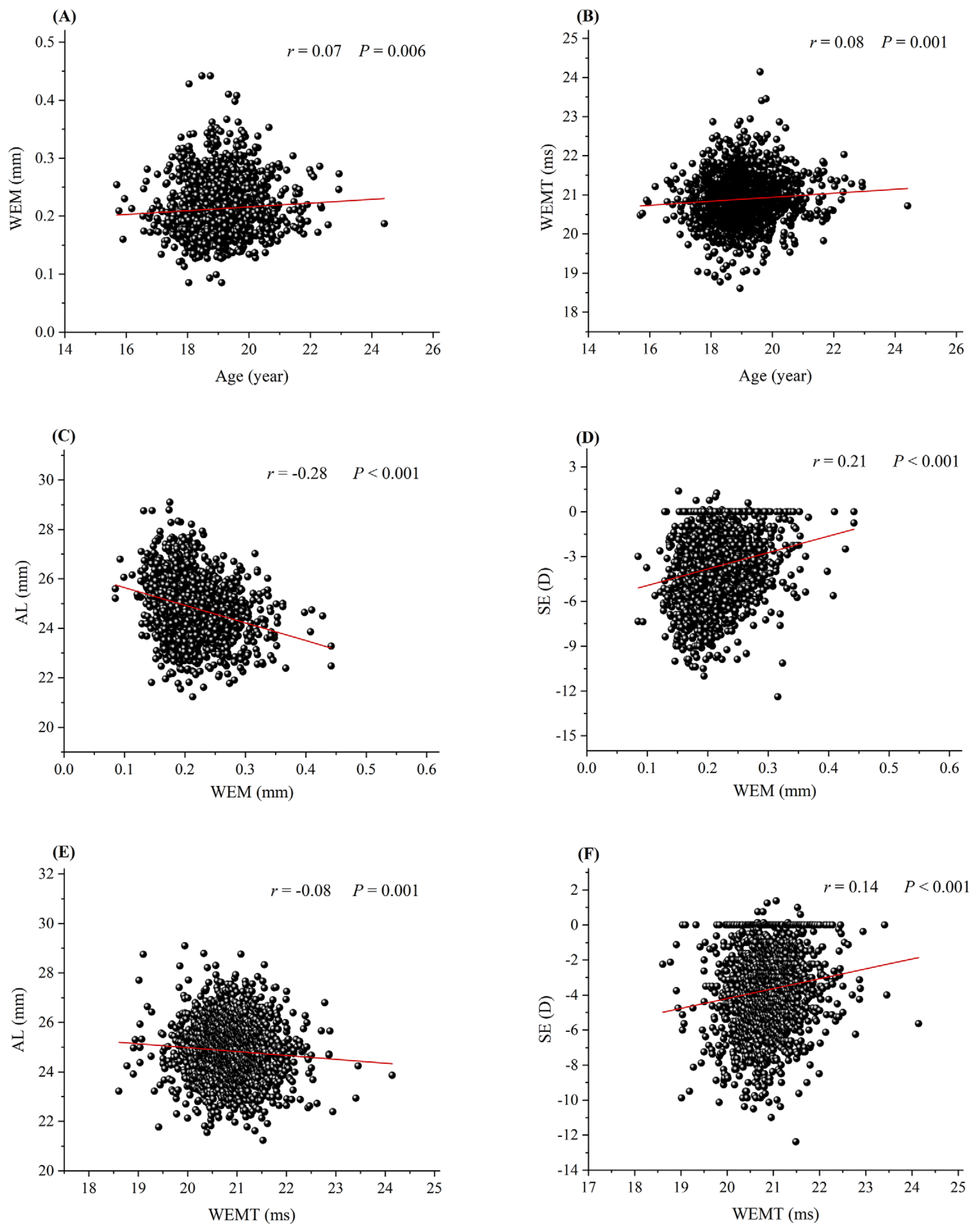

Figure 2. Correlation between age, refractive status, axial length and eye movement. (**A**) Age-WEM; (**B**) Age-WEMT; (**C**) WEM-AL; (**D**) WEM-SE; (**E**) WEMT-AL; (**F**) WEMT-SE.

Significant correlations were observed between AL, SE and WEM, and WEMT (Figs. 2C–F). AL was negatively correlated with WEM and WEMT ($r_{WEM} = -0.28$, $r_{WEMT} = -0.08$; both $P < 0.05$), and SE was positively correlated with WEM and WEMT ($r_{WEM} = 0.21$, $r_{WEMT} = 0.14$; both $P < 0.05$).

Table 2 shows the associations between WEM and WEMT SE and AL. In both the crude and age- and sex-adjusted models, the associations with SE and AL were statistically significant for each unit or quartile increase in WEM and WEMT (all $P < 0.05$). Specifically, after adjusting for sex and age, we found that for each 1 mm increase in WEM, the SE value increases by 10.86 D and the AL decreases by 7.42 mm, whereas for each 1 ms increase in WEMT, the SE value increases by 0.54 D, and the AL decreases by 0.21 mm.

For the risk of high myopia, restricted cubic spline analysis showed that the knots of the significant steep downward trends of WEM and WEMT were 0.27 mm and 20.4 ms, respectively. These breakpoints were used as cutoff values in further analysis. In the restricted cubic spline model adjusted for sex and age, it was observed that the risk of high myopia decreased as

Table 2. Linear Regression Analyses of Associations Between WEM, WEMT, and Refractive Parameters

	SE (D)				AL (mm)			
	Crude Model		Age-Sex-Adjusted Model		Crude Model		Age-Sex-Adjusted Model	
	β (95 % *CI*)	*P*	*β* (95 % *CI*)	*P*	*β* (95 % *CI*)	*P*	*β* (95 % *CI*)	*P*
WEM (mm)								
Per mm increase	11.04 (8.54, 13.55)	<0.001	10.86 (8.35, 13.37)	<0.001	−7.16 (−8.37, −5.95)	<0.001	−7.42 (−8.60, −6.24)	<0.001
R^2	0.04		0.05		0.08		0.14	
Each quartile increase	0.44 (0.34, 0.54)	<0.001	0.43 (0.33, 0.54)	<0.001	−0.27 (−0.32, −0.22)	<0.001	−0.28 (−0.32, −0.23)	<0.001
R^2	0.04		0.05		0.06		0.12	
WEMT (ms)								
Per ms increase	0.57 (0.37, 0.76)	<0.001	0.54 (0.34, 0.73)	<0.001	−0.16 (−0.25, −0.06)	0.001	−0.21 (−0.30, −0.12)	<0.001
R^2	0.02		0.02		0.01		0.07	
Each quartile increase	0.28 (0.18, 0.38)	<0.001	0.26 (0.16, 0.37)	<0.001	−0.08 (−0.13, 0.03)	0.003	−0.10 (−0.15, −0.05)	<0.001
R^2	0.02		0.02		0.01		0.06	

CI, confidence interval.

WEM values increased below 0.27 mm and as WEMT values increased above 20.4 ms (Fig. 3).

Consistently, we further analyzed the association of WEM and WEMT with AL and SE in a piecewise linear regression model. The results revealed that the association between AL, SE, and WEM was not significant when the value exceeded 0.27 mm (Figs. 4A, 4B). However, a significant decrease in AL and an increase in SE were observed as WEMT increased beyond 20.4 ms (Figs. 4C, 4D).

Discussion

Our study provides population-based data on the relationship between eye movement and myopia and AL. The findings suggest that larger WEM and WEMT are associated with a lower degree of myopia and shorter AL, especially at WEM values less than 0.27 mm and WEMT greater than 20.4 ms. In addition, eye movements better explain changes in AL than they explain changes in SE.

In the current study, the mean values of WEM and WEMT were lower than those of Abdi et al.[24] and Li et al.[25] Age may be the largest explanation for the fact that our subjects were younger. In addition, WEM and WEMT were positively associated with age, which was consistent with previous studies.[24,26] This correlation may be due to changes in retrobulbar fat composition with age. As individuals age, retrobulbar fat decreases, and eye displacement and time increase.[27] Based on a small sample, Hwang et al.[6] found that females had a larger MEM than males, whereas our study found the opposite result. Currently, there is no biological mechanism supporting the sex differences in eye movements. Thus the observed differences might be explained by chance findings. Additionally, variations in sample size, age, refractive errors, and orbital structures, could contribute to the inconsistent results.

To date, eye movement has been found to be associated with various eye diseases, such as thyroid eye disease, glaucoma and keratoconus.[8,15,28–30] Shorter WEMT was independently associated with more severe visual field defects in normal tension glaucoma.[8,14] WEM was smaller in patients with Graves orbitopathy or thyroid orbitopathy than in healthy subjects.[15,31] As we know, AL and refractive status are closely related to these diseases, but there are few studies that directly study eye movement and AL and refractive status. We directly explored the relationship between these and found that AL and SE are related to eye movements. Regarding the relationship, the explanation is mainly based on globe compliance and optic nerve traction.

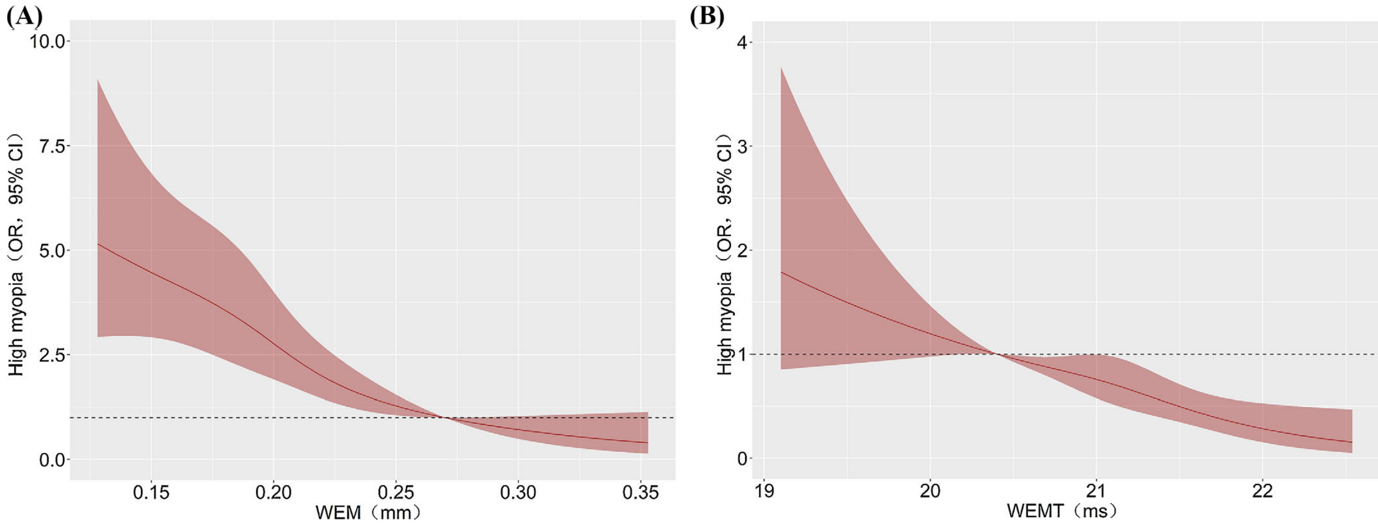

Figure 3. Association of WEM and WEMT with the risk of high myopia. (**A**) WEM-high myopia, the reference was 0.27 mm of WEM; (**B**) WEMT-high myopia, the reference was 20.4 ms of WEMT. OR, odds ratio; CI, confidence interval; adjusted for gender and age.

Previous studies have shown that optic nerve traction exerted on the eyeball during eye movements deforms the optic nerve head, and this effect is more pronounced during adduction than during abduction.[32,33] When looking at close objects, the eye movement is in the adducted state, which may cause transient axial elongation.[34] In highly myopic eyes, the eyeball is overly elongated, which "relieves" some of the inherent optic nerve traction so that the same air-blowing induces less eye movement.[16,35]

Besides, based on growth, deformation, and stress linkages within the eyeball, forces generated by the extraocular muscles during eye movements may be responsible for the axially convergent elongation.[16] However, the direction of extraocular muscle forces is not axial, so it is unlikely that these forces cause scleral remodeling to produce posterior dilation of the globe.[36] In cases of axial length elongation and high myopia, the deformability of the eyeball increases as it elongates axially; that is, the elongation is typically accompanied by a reduction in collagen fiber bundles within the sclera, making it thinner and more elastic. As a result, the compliance of the eyeball increases, allowing for better deformation under force, and the overall movement of the eyeball decreases.[13,24,37–39]

The cornea and sclera are nonlinear, anisotropic, and viscoelastic soft tissues. The extraocular fat and muscles also exhibit significant viscoelasticity.[39,40] Therefore eye movements are also generally nonlinear. Interestingly, our results found a threshold effect on the relationship between eye movement and AL and SE, that is, the relationship is only meaningful when WEM is less than 0.27 mm and WEMT is greater than 20.4 ms. This result shows the nonlinear process of eye movement, but the specific value and phenomenon have not been revealed in a previous study, and the mechanism needs to be further explored in the future. Besides, in the visual system, a series of muscles in our eyeballs are responsible for controlling eye movement.[12] Lin et al.[41] found that inflammation is associated with the development of myopia. In the active inflammation phase, edema and swelling of extraocular muscles, connective tissue, and orbital fat can lead to increased intraocular pressure through ocular hyperemia and increased adventitial venous pressure, followed by decreased orbital compliance leading to slowed eye movements.[31,42,43]

Although both SE and AL are parameters representing the degree of myopia, our analysis showed that eye movements explained more of the variation in AL than in SE. A study by Hagen et al.[44] proposed that sustained elongation of AL is compensated for by refraction of the lens, which involves a reduction in lens power and a deepening of the anterior chamber, thereby delaying the onset of myopia. Additionally, it has been suggested that AL is a better indicator of eye size than SE.[45] Furthermore, it is worth exploring the possibility of a mechanical or physical relationship between eye movements and AL. This relationship warrants further investigation to determine the exact cause and underlying mechanism.

The current study highlights the nonlinear relationship between eye movements and refractive error, suggesting that ocular movement parameters have the potential to serve as new indicators for assessing the risk of myopia. In future diagnostic and predictive

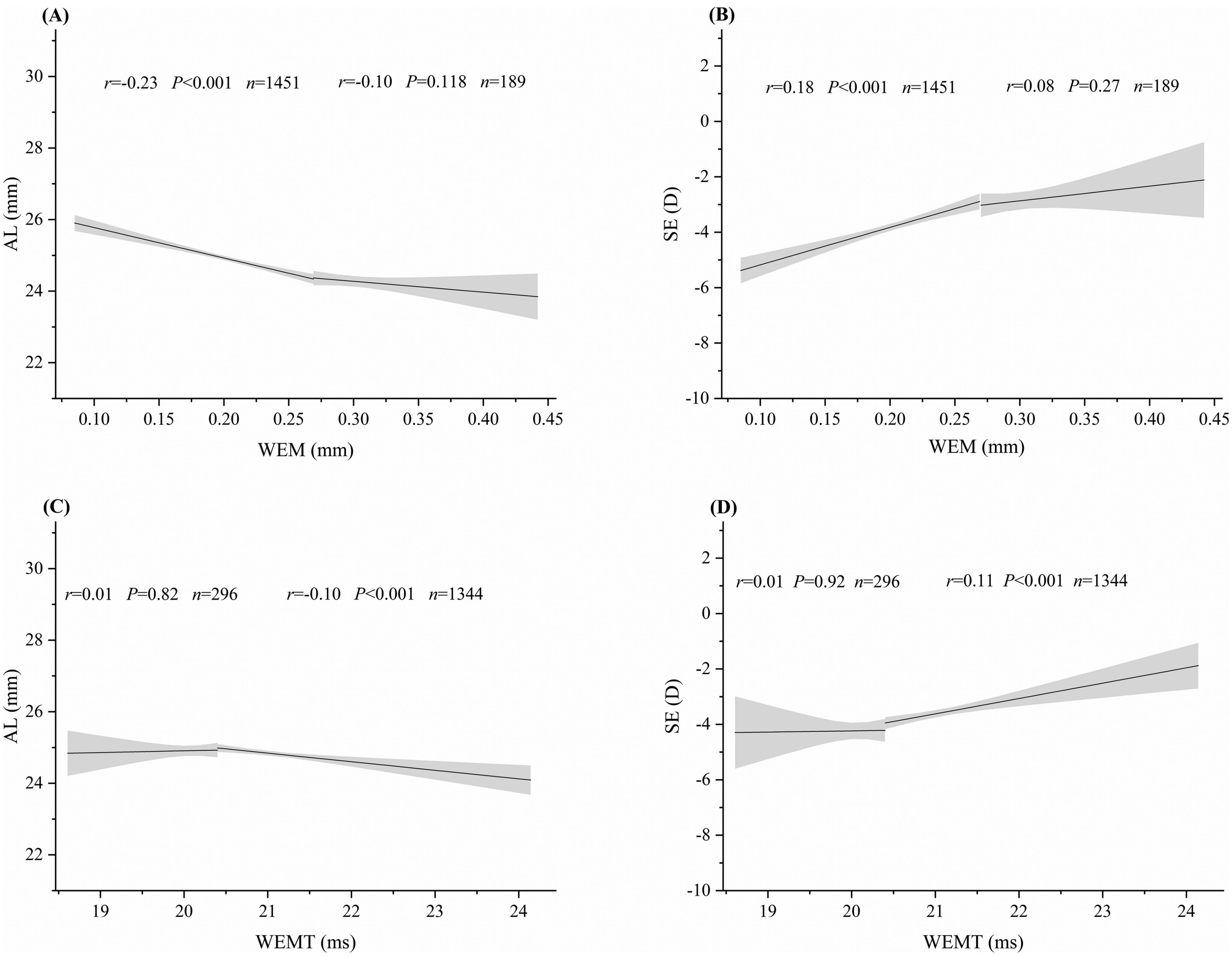

Figure 4. The piecewise linear regression association of WEM and WEMT with SE and AL. (**A**) WEM-AL; (**B**) WEM-SE; (**C**) WEMT-AL; (**D**) WEMT-SE.

models of myopia, eye movement indicators might be included to improve accuracy and help early screening and prevention of myopia onset and progression.

This study explored the relationship between eye movement and myopia based on a large sample of healthy people, but there are still some limitations. Firstly, the study design is cross-sectional, which cannot be used to infer the causal relationships. It is also likely that different refractive status might lead to changes in eye movements. Secondly, the population in this study only included adolescents aged 15–24 years, which limits the generalization of the conclusions to other age groups. Expanding the participant pool to encompass a more diverse age demographic could offer more valuable insights in future research endeavors. Finally, some other factors that may affect the observed association, such as genetic and visual accommodation factors, were not considered in our analysis. Future studies need to control these confounding factors as much as possible.

Conclusions

This study explored the correlation between eye movement and refractive status among Chinese university students. The findings showed that eye movement distance and duration were negatively correlated with longer ALs and more myopic refractive error, and there was a threshold effect. In addition, changes in eye movements are more closely related to AL than SE. These results inform base data for ophthalmologists and other populations and have implications for understanding the role of eye movements in relation to refractive errors and developing the clinical abnormal values for eye movement indicators.

Acknowledgments

The authors thank all participants and the schools involved in the survey, as well as other staff members on the scene.

Funded by the National Natural Science Foundation of China (Grant No. 82160204 and No. 82122059) and Nankai University Eye Institute (NKYKD202206).

Disclosure: **D.-L. Li**, None; **Y. Qin**, None; **Y.-J. Zheng**, None; **Z.-J. Yin**, None; **Y.-Z. Li**, None; **R. Ma**, None; **G. Liang**, None; **C.-W. Pan**, None

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