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

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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<0.01). 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 century1,2. Over the last few decades, the prevalence of myopia has increased worldwide, especially in East and Southeast Asia3-5. 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 epidemic6. As myopia progresses, numerous vision-threatening ocular complications can develop, including lacquer crack, chorioretinal atrophy, retinal detachment, retinoschisis, macular degeneration, choroidal neovascularisation, glaucoma, and cataracts7-8. 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, respectively9. The increasing prevalence of myopia has brought a huge economic burden to society10. 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 way12. Paired with the split-spectrum amplitude-decorrelation angiography (SSADA) algorithm, there have been significant increases in the signal-to-noise ratio while...
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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. 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 AngloVue 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.
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, SBP, 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 (\(r=-0.37, p<0.001;\) \(r=-0.28, p<0.001;\) \(r=-0.30,\)
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Table II. Macular vascular density parameters among the three myopic groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mild myopia</th>
<th>Moderate myopia</th>
<th>High myopia</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAZ area (mm²)</td>
<td>0.279 ± 0.058</td>
<td>0.287 ± 0.061</td>
<td>0.297 ± 0.065</td>
<td>0.371</td>
</tr>
<tr>
<td>Outer retinal flow area (mm²)</td>
<td>1.013 ± 0.381</td>
<td>1.082 ± 0.345</td>
<td>1.169 ± 0.271</td>
<td>0.078</td>
</tr>
<tr>
<td>CC flow area (mm²)</td>
<td>2.092 ± 0.106</td>
<td>2.051 ± 0.132</td>
<td>2.012 ± 0.176</td>
<td>0.029</td>
</tr>
<tr>
<td>Superficial VD (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole image</td>
<td>46.57 ± 1.97</td>
<td>45.02 ± 2.73</td>
<td>42.92 ± 2.47</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Foveal</td>
<td>16.73 ± 3.39</td>
<td>16.23 ± 3.43</td>
<td>17.23 ± 3.18</td>
<td>0.268</td>
</tr>
<tr>
<td>Temporal</td>
<td>48.14 ± 2.12</td>
<td>46.56 ± 3.16</td>
<td>44.63 ± 2.87</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Superior</td>
<td>51.58 ± 2.09</td>
<td>49.66 ± 2.69</td>
<td>46.70 ± 2.84</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Nasal</td>
<td>48.66 ± 2.97</td>
<td>47.29 ± 3.24</td>
<td>44.86 ± 3.20</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Interior</td>
<td>49.12 ± 3.12</td>
<td>48.37 ± 3.46</td>
<td>46.22 ± 2.81</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Deep VD (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole image</td>
<td>50.50 ± 3.59</td>
<td>49.43 ± 3.56</td>
<td>48.44 ± 4.41</td>
<td>0.041</td>
</tr>
<tr>
<td>Foveal</td>
<td>32.73 ± 6.18</td>
<td>33.20 ± 7.36</td>
<td>34.43 ± 5.66</td>
<td>0.413</td>
</tr>
<tr>
<td>Temporal</td>
<td>53.86 ± 3.74</td>
<td>53.09 ± 3.51</td>
<td>51.89 ± 4.58</td>
<td>0.052</td>
</tr>
<tr>
<td>Superior</td>
<td>53.56 ± 4.17</td>
<td>51.19 ± 4.03</td>
<td>50.48 ± 3.81</td>
<td>0.007</td>
</tr>
<tr>
<td>Nasal</td>
<td>54.09 ± 4.17</td>
<td>52.98 ± 3.80</td>
<td>51.92 ± 5.15</td>
<td>0.064</td>
</tr>
<tr>
<td>Inferior</td>
<td>51.87 ± 5.16</td>
<td>51.09 ± 4.51</td>
<td>49.66 ± 4.76</td>
<td>0.073</td>
</tr>
</tbody>
</table>

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

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). The decrease in VD might be attributed to the elongation of AL, which may lead to the narrowing of the retinal vessels. 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, although this is not always the case. 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. 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.

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

All variables were calculated by one-way ANOVA.
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. 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. Consistent with several studies, we observed no difference in FAZ area between the three groups (Table II). However, the FAZ area can be influenced by many other factors, such as age, gender, axial length, and choroidal thickness. 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. 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. 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. 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. 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 (e.g., in some studies, the CC flow was not related to axial length or spherical equivalent).
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. 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.

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. 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. 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.

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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.

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References


