European Review for Medical and Pharmacological Sciences 2022; 26: 5736-5744

Changes in macular vascular density and retinal thickness in young myopic adults without pathological changes: an OCTA study

Y. MENG[1], Z.-H. YI[1], Y.-S. XU[1], L. HE[2], L. LI[1], C.-Z. CHEN[1]

[1]Department of Ophthalmology, [2]Physical Examination Center, Renmin Hospital of Wuhan University, Wuhan, China

Lu Li and Changzheng Chen contributed equally to this paper

Abstract. – OBJECTIVE: The aim of the study was to quantify the macular vascular density and retinal thickness in the eyes of young myopic people with myopia without pathological changes using optical coherence tomography angiography (OCTA).

PATIENTS AND METHODS: In this cross-sectional study, 160 eyes of 80 myopia subjects without pathological changes were classified into three groups: mild myopia (N=40 eyes), moderate myopia (N=66 eyes), and high myopia (N=54 eyes). Macular vascular density (VD), retinal thickness, area of the foveal avascular zone, the flow area of the outer retina and choriocapillaris (CC) were measured using OCTA. The effects of other confounding factors including axial length, the spherical equivalent, and some systemic factors (blood pressure, height, weight, etc.) were also considered.

RESULTS: As the severity of myopia increases, the CC flow area decreased (p=0.029). The superficial VD in the temporal, superior, nasal, and inferior regions was significantly lower in high myopia group compared to moderate and low myopia groups (all p<0.001). With increasing myopia, a significant reduction of deep VD was found in the superior region of the macula (p=0.007). In the fovea, there was no difference in the superficial or deep VD across groups (p=0.268 and p=0.413, respectively). Parafoveal retinal thickness was thinnest in the high myopia group and thickest in the mild myopia group (all p<0.05). The fovea was thickest in the high myopia group and thinnest in the mild myopia group (p=0.030).

CONCLUSIONS: In young myopic people without pathological changes, superficial VD and retinal thickness decreased with myopia progression, except in the fovea. The CC flow area decreased with increasing myopia.

Key Words:
Myopia, OCTA, Vessel density, Retinal thickness, Choriocapillaris.

Introduction

Myopia, which results in vision loss, is one of the most common ophthalmic conditions and is ranked as a major global public health concern for the 21st century[1,2]. Over the last few decades, the prevalence of myopia has increased worldwide, especially in East and Southeast Asia[2-5]. Approximately 80-90% of young adults in these regions have myopia, where the environmental influences (e.g., educational performance pressure, limited time outdoors) are thought to play a more important role than genetic factors in the myopia epidemic[5]. As myopia progresses, numerous vision-threatening ocular complications can develop, including lacquer crack, chorioretinal atrophy, retinal detachment, retinoschisis, macular degeneration, choroidal neovascularisation, glaucoma, and cataracts[6-8]. Based on current trends, it has been predicted that by 2050, there will be 4758 million and 938 million people (49.8% and 9.8% of the global population) with myopia and high myopia, respectively[9]. The increasing prevalence of myopia has brought a huge economic burden to society[10]. In urban China, 143.6 million people have myopia, and the annual economic burden was estimated to be 173.6 billion CNY (26.3 billion USD)[11].

We are now able to better study the progression and causes of myopia due to technological advances. Over the past few years, optical coherence tomography angiography (OCTA) devices have gained huge popularity in the ophthalmology field after their commercialization. These devices detect retinal structure and blood flow in a rapid and non-invasive way[12]. Paired with the split-spectrum amplitude-decorrelation angiography (SSADA) algorithm, there have been significant increases in the signal-to-noise ratio while

Corresponding Authors: Lu Li, MD; e-mail: lilu-000000@163.com
Changzheng Chen, MD; e-mail: chenchangzheng@whu.edu.cn

enhancing the reliability of flow detection[13]. While several previous studies have explored macular microvascular changes in myopic patients, they have tended to focus on subjects of older age and only include relatively small sample sizes without excluding pathological myopia[8,14]. This has resulted in several contradictory findings, such as whether choriocapillaris (CC) blood flow decreases or remains the same in more myopic eyes compared with less myopic eyes or healthy eyes[15,16].

Therefore, the aim of this study is to evaluate the macular microvascular changes and their correlations with retinal structure in the myopic eyes of young people who do not possess pathological changes. Possible associated factors are also investigated.

Patients and Methods

This study is a cross-sectional study. All subjects were recruited between December 2021 to January 2021 at Renmin Hospital of Wuhan University. This study was conducted in strict accordance with the Declaration of Helsinki and approved by the Ethical Review Committee of the Renmin Hospital of Wuhan University. To be included, subjects had to be: a) aged 18 to 39; b) have a best-corrected visual acuity (BCVA) ≤0.00 logMAR in each eye; c). SE ≤ -0.50 D; d). IOP between 10-21 mmHg. The exclusion criteria were as follows: a) a history of ocular surgery or trauma; b) any systemic disease; c) any ocular disease other than myopia. Informed consent was obtained from each subject.

All participants underwent a comprehensive ocular examination that included BCVA tests, slit-lamp biomicroscopy of the anterior and posterior segment, subjective refraction (performed using RT-5100; NEDEK, Gamagori, Japan), axial length (AL) measurement (IOL Master; Carl Zeiss, Germany), and OCTA (RTVue XR Avanti; Optovue Inc., Fremont, CA, USA). Intraocular pressure (IOP) was measured by non-contact tonometry (FT-100 TOMEY; Nagoya, Japan). Spherical equivalent (SE) was calculated as sphere + 1/2 cylinder.

OCTA was performed using the RTVue XR Avanti device with the 3x3 mm Angio Retina mode. All OCTA exams are done by the same experienced physician. Blood flow was estimated using the SSADA algorithm, which allows quantifying retinal and choroidal blood flow noninvasively with the built-in AngioVue software[13,17]. Vascular density refers to the percentage of large blood vessels and microvessels in an area. The calculation of vascular density (VD) was based on 1- and 3-mm Early Treatment Diabetic Retinopathy Study (ETDRS) circles centered on the fovea. The 1 mm circle represented the fovea. The annular area between the 1 mm and 3 mm concentric circles represented the parafoveal region, which was divided into four parts: temporal, superior, nasal, and inferior. During scanning, the SSADA algorithm computes the decorrelation between two different OCT amplitudes taken from the same scanning position, improving blood flow detection and estimation of the connectivity of retinal microvascular networks[17]. The superficial VD referred to the VD of the superficial retinal capillary plexus (from the internal limiting membrane to 9 μm below the inner plexiform layer) while the deep VD referred to the VD of the deep retinal capillary plexus (from 9 μm below the inner plexiform layer to 9 μm above the outer plexiform layer). The AngioVue software also allows quantitative measurements of the blood flow in the outer retina and the choriocapillaris. The outer retina was automatically set to be between the inner plexiform layer and the retinal pigment epithelium (RPE), and the choriocapillaris was from the RPE to 31 μm below the RPE. Full retinal thickness, defined as from the inner limiting membrane to the outer boundary of the RPE, was also obtained in the OCTA scan.

Each subject's demographic information and medical history were recorded. Their height, weight, heart rate (HR), and blood pressure (BP) were recorded. Subjects were asked to rest for at least 15 minutes before BP measurements.

Statistical Analysis

All data were processed and analyzed using SPSS software (Version 26.0; IBM Corp., Armonk, NY, USA). Variables are expressed as mean ± standard deviation (SD). Intergroup comparisons of variables among groups were analyzed by one-way analysis of variance (ANOVA). Pearson correlation coefficients (r values) were used to test the associations between axial length and macular vascular density as well as retinal thickness. The relationship between axial length, macular vascular density, and retinal thickness was analyzed by univariate linear regression. The sex composition ratio of eyes between the three groups was analyzed by chi-square test. All p-values were 2-sided and $p<0.05$ was considered statistically significant.

Table I. The demographic characteristics of the three myopic groups.

Variables	Mild myopia	Moderate myopia	High myopia	*p*-value
No. of eyes	40	66	54	
Sex (females/males)	20:20	40:26	28:26	0.482
Age (year)	27.31 ± 5.17	26.31 ± 4.95	26.34 ± 4.40	0.538
HR (beats/min)	78.72 ± 8.47	77.76 ± 7.28	76.17 ± 8.07	0.294
SBP (mmHg)	119.72 ± 8.28	118.32 ± 5.52	118.29 ± 7.07	0.522
DBP (mmHg)	74.08 ± 4.99	73.89 ± 4.92	74.55 ± 4.48	0.748
Height (cm)	167.00 ± 8.64	166.06 ± 10.37	167.37 ± 9.56	0.748
Weight (kg)	62.27 ± 9.33	60.34 ± 9.67	63.49 ± 9.78	0.201
BMI†	22.25 ± 2.22	21.77 ± 1.73	22.53 ± 1.61	0.071
IOP (mmHg)	15.82 ± 1.84	16.21 ± 2.09	15.80 ± 1.92	0.457
AL (mm)	24.30 ± 0.67	25.64 ± 0.57	26.77 ± 0.76	< 0.001
SE (D)	-1.87 ± 0.64	-4.38 ± 0.79	-7.43 ± 0.78	< 0.001

HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; BMI, body mass index; IOP, intraocular pressure; AL, axial length; SE, spherical equivalent. BMI† = weight (kg)/height (m)^2. The sex composition ratio of eyes between the three groups was analyzed by chi-square test, and other variables were calculated by one-way ANOVA.

Results

The eyes of 80 subjects (44 females and 36 males) were analyzed. The age and SE of the studied subjects were 26.57 ± 4.81 years and -4.78 ± 2.27 D, respectively. According to SE, there were 40 eyes in the mild myopia group (-0.50 D<SE≤-3.00 D), 66 eyes in the moderate myopia group (-3.00 D < SE ≤-6.00 D), and 54 eyes in the high myopia group (SE<-6.00 D). The average demographic characteristics of the subjects are presented in Table I. There were no differences between the three groups in terms of gender composition, age, HR, SDP, DBP, weight, height, BMI, and IOP (all p>0.05). There were differences among the three groups in terms of SE and AL (p<0.001 and p<0.001, respectively).

The whole and regional macular vascular density parameters of each group are shown in Table II. With increasing myopic severity, the choriocapillaris flow area decreased (p=0.029), but the foveal avascular zone (FAZ) area (p=0.371), and the outer retina flow area (p=0.078) did not. The VD in the superficial whole image, temporal, superior, nasal, and inferior macula decreased in more myopic eyes compared to less myopic ones (all p<0.001), while the superficial foveal VD remained the same across all three levels of severity (p=0.268). The VD in the deep whole image and superior macula also decreased with increasing myopia (p=0.041 and p=0.007, respectively). However, there was no difference in the VD in the deep foveal, temporal, nasal, and inferior macula (p=0.413, p=0.052, p=0.064, and p=0.073, respectively) across myopic severity levels.

Table III shows the whole and regional macular retinal thickness parameters between the myopic severity groups. As myopia progressed, the retina became thinner in the whole image, temporal, superior, nasal, and inferior part of the macula (all p<0.05), while the foveal thickness increased (p=0.030). In general, the retina was thicker in less myopic individuals, except for the foveal region, where the more myopic individuals tend to have a thicker retinal thickness.

Pearson's correlation coefficient and linear regression analysis between AL and superficial macular vascular density were performed. AL was negatively correlated with vascular density in the superficial whole image, temporal, superior, nasal, and inferior regions of the macula (r=-0.43, r=-0.37, r=-0.51, r=-0.33, and r=-0.31, respectively; all p<0.001) (Figure 1). There was no correlation between AL and vascular density in the superficial fovea (r=-0.03, p=0.757).

AL was negatively correlated with vascular density in the deep inferior region of the macula (r=-0.17, p=0.036); otherwise there was no relationship between AL and deep macular vascular density in the whole image, foveal, temporal, superior, and nasal regions was found (r=-0.13, p=0.108; r=0.05, p=0.513; r=-0.12, p=0.134 r=-0.13, p=0.092; r=-0.10, p=0.222; respectively) (Figure 2).

We then analyzed the correlation between the AL and the retinal thickness at different locations (Figure 3). AL was negatively correlated with retinal thickness in the whole image, temporal, superior, nasal, and inferior regions of the macula (r=-0.37, p<0.001; r=-0.28, p<0.001; r=-0.30,

Table II. Macular vascular density parameters among the three myopic groups.

Variables		Mild myopia	Moderate myopia	High myopia	*p*-value
FAZ area (mm^2)		0.279 ± 0.058	0.287 ± 0.061	0.297 ± 0.065	0.371
Outer retina flow area (mm^2)		1.013 ± 0.381	1.082 ± 0.345	1.169 ± 0.271	0.078
CC flow area (mm^2)		2.092 ± 0.106	2.051 ± 0.132	2.012 ± 0.176	0.029
Superficial VD (%)	Whole image	46.57 ± 1.97	45.02 ± 2.73	42.92 ± 2.47	< 0.001
	Foveal	16.73 ± 3.39	16.23 ± 3.43	17.23 ± 3.18	0.268
	Temporal	48.14 ± 2.12	46.56 ± 3.16	44.63 ± 2.87	< 0.001
	Superior	51.58 ± 2.09	49.66 ± 2.69	46.70 ± 2.84	< 0.001
	Nasal	48.66 ± 2.97	47.29 ± 3.24	44.86 ± 3.20	< 0.001
	Inferior	49.12 ± 3.12	48.37 ± 3.46	46.22 ± 2.81	< 0.001
Deep VD (%)	Whole image	50.50 ± 3.59	49.43 ± 3.56	48.44 ± 4.41	0.041
	Foveal	32.73 ± 6.18	33.20 ± 7.36	34.43 ± 5.66	0.413
	Temporal	53.86 ± 3.74	53.09 ± 3.51	51.89 ± 4.58	0.052
	Superior	53.56 ± 4.17	51.19 ± 4.03	50.48 ± 5.81	0.007
	Nasal	54.09 ± 4.17	52.98 ± 3.80	51.92 ± 5.15	0.064
	Inferior	51.87 ± 5.16	51.09 ± 4.51	49.66 ± 4.76	0.073

FAZ, foveal avascular zone; CC, choriocapillaris. All variables were calculated by one-way ANOVA.

$p<0.001$; r=-0.26, $p=0.001$; r=-0.27, $p=0.001$; respectively).

Discussion

Here, the macular vascular density and macular retinal thickness of young people with myopic eyes were quantified using OCTA and compared between cases that were mild, moderate, or severe in their myopia. With progression of myopia, we detected reduced macular vascular density, a reduced choriocapillaris flow area, and an increased foveal thickness. There were no differences in FAZ area and outer retina flow across severity levels.

Consistent with previous studies, we found that more myopic subjects had significantly lower superficial macular vascular density than less myopic ones, and there was a negative correlation between superficial vascular density and axial length except in the foveal region (Table II and Figure 1)[18-21]. The decrease in VD might be attributed to the elongation of AL, which may lead to the narrowing of the retinal vessels[22-24]. Deep vascular density also seemed to decrease with the progression of myopia, although this trend was only statistically different in the whole image, and the superior region (Table II). Some studies have found that both the superficial and deep VD reduced significantly in highly myopic patients[19,21]; although this is not always the case[20,25,26]. A recent study revealed that the alteration of deep VD and outer retinal sublayer thicknesses occurred in pathological myopia and could play significant roles in the mechanism of the visual impairment happened in pathological myopia[27]. We only included myopic eyes with normal BCVA and without pathological changes, which may explain why the deep VD was not greatly influenced by myopia alone. We speculate that the decrease in superficial VD may occur earlier than that in deep VD in myopia eyes of young people. Moreover, macular ves-

Table III. Macular retinal thickness parameters among the three myopic groups.

Variables	Mild myopia	Moderate myopia	High myopia	*p*-value
Whole image (μm)	321.3 ± 8.8	316.9 ± 10.3	306.2 ± 12.2	< 0.001
Foveal (μm)	242.9 ± 12.1	247.1 ± 11.0	249.0 ± 10.6	0.030
Temporal (μm)	322.3 ± 10.2	320.9 ± 11.2	310.5 ± 10.5	< 0.001
Superior (μm)	329.3 ± 9.7	327.3 ± 11.0	316.2 ± 14.3	< 0.001
Nasal (μm)	329.6 ± 10.4	333.8 ± 10.9	318.5 ± 12.8	< 0.001
Inferior (μm)	325.1 ± 9.4	322.2 ± 10.3	314.9 ± 11.7	< 0.001

All variables were calculated by one-way ANOVA.

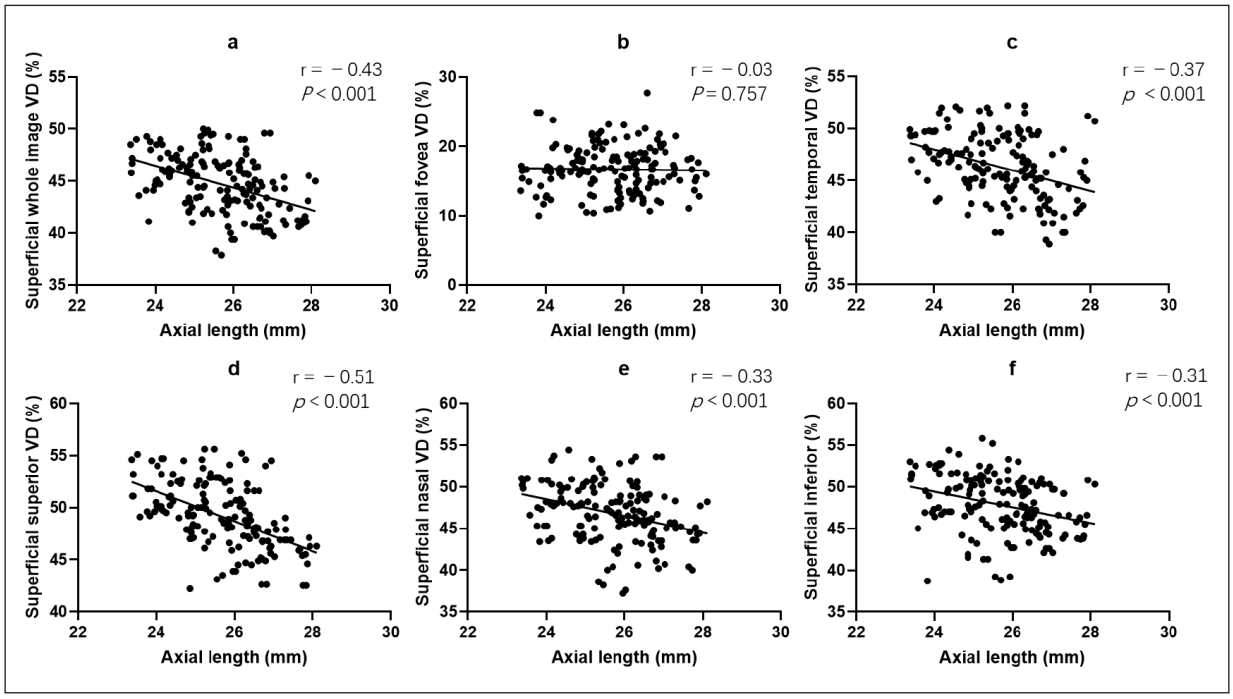

Figure 1. Correlations between axial length and superficial macular vascular density. Scatterplots and regression lines showing the correlations in the whole image (***a***), foveal (***b***), temporal (***c***), superior (***d***), nasal (***e***), and inferior (***f***) regions. Negative correlations could be detected in ***a***, ***c***, ***d***, ***e***, and ***f***.

sel density decreases with age and individuals included in other studies typically have a larger mean age, which may lead to overestimation of the reduction of deep VD[25,28,29]. We observed no difference in superficial and deep foveal VD between the three myopic groups, which may be due to the high metabolism of the FAZ, where the autoregulation of the retina might help maintain relatively stable and sufficient blood flow to meet metabolic needs[23]. Consistent with several studies, we observed no difference in FAZ area between the three groups (Table II;[18-20]). However, the FAZ area can be influenced by many other factors, such as age, gender, axial length, and choroidal thickness[28-31]. Alternatively, the lack of difference may have resulted from deviation from the built-in software (which may also account for lack of differences detected in the outer retina flow area between eyes of varying severity; Table II). While there may be no effect of myopia on the outer retina flow area, it should be noted that the common presence of projection artifacts makes it difficult to accurately understand the true conditions of the deep blood circulation[32]. Although the OCTA device used has a built-in automatic projection artifact removal algorithm, the algorithm may have been affected by slight superficial VD in myopic eyes, resulting in enhanced preservation of images of deeper vessel layers[8,32]. However, as there are relatively few studies using the outer retina flow area as an assessment in myopic eyes, the exact changes need to be further explored.

We also found that the CC flow area decreased with the progression of myopia (Table II). This finding, which is consistent with prior studies, suggests that the choroidal circulation may be disturbed in myopic eyes[14,15,33]. Histologically, the choriocapillaris is a network of capillaries that is highly anastomosed; however, this complex anatomy can make it difficult to achieve accurate segmentation of CC[34]. Here, the choriocapillaris was automatically segmented by built-in software such that the actual measured flow area included larger-sized choroidal vessels in the Sattler's layer in addition to the choriocapillaris. Furthermore, the choriocapillaris perfusion tends to have a wide topographic variation in both healthy and myopic eyes, which means that if studies selected different parts of CC, different results might be reached[35,36] (e.g., in some studies, the CC flow was not related to axial length or spherical equivalent[16,37]).

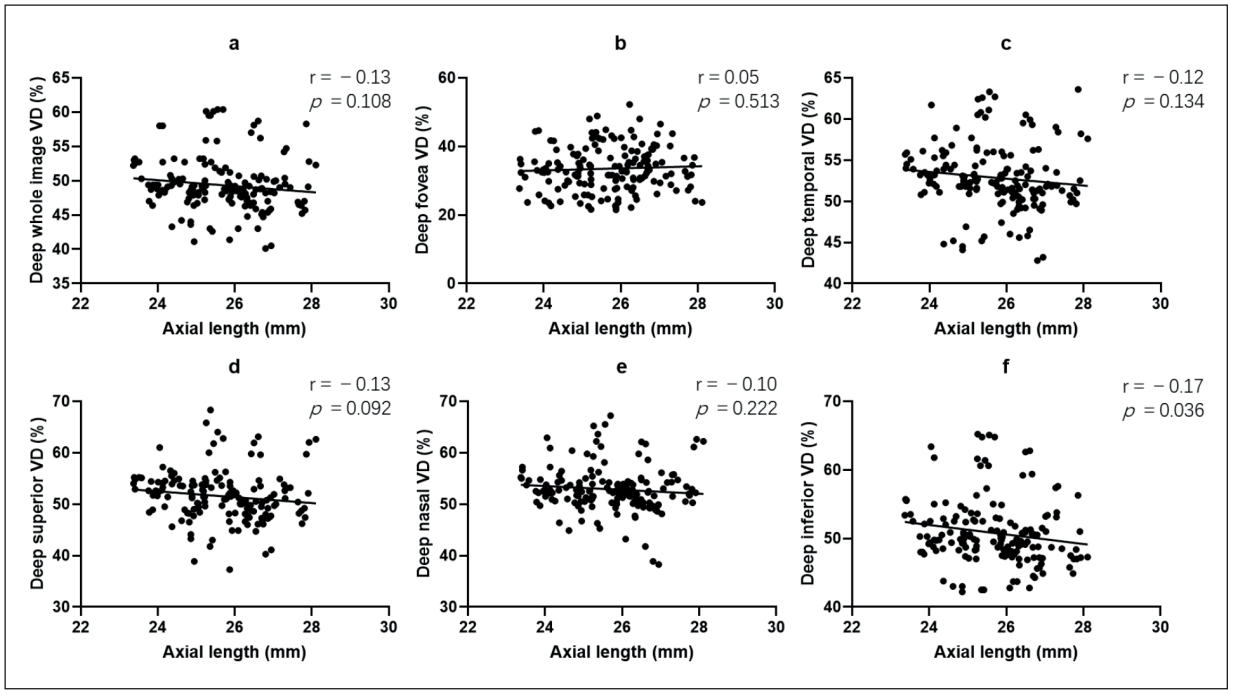

Figure 2. Correlations between axial length and deep macular vascular density. Scatterplots and regression lines showing the correlations in the whole image (**a**), foveal (**b**), temporal (**c**), superior (**d**), nasal (**e**), and inferior (**f**) regions. Negative correlations could be detected in **f**.

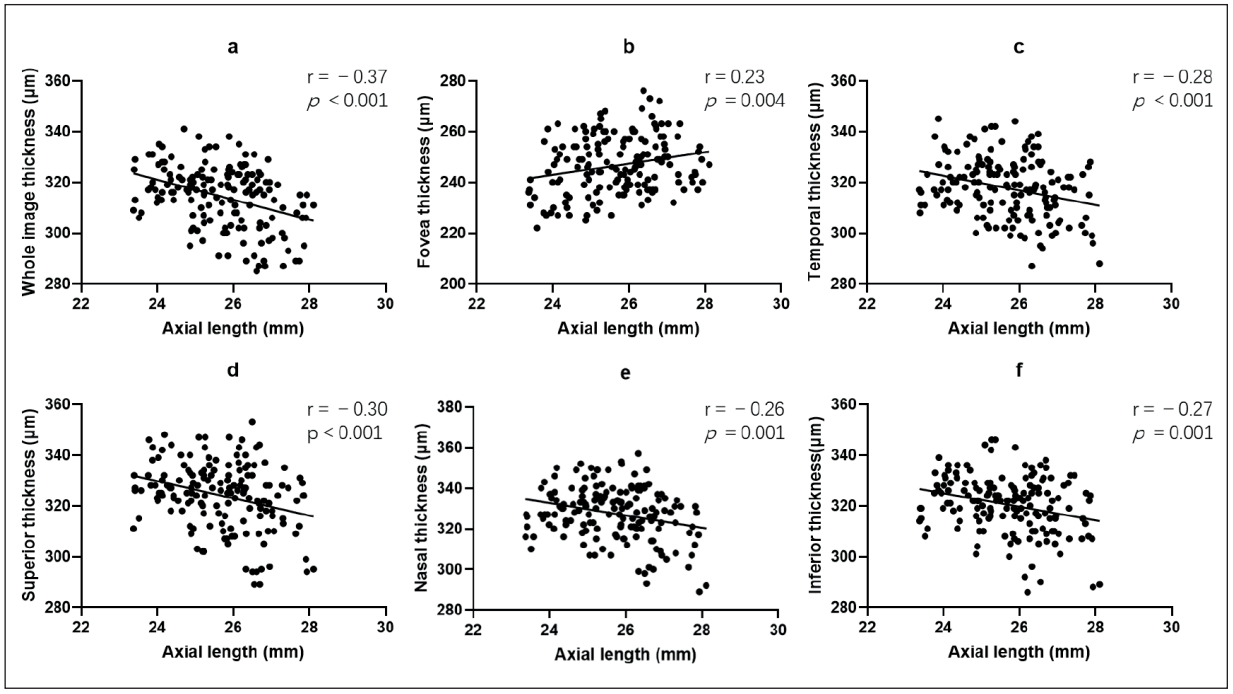

Figure 3. Correlations between axial length and macular retinal thickness. Scatterplots and regression lines showing the correlations in the whole image (**a**), foveal (**b**), temporal (**c**), superior (**d**), nasal (**e**), and inferior (**f**) regions. Negative correlations were observed in **a**, **c**, **d**, **e**, and **f**; a positive correlation can be seen in **b**.

Differences were observed in macular retinal thicknesses for each location between the low, moderate, and high myopia groups (Table III). More myopic eyes appeared to have higher foveal thickness and lower parafoveal retinal thickness than less myopic eyes. Additionally, AL was negatively correlated with retinal thicknesses in all regions, except for the fovea, where it was positively correlated (Figure 3). These findings are supported by several previous articles, which suggest that the thinning of parafoveal retinal detected in myopic eyes is due to mechanical stretching of the enlarged eyeball secondary to the increased axial length[38-42]. In the meanwhile, the fovea was elevated due to the stretching and flattening tendency of the internal limiting membrane as well as the traction of the posterior vitreous[39,43].

Our study did have several limitations. First is the cross-sectional design and small age range of the subjects. It has been widely recognized that age can significantly affect retinal vessel density, retinal thickness, FAZ area, and CC blood flow[25,28,29,44-46]. In addition, we intentionally excluded individuals with pathological changes, so the findings may not be directly generalized to all myopic populations. Future studies with a larger sample size and a wider age range of subjects may help further identify the changes in retinal blood flow and thickness in myopic eyes. Second, more advanced swept-source OCTA (SS-OCTA) devices with higher scan rates, and greater scan depth have recently become commercially available[47,48]. Better visualization of the retinal and choroidal vasculature and structure by SS-OCTA may provide new insights into unresolved controversies and differences between this and previous studies. Third, due to the limited scanning range of the OCTA device, the retina beyond the macula has not been studied. Fourth, in our study we assessed the full thickness of the retina without subdividing the layers of the retina, which may have missed important variations.

Conclusions

In this present study, we found reduced CC flow area in the myopic eyes of young people. The reduction of macular blood flow was mainly concentrated in the superficial VD. This suggests that superficial VD is more susceptible than deep VD when myopic changes occur, although further work is needed to fully understand this mechanism. Both the superficial and deep VD in the fovea did not differ among the three myopia groups, possibly due to the high metabolism and blood needs of the FAZ. With increasing AL, the parafoveal retinal thickness decreased while the foveal thickness increased; this is likely due to the stretching of the eyeball and the traction of the vitreous. More broadly, we establish that OCTA provides a non-invasive way to evaluate changes in retinal structure and blood flow before vision-threatening pathological changes appear. These findings advance our understanding of the mechanisms underlying myopia and facilitate its prevention and control.

Financial Support

This work was supported by the National Natural Science Foundation of China (grant number 81600740), and Independent Scientific Research of Wuhan University (grant number 2042019kf0071). The sponsors had no role in the study design; the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the article for publication.

Ethics Statement

The Ethics Committee of Renmin Hospital of Wuhan University reviewed and approved the research protocol. This study complies with the Declaration of Helsinki.

Informed Consent

Written informed consent for participation has been obtained from the patients.

Authors' Contribution

YM, ZY, YX, LH, LL, CC: Conceptualization; YM, ZY, YX: Data curation; LL, CC: Formal analysis; YM, LH, LL, CC: Investigation; YM, ZY, YX, CC: Methodology; YM, YX, LL, CC: Project administration; LH, LL, CC: Resources; YM, ZY, YX, LL: Software; LL, CC: Supervision; YM, ZY, YX, LH, LL, CC: Validation; YM, ZY, YX, LL, CC: Visualization; YM, ZY, YX, LH, LL, CC: Roles/Writing - original draft; LL, CC: Writing - review & editing.

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We would like to thank all the participants in this research for helping us to improve our understanding of myopia.

References

1) Foo LL, Ng WY, Lim GYS, Tan TE, Ang M, Ting DSW. Artificial intelligence in myopia: current and future trends. Curr Opin Ophthalmol 2021; 32: 413-424.
2) Cai XB, Shen SR, Chen DF, Zhang Q, Jin ZB. An overview of myopia genetics. Exp Eye Res 2019; 188: 107778.
3) Han SB, Jang J, Yang HK, Hwang JM, Park SK. Prevalence and risk factors of myopia in adult Korean population: Korea national health and nutrition examination survey 2013-2014 (KNHANES VI). PLoS One 2019; 14: e0211204.
4) Jonas JB, Ang M, Cho P, Guggenheim JA, He MG, Jong M, Logan NS, Liu M, Morgan I, Ohno-Matsui K, Parssinen O, Resnikoff S, Sankaridurg P, Saw SM, Smith EL, 3rd, Tan DTH, Walline JJ, Wildsoet CF, Wu PC, Zhu X, Wolffsohn JS. IMI Prevention of Myopia and Its Progression. Invest Ophthalmol Vis Sci 2021; 62: 6.
5) Morgan IG, French AN, Ashby RS, Guo X, Ding X, He M, Rose KA. The epidemics of myopia: Aetiology and prevention. Prog Retin Eye Res 2018; 62: 134-149.
6) Cooper J, Tkatchenko AV. A Review of Current Concepts of the Etiology and Treatment of Myopia. Eye Contact Lens 2018; 44: 231-247.
7) Morgan IG, Ohno-Matsui K, Saw S-M. Myopia. The Lancet 2012; 379: 1739-1748.
8) Milani P, Montesano G, Rossetti L, Bergamini F, Pece A. Vessel density, retinal thickness, and choriocapillaris vascular flow in myopic eyes on OCT angiography. Graefes Arch Clin Exp Ophthalmol 2018; 256: 1419-1427.
9) Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, Wong TY, Naduvilath TJ, Resnikoff S. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology 2016; 123: 1036-1042.
10) Ramamurthy D, Lin Chua SY, Saw SM. A review of environmental risk factors for myopia during early life, childhood and adolescence. Clin Exp Optom 2015; 98: 497-506.
11) Ma Y, Wen Y, Zhong H, Lin S, Liang L, Yang Y, Jiang H, Chen J, Huang Y, Ying X, Resnikoff S, Lu L, Zhu J, Xu X, He X, Zou H. Healthcare utilization and economic burden of myopia in urban China: A nationwide cost-of-illness study. J Glob Health 2022; 12: 11003.
12) Kashani AH, Chen CL, Gahm JK, Zheng F, Richter GM, Rosenfeld PJ, Shi Y, Wang RK. Optical coherence tomography angiography: A comprehensive review of current methods and clinical applications. Prog Retin Eye Res 2017; 60: 66-100.
13) Jia Y, Tan O, Tokayer J, Potsaid B, Wang Y, Liu JJ, Kraus MF, Subhash H, Fujimoto JG, Hornegger J, Huang D. Split-spectrum amplitude-decorrelation angiography with optical coherence tomography. Opt Express 2012; 20: 4710-4725.
14) Al-Sheikh M, Phasukkijwatana N, Dolz-Marco R, Rahimi M, Iafe NA, Freund KB, Sadda SR, Sarraf D. Quantitative OCT Angiography of the Retinal Microvasculature and the Choriocapillaris in Myopic Eyes. Invest Ophthalmol Vis Sci 2017; 58: 2063-2069.
15) Wu H, Zhang G, Shen M, Xu R, Wang P, Guan Z, Xie Z, Jin Z, Chen S, Mao X, Qu J, Zhou X. Assessment of Choroidal Vascularity and Choriocapillaris Blood Perfusion in Anisomyopic Adults by SS-OCT/OCTA. Invest Ophthalmol Vis Sci 2021; 62: 8.
16) Scherm P, Pettenkofer M, Maier M, Lohmann CP, Feucht N. Choriocapillary Blood Flow in Myopic Subjects Measured With OCT Angiography. Ophthalmic Surg Lasers Imaging Retina 2019; 50: e133-e139.
17) Tokayer J, Jia Y, Dhalla AH, Huang D. Blood flow velocity quantification using split-spectrum amplitude-decorrelation angiography with optical coherence tomography. Biomed Opt Express 2013; 4: 1909-1924.
18) Wang T, Li H, Zhang R, Yu Y, Xiao X, Wu C. Evaluation of retinal vascular density and related factors in youth myopia without maculopathy using OCTA. Sci Rep 2021; 11: 15361.
19) Ucak T, Icel E, Yilmaz H, Karakurt Y, Tasli G, Ugurlu A, Bozkurt E. Alterations in optical coherence tomography angiography findings in patients with high myopia. Eye (Lond) 2020; 34: 1129-1135.
20) Min CH, Al-Qattan HM, Lee JY, Kim JG, Yoon YH, Kim YJ. Macular Microvasculature in High Myopia without Pathologic Changes: An Optical Coherence Tomography Angiography Study. Korean J Ophthalmol 2020; 34: 106-112.
21) Yang Y, Wang J, Jiang H, Yang X, Feng L, Hu L, Wang L, Lu F, Shen M. Retinal Microvasculature Alteration in High Myopia. Invest Ophthalmol Vis Sci 2016; 57: 6020-6030.
22) Shimada N, Ohno-Matsui K, Harino S, Yoshida T, Yasuzumi K, Kojima A, Kobayashi K, Futagami S, Tokoro T, Mochizuki M. Reduction of retinal blood flow in high myopia. Graefes Arch Clin Exp Ophthalmol 2004; 242: 284-288.
23) Li M, Yang Y, Jiang H, Gregori G, Roisman L, Zheng F, Ke B, Qu D, Wang J. Retinal Microvascular Network and Microcirculation Assessments in High Myopia. Am J Ophthalmol 2017; 174: 56-67.
24) Zheng Q, Zong Y, Li L, Huang X, Lin L, Yang W, Yuan Y, Li Y, He H, Gao Q. Retinal vessel oxygen saturation and vessel diameter in high myopia. Ophthalmic Physiol Opt 2015; 35: 562-569.
25) Leng Y, Tam EK, Falavarjani KG, Tsui I. Effect of Age and Myopia on Retinal Microvasculature. Ophthalmic Surg Lasers Imaging Retina 2018; 49: 925-931.
26) Yang S, Zhou M, Lu B, Zhang P, Zhao J, Kang M, Wang R, Wang F, Sun X. Quantification of Macular Vascular Density Using Optical Coherence Tomography Angiography and Its Relationship with Retinal Thickness in Myopic Eyes of Young Adults. J Ophthalmol 2017; 2017: 1397179.
27) Ye J, Wang M, Shen M, Huang S, Xue A, Lin J, Fan Y, Wang J, Lu F, Shao Y. Deep Retinal Capil-

lary Plexus Decreasing Correlated With the Outer Retinal Layer Alteration and Visual Acuity Impairment in Pathological Myopia. Invest Ophthalmol Vis Sci 2020; 61: 45.

28) Iafe NA, Phasukkijwatana N, Chen X, Sarraf D. Retinal Capillary Density and Foveal Avascular Zone Area Are Age-Dependent: Quantitative Analysis Using Optical Coherence Tomography Angiography. Invest Ophthalmol Vis Sci 2016; 57: 5780-5787.

29) Falavarjani KG, Shenazandi H, Naseri D, Anvari P, Kazemi P, Aghamohammadi F, Alissmail F, Alemzadeh SA. Foveal Avascular Zone and Vessel Density in Healthy Subjects: An Optical Coherence Tomography Angiography Study. J Ophthalmic Vis Res 2018; 13: 260-265.

30) Gomez-Ulla F, Cutrin P, Santos P, Fernandez M, Abraldes M, Abalo-Lojo JM, Gonzalez F. Age and gender influence on foveal avascular zone in healthy eyes. Exp Eye Res 2019; 189: 107856.

31) Tan CS, Lim LW, Chow VS, Chay IW, Tan S, Cheong KX, Tan GT, Sadda SR. Optical Coherence Tomography Angiography Evaluation of the Parafoveal Vasculature and Its Relationship With Ocular Factors. Invest Ophthalmol Vis Sci 2016; 57: OCT224-234.

32) Anvari P, Ashrafkhorasani M, Habibi A, Falavarjani KG. Artifacts in Optical Coherence Tomography Angiography. J Ophthalmic Vis Res 2021; 16: 271-286.

33) Mo J, Duan A, Chan S, Wang X, Wei W. Vascular flow density in pathological myopia: an optical coherence tomography angiography study. BMJ Open 2017; 7: e013571.

34) Nickla DL, Wallman J. The multifunctional choroid. Prog Retin Eye Res 2010; 29: 144-168.

35) Borrelli E, Uji A, Toto L, Viggiano P, Evangelista F, Mastropasqua R. In Vivo Mapping of the Choriocapillaris in Healthy Eyes: A Widefield Swept-Source OCT Angiography Study. Ophthalmol Retina 2019; 3: 979-984.

36) Mastropasqua R, Viggiano P, Borrelli E, Evangelista F, Libertini D, Di Antonio L, Toto L. In Vivo Mapping of the Choriocapillaris in High myopia: a Widefield Swept Source Optical Coherence Tomography Angiography. Sci Rep 2019; 9: 18932.

37) Wang Q, Chan S, Yang JY, You B, Wang YX, Jonas JB, Wei WB. Vascular Density in Retina and Choriocapillaris as Measured by Optical Coherence Tomography Angiography. Am J Ophthalmol 2016; 168: 95-109.

38) Zereid FM, Osuagwu UL. Myopia and Regional Variations in Retinal Thickness in Healthy Eyes. J Ophthalmic Vis Res 2020; 15: 178-186.

39) Wu PC, Chen YJ, Chen CH, Chen YH, Shin SJ, Yang HJ, Kuo HK. Assessment of macular retinal thickness and volume in normal eyes and highly myopic eyes with third-generation optical coherence tomography. Eye (Lond) 2008; 22: 551-555.

40) Hwang YH, Kim YY. Macular thickness and volume of myopic eyes measured using spectral-domain optical coherence tomography. Clin Exp Optom 2012; 95: 492-498.

41) Lim MC, Hoh ST, Foster PJ, Lim TH, Chew SJ, Seah SK, Aung T. Use of optical coherence tomography to assess variations in macular retinal thickness in myopia. Invest Ophthalmol Vis Sci 2005; 46: 974-978.

42) Song AP, Wu XY, Wang JR, Liu W, Sun Y, Yu T. Measurement of retinal thickness in macular region of high myopic eyes using spectral domain OCT. Int J Ophthalmol 2014; 7: 122-127.

43) Sato A, Fukui E, Ohta K. Retinal thickness of myopic eyes determined by spectralis optical coherence tomography. Br J Ophthalmol 2010; 94: 1624-1628.

44) Ichioka A, Ooto S, Uji A, Manabe S, Shiragami C, Tsujikawa A. Correlations among age, sex, axial length, and subfoveal choroidal thickness in the choriocapillaris structure analyzed using multiple en face image averaging optical coherence tomography angiography. PLoS One 2021; 16: e0259880.

45) Lauermann JL, Eter N, Alten F. Optical Coherence Tomography Angiography Offers New Insights into Choriocapillaris Perfusion. Ophthalmologica 2018; 239: 74-84.

46) Park SH, Cho H, Hwang SJ, Jeon B, Seong M, Yeom H, Kang MH, Lim HW, Shin YU. Changes in the Retinal Microvasculature Measured Using Optical Coherence Tomography Angiography According to Age. J Clin Med 2020; 9: 883.

47) Told R, Ginner L, Hecht A, Sacu S, Leitgeb R, Pollreisz A, Schmidt-Erfurth U. Comparative study between a spectral domain and a high-speed single-beam swept source OCTA system for identifying choroidal neovascularization in AMD. Sci Rep 2016; 6: 38132.

48) Lains I, Wang JC, Cui Y, Katz R, Vingopoulos F, Staurenghi G, Vavvas DG, Miller JW, Miller JB. Retinal applications of swept source optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA). Prog Retin Eye Res 2021; 84: 100951.