Characteristics of the peripapillary structure and vasculature in patients with myopic anisometropia

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Abstract

Background

To evaluate the interocular differences of the peripapillary structural and vascular parameters and that of association with axial length (AL) in participants with myopic anisometropia using swept-source optical coherence tomography (SS-OCT).

Methods

This prospective cross-sectional study included 88 eyes of 44 participants. Eyes were classified into the longer and the shorter eye group according to ALs. The $\beta$- and $\gamma$-parapapillary atrophy (PPA) areas, Bruch’s membrane opening distance (BMOD), border length (BL), and border tissue angle (BTA) were measured manually. MATLAB software determined peripapillary choroidal vascularity index (CVI) and choroidal thickness (CT) values in superior, nasal, inferior, and temporal.

Results

The interocular difference in spherical equivalent (SE) was highly correlated with that of the AL. The $\beta$- and $\gamma$-PPA areas, BMOD, and BL were greater in longer eyes. The mean and inferior peripapillary CVI and the mean, superior, and inferior peripapillary CT were lower in the longer eye group. The interocular difference in AL was significantly positively correlated with the $\gamma$-PPA area and BL and negatively correlated with the temporal CVI and mean, inferior, and temporal peripapillary CT. There was an independent correlation between the interocular differences in AL and the $\gamma$-PPA area, inferior and temporal peripapillary CT.

Conclusions

Significant differences between both groups were detected in most peripapillary parameters. The $\gamma$-PPA area, BL, and peripapillary CVI and CT were sensitively affected by the elongation of AL. The characteristics of peripapillary parameters may be useful in the prediction of AL elongation.

Background

Myopia is an increasingly common visual disorder worldwide, particularly in East Asia. (1–3) Most myopia is considered a failure of emmetropization owing to asymmetrically excessive ocular axial elongation. (1, 4–7) Uneven mechanical or optical factors can induce unequal ocular growth, which can lead to myopic anisometropia. (6) Myopic anisometropia causes several visual function disorders and myopia-related complications, such as diplopia, decreased stereopsis, and even amblyopia in the more myopic eye. (6, 8) Recently, myopic changes in the optic nerve head (ONH) have attracted significant
interest. (9–11) There are a series of retinal and choroidal complications surrounding the ONH, such as choroid neovascularization, optic disc tilted and rotation, and the parapapillary temporal crescent of chorioretinal atrophy. (12–14) Anisometropia is also associated with alterations in ONH morphology. (6, 15, 16) Serious anisometropia is always parallel with abnormal ocular development, leading to retinal and choroidal disorders, such as optic nerve hypoplasia (17) and unilateral extensive myelination. (18) Therefore, it is necessary to investigate the peripapillary characteristics of anisometric patients to demonstrate the potential mechanisms of myopia.

Previous studies have identified that some structural ONH changes in myopic eyes were associated with the progressive mechanical stretch of the globe posterior, such as parapapillary atrophy (PPA), nasal elevation (ie, superior traction), tilted and rotated discs, and scleral deformation between the macular and the ONH. (11, 13, 19–22) However, the characteristics of ONH in myopic asymmetrical ocular growth remain unknown. (23–27) With the advent of swept-source optical coherence tomography (SS-OCT) technology, visualization of a larger area with reduced motion artifact and better visualization of the choroidal vasculature system is possible. (23) SS-OCT has been widely applied in studies on myopia and ocular diseases centered on the fovea. (2, 28–34) However, despite the advantages of these techniques, knowledge concerning the characteristics of the peripapillary structure and vasculature using SS-OCT is limited.

In this study, we assessed the characteristics of the β- and γ-PPA areas, Bruch's membrane opening distance (BMOD), border length (BL), border tissue angle (BTA), peripapillary choroidal vascularity index (CVI), and choroidal thickness (CT) in patients with myopic anisometropia. In addition, we analyzed the relationship between interocular differences in these parameters and axial length (AL). This method of examining interocular differences in both eyes of the same individual minimizes the confounding effects of individual parameters such as age, sex, and gender; thus, typical results could be found in a smaller sample size. (2, 6, 28) This study aims to demonstrate the myopic anisometric changes in the peripapillary structure and vasculature.

Methods

Participants

This study was approved by the Ethics Committee of the Eye Hospital affiliated with Wenzhou Medical University. All the procedures in this study adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all the participants. A total of 45 participants were enrolled from among patients who had visited the Refractive Surgery Center at the Affiliated Eye Hospital of Wenzhou Medical University, Hangzhou, between October 2021 and January 2022.

The inclusion criteria were as follows: age between 18 and 40 years old; spherical equivalent (SE) between −8.00 diopters (D) and −1.00 D in the longer eye group and between −7.00 D and 0.00 D in the shorter eye group; myopic anisomyopes with an interocular difference in SE of at least 1.00 D and less.
than 3.00 D; best-corrected visual acuity (BCVA) of 0.00 log minimum angle of resolution (logMAR, Logarithm of the Minimum Angle of Resolution) or better in each eye (28); stable myopia for more than two years; intraocular pressure (IOP) of 21 mmHg or less; and normal ONH without glaucomatous changes, such as neuroretinal rim narrowing and peripapillary hemorrhage. The exclusion criteria were as follows: compliments of pathological myopia, including posterior staphyloma, lacquer cracks, and myopic choroidal neovascularization; vitreoretinal disorders such as macular holes or chorioretinal atrophy (35); previous intraocular or refractive surgery; and history of ocular or systemic diseases, including congenital cataract and glaucoma, hypertension, and diabetes. (36) Both eyes of all participants were included for statistical analysis.

Ophthalmic Examination And Measurements

All participants enrolled in this study underwent a series of ophthalmic screening examinations, including non-cycloplegic subjective refraction measurements, ocular health evaluations, and non-connected IOP measurements. (2) Subjective refractive indices were obtained by a trained optometrist (Wu et al., 2021). Refractive data were converted to SE, which was calculated as the spherical dioptric power plus half the cylindrical dioptric power. (30) The ocular health evaluations were conducted by an experienced ophthalmologist (CD).

The enrolled participants were instructed to undergo a comprehensive ophthalmologic evaluation after screening. Ocular biometric parameters were measured using IOL Master (Zeiss 700; Carl Zeiss Meditec, Inc, Dublin, CA), (30) including central corneal thickness (CCT), anterior chamber depth (ACD), lens thickness (LT), and AL. The vitreous chamber depth (VCD) was defined as AL − (CCT + ACD + LT). The choroidal and peripapillary structures were measured using SS-OCT. (2) All measurements were conducted between 9 AM and 4 PM.

Swept-source Optical Coherence Tomography Image Acquisition And Analysis

The commercial SS-OCT device (VG200; SVision Imaging, Ltd., Henan, China) contained an SS laser with a central wavelength of approximately 1050 nm (990–1100 nm full width) and a scanning rate of 200,000 A-scans per second. (37) Detailed information on the acquisition protocols for this device has been previously reported. (2, 28, 30, 38) Based on a review by an experienced researcher, OCT and OCTA images were selected according to the following exclusion criteria: (1) signal score < 6, (2) poor clarity, (3) residual motion artifacts visible as irregular vessel patterns or disc boundary on en face angiogram, (4) local weak signal, and (5) choroidal-layer segmentation unclarity. (39, 40)

The en face images were acquired from an ONH of 6×6 mm² (Fig. 1A1). The β-PPA area was defined as the size of the zone with complete retinal pigment epithelium (RPE) loss with the presence of Bruch’s membrane (BM). The γ-PPA area was defined as the size of the zone without the BM (Fig. 1A2, A3). The structural OCT B-scan image was acquired by focusing on the intersection of the longest axial and
shortest axial of the ONH. Both ends of the Bruch's membrane opening (BMO) were marked, and the two points were connected to draw the BMO reference plane. The distance between these two points in the BMO was defined as the BMOD. BL was measured and defined as the distance between the temporal BMO point and the border tissue and scleral end where the BM was absent, provided there was border tissue at the temporal parapapillary optic disc (Fig. 1B). BMOD and BL were measured using the SS-OCT software. The BTA was defined as the angle between the BMOD and BL planes and was measured using the ImageJ image processing software (available at http://rsb.info.nih.gov/ij/index.html). (11, 21) The image size was adjusted for differences in magnification owing to the difference in AL among the eyes. (2, 28)

The choroidal area on OCT was defined as the zone between the RPE-BM complex and the lower border of the light pixels at the choroid-scleral interface. (39) The CVI was defined as the ratio of vascular area to the total choroidal area. (25) CT was defined as the thickness of the choroidal area. Peripapillary CVI and CT were measured based on a 3.4 mm-sized ONH circular scan (Fig. 1C1) using MATLAB R2021a (MathWorks, Natick, MA, USA). (2, 28) After segmenting semi-automatically, the borders of the choroidal area were adjusted. The CVI and CT of each region were calculated following binarization with Niblack's autolocal threshold. (2) The circular B-scan image was separated into five regions, including superotemporal (TS), superior (S), nasal (N), inferior (I), and inferotemporal (TI) regions from left to right in the right eye; this order was reversed in the left eye. The TS and TI regions were combined into a single temporal (T) region (Fig. 1C2, C3).

Statistical Analysis

Statistical analysis was performed using SPSS Statistics 25.0 (IBM, Armonk, NY, USA). All continuous variables were presented in two forms: means and standard deviations and 95% confidence intervals (CI). Normality of the data was evaluated using the Shapiro-Wilk test. Two-way repeated-measures ANOVAs were performed to analyze the peripapillary choroidal parameters, including analyses of two factors (eyes and regions). Bonferroni adjustments for multiple comparisons were applied to adjust the $P$-value. Paired t-tests or Wilcoxon signed-rank tests were used to assess interocular differences between the eyes of individuals. The interocular differences were calculated by subtracting the shorter eye from the longer eye. Pearson’s correlation or Spearman’s correlation was used to calculate the degree and statistical significance of the associations between the interocular AL differences and other parameters. A multiple linear regression model was established to explore the association between the interocular differences in AL and interocular differences in parameters that were significantly correlated with AL. All $P$ values were two-sided, and $P<0.05$ were considered significant.

Results

Demographic Data
Owing to one case of missing data, forty-four patients (88 eyes) were enrolled in this study. Eleven were male patients (25.00%) and 33 were female patients (75.00%). The mean patient age was 27.58 ± 5.81 yrs (18 to 39 yrs).

There were significant interocular differences in terms of SE, AL, ACD, LT, and VCD. Compared to the shorter eye group, the longer eye group had lower SE and LT ($P < 0.001$ and $P = 0.044$, respectively) and higher AL, ACD, and VCD (all $P < 0.001$). No significant differences were found in IOP and CCT between eyes ($P = 0.945$ and 0.308, respectively) (Table 1).

### Table 1

**Ocular Biometrics Parameters in Myopic Anisometropic Patients**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Longer Eye Group (N = 44)</th>
<th>Shorter Eye Group (N = 44)</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>95% CI</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>SE (D)</td>
<td>-5.43 ± 1.79</td>
<td>-5.98 ~ -4.88</td>
<td>-3.80 ± 1.98</td>
</tr>
<tr>
<td>IOP (mmHg)</td>
<td>13.81 ± 2.92</td>
<td>12.92 ~ 14.71</td>
<td>13.74 ± 2.92</td>
</tr>
<tr>
<td>AL (mm)</td>
<td>25.58 ± 0.93</td>
<td>25.29 ~ 25.86</td>
<td>24.96 ± 0.98</td>
</tr>
<tr>
<td>ACD (mm)</td>
<td>3.64 ± 0.26</td>
<td>3.57 ~ 3.72</td>
<td>3.61 ± 0.25</td>
</tr>
<tr>
<td>LT (mm)</td>
<td>3.72 ± 0.20</td>
<td>3.65 ~ 3.78</td>
<td>3.73 ± 0.20</td>
</tr>
<tr>
<td>CCT (µm)</td>
<td>535.28 ± 36.24</td>
<td>524.13 ~ 546.43</td>
<td>536.44 ± 35.78</td>
</tr>
<tr>
<td>VCD (mm)</td>
<td>17.68 ± 0.91</td>
<td>17.40 ~ 17.96</td>
<td>17.08 ± 0.97</td>
</tr>
</tbody>
</table>

SD, standard deviation; CI, confidence interval; SE, spherical equivalent; D, diopter; IOP, intraocular pressure; AL, axial length;

CCT, central corneal thickness; ACD, anterior chamber depth; LT, lens thickness; VCD, vitreous chamber depth.

* $P$-value determined using the paired $t$-test;

† $P$-value determined using the Wilcoxon signed-rank test.

**Interocular Differences In Peripapillary Structure And Vasculature**

The $\beta$- and $\gamma$-PPA areas were both significantly greater in the longer eye group ($P = 0.010$ and $P = 0.001$, respectively). Larger BMOD and BL were found in longer eyes than in shorter eyes ($P = 0.009$ and $P = 0.016$, respectively). There was no significant difference in the BTA ($P = 0.718$) (Table 2).
<table>
<thead>
<tr>
<th>Peripapillary Structural Parameters</th>
<th>Mean</th>
<th>Range</th>
<th>Mean</th>
<th>Range</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β-PPA area (mm²)</strong></td>
<td>0.48 ± 0.29</td>
<td>0.39 ~ 0.57</td>
<td>0.40 ± 0.46</td>
<td>0.26 ~ 0.54</td>
<td>0.010†</td>
</tr>
<tr>
<td><strong>γ-PPA area (mm²)</strong></td>
<td>0.69 ± 0.35</td>
<td>0.59 ~ 0.80</td>
<td>0.53 ± 0.37</td>
<td>0.42 ~ 0.65</td>
<td>0.001†</td>
</tr>
<tr>
<td><strong>BMOD (µm)</strong></td>
<td>1796.70 ± 260.90</td>
<td>1716.41 ~ 1876.99</td>
<td>1714.60 ± 290.90</td>
<td>1625.07 ~ 1804.12</td>
<td>0.009†</td>
</tr>
<tr>
<td><strong>BL (µm)</strong></td>
<td>461.61 ± 222.70</td>
<td>393.08 ~ 530.15</td>
<td>363.98 ± 274.15</td>
<td>279.61 ~ 448.35</td>
<td>0.016†</td>
</tr>
<tr>
<td><strong>BTA (°)</strong></td>
<td>42.05 ± 17.64</td>
<td>36.62 ~ 47.47</td>
<td>41.77 ± 24.74</td>
<td>34.15 ~ 49.38</td>
<td>0.718†</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Peripapillary Choroidal Vascularity Index (%)</th>
<th>Mean</th>
<th>Range</th>
<th>Mean</th>
<th>Range</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean</strong></td>
<td>50.14 ± 4.85</td>
<td>48.65 ~ 51.64</td>
<td>51.80 ± 4.93</td>
<td>50.29 ~ 53.32</td>
<td>0.016*</td>
</tr>
<tr>
<td><strong>Superior</strong></td>
<td>51.26 ± 5.51</td>
<td>49.56 ~ 52.96</td>
<td>52.81 ± 4.97</td>
<td>51.28 ~ 54.34</td>
<td>0.333†</td>
</tr>
<tr>
<td><strong>Nasal</strong></td>
<td>52.07 ± 5.15</td>
<td>50.49 ~ 53.66</td>
<td>53.31 ± 6.18</td>
<td>51.41 ~ 55.22</td>
<td>0.587*</td>
</tr>
<tr>
<td><strong>Inferior</strong></td>
<td>51.05 ± 5.86</td>
<td>49.24 ~ 52.85</td>
<td>52.97 ± 6.41</td>
<td>51.00 ~ 54.95</td>
<td>0.030*</td>
</tr>
<tr>
<td><strong>Temporal</strong></td>
<td>45.26 ± 7.20</td>
<td>43.05 ~ 47.48</td>
<td>47.08 ± 7.38</td>
<td>44.81 ~ 49.35</td>
<td>0.178*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Peripapillary Choroidal Thickness (µm)</th>
<th>Mean</th>
<th>Range</th>
<th>Mean</th>
<th>Range</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean</strong></td>
<td>195.24 ± 53.24</td>
<td>178.86 ~ 211.63</td>
<td>216.74 ± 60.08</td>
<td>198.25 ~ 235.23</td>
<td>0.001†</td>
</tr>
<tr>
<td><strong>Superior</strong></td>
<td>221.51 ± 62.78</td>
<td>202.19 ~ 240.83</td>
<td>242.09 ± 70.38</td>
<td>220.43 ~ 263.75</td>
<td>0.021*</td>
</tr>
<tr>
<td><strong>Nasal</strong></td>
<td>212.86 ± 64.91</td>
<td>192.88 ~ 232.84</td>
<td>229.67 ± 58.97</td>
<td>211.53 ~ 247.82</td>
<td>0.099†</td>
</tr>
<tr>
<td><strong>Inferior</strong></td>
<td>182.01 ± 47.92</td>
<td>167.26 ~ 196.75</td>
<td>196.53 ± 54.55</td>
<td>179.74 ~ 213.32</td>
<td>0.060†</td>
</tr>
<tr>
<td><strong>Temporal</strong></td>
<td>165.13 ± 52.62</td>
<td>148.93 ~ 181.32</td>
<td>199.37 ± 77.48</td>
<td>175.52 ~ 223.21</td>
<td>0.000†</td>
</tr>
</tbody>
</table>

PPA, parapapillary atrophy; BMOD, Bruch's membrane opening distance; BL, border length; BTA, border tissue angle.

* P-value determined using the paired t-test;
† P-value determined using the Wilcoxon signed-rank test.
### Peripapillary Structural Parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Longer Eye Group</th>
<th>Shorter Eye Group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>95%CI</td>
<td>Mean ± SD</td>
</tr>
</tbody>
</table>

For peripapillary CVI values, the interactive effect among the eyes and regions was not significant (eyes × regions, $F = 0.376, P = 0.825$). All CVI values were greater in the shorter eye group (Fig. 2A). The mean and inferior CVI values in the shorter eye group were significantly greater ($P = 0.003$ and $P = 0.006$, respectively), whereas no significant differences were found in the superior, nasal, and temporal CVI values ($P > 0.05$) (Table 2).

For peripapillary CT values, the interactive effect among the eyes and regions was significant (eyes × regions, $F = 6.262, P < 0.001$). All CT values were greater in the shorter eye group (Fig. 2B). The mean, superior, and temporal CT values in the shorter eye group were significantly greater than those in the longer eyes ($P < 0.001$, $P = 0.004$, and $P < 0.001$, respectively), whereas no significant differences were found for nasal and inferior CT values ($P > 0.05$) (Table 2).

### Factors Associated With The Interocular Difference In AL

The interocular difference in AL was significantly positively correlated with that in VCD ($r = 0.983, P < 0.001$) and negatively correlated with that in SE ($r = -0.686, P < 0.001$). There was a correlation between γ-PPA ($r = 0.361, P = 0.015$) and BL ($r_s = 0.342, P = 0.023$) and the AL difference. The AL difference was significantly correlated with the temporal CVI values and the mean, inferior, and temporal CT values ($r = -0.295, P = 0.049; r = -0.339, P = 0.023; r = -0.394, P = 0.007$, and $r = -0.504, P < 0.001$, respectively) (Fig. 3).

The AL difference was positively correlated with the area difference of γ-PPA ($P = 0.016$), whereas it was negatively correlated with the interocular difference in the inferior and temporal CT values ($P = 0.015$ and $P = 0.007$, respectively) (Table 3).
Table 3

Multiple Linear Regression Analysis of Interocular Differences in AL and Parameters in Myopic Anisometropic Patients

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Unstandardized Coefficient</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>γ-PPA area (mm²)</td>
<td>0.271</td>
<td>0.06 ~ 0.25</td>
<td>0.016</td>
</tr>
<tr>
<td>BL (µm)</td>
<td>0.000</td>
<td>11.98 ~ 183.29</td>
<td>0.780</td>
</tr>
<tr>
<td>CVI _ Temporal (%)</td>
<td>-0.007</td>
<td>-3.78 ~ 0.15</td>
<td>0.158</td>
</tr>
<tr>
<td>CT _ Mean (µm)</td>
<td>0.002</td>
<td>-31.78 ~ -11.21</td>
<td>0.157</td>
</tr>
<tr>
<td>CT _ Inferior (µm)</td>
<td>-0.002</td>
<td>-26.24 ~ -2.80</td>
<td>0.015</td>
</tr>
<tr>
<td>CT _ Temporal (µm)</td>
<td>-0.003</td>
<td>-48.80 ~ -19.68</td>
<td>0.007</td>
</tr>
</tbody>
</table>

CI, confidence interval; PPA, parapapillary atrophy; BL, border length; CVI, choroidal vascularity index; CT, choroidal thickness.

Discussion

In the current study, SS-OCT was used to investigate the relationship between the interocular difference in AL and the peripapillary structure and vasculature in patients with myopic anisometropia. The results showed that the areas of β-PPA, γ-PPA, BMOD, and BL were significantly larger in the longer eye group than in the shorter eye group. In contrast, the mean and inferior peripapillary CVI values and the mean, superior, and temporal peripapillary CT values were significantly lower in the longer eye group. The interocular AL difference was significantly positively correlated with the γ-PPA area and BL, whereas it was significantly negatively correlated with the temporal CVI and the mean, inferior, and temporal CT. Moreover, the AL difference was positively associated with the γ-PPA area difference and negatively correlated with the interocular differences in inferior and temporal CT.

In recent years, OCT technology has been developed with increasing demand for choroidal visualization. Compared to conventional SD-OCT, SS-OCT makes it possible to obtain detailed information on the choroid-scleral interface owing to its faster scan rate and tunable swept laser enabling longer wavelengths. Moreover, SS-OCT reduces motion artifacts and permits high-speed, high-resolution imaging and better visualization of the ONH. (23, 24, 41) In addition, SS-OCT showed excellent repeatability and reproducibility in ONH parameters. (42) Therefore, the current study used SS-OCT to analyze ONH characteristics in myopic anisometropia.

We found that the areas of β-PPA and γ-PPA were significantly larger in longer eyes, and the interocular difference in the γ-PPA area was positively correlated with that of AL. Previous studies have demonstrated that with the elongation of the ocular axis, retinal stretching might not be the same as scleral growth, resulting in scleral slipping to the retina. (43) Some clinical studies showed that the β-PPA...
was associated with glaucoma and myopia, whereas the γ-PPA was merely associated with myopia. (44, 45) Kyoung Min Lee suggested that the enlargement of the β-PPA during axial elongation was affected by the extent and direction of vascular trunk dragging, thus implicating disproportionate growth between the retina and sclera. (46) In this study, our findings suggested that the changes in the PPA area mostly resulted from myopic ocular axial elongation, as all participants enrolled in the study were not diagnosed with glaucoma. These results are similar to those of the previous studies. However, we hypothesized that the longer eye in myopic anisometropic adults might be more vulnerable to glaucomatous damage owing to the increasing β-PPA area. It might be necessary to monitor the IOP and screen for glaucoma regularly in myopic anisometropic adults.

We found that the BMOD and BL were significantly greater in the longer eye group than in the shorter eye group. However, there was no significant interocular difference between the BTA and AL groups. Kim conducted a longitudinal observational study of 23 myopic children. They found that the nasal BL increased and the BTA decreased, whereas the BMOD was relatively stable when the ONH structure was changed by axial elongation. (11) Aarti Patel evaluated the longitudinal changes of ONH parameters in 352 full-time infants and children and reported that the BMOD showed an increasing trend without statistical significance during the development of myopia. (47) In our study, the interocular difference in BMOD was significant. We believe that the different findings in BMOD were caused by differences in the participants.

Few investigations have focused on peripapillary CVI values in patients with myopic anisometropia. In this study, we found significant differences in the peripapillary CVI values between eyes of myopic anisometropic patients. We found that the mean and inferior peripapillary CVI values were significantly lower in the longer eye group, and a negative correlation between the temporal CVI and AL difference was also found. These findings suggest that the temporal peripapillary CVI may be a predictor of asymmetric ocular axial elongation.

Previous studies on peripapillary CT values in myopic eyes remain controversial. Bitirgen evaluated peripapillary CTs in children with unilateral hyperopic anisometropic amblyopia using SD-OCT and found that hyperopic amblyopic eyes had significantly higher CT values in all regions compared to control eyes. In addition, differences in average, temporal, and inferior peripapillary CT values were still significant after adjusting for the effects of AL. (48) Dongmei Cui compared the peripapillary CT in young myopic patients and found that the superonasal CT was the thickest and the inferotemporal CT was the thinnest. (49) Martha Kim reported that the global and sectoral peripapillary CT and the retinal nerve fiber layer were not changed in myopic patients during myopic axial elongation and for 4 years. (50) Our results were similar to the results proposed by Gulfidan Bitirgen and Dongmei Cui. In our study, we found that the peripapillary temporal and inferior CT values were thinner than the peripapillary superior and nasal CT values. The mean, superior, and temporal peripapillary CT values were significantly greater in the shorter eye group than in the longer eye group. In addition, there was a significant association between the interocular differences in the mean, temporal, and inferior peripapillary CT values and AL. The dysfunction of the whole choroid was obvious, despite the SE interocular difference being strictly maintained between 1.00
D to 3.00 D. We propose that interocular differences in peripapillary CT result from AL differences. In addition, peripapillary CT values may be more sensitive parameters than peripapillary CVI values.

The choroid is one of the most vascularized structures in the human body, supplying most of the blood, nutrients, and oxygen to the retina. (14, 24, 51) More evidence has shown two other functions of the choroid: adjusting the position of the retina by changing the CT and releasing growth factors to regulate the modulation of vascularization and scleral remodeling, as well as promoting ocular growth. (52, 53) Variations in CT may be predominantly driven by changes in choroidal blood flow, given that the choroid is essentially a vascular structure capable of quickly altering blood flow. Thus, reduced choroidal blood flow may contribute to scleral ischemia and hypoxia, resulting in abnormalities in the scleral structure and myopia. (28, 52, 53) We hypothesize that the choroid grows unevenly during myopic development, thereby changing the position of the retina by adjusting the CT and blood flow and thus leading to unequal excessive ocular axial elongation.

The main limitation of this study was the relatively small sample size. Further studies with a larger sample size are needed to confirm these results. Second, SS-OCT analysis may not accurately represent histological changes in myopia. However, further animal studies are required.

Conclusions

A strong relationship was found between interocular differences in AL and ONH parameters in myopic anisometropic adults. These findings may provide new insights into the role of the choroid in the development of human myopia. Further longitudinal investigations are necessary regarding the predictive value of decreased peripapillary CVI and CT values with increased asymmetry of ocular axial elongation. Early interventions can be aimed at delaying the development of myopia.

Abbreviations

ONH
optic nerve head
PPA
parapapillary atrophy
SS-OCT
swept-source optical coherence tomography
BMOD
Bruch's membrane opening distance
BL
border length
BTA
border tissue angle
CVI
Declarations

Ethics approval and consent to participate

The design and procedure of this research adhered to the principles of the Declaration of Helsinki. This study was approved by the Ethics Committee of the Eye Hospital affiliated with Wenzhou Medical University (No. 2019-078-K-77). Written informed consent was obtained from each participant.

Consent for publication

Not applicable.

Declarations

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YQ: data collection, statistical analysis, and writing the manuscript; DC: statistical analysis and writing the manuscript; KR, JY: analysis and interpretation; ZZ, YQ: statistical analysis; WG, MW, XZ, YY: data collection and critical revision; MS: software technical support and data analysis; LS: conception, design, and critical revision.

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References


Unsectioned Figure Details

A

Fig. 1
Measurement of peripapillary structural and vascular parameters. The measurement method using the right eye as an example. A. Determination of the β- and γ-parapapillary atrophy (PPA) areas. The orange, white and blue lines present the boundaries of the retinal pigment epithelium (RPE), Bruch's membrane (BM), and optic disc edge, respectively (A1 and A2). The β-PPA is marked in light green and the γ-zone PPA is marked in dark green (A3). B. Measurement of the Bruch's membrane opening (BMO) distance, border length (BL), and border tissue angle (BTA). BMO distance (BMOD) was measured as the distance between the two sides of the BMO. The BL was measured as the distance between the temporal BMO end and the scleral end. The BTA was defined as the angle between the BMOD and BL. C. The peripapillary choroidal vascularity index (CVI) and choroidal thickness (CT) were measured from the 3.4-mm-sized ONH circle scan image (C1 and C2) and analyzed using an identified imaging software in MATLAB. CVI and CT values were calculated for five regions, including the superotemporal (TS), superior (S), nasal (N), inferior (I), and inferotemporal (TI) regions. TS and TI were combined into a single temporal (T) region (C3).

A

Fig. 2
Distribution of peripapillary CVI (A) and CT (B) in fellow eyes of myopic anisometricopic patients (N = 44).
A
Fig. 3
Scatter plot of the correlation between the interocular differences in the peripapillary parameters and that of axial length (AL). A. β-PPA area; B. γ-PPA area; C. BMOD; D. BL; E. BTA; F. CVI_Mean; G. CVI_Superior; H. CVI_Nasal; I. CVI_Inferior; J. CVI_Temporal; K. CT_Mean; L. CT_Superior; M. CT_Nasal; N. CT_Inferior; O. CT_Temporal. Regression lines were fitted for the parameters with a significant correlation with the interocular difference in AL. BMOD, Bruch’s membrane opening distance; BL, border length; BTA, border tissue angle; CVI, choroidal vascularity index; CT, choroidal thickness.

Unsectioned Paragraphs

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Figure 2

Figure 3

Figure Legends