ORIGINAL RESEARCH

Association Between Peripheral Retinal Defocus and Myopia by Multispectral Refraction Topography in Chinese Children

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Objective: To investigate the association between the peripheral refractive errors of the fundus in different regions and moderate and high myopia.

Methods: In this case-control study, 320 children and adolescents aged 6 to 18 years were recruited. Peripheral refractive errors were measured using multispectral retinal refractive topography (MRT). Spherical equivalent (SE) and cylinder errors were classified into low, moderate, and high categories based on the magnitude range. Logistic regression was performed to test the factors associated with myopia.

Results: There were 152 participants with low myopia and 168 participants with moderate and high myopia included in the current study. Participants with moderate and high myopia were most likely to be older, with larger axial length (AL), lower SE, less time to watch electronic devices on the weekend, a higher difference between central refractive error and paracentral refractive error from the superior side of the retina (RDV-S), but a smaller difference between the central refractive error and paracentral refractive error from the inferior side of the retina (RDV-I) than those with low myopia (all P <0.05). After logistic analysis, female sex (odds ratio [OR] = 4.14; 95% confidence interval [CI] = 2.16–7.97, P <0.001), AL (OR = 6.88, 95% CI = 4.33–10.93, P <0.001), and RDV-I (OR = 0.52, 95% CI = 0.32–0.86, P = 0.010) were independent factors for moderate and high myopia.

Conclusion: Our study demonstrated that the retina peripheral refraction of the eyes (RDV-I) was associated with moderate and high myopia, and RDV-S was only associated with high myopia.

Keywords: peripheral refractive errors, myopia, spherical equivalent, logistic analysis, ocular biometrics

Introduction

Myopia is one of the most common refractive errors, and its incidence increases annually; thus, it has become an important public issue worldwide.[1] Globally, it is estimated that the number of people suffering from myopia is approximately 1.45 billion, with the highest prevalence rate in Asia.[2,3] The mechanism of myopia development is still unclear; however, current evidence indicates that peripheral retinal refractive status may be related to occurrence of myopia.[4–6] More outdoor activities may reduce the process of myopia due to modifying retinal refractive status.[7,8] The peripheral retina of emmetropia is associated with a mild relative myopic refractive state, while the peripheral retina of uncorrected hyperopia is closely related to a slightly higher relative myopic refractive status.[9]

After light enters the eye, the central image can be focused on the retina, but the peripheral focus is located before and after the retina. When the object is focused on the retina, it will promote the growth of the eye axis, leading to myopia. Multispectral refraction topography (MRT) uses single spectra to respond to light of a special wavelength to sequentially collect fundus images.[8] Using a deep development computer algorithm (ie, a series of neural network-based U-Nets), the multispectral images

after lens compensation were compared and analyzed, and the corresponding terrain map was drawn after calculating and summarizing the actual refractive values of each pixel. This method can be used to predict the occurrence and development of myopia in advance, and to scientifically evaluate the effectiveness of various forms of myopia prevention and control. To date, many previous studies have investigated the association between MRT measurements and myopia; however, those studies did not adjust variables such as body mass index, or lifestyle factors.[10–13] Therefore, this study aimed to investigate the association between peripheral retinal defocus measurements and myopia.

Methods
Study Design and Subjects
In this cross-sectional observational study, we collected information on 320 patients with myopia who were seen at Chifeng Chaoju Eye Hospital between January and June 2023. Ethical approval was obtained from the Ethics Committee of the Chifeng Chaoju Eye Hospital. Written informed consent was obtained from the child's parents or guardian.

Eye Examination and Questionnaire
Patients with spherical equivalent (SE) errors in both eyes of at least −0.5 diopters (D) seen in the ophthalmology outpatient department of Chifeng Chaoju Eye Hospital between June 1 and September 30, 2023 were eligible for the current study. The inclusion criteria were as follows: (1) between the ages of 6 and 18 years, and (2) best-corrected visual acuity (BCVA) of 20/20 in both eyes. The exclusion criteria were as follows: (1) any ocular diseases or previous ocular surgery history, (2) a history of corneal contact lenses or atropine eye drops, and (3) a history of any severe systemic disease. The study included only the right eye.

All children and adolescents underwent a questionnaire and comprehensive eye examination. Demographic information, family history, and lifestyle factors such as time to look at electronic devices and time spent outdoors were collected. The time was categorized as low (<2 hours), normal (2–4 hours) and high (>4 hours). Body weight and height were measured and BMI was calculated using the formula: BMI = body weight(kg)/height(2) (m(2)). Refractive examination was performed using an autorefractometer (AR-360A, NIDEK Co. Ltd., Japan) after full cycloplegia, using mixed eye drops containing 0.5% tropicamide and 0.5% phenylephrine (SINQI Pharmaceutical Co., Ltd., Shenyang, China) for mydriasis, every 10 minutes, followed by 3 drops and observation for 10 minutes. Photometry was performed in a semi-dark room environment. This examination was completed by an experienced optometrist. Refractive error value was presented as sphere (S) and cylinder (C) measurements. The final refractive error was recorded as the spherical equivalent (SE), and the SE value (D) was SE = S + C/2. The intraocular pressure (IOP) was measured using a non-contact tonometer NT-4000 (Nidek Co. Ltd., Gamagori, Japan). The axial length (AL) was measured by IOL Master Biometry (Master 2000, Zeiss Co., Germany). The mean of three measurements was collected as the final result. Retinal defocus measurements were tested using multispectral refraction topography (version 1.0.5T05C; Thondar, Inc.). The parameters were defined as follows: peripheral refractive errors (RPRE); peripheral refractive error from center to peripheral 53°of retina (TRDV) and four regions − RDV-Superior (RDV-S), RDV-Inferior (RDV-I), RDV-Temporal (RDV-T), and RDV-Nasal (RDV-N) − from the fovea to 53 degrees (RDV-15, RDV-30, RDV-45) (Figure 1).

Myopia Definition and Category
Participants were classified into two refractive groups according to central SE refractive error: low myopia was defined as an SE of 0 to −2.99 D, moderate myopia as an SE of −3D and −6, and high myopia as an SE of > −6D. In this study, we combined both moderate and high myopia into one group.

Statistical Analysis
All statistical analysis was performed using SPSS 26.0 (SPSS Inc., Chicago, IL, USA). Data were presented as mean ± standard deviation (SD) for continuous measures and analyzed by the independent sample t-test. On the other hand, categorical measurements were presented as percentages and compared using Pearson chi-square test. Logistic regression analysis was used to analyze the relationship between biomedical ocular information, demographic information, lifestyle indicators, and myopia. Statistical significance was interpreted as a P-value of less than 0.05.
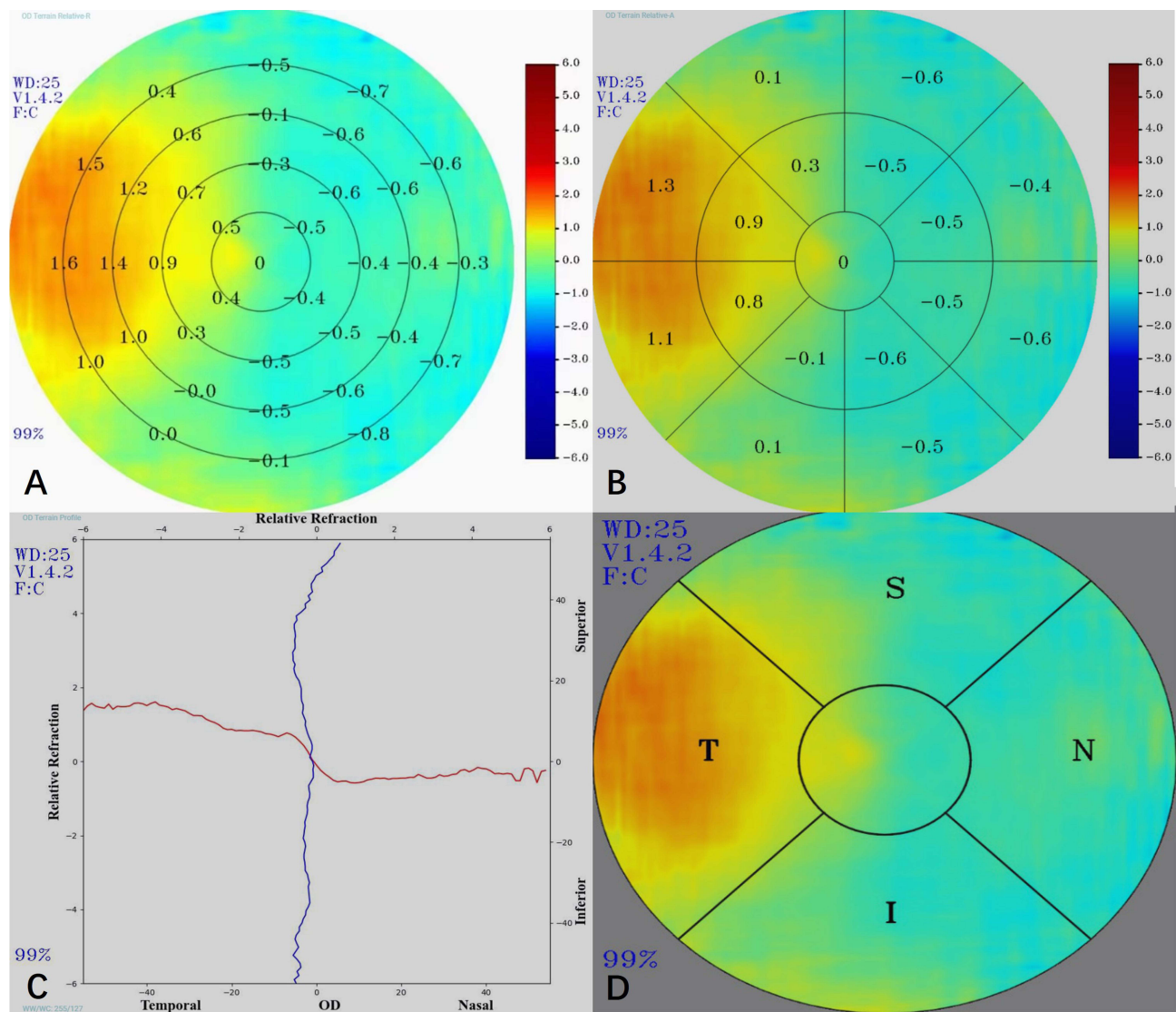
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Figure 1 Multispectral refractive topography. (**A**) Mean-R; (**B**) Relative-R; (**C**) Profile; (**D**) Quadrant.

Results

Currently, 320 children and adolescents (320 eyes) involving 161 boys and 159 girls aged 6 to 18 years were included. Of which, 152 had low myopia (mean SE: −1.75 ± 1.0 D), and 168 had moderate to high myopia (mean SE: −4.25 ± 1.94 D). Compared with low myopia, participants with moderate and high myopia were most likely to be older, with larger AL, lower SE, less time to watch electronic devices on the weekend, higher RDV-S but lower RDV-I than those with low myopia (all P <0.05; Table 1).

In the multivariate analysis using logistic regression, female sex (OR = 4.14; 95% CI = 2.16–7.97, P <0.001), AL (OR = 6.88, 95% CI = 4.33–10.93, P <0.001), and RDV-I (OR = 0.52, 95% CI = 0.32–0.86, P = 0.010) was significantly correlated with moderate and high myopia (Table 2).

In subgroup analysis, female sex (OR = 3.62, 95% CI = 1.86–7.04, P <0.001) and AL (OR = 5.35, 95% CI = 3.37–8.49, P <0.001) were associated with moderate myopia. Furthermore, female sex (OR = 4.64, 95% CI = 1.81–11.87, P <0.001), age (OR = 1.31, 95% CI = 1.05–1.61, P = 0.015), AL (OR = 18.29, 95% CI = 9.34–35.83, P <0.001), and RDV-S (OR = 2.71, 95% CI = 1.34–5.49, P = 0.006) were associated with high myopia (Table 3).

Table 1 Demographic and Ocular Characteristics of the Two Refractive Groups

	Low Myopia (n = 152)	Moderate and High Myopia (n = 168)	P
Demographic Characteristics			
Age (years)	10.00 (4)	12.00 (3)	**<0.001***
Sex (female, %)	70 (46.10%)	89 (53.00%)	0.216
BMI	18.10 (5.70)	19.10 (5.80)	0.052
Ocular Characteristics			
IOP (mmHg)	17.00 (4)	17.00 (5)	0.356
AL (mm)	24.23 (1.08)	25.30 (1.12)	**<0.001***
SE	−1.75 (1)	−4.25 (1.94)	**<0.001***
Parental myopia (yes, %)	75 (49.30%)	79 (47.00%)	0.679
Reading and writing at close range (yes, %)	127 (83.60%)	141 (83.90%)	0.927
Improper reading and writing posture (yes, %)	128 (84.20%)	135 (80.40%)	0.368
Time to watch electronic devices Monday to Friday			
<2	120 (78.90%)	137 (81.50%)	
2~4	22 (14.50%)	21 (12.50%)	0.568
>4	10 (6.60%)	10 (6.00%)	
Time to watch electronic devices on the weekend			
<2	59 (38.80%)	87 (51.80%)	
2~4	66 (43.40%)	59 (35.10%)	**0.023***
>4	27 (17.80%)	22 (13.10%)	
Time spent outdoors Monday to Friday			
<2	70 (46.10%)	95 (56.50%)	
2~4	77 (50.70%)	67 (39.90%)	0.079
>4	5 (3.30%)	6 (3.60%)	
Time spent outdoors on the weekend			
<2	78 (51.70%)	93 (55.40%)	
2~4	60 (39.70%)	61 (36.30%)	0.542
>4	13 (8.60%)	14 (8.30%)	
RPRE			
TRDV	−0.03 (0.52)	−0.02 (0.56)	0.484
RDV-15	−0.06 (0.09)	−0.07 (0.06)	0.525
RDV-30	−0.09 (0.23)	−0.07 (0.21)	0.793
RDV-45	−0.01 (0.41)	−0.03 (0.46)	0.338
RDV-S	−0.54 (0.93)	−0.36 (0.64)	**0.007***
RDV-I	0.13 (0.67)	−0.04 (0.70)	**0.007***
RDV-T	0.19 (0.80)	0.12 (0.70)	0.318
RDV-N	0.02 (0.86)	0.10 (0.86)	0.832

Notes: n, number of eyes. Data were expressed as n (%) or median (IQR). * means statistically significant.
Abbreviations: SD, standard deviation; BMI, body mass index; SE, spherical equivalent; IOP, intraocular pressure; AL, axial length; RPRE, peripheral refractive errors; TRDV, peripheral refractive error from center to peripheral 53°of retina; RDV-15, the difference between central refractive error and paracentral refractive error from center to 1*5° of retina; RDV-30, the difference between central refractive error and paracentral refractive error from 15° to 30° of retina; TRV-45, the difference between central refractive error and paracentral refractive error from 30° to 45° of retina; RDV-S, the difference between central refractive error and paracentral refractive error from superior side of retina; RDV-I, the difference between central refractive error and paracentral refractive error from inferior side of retina; RDV-T, the difference between central refractive error and paracentral refractive error from temporal side of retina; RDV-N, the difference between central refractive error and paracentral refractive error from nasal side of retina.

Discussion

With the development of socio-economic improvements, myopia among children and adolescents has gradually become the focus of public health measures. Early screening and mechanisms of investigation are important. MRT is new equipment using multispectral imaging technology. This instrument collects ocular fundus images, and parameters are calculated by a novel

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Table 2 Risk Factors Associated with Moderate to High Myopia

	β	SE β	Wald's χ^2	P	OR (95% CI)
Sex (male reference)	−1.422	0.333	18.192	**<0.001***	**4.14 (2.16–7.97)**
Age	0.076	0.066	1.328	0.249	1.08 (0.95–1.23)
BMI	−0.017	0.038	0.205	0.651	0.98 (0.91–1.06)
IOP	−0.095	0.050	3.616	0.057	0.91 (0.82–1.00)
AL	1.928	0.236	66.630	**<0.001***	**6.88 (4.33–10.93)**
RDV-I	−0.644	0.249	6.681	**0.010***	**0.52 (0.32–0.86)**

Notes: *$p<0.05$ is considered statistically significant; Bold text means statistically significant.
Abbreviations: RPRE, peripheral refractive errors; BMI, body mass index; SE, spherical equivalent; IOP, intraocular pressure; AL, axial length; RDV-I, the difference between central refractive error and paracentral refractive error from inferior side of retina; CI, confidence interval; OR, odds ratio.

Table 3 Risk Factors Associated with Moderate and High Myopia

	$β^a$	$β^b$	SE $β^a$	SE $β^b$	Wald's χ^{2a}	Wald's χ^{2b}	P^a	P^b	OR (95% CI)^a	OR (95% CI)^b
Sex (male reference)	1.287	0.263	0.339	0.480	14.421	10.237	**<0.001***	**0.001***	**3.62 (1.86–7.04)**	**4.64 (1.81–11.87)**
Age	0.035	0.060	0.069	0.108	0.258	5.964	0.612	**0.015**	1.03 (0.91–1.18)	**1.31 (1.05–1.61)**
BMI	−0.021	−0.043	0.039	0.058	0.289	1.055	0.591	0.304	0.97 (0.91–1.05)	1.06 (0.94–1.19)
IOP	−0.081	2.907	0.050	0.070	2.619	0.383	0.106	0.536	0.92 (0.83–1.01)	0.95 (0.83–1.09)
AL	1.679	0.998	0.235	0.343	50.890	71.872	**<0.001***	**<0.001***	**5.35 (3.37–8.49)**	**18.29 (9.34–35.83)**
RDV-S	0.091	1.535	0.229	0.360	0.156	7.703	0.693	**0.006***	1.09 (0.69–1.71)	**2.71 (1.34–5.49)**

Notes: [a]Moderate myopia (reference: low myopia). [b]High myopia (reference: low myopia). *$p<0.05$ is considered statistically significant; Bold text means statistically significant.
Abbreviations: RPRE, peripheral refractive errors; BMI, body mass index; SE, spherical equivalent; IOP, intraocular pressure; AL, axial length; RDV-S, the difference between central refractive error and paracentral refractive error from superior side of retina; CI, confidence interval; OR, odds ratio.

computer algorithm according to subtle differences in fundus images of different wavelengths. MRT can reveal the refractive status of some points of the retina within 53 degrees by successively collecting fundus images with different wavelengths of a single spectral light, which has been reported elsewhere.[14] However, the association between its parameters and moderate and high myopia has not been fully verified and affirmed in clinical practice.

In the current study, it is noteworthy that participants had higher RDV-S but lower RDV-I than those with low myopia. Furthermore, female sex, AL, and RDV-I were significantly correlated with moderate and high myopia. Generally, compared with low myopia, participants with a higher difference between central refractive error and paracentral refractive error from the inferior side of the retina had a 0.52 times higher risk for moderate and high myopia; while participants with a higher difference between central refractive error and paracentral refractive error from the superior side of the retina had a 2.71 times higher risk for high myopia. Recently, another relative sample size study indicated that children had a myopia defocus within 15° eccentricity.[10] Moreover, the retina defocus of the fovea area has less influence on the occurrence of myopia. Generally, hyperopia defocus at 30° and 45° eccentricity of fundus is observed among children with high myopia, while children with low and moderate myopia present hyperopia at 45° eccentricity. In view of the peripheral refractive errors, the hyperopic shift was larger in eyes with moderate myopia than in those with low myopia.[6]

Peripheral defocus refers to the myopia degree state of the peripheral retina; the optics of the eyeball and the curve of the retina both contribute to the peripheral refraction of the retina.[15] Defocus of the peripheral retina has benefits in controlling the growth in axial length, which may be associated with reducing changes in choroidal thickness.[16] A previous study indicated that the defocused signals around the retina occupy a dominant position in the process of growth in axial length.[17] Generally, both the central and peripheral retina provide visual signals to the retina, thereby directly influencing refractive development and ocular growth. It can be inferred that differences in the distribution and sensitivity of visual neurons from the central and peripheral retina may be important factors in the different responses of the retina to peripheral defocus in

different regions, with different impacts on growth of the eyeball. Herein, understanding the association between central and peripheral retinal defocus may have key implications for the control of myopia.

Furthermore, children with peripheral hyperopia defocus experience it two years before the development of myopia, which indicates that peripheral hyperopia defocus may appear in emmetropia.[18] Unfortunately, there is no emmetropia included in the current study; thus, we cannot investigate the association between peripheral hyperopia defocus and low myopia, or even its predictive significance for the occurrence of myopia.

In the four quadrants, we found that RDV-I in our study was associated with moderate and high myopia. Moreover, the higher was the degree of myopia, the larger was its significance. Another study evaluated the peripheral refractive errors in horizontal and vertical positions, and two diagonal meridians, and suggested that the hyperopic shift was larger toward the inferior visual field than toward the superior visual field in the moderate and high myopia groups.[19] In contrast, Gregor F. Schmid and co-researchers indicated that the steepening of the relative peripheral eye length varied significantly in the superior retina.[20] The exact mechanism of the role of peripheral refractive error in myopic occurrence remains unclear. On the one hand, peripheral hyperopic defocus is associated with axial elongation during myopia development. On the other hand, peripheral hyperopia may be a result of eye growth. Further studies are warranted to explore the specific mechanism between peripheral hyperopic defocus and myopia.

In our study, we found that myopes with more diopters used digital devices for fewer hours on the weekend. This may be due to them spending more time studying on weekends, so although they spend less time watching electronic devices, they have a higher degree of myopia. Another scenario is that because this study is cross-sectional, those with high myopia were asked to reduce their electronic devise usage time on weekends. These are all our speculations, and further investigation is needed to confirm them.

A strength of the current study is the association between MRT indicators and myopia adjusted with more variables. There are several limitations in our study too, however. First, the findings are limited by the small sample size and the case-control design. Herein, further prospective studies with a larger sample size are needed to confirm the present findings. Second, we only included participants with myopia and no subjects with emmetropia; therefore, our findings should be interpolated with some caution.

Conclusion

In summary, our findings suggest that the RDV in the inferior retina is associated with both moderate and high myopia, and RDV in the superior side of retina is only associated with high myopia. Consequently, the study concluded that peripheral hyperopic defocus components may be identified as a factor related to myopia.

Data Sharing Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval

The study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments and approved by the Ethics Committee of Chifeng Chaoju Eye Hospital. All participants were aware of the collection of their data for this study and informed consent was obtained from each participant.

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Disclosure

All authors declare that they have no competing interests in this work.

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