Alterations in Choroidal Volume and Determinants of Choroidal Volume and Visual Acuity in Entire Macula-involved Myopic Retinoschisis

Shiwei Li

Shanghai Jiaotong University Affiliated Sixth People's Hospital

Tingting Li

Shanghai Jiaotong University Affiliated Sixth People's Hospital

Bin Lu

Shanghai Jiaotong University Affiliated Sixth People's Hospital

Yan Chen

Shanghai Jiaotong University Affiliated Sixth People's Hospital

Xueyan Zhang

Shanghai Jiaotong University Affiliated Sixth People's Hospital

Jianyan Hu

Shanghai Jiaotong University Affiliated Sixth People's Hospital

Qiang Wu (✉ qiang.wu@shsmu.edu.cn)

Shanghai Jiaotong University Affiliated Sixth People's Hospital

Research Article

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Abstract

Background

To evaluate alterations in the choroidal volume (CV) of eyes with entire macula-involved myopic retinoschisis (MRS) and to investigate predictive factors for CV and visual acuity.

Methods

This cross-sectional observational study recruited 32 MRS eyes, 52 non-MRS highly myopic eyes, and 55 emmetropic eyes. Retinal and choroidal morphological findings were obtained using SD-OCT. The CV of the three groups was compared, and factors associated with CV and BCVA were analyzed.

Results

The macular CV was significantly lower in MRS eyes than in emmetropic eyes ($P < 0.0001$) and in non-MRS highly myopic eyes ($P < 0.05$). The difference in CV for MRS eyes among the superior ($0.34 \pm 0.16 \text{ mm}^3$), inferior ($0.33 \pm 0.17 \text{ mm}^3$), nasal ($0.27 \pm 0.12 \text{ mm}^3$) and temporal ($0.34 \pm 0.21 \text{ mm}^3$) quadrants was not significant ($P = 0.3755$). Multivariate regression analysis showed that the total macular CV in MRS eyes was negatively correlated with axial length ($P = 0.0459$), decreasing by 0.19 mm^3 for each millimeter of axial length. Refractive error and defects in the ellipsoid zone (EZ) were associated with BCVA in logMAR units ($P = 0.0075$ and 0.0002 , respectively); BCVA decreased by 0.027 logMAR units for each diopter of myopia. The total macular retinal volume (RV) in MRS eyes with EZ defects was higher than that in eyes with intact or partially continuous EZs ($P = 0.0460$).

Conclusion

In MRS eyes, the choroid is thinner, the total macular CV decreases as the axial length increases, and the severity of myopia and the integrity of the EZ, associated with the schisis extent are predictors of visual acuity, and the decrease of the macular CV is not the influencing factor of the visual function.

Background

The prevalence of high myopia is estimated to be as high as 4% worldwide and continues to increase [1–5]. The macular complications of high myopia are major causes of visual impairment [6–8]. Myopic retinoschisis (MRS) is a common pathological comorbidity of myopic traction maculopathy, and severe and progressive MRS can threaten visual function [9]. MRS is found in 6.5–31.3% of patients with high myopia according to different hospital-based and population-based studies [10, 11]. Cross-sectional and retrospective studies have revealed that the opposing mechanical forces of eyeball expansion, uneven

outward protrusions in posterior staphyloma and vitreoretinal attachments may promote the occurrence of MRS [12–15]. The cleavage of intraretinal tissue in the macula resulting from mechanical traction, retinal microstructural alterations such as disruption of the ellipsoid zone (EZ) and the presence of myopia-related macular degeneration in the retina can lead to varied degrees of visual loss in MRS, and MRS eyes with outer retinoschisis involving the entire macula have a much poorer visual prognosis [10, 12, 16]. It is generally considered that excessive stretching of the eyeball can damage the choroidal capillaries and further cause choroid thinning, which may lead to insufficient nutrition to the outer retina in high myopia [17, 18]. Studies have reported that the choroid is thinner in highly myopic eyes than in normal emmetropic eyes and may be a predictor of poor visual acuity [19–21], particularly in highly myopic eyes that have not yet progressed to the stage of pathological myopia [22]. However, the measurements of choroidal thickness at fixed points may not be useful for fully assessing the overall changes in the choroid due to unevenness of the choroidal thickness caused by the irregularity of the choroidal-scleral surface and the presence of posterior staphyloma [23, 24]. Researchers have used the enhanced depth imaging (EDI) mode on spectral domain optical coherence tomography (SD-OCT) to measure choroidal volume (CV) to compensate for the shortcomings of these choroidal thickness measurements and have found that the CVs in eyes with myopic traction maculopathy are lower than those in highly myopic eyes without choroidoretinal lesions [25]. However, these studies did not determine the variations in CV and the factors influencing CV in MRS eyes exclusively, especially in eyes with MRS involving the entire macula, which may represent a much severe status, or analyze the roles played by variations in CV and retinal morphological changes derived from mechanical traction on visual vision in these eyes.

Our study aimed to describe variations in CV in eyes with entire macula-involved MRS and to explore the predictive factors of CV and the associations of ocular characteristics with visual acuity.

Methods

Patients

This cross-sectional study recruited patients from the Department of Ophthalmology of the Sixth People's Hospital Affiliated with Shanghai Jiao Tong University from October 2019 to November 2020. We divided the patients into three groups: 1) patients with MRS involving the entire macular area (stage S4 as described by Shimada et al [14]) on SD-OCT; 2) highly myopic patients without MRS; and 3) normal emmetropic patients. Inclusion criteria for highly myopic eyes were an axial length ≥ 26 mm and a refractive error ≥ -6.00 diopter (D), and those for normal emmetropic patients were a refractive error from -0.5 D to $+0.5$ D and an axial length from 23.5 mm to 24.5 mm. The exclusion criteria were 1) high myopia in which peripapillary diffuse choroidal atrophy was observed within a circular area 6 mm in diameter centered on the fovea; 2) retinal diseases such as full-thickness macular holes or choroidal neovascularization; 3) a history of vitreoretinal surgery, glaucoma or ocular trauma; 4) any systemic disease that could affect choroidal perfusion such as uncontrolled hypertension [25] or diabetes; and 5) significant media opacity decreasing the quality of OCT imaging. The study complied with the tenets of

the Helsinki Declaration and was approved by the Ethics Committee of Sixth People's Hospital Affiliated with Shanghai Jiao Tong University. The study was also registered in the Chinese clinical trial registry (<http://www.chictr.org.cn/>, registration number: ChiCTR2000038824). Written informed consent for participation was obtained from all patients.

Clinical Examinations

All patients were measured for refractive error and best corrected visual acuity (BCVA) in Snellen units by refractometer, noncontact intraocular pressure, and axial length by an IOL-Master (Carl Zeiss Meditec AC, Jena, Germany) and imaged for the presence of posterior staphyloma by B-scan ultrasonography, and posterior polar lesions by color fundus photography (Optos 200Tx scanning laser ophthalmoscope; Optos PLC, Dunfermline, United Kingdom). The Snellen units for BCVA were converted to logarithm of the minimal angle of resolution (logMAR) units for statistical analysis. The refractive error was calculated as the sum of the spherical power and half of the cylinder power. Myopic maculopathy was defined as the lack of myopic retinal degenerative lesions, a tessellated fundus, diffuse chorioretinal atrophy, patchy chorioretinal atrophy or macular atrophy according to the International Meta-Analysis for Pathologic Myopia (META-PM) classification system based on fundus photographs^[26]. Diffuse chorioretinal atrophy was further classified into peripapillary diffuse choroidal atrophy and macular diffuse choroidal atrophy^[22]. All patients underwent SD-OCT examination (Heidelberg Engineering, Heidelberg, Germany), consisting of horizontal and vertical A-scans with a length about 9.1 mm and a B-scan containing 31 scanning lines (covering a 30°*25°/ about 9.1 mm*7.6 mm area) at an interval of 240 µm through the center of the fovea in the horizontal direction. Before acquiring the image, we input the data of corneal curvature and axial length of highly myopic eyes in built-in software of SD-OCT in order to correct the error caused by the magnification effect. The Early Treatment Diabetic Retinopathy Study (ETDRS) grids were automatically generated by built-in Spectralis mapping software. In summary, the macula was divided into a central ring with a diameter of 1 mm centered on the fovea, an inner ring with a diameter between 1 mm and 3 mm, and an outer ring with a diameter between 3 mm and 6 mm; the three rings were then sectioned into superior, inferior, nasal and temporal quadrants, and the retinal volumes (RVs) in the entire macula and the 9 subfields were obtained, as the upper segmentation line lied in the internal limiting membrane, and the lower segmentation line was in line with the lower border of the retinal pigment epithelium (RPE)-Bruch's membrane complex. Examiners made manual adjustments when the segmentation lines did not correspond to the respective retinal tissue. Subsequently, the scanning mode was adjusted to EDI mode, and the same B-scan scanning method as above was applied. The segmentation line of the automatically marked internal limiting membrane was moved down to the layer of the RPE-Bruch's membrane complex, and the segmentation line of the automatically marked RPE-Bruch's membrane complex was moved down to the layer of the choroidoscleral boundary. Then, the software calculated the CVs in the nine subfields and the entire macula (Fig. 1). The CV was measured by two independent retina ophthalmologists. The MRS subgroup (outer schisis and inner schisis [occurring in the inner plexiform layer]), the integrity (intact, partially continuous, or defective) of the EZ, partial

posterior vitreous detachment (PVD) and epimacular membrane were assessed based on SD-OCT. OCT examinations for all patients were performed from 10 am to 3 pm to reduce the influence of diurnal fluctuations [27].

Statistical Analysis

Statistical analysis was performed using SAS software version 9.13 (SAS Institute Inc., Chicago, IL). Categorical variables were depicted as numbers, and continuous variables were depicted as the mean $\pm$ standard deviation (SD). One-way analysis of variance and the Kruskal-Wallis test was used for comparing continuous variables among the three groups, and the independent t-test was used for comparing continuous variables between the two groups. If the data did not conform to a normal distribution, the Kruskal-Wallis test and the Wilcoxon rank-sum test were performed. The chi-square test was used to compare the differences in categorical variables. Correlations between the different related factors were analyzed by applying Spearman correlation analysis. Multivariate regression analysis was used to determine the factors influencing CV and BCVA. The intraclass correlation coefficient was adopted to test the interobserver agreement and reliability. $p < 0.05$ was considered statistically significant.

Results

Clinical Characteristics

A total of 139 eyes from 139 patients were studied, including 32 MRS eyes, 52 non-MRS highly myopic eyes, and 55 normal emmetropic eyes. There were no significant differences among the three groups in terms of age, sex, or IOP ($P = 0.2621, 0.8376$, and 0.4286 , respectively), and there were no significant differences in refractive error, axial length, or the presence of posterior staphyloma between the MRS group and the non-MRS group ($P = 0.6850, 0.6058$, and 0.3931 , respectively). The type of myopic maculopathy was distributed differently between the MRS group and the non-MRS group ($P = 0.0183$). MRS eyes had higher proportions of partial PVD and epimacular membrane than non-MRS highly myopic eyes ($P = 0.0361$ and 0.0389 , respectively). The BCVA in MRS eyes was worse than that in non-MRS eyes ($P < 0.0001$) (Table 1). In MRS group, 12 eyes had outer retinoschisis only, and 20 eyes had both outer and inner retinoschisis, the EZ was defective in 7 eyes and intact or partially continuous in 25 eyes.

Table 1
Clinical Characteristics of the MRS, non-MRS High Myopia and Emmetropia Groups

	MRS (n = 32)	High Myopia without MRS (n = 52)	Emmetropia (n = 55)	<i>P</i>	<i>P</i> ₁	<i>P</i> ₂	<i>P</i> ₃
Age (years)	65.1 ± 9.58	64.7 ± 9.78	67.7 ± 7.81	0.2621	0.9323	0.1864	0.1095
Sex (n) F:M	8/24	16/36	15/40	0.8376	0.5698	0.8167	0.6903
Refractive error (D ± SD)	-12.7 ± 5.33	-12.0 ± 3.72	0.30 ± 0.77	< 0.0001	0.6850	< 0.0001	< 0.0001
Axial length(mm)	29.4 ± 1.53	29.0 ± 1.41	23.9 ± 0.48	< 0.0001	0.6058	< 0.0001	< 0.0001
Posterior staphyloma(n) (present/absent)	26/6	38/14	0	-	0.3931	-	-
Type of myopic maculopathy				-	0.0183	-	-
no myopic retinal degenerative lesion	0	0	-				
tessellated fundus	1	4	-				
PDCA	11	27	-				
MDCA	16	20	-				
patchy chorioretinal atrophy	4	1	-				
macular atrophy	0	0	-				
Partial PVD (present/absent)	7/25	6/46	0	-	0.0361	-	-
epimacular membrane (present/absent)	15/17	13/39	0	-	0.0389	-	-
IOP (mmHg)	14.7 ± 2.15	14.5 ± 1.92	14.4 ± 2.22	0.4286	0.3940	0.4333	0.3051

D diopter; *SD* standard deviation; *PDCA* peripapillary diffuse choroidal atrophy; *MDCA* macular diffuse choroidal atrophy; *IOP* intraocular pressure; *LogMAR* logarithm of the minimal angle of resolution

	MRS (n = 32)	High Myopia without MRS (n = 52)	Emmetropia (n = 55)	<i>P</i>	<i>P</i> ₁	<i>P</i> ₂	<i>P</i> ₃
BCVA (logMAR)	0.50 ± 0.25	0.26 ± 0.18	0.08 ± 0.10	< 0.0001	< 0.0001	< 0.0001	< 0.0001
<i>D</i> diopter; <i>SD</i> standard deviation; <i>PDCA</i> peripapillary diffuse choroidal atrophy; <i>MDCA</i> macular diffuse choroidal atrophy; <i>IOP</i> intraocular pressure; <i>LogMAR</i> logarithm of the minimal angle of resolution							

Choroidal Volume Of The Three Groups

The intraclass correlation coefficients for the CV at all locations in the three groups ranged from 0.89 to 0.93. The CVs of the nine subfields and the entire macula in highly myopic eyes with and without MRS were significantly lower than those in emmetropic eyes (all $P < 0.0001$). MRS eyes had significantly lower CVs than non-MRS highly myopic eyes in the ETDRS subfields and the entire macula (all $P < 0.05$) (Table 2) (Fig. 2). Among MRS eyes, there was no significant difference in the CV among the superior ($0.34 \pm 0.16 \text{ mm}^3$), inferior ($0.33 \pm 0.17 \text{ mm}^3$), nasal ($0.27 \pm 0.12 \text{ mm}^3$) and temporal ($0.34 \pm 0.21 \text{ mm}^3$) quadrants ($P = 0.3755$).

Table 2
Comparison of the Choroidal Volume (mm³) of 9 Grids Among MRS, Non-MRS high myopia and Emmetropia groups

	MRS (n = 32)	non-MRS high myopia (n = 52)	Emmetropia (n = 55)	<i>P</i>	<i>P</i> ₁	<i>P</i> ₂	<i>P</i> ₃
Total (mm ³)	1.36 ± 0.62	1.66 ± 0.57	5.37 ± 1.45	< 0.0001	0.0083	< 0.0001	< 0.0001
subfoveal (mm ³)	0.03 ± 0.02	0.05 ± 0.20	0.16 ± 0.05	< 0.0001	0.0491	< 0.0001	< 0.0001
Inner superior (mm ³)	0.08 ± 0.03	0.10 ± 0.04	0.33 ± 0.10	< 0.0001	0.0117	< 0.0001	< 0.0001
Outer superior (mm ³)	0.27 ± 0.13	0.35 ± 0.13	1.10 ± 0.26	< 0.0001	0.0039	< 0.0001	< 0.0001
Inner inferior (mm ³)	0.07 ± 0.03	0.09 ± 0.03	0.30 ± 0.09	< 0.0001	0.0179	< 0.0001	< 0.0001
Outer inferior (mm ³)	0.26 ± 0.14	0.34 ± 0.14	0.98 ± 0.32	< 0.0001	0.0080	< 0.0001	< 0.0001
Inner nasal (mm ³)	0.06 ± 0.03	0.08 ± 0.04	0.33 ± 0.19	< 0.0001	0.0149	< 0.0001	< 0.0001
Outer nasal (mm ³)	0.21 ± 0.09	0.25 ± 0.08	0.83 ± 0.34	< 0.0001	0.0421	< 0.000	< 0.0001
Inner temporal (mm ³)	0.07 ± 0.04	0.09 ± 0.04	0.32 ± 0.09	< 0.0001	0.0274	< 0.0001	< 0.0001
Outer temporal (mm ³)	0.27 ± 0.17	0.33 ± 0.16	1.05 ± 0.28	< 0.0001	0.0170	< 0.0001	< 0.0001

Factors Associated with the Total Choroidal Volume in the MRS Group

In MRS eyes, Spearman correlation analysis showed that axial length had a significant negative correlation with the total CV (correlation coefficient = -0.54088, *P* = 0.0096), while age, refractive error, and total RV (12.50 ± 2.75 mm³) were not (*P* = 0.7290, 0.1476, and 0.0704, respectively). On multivariate regression analysis, axial length was the only factor associated with the total CV (*P* = 0.0459); the total CV decreased by 0.19 mm³ per millimeter of axial length. By contrast, age, sex, IOP, refractive error, the presence of posterior staphyloma, partial PVD, epimacular membrane, type of myopic maculopathy, the presence of EZ defects, retinoschisis subgroup and the total RV were not found to have a significant correlation with the total CV (*P* = 0.5900, 0.5676, 0.6790, 0.4990, 0.7724, 0.1781, 0.3087, 0.1890, 0.8576, 0.1917 and 0.2688, respectively) (Table 3).

Table 3

Multivariate Regression Analysis of Factors Affecting Total Choroidal Volume (mm³) of MRS

	Parameter estimate	<i>P</i>
Intercept	7.92227	0.0060
Age(years)	0.00653	0.5900
Sex	0.13176	0.5676
IOP (mmHg)	-0.02413	0.6790
Refractive error (D ± SD)	-0.01702	0.4990
Axial length (mm)	-0.18843	0.0459
Posterior staphyloma	-0.07950	0.7724
Partial PVD	-0.42914	0.1781
Epimacular membrane	-0.27290	0.3087
Type of myopic maculopathy	-0.31988	0.1890
Defect of EZ	0.05324	0.8576
Retinoschisis Subgroup	-0.37419	0.1917
RV(Total,mm ³)	-0.05353	0.2688
<i>IOP</i> intraocular pressure; <i>D</i> diopter; <i>SD</i> standard deviation; <i>PVD</i> posterior vitreous detachment; <i>EZ</i> ellipsoid zone; <i>RV</i> retinal volume		

Factors Associated with BCVA and the Integrity of the Ellipsoid Zone in the MRS Group

In MRS eyes, refractive error was inversely correlated with BCVA (correlation coefficient = -0.44525, $P=0.0107$) by Spearman correlation analysis, while age, axial length, subfoveal RV and subfoveal CV showed no significant association with BCVA ($P=0.8047$, 0.2782, 0.1168, and 0.7454, respectively). In the subsequent multivariate regression analysis, refractive error and the presence of defects in EZ were correlated with BCVA ($P=0.0075$ and 0.0002, respectively) and the BCVA decreased by 0.027 logMAR units for each diopter of myopia, while age, sex, axial length, the presence of posterior staphyloma, partial PVD, epimacular membrane, the type of myopic maculopathy, retinoschisis subgroup, the subfoveal RV and the subfoveal CV had no significant association with BCVA ($P=0.5302$, 0.5705, 0.5227, 0.6917, 0.7890, 0.3190, 0.2023, 0.4140, 0.2240 and 0.8644, respectively) (Table 4). MRS eyes with EZ defects had a significantly greater total RV than MRS eyes with an intact or partially continuous EZ ($P=0.0460$). There were no significant differences in age, refractive error, axial length, the presence of posterior staphyloma, partial PVD, epimacular membrane, retinoschisis subgroup, subfoveal RV, total CV, or subfoveal CV between MRS eyes with intact or partially continuous EZs and MRS eyes with defective EZs

($P = 0.0901, 0.3494, 0.6322, 0.7321, 0.5687, 0.1317, 0.1512, 0.0641, 0.2271$, and 0.4482 , respectively) (Table 5).

Table 4
Multivariate Regression Analysis of Factors Affecting BCVA of MRS

	Parameter estimate	<i>P</i>
Intercept	1.20143	0.1756
Age(years)	0.00247	0.5302
Sex	-0.05165	0.5705
Refractive error ($D \pm SD$)	-0.02668	0.0075
Axial length (mm)	-0.01969	0.5227
Posterior staphyloma	-0.03545	0.6917
Partial PVD	-0.02582	0.7890
Epimacular membrane	0.08892	0.3190
Type of myopic maculopathy	-0.10234	0.2023
Defect of EZ	-0.39674	0.0002
Retinoblastoma subgroup	-0.07383	0.4140
RV(Sufoveal,mm ³)	-0.53715	0.2240
CV(Sufoveal,mm ³)	-0.37070	0.8644
<i>D</i> diopter; <i>SD</i> standard deviation; <i>PVD</i> posterior vitreous detachment; <i>EZ</i> ellipsoid zone; <i>RV</i> retinal volume; <i>CV</i> Choroidal volume		

Table 5
Association Between Clinical Characteristics and Integrity of the Ellipsoid Zone of MRS

Factor	Intact or partially continuous in EZ (n = 25)	Defect in EZ (n = 7)	<i>P</i>
Age(years)	61.8 ± 9.18	66.3 ± 11.6	0.0901
Refractive error (D ± SD)	-12.03 ± 4.58	-15.0 ± 7.4	0.3494
Axial length (mm)	29.3 ± 1.44	29.9 ± 1.84	0.6322
Posterior staphyloma (n)			0.7321
present	20	6	
absent	5	1	
Partial PVD (n)			
present	6	1	0.5687
absent	19	6	
Epiretinal membrane (n)			0.1317
present	10	5	
absent	15	2	
Retinochisis subgroup (n)			0.1512
outer	11	1	
outer + inner	14	6	
RV(total,mm ³)	11.8 ± 2.40	14.9 ± 2.67	0.0460
RV(subfoveal,mm ³)	0.32 ± 0.08	0.41 ± 0.12	0.0641
CV(total,mm ³)	1.36 ± 0.61	1.08 ± 0.39	0.2271
CV(subfoveal,mm ³)	0.04 ± 0.02	0.04 ± 0.01	0.4482
<i>D</i> diopter; <i>SD</i> standard deviation; <i>PVD</i> posterior vitreous detachment; <i>RV</i> retinal volume; <i>CV</i> Choroidal volume			

Discussion

The measurement of the CV in MRS can help evaluate the overall changes in the choroid. Our results showed that the entire macula-involving MRS eyes group had much lower CVs than the emmetropic eyes group and presented significantly lower CVs in the entire macula and EDTRS subfields than the non-MRS highly myopic eyes group. There was no difference in the distribution of the CV in the four quadrants.

Axial length was the most important factor affecting the total CV in MRS eyes, myopic refractive error and integrity of the EZ were predictive of visual acuity, and defects in the EZ were associated with a greater total macular RV.

It is well recognized that highly myopic eyes have a thin choroid, and the presence of myopic traction maculopathy is related to subfoveal choroidal thinning ^[22,28-30]. In the present study, when compared with emmetropic eyes, highly myopic eyes, including MRS and non-MRS eyes, exhibited much lower macular CVs in the entire macula and all ETDRS subfields. In the research of Barteselli et al ^[25], the macular total CV in 21 eyes with myopic traction maculopathy (including 3 foveoschisis eyes) was lower than that in 36 highly myopic eyes without choroidoretinal pathology, which may be related to the difference in the average axial length (28.4 mm vs 27.6 mm) and the different prevalence of posterior staphyloma (16/21 eyes vs 9/36 eyes) between the two groups. In our study, MRS eyes had a lower macular CV than non-MRS highly myopic eyes, probably mainly due to the more serious degree of macular maculopathy in MRS eyes than in non-MRS eyes, even if no difference was found in axial length or the presence of posterior staphyloma between the two groups. Previous reports have indicated that in high myopia, the nasal quadrant is the thinnest region in the macula as measured with the ETDRS grid method, regardless of choroidal thickness or volume ^[19, 22, 25, 31]. We found that there was no significant difference in CV among the superior, inferior, temporal and nasal locations in MRS eyes, although the nasal CV presented the lowest value, which may be related to our exclusion of patients whose PDCA was localized to within an area with a 6 mm diameter centered on the fovea in our study. As the CV in the PDCA region is close to zero, manual measurements can easily cause errors in these cases.

In the current study, multivariate regression analysis indicated that the total macular CV was most strongly associated with axial length and not related to the total RV. Previous studies have confirmed that the choroidal thickness in foveal and parafoveal regions decreases with increasing axial length in high myopia ^[22, 25] and calculated that the subfoveal choroid thickness decreases between 19.63 μm and 32 μm for every millimeter increase in axial length in adults older than 60 years ^[17, 32]. Barteselli et al ^[25] found that the total macular CV decreased 0.32 mm^3 for every millimeter of axial length in highly myopic eyes, including those with MRS, choroidal neovascularization and no choroidoretinal lesions. Choroidal growth is restrained by axial growth of the eyeball during the development of myopia ^[33], and continuous axial-related choroidal thinning is observed in every stage of myopic maculopathy ^[22]. Eyeball elongation was found to be an important predictor of total choroidal volume alterations in high myopia and was simultaneously considered the initial tractional factor in the occurrence and development of MRS ^[34]. Whereas, the changes in the choroid appeared to be inconsistent with severity of MRS, as shown in the measurement of RV, we presume that different types and degrees of posterior staphyloma may lead to markedly unbalanced or disproportionate choroidal thinning; furthermore, the pathogenesis of MRS could possibly be attributed to a more complicated mechanism, such as the inward force generated by the asymmetrical progression of posterior vitreous detachment and its different adhesive sites on the retina^[14], in addition to the outward force imposing on the retina and choroid.

In this study, factors such as myopic refractive error and defects in the EZ were determinants of logMAR BCVA in MRS eyes; the BCVA decreased by 0.027 logMAR units for each diopter of myopia, and a greater RV was found in MRS eyes with EZ defects on further analysis. However, the subfoveal CV was not responsible for logMAR BCVA or the integrity of the EZ. Recent studies have investigated the factors affecting the visual acuity of high myopia and found that subfoveal choroidal thickness was an important predictor of BCVA in middle-age and elderly adult high myopia without macular chorioretinopathy ^[19–21], suggesting that structural alterations in the choroid in high myopia may reflect the inability of the choroid to supply oxygen and nutrients to photoreceptors of the outer retina, which may lead to damage to the photoreceptors and consequent visual dysfunction. However, other findings suggest that the subfoveal choroidal thickness alone is not a sensitive indicator of visual acuity in pathological myopia except at the choroidal neovascularization stage ^[22, 31]. Disruption of the EZ on OCT images has been regarded as a sign of damage to the photoreceptors. Ye et al found that the choroid affects visual vision through its interaction with the complex of the myoid zone and the EZ in pathological myopia ^[35]. Cheng et al demonstrated that the severity of the schisis cavity affected the integrity of the EZ and visual prognosis. In their study, eyes with MRS involving the entire macula had a significantly higher prevalence of EZ defects (50%, 13/26 eyes) and a worse mean logMAR BCVA (0.45) than eyes with less extensive MRS ^[16]. We speculate that mechanical forces resulting in morphological destruction of the retina, including schisis enlargements other than the reduced CV, probably played a more important role in the disruption and even loss of the EZ and the subsequent visual deterioration. There are at least three possible explanations for the insensitivity of the subfoveal CV in predicting visual acuity in our study. First, 96.9% (31/32 eyes) of MRS had pathological myopia, which made the subfoveal CV unpredictable for BCVA. Second, the variable choroidal thinning may insufficiently reflect the blood supply of the choroid to the outer layer of the retina compared with the changes in choroidal vascular flow. Third, choroidal thinning or decreased choroidal blood perfusion is an adaptive process resulting from damage to the photoreceptors due to mechanical stress and the reduced nutrition requirement of the photoreceptors from the choroid in MRS.

There are some limitations in our study. First, we did not examine the type of posterior staphyloma in the MRS eyes due to the limited scanning range of the conventional SD-OCT device, as posterior staphyloma plays a key role in the development of MRS ^[12] and may affect the determination of the ETDRS grids in the macula, which can cause the included RV and CV to be larger than the actual values. Second, due to the lack of built-in software for automatic measurement, the CV had to be manually measured, which inevitably produced measurement errors, especially in MRS eyes with a steep curvature of posterior staphyloma.

Conclusions

The macular CV was reduced in MRS eyes relative to non-MRS eyes in all regions, and the CV in the nasal region of the macula did not differ from that in the other quadrants. The decreased total macular CV in MRS was associated with axial length, a more myopic status and defects in the EZ played vital roles in

visual loss. The photoreceptor dysfunction may be mainly brought by mechanical traction exerted on the retina, and the variations in the macular choroid alone insufficiently indicated photoreceptor dysfunction and visual disturbance. Therefore, in MRS, clinicians should pay particular attention to the damage caused by mechanical factors and take measures to postpone this damage, and future studies should focus on changes in choroidal vascular structures and their impact on visual acuity.

Abbreviations

MRS
Myopic retinoschisis
EZ
Ellipsoid zone
EDI
enhanced depth imaging
SD-OCT
Spectral domain optical coherence tomography
CV
Choroidal volume
BCVA
Best corrected visual acuity
Log MAR
Logarithmic minimal angle of resolution
ETDRS
Early Treatment Diabetic Retinopathy Study
RV
Retinal volume
RPE
Retinal pigment epithelium
PVD
Posterior vitreous detachment
SD
standard deviation

Declarations

Ethics approval and consent to participate

The study was following the guidelines of the Helsinki Declaration and was approved by the Ethics Committee of Sixth People's Hospital Affiliated to Shanghai Jiao Tong University, Shanghai, China (Approval NO.: 2020-073). The study was registered in the Chinese clinical trial registry

(<http://www.chictr.org.cn/>, Registration number: ChiCTR2000038824). All patients had signed written informed consent for participation.

Consent for publication

All presentations of the cases have consent for publication.

Availability of data and materials

The data used and analyzed during the current study are available from the corresponding author on reasonable request. The data supporting our findings can also be found in the Chinese clinical trial registry (<http://www.chictr.org.cn/>, Registration number: ChiCTR2000038824).

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LS and WQ were responsible for conceiving and designing the study. LS, LT and HJ performed the experiments. LS, LB, CY and ZX collected and analyzed the data. LS wrote the draft. LS and WQ discussed the results and WQ critically reviewed the manuscript. All authors read and approved the final manuscript.

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Authors' information

¹Department of Ophthalmology, Shanghai Jiaotong University Affiliated Sixth People's Hospital, 600 Yishan Road, Shanghai 200233, China.

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Figures

Figure 1

Measurement mode of retinal and choroidal volume. SD-OCT B-scan protocol from routine mode in the horizontal direction (a). Automated segmentation for retinal volume (b). Measurements of retinal volume on the ETDRS grid (c). SD-OCT B-scan protocol from enhanced depth imaging mode in the horizontal direction (d). Manual segmentation for choroidal volume (e). Measurements of choroidal volume on the ETDRS grid (f).