Retinal and Choroidal Changes in Children with Moderate-to-High Hyperopia

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Purpose. This study aimed to investigate the characteristics of retinal nerve fiber layer (RNFL) thickness, ganglion cell layer (GCL) thickness, and choroidal thickness in children with moderate-to-high hyperopia (MHH). Methods. This was a cross-sectional study that enrolled 53 children with MHH and 53 emmetropic children. Subjects with a spherical equivalent refraction (SER) of +4.0 D or higher were included in the MHH group, and subjects with SER between −1.0 D and +1.0 D were included in the emmetropic group. Ophthalmic examinations, including uncorrected visual acuity, cycloplegic refraction, slit-lamp examination, axial length, and swept-source optical coherence tomography (SS-OCT; DRI OCT Triton-1, Topcon, Tokyo, Japan), were performed. Results. The RNFL and GCL in the temporal and inferior quadrants in 1–3 mm of the macular fovea were thinner in the MHH group than in the emmetropic group (all \(P < 0.05\)). The MHH group also had a thicker choroidal thickness in all regions (all \(P < 0.05\)). SER was independently correlated with the average choroidal thickness in the optic disc and fovea (coefficient \(= 4.853, P < 0.001\) for the optic disc; coefficient \(= 5.523, P = 0.004\) for the fovea), while axial length was negatively correlated with choroidal thickness (coefficient \(= −12.649, P < 0.001\)). Axial length was positively associated with RNFL and GCL thickness in the temporal quadrant in 1–3 mm of the macular fovea (coefficient \(= 0.966, P = 0.007\) for RNFL and coefficient \(= 1.476, P = 0.011\) for the macular fovea). Conclusion. Compared with emmetropic children, MMH children had greater choroidal thickness. The characteristics of the RNFL and GCL thickness in MMH children were different from those in emmetropic children.

1. Introduction

The refractive status of healthy children gradually changes from hyperopia to emmetropia [1]. However, in approximately 3.2% of children [2], the spherical equivalent refraction (SER) is maintained at moderate-to-high hyperopia (MHH) (SER ≥ 4.00 D) [2] and the speed of emmetropization is very slow [3]. Because it is difficult to form a clear image in the retinal plane under hyperopic conditions, such children often have poor vision. Furthermore, as the eyeball is smaller and the iris and lens are thicker and located more anteriorly, the risk of the peripheral iris tissue blocking the anterior chamber angle is higher. This makes MHH an additional risk factor for angle-closure glaucoma (ACG) [4, 5]. Once it develops, ACG can cause irreversible vision loss. However, the development of glaucoma in children is insidious; it usually affects younger children and leads to few complaints. Moreover, visual field examination cannot be performed easily and the measurement of intraocular pressure is affected by corneal curvature, central corneal thickness, and corneal biomechanics [6], making the early diagnosis of glaucoma difficult.

In addition to intraocular pressure and visual field examination, thinning of the retinal nerve fiber layer (RNFL)
(including the pRNFL) and the ganglion cell layer (GCL) (including the macular ganglion cell layer) [7] is also known to provide important evidence suggestive of a diagnosis of glaucoma. However, the existing database of RNFL and GCL thickness in children is based on data from children with emmetropia or low and moderate diopter SER [8–10]. In our opinion, this database may not be suitable for the diagnosis of glaucoma in children with MHH. Tas et al. [11] and Dikkaya and Karaman Erdur [12] found no difference in inner macular GCL (mGCL) thickness between the two groups. There are only a few reports of RNFL and GCL thickness in MHH children, and all existing data are from European populations. To date, a growing number of researchers have suggested that the choroid in angle-closure glaucoma is thicker, and an increase in choroidal volume may cause a decrease in the anterior segment space [14–16]. However, there is still a lack of data on choroidal thickness in MHH children.

In our study, RNFL, GCL, and choroid thickness in MHH and emmetropic children were measured using SS-OCT, and the differences between the two groups were compared. This study aimed to explore characteristics of the changes in RNFL, GCL, and choroidal thickness in MHH children.

2. Patients and Methods

This hospital-based case-control study was approved by the ethics committee of Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine (approval number: No. 2020KY018), and conducted in accordance with the ethical standards stipulated in the Declaration of Helsinki in 1964. After obtaining informed consent from the subjects or legal guardians of these children, the children were examined and their personal data were strictly protected.

From October 2019 to January 2020, the subjects were selected from children who were outpatients at the Shanghai Eye Disease Prevention and Treatment Center. The inclusion criteria were as follows: (1) MHH group: SER ≥ 4.0 D in either eye; (2) emmetropic group: −1.0 D ≤ SER ≤ 1.0 D in either eye; (3) intraocular pressure in the range of 10–21 mmHg; and (4) age < 18 years. The exclusion criteria were as follows: (1) an earlier history of eye disease, such as strabismus, corneal disease, lens disease, glaucoma, maculopathy, and other eye diseases, that may cause retinopathy; (2) a history of ocular surgery; (3) presence of systemic diseases such as hypertension or diabetes; and (4) uncooperative during the examination or the OCT image obtained not being clear and unable to be used for analysis.

An experienced clinical ophthalmologist (Y. Q.) recorded the age, height, weight, and other basic information of the subjects and completed the following ophthalmic examinations: uncorrected visual acuity test, slit-lamp biomicroscopy (SL130, Zeiss, Germany) examination; axial length (AL) was measured using an IOL Master 700 (Carl Zeiss Meditec, Dublin, CA, USA). After pupil dilation, the diopter was measured using an automatic refractometer (KR-8900, Topcon, Tokyo, Japan). An experienced optometrist conducted subjective optometry of the subjects. The best-corrected visual acuity (BCVA) was assessed using the international standard logMAR visual chart.

SS-OCT (DRI OCT Triton-1, Topcon, Tokyo, Japan) was used to evaluate the retina and choroid of the subjects. The optic disc center and the macular fovea were taken as center points with a 6 mm diameter, and 12-line radial scan patterns with a resolution of 1,024 DPI were used to scan the optic disc and macula. The optic disc and macula were divided into three rings with diameters of 1 mm (center), 3 mm (inner), and 6 mm (outer) (Figures 1(a) and 1(b)). The inner and outer rings were divided into four quadrants: temporal, superior, nasal, and inferior. The thickness of each layer of the retina and choroid was analyzed using the built-in software of the SS-OCT device. In this study, RNFL (the interface between the nerve fiber layer and ganglion cell layer to the inner limiting membrane), GCL (the interface between the nerve fiber layer and ganglion cell layer to the interface between the inner plexiform layer and inner core layer), and choroid (Bruch membrane to the choroid-sclera interface) thicknesses were selected for analysis (Figures 1(c)–1(e)).

The sample size was calculated according to the mean and standard deviation of pRNFL thickness in high and low hyperopic children in Dikkaya’s and Karaman Erdur study [12], using a two-sample t-test, which allowed for unequal variance following the method in PASS 15.0.5 (NCSSs, LLC). The parameters were \( \mu_1 \) (113.2 \( \mu \)), \( \sigma_1 \) (13.1 \( \mu \)), \( \mu_2 \) (101.4 \( \mu \)), \( \sigma_2 \) (7.0 \( \mu \)), \( \alpha \) (0.05), and power (0.9). In this study, the ratio of the size of the MHH group to that of the emmetropic group was 1:1, and the basic sample size requirement of each group was 18 eyes.

Body mass index (BMI) was calculated as body weight (kg)/height\(^2\) (m\(^2\)). SER was calculated as spherical power +1/2 cylindrical power. For the MHH and control groups, the data from any eye that met the requirements of this study were included in the statistical analysis.

SPSS (version 23.0; SPSS for Windows, Chicago, IL, USA) was used for all statistical analyses. Continuous variables were presented as mean ± standard deviation, and categorical data were presented as rates (proportions). The data distribution was examined using the Kolmogorov–Smirnov test; Levene’s test was used to examine the variance of the data. If the data were normally distributed and had homogeneous variance, the data were analyzed using the two independent samples t-test; otherwise, the Mann–Whitney test was used. The chi-square test was used to analyze the categorical data. The independent factors related to RNFL, GCL, and choroidal thickness were determined using stepwise multiple linear regression analysis.
3. Results

There were 53 children (19 males, 34 females) with MHH who met the inclusion criteria. Another 53 children (27 male, 26 female) with emmetropia in the same period were also recruited to the emmetropic group. The sex and age of the two groups were matched. Compared with the emmetropic group, the MHH group had significant differences in axial length, SER, BMI, and BCVA (Table 1).

The thickness of the pRNFL was generally greater in the MHH group than in the emmetropic group (Table 2). However, except for the macular fovea, which was significantly thicker in the MHH group than in the emmetropic group, the MHH group had a significantly thinner RNFL than the emmetropic group in the temporal and inferior quadrants in the inner ring of the macula (Table 3). The thickness of the GCL in the optic disc area of the MHH group was generally greater than that of the emmetropic group (Table 2). However, the GCL in the temporal and inferior quadrants of the inner macula in the MHH group were thinner than those in the emmetropic group. The outer macula in the MHH group was thicker and the average thickness of the macula was greater than that in the emmetropic group (Table 3). All quadrants and the average thickness of the choroid in the macula and optic disc in the MHH group were significantly greater than those in the emmetropic group (Tables 2 and 3).

The significantly correlated factors in the single-factor analysis included sex, age, BMI, SER, and AL. These factors were used as dependent variables in the stepwise multiple linear regression analysis. The results showed that there was no correlation between the thickness of the GCL and RNFL.

Figure 1: Optical coherence tomography schematic diagram. (a) The Early Treatment Diabetic Retinopathy Study (ETDRS) grid: central circle (diameter = 1 mm), macular inner circle (diameter = 3 mm), and macular outer circle (diameter = 6 mm). (b) ETDRS grid: central circle (diameter = 1 mm), optic disc inner circle (diameter = 3 mm), and optic disc outer circle (diameter = 6 mm). (c) RNFL thickness (the interface between the nerve fiber layer and ganglion cell layer to the inner limiting membrane). (d) GCL thickness (the interface between the nerve fiber layer and ganglion cell layer to the interface between the inner plexiform layer and inner core layer). (e) Choroidal thickness (Bruch’s membrane to the choroid-sclera interface).
in the fovea and the selected independent variables. SER was an independent factor for pRNFL thickness and average choroidal thickness in the optic disc and fovea. Axial length was negatively correlated with mGCL and choroidal thickness in the macula. Age was positively associated with pRNFL and GCL in the optic disc (Table 4).

### 4. Discussion

This study indicated that the RNFL and the GCL in the inferior and temporal quadrants in the 1 mm to 3 mm diameter of the macular fovea in MHH children were thinner than those in emmetropic children, and the choroid in MHH children was generally thicker than that in emmetropic children. To the best of our knowledge, these results have not been reported in previous studies.

Regarding the characteristics of RNFL thickness, our research found that the pRNFL in the temporal quadrant was significantly thicker in the MHH group than in the emmetropic group. This is similar to the results reported by Tas et al. [11], Dikkaya and Karaman Erdur [12], and...
To date, it is not clear whether the thickness of the RNFL and GCL in MHH children is increased or decreased. This may be due to the influence of retinal development in children, which might lead to the thickening of the GCL and RNFL in these areas [17].

Due to the characteristic anatomy of the eyeballs of MHH children, the development of glaucoma is possible. In addition to evaluating the thickness of the pRNFL in glaucoma, the thickness of the mGCL can also reflect the damage to macular function in glaucoma [7]. Hood et al. [19] found that, in patients with early glaucoma, the change in the mGCL preceded that in the pRNFL. Hood et al. [20] and Schiefer et al. [21] also found that the mGCL in the inferior quadrant of glaucoma patients was thinner. Children with MHH show a thinner RNFL and GCL in the inner macula in childhood, and this anatomical structure may indicate that they are more likely to suffer from glaucoma in adulthood, which also explains why MHH is a risk factor for glaucoma [22].

The choroid is an important tissue in the eyeball and is rich in blood vessels. Some studies have found that a thicker choroid might affect the process of emmetropization in children with MHH [23]. Troilo et al. showed that choroidal thickening in primates is related to hyperopia [23]. They suggested that normal choroidal thickening is a method of...
controlling the growth of the eyeball and can appropriately slow the increase in AL during the rapid growth of the eyeball. Our study showed that the choroidal thickness in MHH children was greater, and the average choroidal thickness in the macula was higher with a higher SER, while the average thickness of the choroid in the macula decreased with increasing AL. Choroidal thickness was negatively correlated with AL, which is similar to the results of previous studies. In a cross-sectional study of the retina of 276 Chinese children aged 7–13 years, Jin et al. [24] found that choroidal thickness was related to axial length in Chinese children. They believed that, in the early stages of myopia, choroidal thinning occurred before retinal thinning. Kaderli et al. [25] found that the macular choroid thickened with an increase in hyperopia and a decrease in AL. At the same time, their study also found that the diameter and area of blood vessels in the macular choroid also increased. Oner et al. [26] found that the choroidal thickness in the fovea decreased with an increase in the AL, and hyperopia was related to the choroidal thickness in the fovea, while amblyopia had no independent significant effect on the choroidal thickness in the fovea. Therefore, our results add evidence to the hypothesis that choroidal thickening may play an important role in the stagnation of the emmetropization process in MHH children.

Through stepwise multiple linear regression analysis, SER, AL, and age were found to be significantly positively correlated with RNFL thickness. This may be because the nerve fiber bundles of the upper and lower arch between the optic disc and macula gradually approached the level of the temporal side, resulting in an increase in thickness [27]. There was a positive correlation between the thickness of the mGCL in the temporal and inferior quadrants, AL, and age. It is possible that the number of amacrine cells in the GCL increased with an increase in AL and age [28]. The mGCL thickness in the outer macula was negatively correlated with AL and age, which may be due to the high density of RGCs in the macula. With the increase in AL, the area of the macula increased, and the density of RGCs decreased accordingly. A greater change was found further away from the fovea [29].

One limitation of this study is its cross-sectional design. In future studies, these children will be followed up to observe changes in the RNFL and GCL in children with MHH, and the examination of intraocular pressure, visual field, and anterior segment OCT will be added. Another limitation is that the number of participants was relatively small because of limited access to MMH children. Future studies must include more children with MHH.

5. Conclusions

Compared with emmetropic children, children with MHH had greater choroidal thickness. The characteristics of RNFL and GCL thickness in MMH children were different from those in emmetropic children.

Data Availability

In our study, the children were examined, and their personal data were strictly protected, after obtaining informed consent of the subjects or legal guardians of these children. Therefore, all the original data are stored in Shanghai Eye Disease Prevention and Treatment Center. If necessary, we can e-mail all the original data to the editorial office.

Additional Points

In brief, we found that RNFL and GCL thicknesses in the temporal and inferior quadrants in the 1 mm to 3 mm diameter of the macular fovea were lesser, and all parts of the choroidal thickness were greater in children with moderate-to-high hyperopia than in emmetropic children.

Conflicts of Interest

The authors declare no conflicts of interest.

Authors’ Contributions

Yu Qian and Yingyan Ma contributed equally to the manuscript.

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