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Research Article

A Comparison of Retinal Oxygen Saturation with Retinal and Choroidal Thickness in Chinese Adults with a Wide Range of Myopia

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Abstract

Introduction

The study aimed to investigate the characteristics of retinal and choroidal thickness, and retinal oxygen saturation in people with a wide range of myopia.

Methods

A single-center, observational cross-sectional study was conducted, with 646 adults included. Subjects were divided into five groups according to their spherical equivalent refractive error: low myopia (LM: -3.00D<SE≤-0.50D), moderate myopia (MM: -6.00D<SE≤-3.00D), high myopia (HM: -9.00D<SE≤-6.00D), and ultra-high myopia (UHM: SE≤-9.00D). Axial length, spherical equivalent refractive error, retinal and choroidal thickness (ChT), and retinal oxygen saturation (arterial and venous) were measured. Retinal thickness was divided into nine regions: foveal or central, inner superior (SI), inner inferior (II), inner nasal (NI), inner temporal (TI), outer superior (SO), outer inferior (IO), outer nasal (NO), and outer temporal (TO).

Results

Of the 645 participants, 320 (49.6%) were males and 325 (50.4%) were females. The mean (SD) age and SE were 26.1 (7.7) years and -5.45 (2.74) D, respectively. Significant differences in choroidal thickness in all regions were observed across the range of myopia. Retinal arterial oxygen saturation showed significant positive correlations with spherical equivalent refractive error (rs=0.31, F=67.2, $p < 0.001$), but was only significantly correlated with inferior macular area thickness (F=4.58, p=0.03). There were no significant correlations between retinal venous oxygen saturation and choroidal or retinal thickness (all $p > 0.05$).

Conclusion

Retinal and choroidal thickness are not associated with retinal oxygen saturation, and we hypothesize that the differences in retinal oxygen saturation may be indirectly caused by changes in retinal and choroidal vascular lumen composition caused by axial length elongation.

Keywords: Retinal Oxygen Saturation; Retinal and Choroidal Thickness; Myopia

Key Summary Points

Why carry out this study?

- Current research indicates that certain changes in the fundus blood flow dynamics are due to differences in refractive error and axial length.
- We further investigated the changes in retinal oxygen saturation in patients with myopia and elucidated the possible factors related to axial length.

What was learned from the study?

- There is a significant correlation between both retinal and choroidal thickness and retinal oxygen saturation across a wide range of myopia.
- This may be due to changes in retinal and choroidal vascular lumen composition caused by axial length elongation and this needs further investigation.

Introduction

Since 2000 the global prevalence of myopia and high myopia have increased significantly. It is projected that by 2050 49.8% of the world population will be myopic and almost 10% of the world population will have high myopia [1]. Myopia can lead to persistent retinal thinning and a series of associated pathological complications, especially at the posterior pole of the eye [2-4].

Retinal oxygen saturation of the arteries and veins and their branches can be detected by retinal oximetry using a multi-wavelength structure function-coupled retinal imaging device [5]. A

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previous large sample study indicated that retinal arterial saturation was associated with younger age, higher myopia, and smaller average keratometry (K) values [5] .We hypothesize that changes in retinal oxygen saturation would alter the retinal and choroidal thickness [6,7].

An important, noncontact and noninvasive approach to measuring the retinal and choroidal structure is provided by optical coherence tomography (OCT) [8]. Reduced choroidal thickness (ChT) increases oxygen diffusion, reducing the amount of oxygen circulating in the retina [9]. A series of studies have shown that myopia progression is accompanied by changes in axial length increase and choroidal thinning [10-12]. The choroidal thickness decrease is mostly attributed to thinning in the stromal component of the choroid. In addition, choroidal blood flow is disturbed in myopia [13].

The purpose of this study was to investigate the characteristics of retinal and choroidal thickness and retinal oxygen saturation in Chinese adults by means of OCT and retinal oximetry.

Methods

Study design

This single-center, cross-sectional study was conducted between December 2023 and March 2024, according to the tenets of the Declaration of Helsinki and was approved by the Medical Ethics Committee of Ineye Hospital of Chengdu University of Traditional Chinese Medicine (2021yh-022) with the guidance of Chengdu University of Traditional Chinese Medicine (TCM). All participants understood the study protocol and gave their informed consent and all examinations were performed between 9 and 11 am.

Subjects

Based on the inclusion and exclusion criteria in Table 1, a total of 682 patients were recruited, but the image quality was poor for 38 subjects, so 645 subjects (645 eyes) were ultimately included. Based on spherical equivalent (SE), participants were assigned into five groups: Emmetropia 127 eyes(-0.50D < SE ≤+ 0.50D); low myopia 129 eyes(LM:-3.00D < SE ≤- 0.50D), moderate myopia 129 eyes(MM:-6.00D < SE ≤- 3.00D), high myopia 130 eyes(HM:-9.00D < SE ≤- 6.00D), and ultra-high myopia 130 eyes(UHM:SE ≤- 9.00 D).

Inclusion criteria	Exclusion criteria
At least 18 years old	Strabismus or amblyopia
Best corrected visual acuity (BCVA) logMAR better than 0.10 logMAR	Systemic and ophthalmic diseases which might affect ocular development (e.g., Rheumatoid arthritis, Diabetes)
Normal ocular health other than myopia and emmetropia	History of ocular inflammation or infection, corneal dystrophy
Willing to participate in the process	Incomplete clinical data or inability to obtain high-quality images
No use of treatments to control the development or progression of myopia	Application of drugs or treatments that may alter the choroidal thickness

Table 1: Inclusion and Exclusion Criteria.

Ophthalmic examinations

An ophthalmologist performed slit-lamp biomicroscopy before measurements were performed. Uncorrected and best-corrected visual acuity were measured using a logMAR chart. The best-corrected visual acuity was measured using a subjective refraction result and all were better than 0.10 logMAR (20/25). Intraocular pressure (IOP) (CT-800, TOPCON Co., Ltd, Tokyo, Japan) and axial length (AL) (Haag-Streit Diagnostics, LS 900; Haag-Streit AG, Koeniz, Switzerland) were measured and the refraction correction was determined after cycloplegia using 0.5% tropicamide eye drops (Mydrin-P; Santen, Osaka, Japan) and spherical equivalent calculated. Finally, indirect fundoscopy was used to rule out retinal pathology.

OCT imaging

Retinal and choroidal thickness were obtained using optical coherence tomography (OCT) (RTVueXR, Optovue, CA). Choroidal thickness was assessed using the Enhanced HD Line (EDI) pattern at the subfoveal region. The image is automatically inverted so that the chorioretinal interface is adjacent to the zero delay (Figure 1A). Masking the refractive status of the participants and using RTVueXR linear measurement tools, two independent experienced ophthalmologists measured choroidal thickness perpendicularly from the outer edge of the hyper-reflective retinal pigment epithelium to the inner sclera at the fovea, the measurements from the two observers were then averaged for analysis. Kendall's W was used to assess the concordance of the analysis of the choroidal thickness. The consistency coefficients were 0.928, which was acceptable.

The retinal map pattern (Figure 1B) automatically generated full retinal thickness measurements in nine subfields: foveal (1mm), inner macular areas (1mm ~ 3mm), and outer macular areas (3mm ~ 5mm). The inner and outer macular areas are further divided into 4 quadrants, which are the superior, inferior, nasal and temporal, so that a total of nine thicknesses were obtained: foveal, inner superior (SI), inner inferior (II), inner nasal (NI), inner temporal (TI), outer superior (SO), outer inferior (IO), outer nasal (NO), outer temporal (TO). The Littmann and modified Bennett formulae were used to correct image size [14].

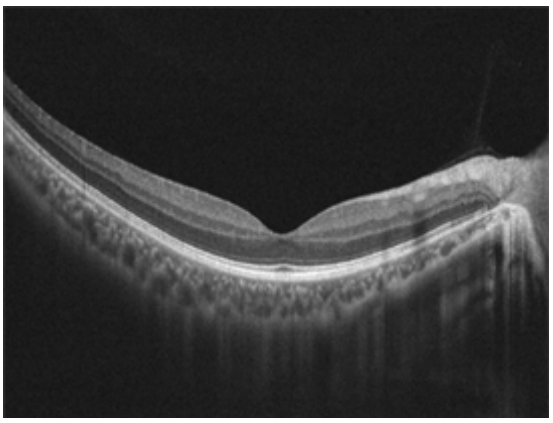

Figure 1A: Choroidal thickness presented by Enhanced HD Line (EDI) pattern.

Oxygen examination

Retinal oxygen saturation was obtained using a multi-wavelength structure function-coupled retinal imaging device (ROSV-M18, HealthSun, China). All images were analyzed using HealthSun retinal image quantification analysis (ROSV-HIQA-1, V1, China). The subjects sat in a dark room for at least five minutes of rest while the pupils dilated to larger than 6 mm. Analysis was made on the retinal vessels with a width ≥8 pixels and a length >50 pixels between two concentric circles with a radius of 1.5 to 3.0-disc diameters centered

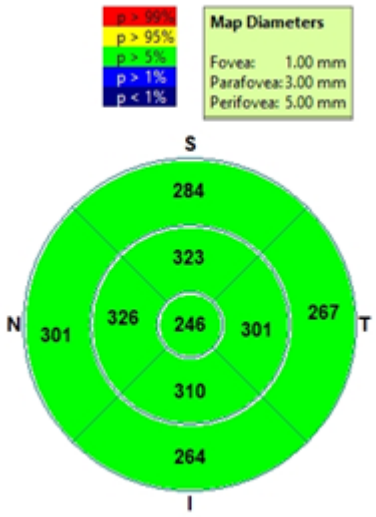

Figure 1B: Retinal map pattern automatically generated full retinal thickness.

on the disc (Figure 2). To correct and balance the effect of retinal oxygen saturation due to range difference, so that it is close to the real average retinal oxygen saturation, the retinal arterial oxygen saturation (SaO_2) and retinal venous saturation (SvO_2) were calculated using the fourfold weighted average equation [7,15,16] (Equation. 1), "S" represents oxygen saturation, and "D" represents vessel diameter.

$$S=\frac{S_1\times D_1^4+S_2\times D_2^4+S_3\times D_3^4+\ldots+S_n\times D_n^4}{D_1^4+D_2^4+D_3^4+\ldots+D_n^4} \quad \text{(Equation 1)}$$

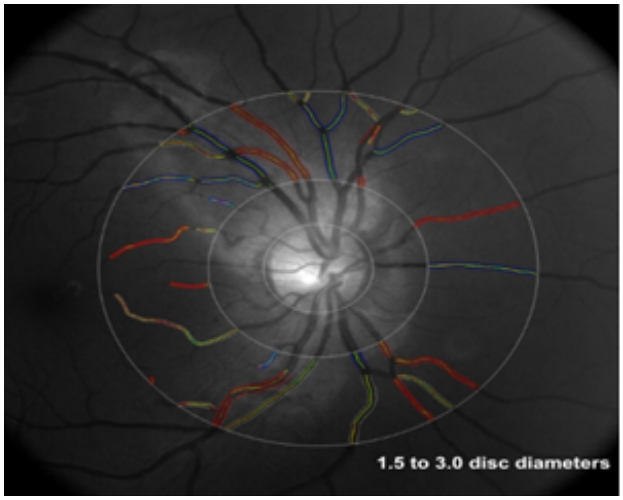

Figure 2: Analyze the retinal vessels between two concentric circles with a radius of 1.5 to 3.0-disc diameters centered on the disc.

Statistical analysis

Data analysis focused solely on the right eye of each participant and the left eye was included if the other eye was unclear. All data were recorded in a database and statistical analyses were conducted using IBM SPSS Statistics 27.0.1 (IBM Corp., Armonk, NY). Quantitative variables were described using means (standard deviations), and categorical variables were presented as absolute and relative frequencies. The Kolmogorov-Smirnov test was used to verify whether the data had a normal distribution. A one-way repeated measure analysis of variance (ANOVA) was conducted to assess if there were any SaO_2, SvO_2, retinal and choroidal thickness differences within varying SE. Simple Linear regression analysis was performed to investigate the correlations between independent parameters, e.g., choroidal thickness, and dependent parameters (SaO_2, and SvO_2). The level of significance was set at $p < 0.05$, for all comparisons.

Results

General characteristics at baseline

Of the 645 participants included in the analyses, 320 [49.6%] were males and 325 [50.4%] were females. The mean (SD) age was 25.99 ± 7.85 years, (range:18 to 54); spherical equivalent was -5.45 (2.74) D, (range:-15.00 to +0.50 D); IOP was 15.9 (2.7) mmHg, (range:10 to 21); K was 43.52 (1.44) D, (range: 39.31 to 47.63); AL was 25.82 (1.19) mm, (range: 22.46 to 29.08).

The analyses of retinal and choroidal thickness between the five groups

In the one-way ANOVA analysis, significant differences in choroidal thickness, inner macular areas and outer macular areas were observed across various refractive errors, except for the fovea (ChT: p<0.001; SI: p=0.003; II: p<0.001; NI: p<0.001; TI: p=0.04; SO: p<0.001; IO: p<0.001; NO: p<0.001; TO: p<0.001). Specifically, choroidal thickness, II, NI, and outer macular areas showed markedly higher differences in varying SE (All p<0.001). Detailed data are given in Table 2.

In the simple linear regression analysis retinal and choroidal thickness among all the regions showed positive correlations with spherical equivalent, except for the fovea (ChT: F=37.04, p<0.001; SI: F=20.87, p<0.001; II: F=27.33, p<0.001; NI: F=18.89, p<0.001; TI: F=8.51, p=0.004; SO: F=42.44, p<0.001; IO: F=82.36, p<0.001; NO: F=37.33, p<0.001; TO: F=47.01, p<0.001; fovea: F=0.90, p=0.34). Correlation analysis of retinal and choroidal thickness across various SE were shown in Figure 3.

Table 3 shows there was a significant difference in retinal oxygen saturation among the five refractive error groups ($F_{4,640}$=20.45, p<0.001; SvO_2: $F_{4,640}$=1.44, p=0.22). Furtehrmore, correlation analysis revealed that retinal oxygen saturation showed a significant positive correlation with myopia level (r_s=0.31, p=0.002) (Figure 4).

The Correlation of Retinal and Choroidal Thickness within Retinal Oxygen Saturation

Table 4 shows that retinal arterial oxygen saturation only positively related to outer inferior macular areas thickness (F=4.58, P=0.03), with other regions showing were no significant correlations with retinal arterial oxygen saturation. There were no significant correlations between retinal venous oxygen saturation and choroidal thickness, retinal thickness (all p>0.05).

Discussion

In this cross-sectional study, we investigated whether there was any association between retinal oxygen saturation and retinal and choroidal thickness in Chinese adults with a wide range of myopia. The results showed that the retinal arterial oxygen saturation had a significant positive correlation with myopia level. In addition,

Index	Emmetropia	LM	MM	HM	UHM	F4,640	p
ChT	307±78	299±52	290±50	273±46	270±44	7.68	<0.001**
Fovea	247±27	251±22	248±19	250±18	252±17	0.68	0.61
SI	318±17	322±26	319±14	316±15	312±15	4.04	0.003*
II	308±18	318±23	313±14	310±15	306±14	7.51	<0.001**
NI	314±16	325±24	320±16	317±17	314±16	5.12	<0.001**
TI	302±16	308±24	304±15	304±15	300±14	2.47	0.04*
SO	289±269	292±26	291±13	284±13	281±15	9.1	<0.001**
IO	277±13	280±20	275±14	268±12	264±15	17.98	<0.001**
NO	304±7	308±25	302±17	297±16	294±15	8.83	<0.001**
TO	278±12	279±27	274±13	270±13	265±15	9.98	<0.001**

Table 2: The differences of retinal and choroidal thickness across various refractive errors

LM = Low Myopia; MM = Moderate Myopia; HM = High Myopia; UHM = Ultra-High Myopia; ChT = Choroidal Thickness; SI = Inner Superior; II = Inner Inferior; NI =Inner Nasal; TI =Inner Temporal; OS = Outer Superior, IO = Outer Inferior, NO =Outer Nasal; TO = Outer Temporal; *p<0.05, **p<0.001.

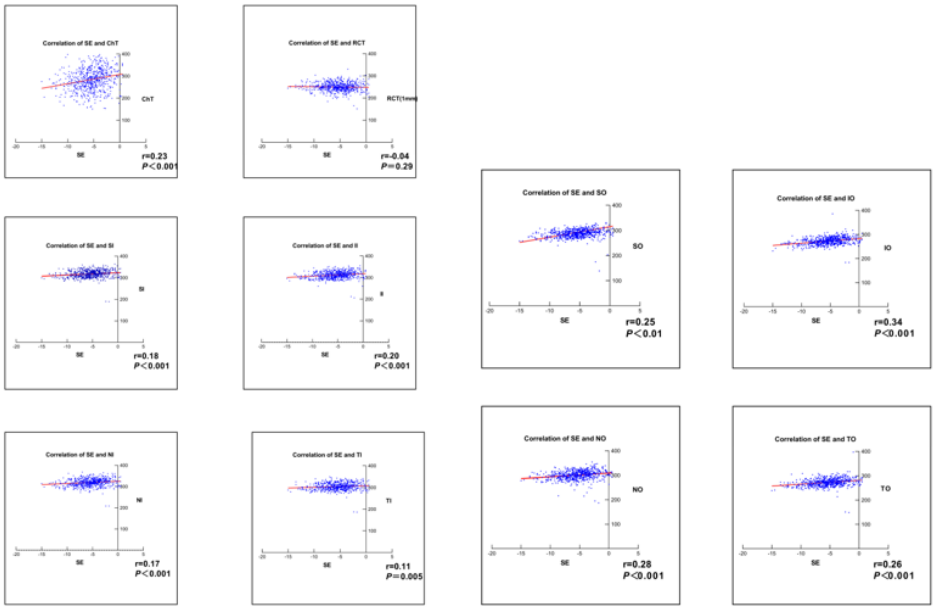

Figure 3: Correlation of retinal and choroidal thickness (ChT) across various spherical equivalent (SE).

Index	Emmetropia	LM	MM	HM	UHM	F4,640	p
SaO_2(%)	95.38±1.23	94.25±1.53	93.76±1.64	93.33±1.77	92.32±1.58	20.45	< 0.001**
SvO_2(%)	63.78±4.32	63.57±3.82	63.40±4.43	62.67±4.42	62.54±4.56	1.44	0.22

Table 3: Comparison of retinal oxygen saturation within spherical equivalent.

LM = Low Myopia; MM = Moderate Myopia; HM = High Myopia; UHM = Ultra-High Myopia; SaO_2 = Retinal Arterial Oxygen Saturation, SvO_2 = Retinal Venous Oxygen Saturation, *p<0.05, **p<0.001.

choroidal thickness and retinal thickness were thinner in the more myopic eyes, except for the fovea region. Retinal arterial oxygen saturation was significantly positive related to the thickness of outer inferior areas of the choroid. There were no correlations between retinal venous oxygen saturation and choroidal or retinal thickness.

It is noteworthy that significant correlations were found between retinal arterial oxygen saturation and the thickness of outer inferior areas. We hypothesise that the differences in retinal arterial oxygen saturation may be caused by changes in retinal and choroidal tissue caused by axial length elongation. Although the exact pathophysiological mechanism of retinal oxygen saturation changes in varying refractive error remains unknown, based on the extensive evidence in the literature, it may be associated with choroidal vascularity and choriocapillaris blood perfusion [13].

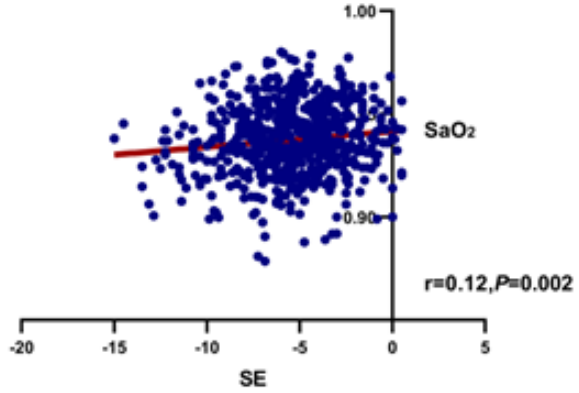

Figure 4: The variation trend of retinal arterial oxygen saturation within spherical equivalent (SE).

		ChT	Fovea	SI	II	NI	TI	SO	IO	NO	TO
SaO_2	rs	0.03	-0.01	0.06	0.05	0.05	0.05	0.06	0.08	0.04	0.06
	P	0.5	0.72	0.14	0.17	0.2	0.24	0.1	0.03*	0.28	0.15

Table 4: Correlation analysis of retinal oxygen saturation and each parameter.

ChT = Choroidal Thickness; SI = Inner Superior; II =Inner Inferior; NI = Inner Nasal; TI = Inner Temporal; SO = Outer Superior; IO = Outer Inferior; NO = Outer Nasal; TO = Outer Temporal; *p<0.05, **p<0.001.

The possible hypotheses for the differences in retinal oxygen saturation include retinal and choroidal degeneration and atrophy [6,7]. Cross-sectional studies have demonstrated choroidal thickness is thinner in myopia, compared with emmetropia and hyperopia [17,18].

All the fundus images were captured using ultra-widefield swept-source optical coherence tomography angiography (SS-OCTA) and uniformly divided into nine regions. Based on the above data, a recent study reported that choroidal thickness and outer retinal thickness were statistically diminished in high myopia [19].

Furthermore, the mechanical elongation of axial length leads to a reduction of choroidal thickness and retinal pigment epithelium thickness [20]. Our current measurements are consistent with these results. Differentially, our present study analyzed full retinal thickness, rather than the outer or inner retinal thickness.

Clinical studies using OCT-angiography (OCTA) have reported that choroidal vascular luminal area (LA) and stromal area (SA) are reduced in high myopia, whereas the area of choriocapillaris flow voids (FVs) are increased and indicating diminished perfusion areas [21,22]. Li [23] performed a cross-sectional study and reported a negative correlation between luminal area and axial length. There are also emerging studies on the reception and conversion of retinal optical signals, which affected by blood flow and further altered retinal oxygen saturation [24,25]. All these studies suggest that the retinal oxygen saturation differences in myopia may be caused by the retinal and choroidal vascular luminal component.

Interestingly, wide-field optical coherence tomography (OCT) suggested that the reason that choroidal thickness is decreased is mostly due to thinning in the stromal component of the choroid, such as the luminal (vascular) component [26]. These findings suggest that choroidal blood circulation may be associated with choroidal thickness, further confirming that there is correlation between retinal choroidal thickness and retinal oxygen saturation. Retinal oximetry can noninvasively measure retinal oxygen saturation, which provides oxygen consumption information in tissues and has a significant impact on retinal diseases as a new potential biomarker [27]. The reproducibility of retinal oximetry is excellent and to some extent, arterial measures are more reliable than venous [28].

A large number of investigations have shown that eyes with more myopia and longer axial length have lower retinal arterial oxygen saturation, consistent with the findings of the present study [5,6,29,30]. According to previous studies, the retinal arterial oxygen saturation decreases in high myopia accompanied by retinal vessel diameter narrowing [31]. Retinal oxygen saturation is affected by age, keratometry value, and refractive errors [5,32]. Narrower retinal vessel diameter is associated with elongated axial length and decreased blood flow [33,34]. Several reports have indicated that there is an interaction between the choroidal thickness thinning effect of myopia development and the normal physiological developmental thickening in childhood [35,36]. Indeed, there is an age-related change in choroidal thickness [37,38], as well as in retinal oxygen saturation [39,40].

The first limitation of the current study is the large age range of the participants and the influence of age on the choroid thickness and retinal oxygen saturation was examined. Second, retinal oxygen saturation can be affected by changes of retinal blood flow and retinal vessel diameter [33,34]. Due to the limitation of the equipment, the retinal and choroidal blood flow index measurements were not performed. Although the results suggest there was a significant correlation between retinal choroidal thickness and retinal oxygen saturation in some areas, the contribution of the retinal and choroidal structure to retinal oxygen saturation remains largely unexplored.

Conclusion

The present study investigated the characteristics of retinal and choroidal thickness, retinal oxygen saturation in people with emmetropia and a wide range of myopia. We found significant differences in choroidal thickness in the inner and outer macular areas across the range of myopia. Furthermore, the retinal oxygen saturation and retinal choroidal thickness are significantly correlated with refractive error. It is worth noting that significant correlations were observed between retinal arterial oxygen saturation and choroidal outer inferior thickness in several areas. It is still unclear what causes the variation in retinal oxygen saturation and retinal choroidal thickness and the underlying mechanisms remains to be determined.

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Author's Contribution

Xiaoqi Ma, Shanshan Ge, Yuanlin Zhou and Yuehua Zhou made substantial contributions to the conception, design of the work, the acquisition, analysis, and interpretation of data. Xiaoqi Ma drafted the work.

Yuehua Zhou revised it critically for important intellectual content; Xiaoqi Ma, Shanshan Ge, Yuanlin Zhou and Yuehua Zhou approved the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy of integrity of any part of the work are appropriately investigated and resolved.

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Medical Writing /Editorial Assistance

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Data Availability

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

Ethical Approval

All study protocols were approved by the Medical Ethics Committee of Ineye Hospital of Chengdu University of TCM (2021yh-022) and were performed in accordance with the Helsinki Declaration of 1964. This study was supported by the Beijing Ming Vision and Ophthalmology, Eye School of the Chengdu University of Traditional Medicine, and Ineye Hospital of the Chengdu University of Traditional Medicine. All participants understood the purpose and methods of the study and provided informed consent by written form.

Conflict of Interest

Xiaoqi Ma, Shanshan Ge, Yuanlin Zhou and Yuehua Zhou declare that they have no competing interests.

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