Retinal and Choroidal Biometry in Highly Myopic Eyes with Spectral-Domain Optical Coherence Tomography

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PURPOSE. Morphologic changes in the retina and choroid are closely related with high myopia–related diseases. This study was conducted to evaluate the morphologic characteristics of normal highly myopic eyes.

METHODS. Thirty-one phakic highly myopic eyes with no posterior abnormalities (18 patients; mean ± SD age, 51.7 ± 11.4 years) were enrolled. Retinal–choroidal thickness at the fovea 1.5 mm superiorly, inferiorly, nasally, and temporally and the choroidal curvature were measured in the 512 × 128 three-dimensional scan mode with spectral-domain optical coherence tomography. The degree of posterior staphyloma was determined as the sum of the vertical distance from the retinal pigment epithelial line beneath the fovea to the nasal, temporal, superior, and inferior edge of the image, including the fovea. The association of clinical data with these parameters was evaluated.

RESULTS. The mean ± SD central retinal thickness was 200.9 ± 39.3 μm. The mean choroidal thickness at the fovea (100.5 ± 56.9 μm) was significantly different from the temporal (125.4 ± 59.7 μm), nasal (81.9 ± 35.0 μm), and superior (129.4 ± 57.5 μm) thicknesses (P < 0.01). Central retinal thickness did not correlate with age, sex, refractive error, axial length, or central choroidal thickness. Central choroidal thickness was significantly associated with refractive error (P < 0.05) and posterior staphycoma height (P < 0.01). Central retinal thickness correlated significantly with age and posterior staphycoma height (P < 0.01).

CONCLUSIONS. Posterior staphyloma formation was a key factor in choroidal thinning in highly myopic eyes. Choroidal thickness had a greater effect than retinal thickness in highly myopic eyes. (Invest Ophthalmol Vis Sci. 2009;50:3876–3880) DOI:10.1167/iovs.08-3325

Myopic degeneration is a major leading cause of visual impairment in many parts of the world, including Asia, Europe, and in some races in the United States, although the degree of its contribution differs depending on race and country. Specific causes of severe visual loss from high myopia include chorioretinal atrophy, macular holes, and choroidal neovascularization. Among them, chorioretinal myopic atrophy results in photoreceptor cell death and thus an irreversible, progressive, and severe loss of central visual function. Myopic choroidal neovascularization also develops into secondary chorioretinal central atrophy, which eventually causes a large central scotoma. Therefore, myopic chorioretinal atrophy is a very common and serious problem; however, the mechanisms and pathologic course are not well understood.

The process of myopic chorioretinal atrophy, especially at the choroidal level, is not clear. Histopathologic studies in postmortem eyes indicate that occlusion and disappearance of large choroidal vessels and capillaries and consequent replacement of the normal choroidal structure with fibrous tissue are common. Although histopathologic studies provide valuable information toward understanding the pathologic course of the disease that generally cannot be obtained in vivo, there are several challenges. These types of studies are usually performed on extreme cases at an older age, and so there has only been limited investigation of the initial stage of the disease. Further, histopathologic studies cannot provide information about the time course, because the tissue is examined at only one time point. Ideally, therefore, the retinal/choroidal anatomic status should be evaluated in vivo.

The choroid is much less accessible than the retina, and it is therefore difficult to assess the choroidal changes in highly myopic eyes. For example, signals from the choroid are almost totally blocked by retinal pigment epithelium (RPE) in fluorescein angiography, which does not allow for evaluation of the choroidal anatomic and vascular status. Therefore, fluorescein angiography is not helpful in observing the choroid, located behind the RPE.

Another option is confocal indocyanine green angiography, which can provide information about the choroidal vessels. Indocyanine green angiography is useful for observing retinal vessels and various pathologic changes specific to high myopia. Lacquer cracks are strongly associated with choroidal neovascularization in highly myopic eyes. However, indocyanine green angiography is invasive. Also, because the choroid has many vessels with multiple layers, it can be difficult to detect minimal choroidal vascular obstruction/loss, even with careful observation. High-resolution magnetic resonance imaging can be used to monitor the choroid in vivo, but the resolution and accuracy of this technique are not satisfactory.

Spectral-domain optical coherence tomography (SD-OCT) is a powerful modality for investigating the retinal/choroidal structure of highly myopic eyes. The low signal-to-noise ratio and higher scanning speed allows for images with higher resolution and a higher scan density than conventional time-domain OCT. This advantage enables us to observe not only the initial retinal changes, but also the choroidal changes in highly myopia–specific disease. For example, subtle photoreceptor changes, which are difficult to detect with conventional methods, can be detected by SD-OCT in highly myopic eyes. The thinned choroid in such highly myopic eyes can also be observed with this technology.

To evaluate the morphologic changes in highly myopic eyes, we used SD-OCT to measure the choroidal thickness and curvature based on the posterior staphyloma formation in normal highly myopic eyes. We also evaluated the choroidal...
thickness and the key factors associated with choroidal thick-

METHODS

Patients

Thirty-one highly myopic, apparently normal eyes of 18 patients who visited the high-myopia clinic at the Department of Ophthalmology, Osaka University Medical School, were enrolled. The research adhered to the tenets of the Declaration of Helsinki and written, informed consent was obtained from the participants before participation in the study. The inclusion criteria were (1) phakic highly myopic eyes, defined as spherical equivalent refractive error less than −6 D; (2) no posterior abnormality such as choroidal neovascularization, foveoschisis, macular hole, or whitish round atrophy at the fovea; (3) choriotectal change grades 0 to 2, according to the classification by Avila et al.; (4) between the ages of 30 and 80; (5) best corrected visual acuity (BCVA) better than 20/40, to obtain a stable central fixation; and (6) both SD-OCT (Cirrus-HD OCT; Carl Zeiss Meditec, Inc., Dublin, CA) data and axial length measured by an inferometer (IOLMaster; Carl Zeiss Meditec, Inc.). The exclusion criteria were (1) the presence of any pathologic structures such as choroidal neovascularization, macular hole, or foveoschisis at the macula in the fellow eye because they reportedly increase the risk of the disease in the study eye and may affect the retinal/choroidal structural parameters; (2) aphakic or pseudophakic eyes; and (3) the presence of severe cataract preventing detailed fundus observation or glaucoma in the study eye.

Examination

A technician masked to the clinical diagnosis of the patient performed all the examinations such as refractive error and axial length measurements using partial optical coherence interferometry (IOLMaster; Carl Zeiss Meditec, Inc.); SD-OCT was performed in all patients by three masked technicians. The scan patterns included the Macular Cube 512 × 128 Combo protocol. This scan protocol generates a cube of data through a 6-mm square grid by acquiring a series of 128 horizontal scan lines comprising 512 A-scans.

Measurement of Retinal/Choroidal Morphologic Parameters

Retinal/choroidal thickness was measured at the fovea, 1.5 mm superiority, 1.5 mm inferiorly, 1.5 mm nasally, and 1.5 mm temporally, by manually using the scale supplied with the software. Retinal thickness was defined as the vertical distance from the RPE (the outermost hyperreflective line at the retina-choroidal interface) to the retinal surface. The choroidal thickness was defined as the distance from the RPE line to the hyperreflective line behind the large vessel layers of the choroid, presumed to be the choroid-sclera interface. All the eyes showed this clear choroid-sclera interface because they had a thinned choroid. If the retina/choroid was tilted, the distance was measured right to this RPE line.

The degree of posterior staphyloma was measured in the OCT image. The posterior staphyloma height was defined as the distance from the RPE line beneath the fovea to the nasal and temporal edge of the horizontal scan and superior and inferior vertical scan including the fovea. The sum of these four measurements was used as posterior staphyloma height in this study (Fig. 1).

Statistical Analysis

The data were analyzed by using a paired t-test, one-way analysis of variance (ANOVA) with Tukey’s post-hoc analysis, or multiple stepwise regression analysis (JMP statistical software package, ver. 7.0; SAS Institute Inc, Cary, NC). $P < 0.05$ was considered to indicate a significant difference.

RESULTS

Patient Demographic Data

Study participants included 5 men and 13 women with a mean age of 51.7 ± 11.4 years (range, 33–75). The median value of best-corrected visual acuity was 1.2 (range, 0.5–1.5). The mean spherical equivalent refractive error and axial length were −15.5 ± 4.3 D (range −6.0 to −23.0 D) and 29.6 ± 1.8 mm (26.21–33.56 mm), respectively.

Retinal Thickness

Table 1 shows the retinal thickness data at the fovea and 1.5 mm from the center temporally, nasally, superiorly, and inferiorly. Retinal thickness was thinnest at the central fovea, and thickest at the nasal side. The thickness of the retina surrounding the fovea was almost 150% that of the fovea, and the retinal thickness was significantly greater at all the other four points compared with that of the central fovea. One-way ANOVA revealed no significant differences in the thickness between the four surrounding points. That is, retinal thickness was similar at the surrounding points.

Choroidal Thickness

Table 2 shows the choroidal thickness data. The mean choroidal thickness was thinnest at the nasal quadrant, greatest at the temporal quadrant, followed by the superior and inferior quadrants. Choroidal thickness at the fovea was significantly greater than that at the nasal quadrant, but significantly lower than that at the temporal and superior quadrants. One-way ANOVA revealed significant differences among the four quadrants.

<table>
<thead>
<tr>
<th>Location</th>
<th>Retinal Thickness (μm)</th>
<th>% Thickness (vs. Central Fovea)</th>
<th>$P$ vs. Fovea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fovea</td>
<td>201.2 ± 40.6</td>
<td>100</td>
<td>NA</td>
</tr>
<tr>
<td>Temporal</td>
<td>290.1 ± 38.3</td>
<td>150.0 ± 37.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Nasal</td>
<td>298.1 ± 30.8</td>
<td>154.1 ± 39.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Superior</td>
<td>279.0 ± 41.1</td>
<td>142.2 ± 24.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Inferior</td>
<td>286.9 ± 46.7</td>
<td>147.0 ± 32.9</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
Tukey’s test revealed a significant difference between superior and nasal quadrant thickness.

**Posterior Staphyloma Height**

Posterior staphyloma height measured on the OCT image was 515 ± 239 \( \mu \text{m} \) temporally, 436 ± 566 \( \mu \text{m} \) nasally, 636 ± 375 \( \mu \text{m} \) superiorly, and 317 ± 492 \( \mu \text{m} \) inferiorly. One-way ANOVA indicated a significant difference among the four quadrants \((P < 0.05)\). Tukey’s test indicated that the height of the superior staphyloma was significantly greater than that of the inferior staphyloma.

**Simple Regression Analysis**

A simple regression analysis for retinal thickness is shown in Table 3. No factors, such as age, refractive error, axial length, foveal choroidal thickness, and posterior staphyloma height, were significantly related with foveal retinal thickness. A simple regression analysis for foveal choroidal thickness is shown in Table 4. Axial length did not correlate with foveal choroidal thickness. Refractive error and posterior staphyloma height correlated significantly, and the factor of age tended to be significant. The factors associated with posterior staphyloma height are shown in Table 5. Posterior staphyloma height did not correlate with age, but correlated significantly with refractive error and axial length.

**Stepwise Multiple Regression Analysis**

A stepwise multiple regression analysis was performed to determine the most important explanatory variables among age, sex, refractive error, axial length, posterior staphyloma height, and retinal/choroidal thickness. None of these factors correlated significantly with retinal thickness. Posterior staphyloma height \((P < 0.01)\) and age \((P < 0.05)\) correlated significantly with choroidal thickness \((R^2 = 0.52)\), but not with error or axial length. Axial length correlated, however, with posterior staphyloma height \((P < 0.01, R^2 = 0.50)\).

**Discussion**

Recently developed technologies enable more accurate measurements of choroidal thickness. In highly myopic eyes, the mean choroidal thickness measured histopathologically is 220 \(\mu \text{m}\).\(^{16}\) Enhanced depth imaging of SD-OCT, however, allows for clear detection of the choroid-retina and choroid-scleral interface and for the total choroidal thickness to be measured in vivo. Using this method, the mean choroidal thickness under the fovea was 308 \(\mu \text{m} \) in healthy volunteers.\(^{17}\) Partial coherence interferometry technology is another useful modality for obtaining axial length measurements and intraocular calculations for cataract surgery (IOLMaster; Carl Zeiss Meditec, Inc.). If choroidal thickness is defined as the distance between the two peaks (P3 and P4), mean choroidal thickness is 307 \(\mu \text{m}\).\(^{18}\) There is still limited access to these technologies, and thus their wide application in observational studies remains challenging.

Commercial SD-OCT uses an 830-nm infrared light source, which has high reflectivity and scattering at the RPE/Bruch’s membrane interface. This fact makes observations of the deep choroid difficult because the signal is attenuated, thus limiting studies of the deep choroid with OCT. Highly myopic patients, however, usually have choroidal thinning, which facilitates detection of the scleral interface. Taking advantage of this characteristic, we attempted to measure choroidal thickness using the commercially available SD-OCT (Cirrus HD-OCT; Carl Zeiss Meditec, Inc.). Our experience suggests that the scleral interface is generally undetectable in eyes with a choroidal thickness greater than 300 \(\mu \text{m} \). None of the study eyes in patients between the ages of 30 to 80, however, had such a thick choroid. Therefore, the results of the present study indicate that choroidal thickness is partly age dependent. Measuring the choroidal thickness in younger patients is difficult, however, because of signal loss. The new generation OCT with a 1-\(\mu \text{m}\)-wavelength band has greater penetration through the RPE-Bruch’s membrane interface,\(^{19,20}\) and may therefore be capable of detecting the scleral interface in young healthy eyes.

SD-OCT was widely used to measure the retinal thickness in retinal thickening disease such as diabetic macular edema. The quantification of the retinal thickness facilitates the evaluation of the disease severity or comparison of the efficacy of treatment options.\(^{21}\) Thus, retinal thickness OCT has become a routine examination in a clinical setting.\(^{22}\) However, a single B-scan is still questionable for representing diseases of a whole macula. Automatic volume measurement by three-dimensional analysis that SD-OCT provides is advantageous in this point. The volume analysis of the choroid would be useful for quantitating the thickness or thinning of the whole choroidal; however, there is no algorithm available for automatic detection of the choroid-scleral interface.
In the present study, mean foveal retinal thickness was 201.2 μm. Another study reported a mean retinal thickness of 258 μm within the 500-μm circle of the fovea in normal subjects using the Cirrus HD-OCT.\textsuperscript{23} We did not use the automated segmentation and thickness measurements of the Cirrus HD-OCT, but rather a manual method to measure the thickness specifically of the central fovea; thus, the foveal thickness in our study is thinner than that found in the other studies. Our study did not include normal subjects as the control, and therefore, we did not examine the difference between highly myopic eyes and nonmyopic eyes with our manual-based method.

Neither refractive error nor axial length was significantly associated with retinal thickness in our study. Previous studies revealed a significant negative correlation between axial length or refractive error and macular thickness on OCT images in adults\textsuperscript{24,25} and children.\textsuperscript{26} The correlation coefficient is low, however, ranging from 0.1 to 0.3. One reason for the disagreement between studies may be that we analyzed a smaller number of subjects. In addition, previous studies used the older version of the OCT, the Stratus, rather than the Cirrus. Because the Stratus is a time-domain OCT and has a different protocol for macular thickness analysis, the thickness is less than that obtained with the Cirrus-HD OCT.\textsuperscript{27} Finally, previous studies used A-scan ultrasound for axial length measurements, and we used partial coherence interferometry. Ultrasound detects the inner surface of the retina as a peak, whereas partial coherence interferometry detects the RPE. These differences may have affected our results and may be why we failed to detect statistically significant correlations. Further studies with a larger number of subjects are needed to clarify this point.

Posterior staphyloma is recognized as a protrusion of the posterior shell of the eye globe, and is a hallmark of high myopia. Several studies have demonstrated that posterior staphyloma formation is closely related to posterior retinal diseases, including macular hole retinal detachment and myopic foveoschisis.\textsuperscript{27–29} This association is probably because deeper posterior staphyloma generates greater inward vector force to detach or split the neural retina, which is facilitated by vitreous cortex shrinkage, epiretinal membrane, or rigid internal limiting membrane.\textsuperscript{30–32} Thus, posterior staphyloma is believed to cause various pathologies in high myopia-specific diseases.

These findings suggest that studies of choroidal disease are useful toward understanding the process of consequent atrophic changes. Further, the quantification of biometric changes is very helpful for monitoring the progression and estimating the relative risks for future development of the disease. In the present study, posterior staphyloma height was strongly correlated with choroidal thinning. Ultrasonography-based posterior staphyloma depth is well correlated with the degree of lacquer cracks, conus, RPE defect, and choroidal atrophy.\textsuperscript{33} We demonstrated that posterior staphyloma height correlates well with axial length and refractive error. Thus, this newly developed parameter of posterior staphyloma height appears to be a good indicator for risk management of choroidal thinning and posterior staphyloma formation, but its correlation with myopia-specific disease must be further investigated.

Of interest, the pattern of choroidal thickness was unique, depending on its location. The nasal choroid was the thinnest, followed by the central foveal and inferior choroid, and then the temporal and superior choroid. One possible reason for this is the watershed zone of the choroid that is typically recognized as a hypofilling area of the choroid in angiography.\textsuperscript{34} The watershed zone indicates the isolation of a choroidal capillary bed supplied by an independent posterior ciliary artery (PCA) that does not anastomose with another end artery, making it prone to ischemia. From one to five PCA branches arise from the ophthalmic artery.\textsuperscript{34} There are many interindividual variations, but the posterior choroid is supplied by two major PCAs, the lateral and medial PCA, in approximately 90% of eyes.\textsuperscript{35} A watershed zone between the medial and lateral PCA is observed vertically between the macula and optic nerve head in 60% of eyes.\textsuperscript{34} Also, the lateral watershed zone is sometimes observed horizontally at the macula. Another possibility is an embryologic event. The optic fissure is closed at the nasal and subfoveal choroid. It remains uncertain why the inner choroid was thinner than the superior choroid. A superior PCA is observed in 10% of eyes, which may be why the superior choroidal thickness was well preserved. Our data indicated that inferior posterior staphyloma height was significantly less than the superior height. Thus, posterior staphyloma expansion seems to be asymmetrical. Better knowledge of the mechanisms of thinning is crucial for understanding myopic disease. Further investigation is needed to clarify the mechanisms and pathogenesis of high myopia disease.

Another interesting point is that, after posterior staphyloma height, choroidal thinning correlated with age. Ramrattan et al.\textsuperscript{36} investigated 95 normal eyes with a histologic approach and found a significantly negative correlation between age and choroidal thickness. Although the association was significant (\textit{p} < 0.01), the correlation coefficient was only 0.18, indicating a weak correlation. Similarly, in the present study, only borderline significance was detected between age and choroidal thickness in simple regression analysis. It is also noteworthy that choroidal thickness correlated strongly with posterior staphyloma height, but posterior staphyloma had no correlation with age. These observations lead us to hypothesize that choroidal thinning is dependent on staphyloma formation and aging, both of which are independent factors.

References


