Abstract

Introduction: This study describes the pathologic changes in the retina of a group of young Asian subjects with myopia worse than –10 diopters spherical equivalent (SE) refraction.

Materials and Methods: The study population consists of 20 male subjects undergoing pre-employment screening for public service for a 1-year period from 2009 to 2010. A detailed series of visual tests of function, fundus examination and grading, ocular biometry and posterior segment optical coherence tomography were performed for all eyes. Results: A total of 21 eyes with mean SE of –10.88 diopters, [standard deviation (SD), 1.28 diopters], and mean age of 21.8 years (SD, 1.3 years) were included. Out of 21 eyes, 17 (81.0%) had beta peripapillary atrophy, 10 (47.6%) had clinically detectable optic disc tilt, 1 (4.8%) had positive T-sign and 18 (85.7%) had retinal tessellation, 4 (19.0%) had posterior vitreous detachment and 14 (66.7%) had peripheral retina degeneration. The mean retinal nerve fibre layer (RNFL) thickness was 92.48 mm (SD, 9.99 mm). Conclusion: None of the 21 highly myopic eyes had features of myopic retinopathy but most of these young males had clinically visible myopia-associated abnormalities of the optic disc, vitreous and peripheral retina. Generally, these eyes had thinner RNFL. Further longitudinal studies are required to investigate if these eyes will eventually develop complications of pathological myopia.
tomography (OCT) correlates inversely with axial length and myopia.\textsuperscript{15,16} However, little is known about the structural changes in the retina of eyes with extremely high myopic refraction that were more than 10 diopters (D) and its associated functional changes. We aim to describe the pathologic changes in the retina of a group of young males with myopia that were worse than \(-10.00\) D.

**Materials and Methods**

The study population consists of 20 young males who are subjects undergoing pre-employment screening for public service for a 1-year period from 2009 to 2010. Of a total of 29,177 subjects aged between 18 and 26 years, 412 had at least 1 eye with spherical equivalent worse than \(-10.00\) D. Of these 412 subjects, 20 were randomly selected and invited to take part in this study. Exclusion criteria included subjects who did not give consent to take part in the study; previous ocular trauma or surgery; subjects who were currently receiving treatment for their ocular conditions which were not related to myopia. Written informed consent were taken from the subjects and their parents/guardians (if they were 21 years old and below). Ethics approval was obtained from the Institutional Review Board of DSO National Laboratories, Singapore. The study was conducted in accordance with the tenets of the World Medical Association’s Declaration of Helsinki.

**Examination and Investigations**

**Medical Questionnaire**

The subjects were asked a series of standardised questions including age, age at which they first wore spectacles to correct their refractive error, previous ocular trauma or surgery, history of ocular diseases, highest academic qualifications, ethnicity, height and weight.

**Ophthalmic Examination and Measurements**

Habitual and best-corrected visual acuity was measured monocularly using the standard Snellen chart. Contrast acuity was measured using Sloan Letters Translucent 5% contrast chart respectively. Refractive error was measured using Canon Autorefractor RK-F1 (Tokyo, Japan). Spherical equivalent of refractive status was used and calculated as the sum of the spherical power and half of the cylinder power. Axial length (AL) of the eye was obtained from the non-contact Zeiss IOLMaster by a trained operator. All the above mentioned tests were carried out by a trained optometrist.

Slit lamp and binocular indirect ophthalmoscopy were performed approximately 30 minutes after topical instillation of 3 drops of tropicamide and 2.5% phenylephrine, given 5 minutes apart. Dilated fundus examination was carried out by a trained ophthalmology resident (Victor Koh). The presence and type of peripheral retinal degenerations and vitreous degenerations were systematically documented.

**Fundus Photography and Grading**

Retinal photographs were performed by trained staff using the Canon CR6-45NM Non-Mydriatic retinal camera using the same standardised protocol. After pupillary dilation with tropicamide and 2.5% phenylephrine, given 5 minutes apart, 7 retinal photographs were taken for each eye — disc-centred rotated at 30 degrees to the right, disc-centred rotated 30 degrees to the left, macular view, and right and left upper and lower arcade periphery views from both eyes.

Grading of the fundus photos was performed by a trained observer (Lan Chang) based on a template used by the grading team of the Blue Mountains Eye study for myopic retinopathy.\textsuperscript{13} The observer was masked to refractive error status and a stereo-viewer was used to evaluate 3-dimensional views of the 2 disc-centred photographs rotated towards the right and left. The grader systematically assessed the size, location and position of pathology following the aforementioned template. Myopic retinopathy was defined as the presence of any of the following features: lacquer cracks, posterior staphyloma, chorioretinal atrophy, choroidal neovascularisation or Fuchs’ spot.\textsuperscript{13} The following showed a brief description of the main myopia-specific fundus changes that were assessed.

1. **Optic disc abnormalities**
   - (i) Disc tilt—stereoscopic confirmation of a tilted disc (Fig. 1) and quantifying it by calculating the ratio of the shortest and longest diameter of the optic disc. A ratio of less than 0.85 was considered significant disc tilt.\textsuperscript{17}
   - (ii) Cup and disc vertical and horizontal diameters.

2. **Beta-peripapillary atrophy**

   This was characterised by marked atrophy of the retinal pigment epithelium and of the choriocapillaries (Fig. 2). Features included small grey fields on a whitish background, good visibility of the large choroidal vessels, thinning of the chorioretinal tissues, round border to the adjacent alpha zone on the peripheral side and to the peripapillary sceral ring on the central side as described by Jonas et al.\textsuperscript{18} This arose from retraction of the chorioretinal tissues from the posterior sceral ring. The location and extent of the lesions (posterior pole, macular, peripapillary, temporal, inferotemporal, annular, inferior, nasal-inferior) were noted.

3. **Staphyloma**

   This lesion was characterised by scleral ectasia resulting in increased visibility of the underlying choroidal vasculature;
relative pallor of the ecstatic area and abrupt dipping of the retinal vessels at the margins. The demarcation was noted as vague or abrupt and graded (grades 1 to 10 according to Curtin’s classification)\(^1\) based primarily on the position and extent of the sclera ectasia. Briefly, the first 5 primary types were classified according to the extent of posterior staphyloma with respect on the optic disc. The next 5 compound types were various combinations of the primary types.

4. Lacquer cracks
These lesions are actually fissures in the Bruch’s membrane. The number of cracks, whether there is branching, position (posterior pole, macular, peripapillary) and the length were noted.

5. Fuchs’ spot
This is typically an elliptical black retinal spot that is well circumscribed and slightly elevated. The position of the Fuch’s spot (macular or peripapillary) was noted.

6. Chorioretinal atrophy
In myopic eyes, the increase in axial length resulted in thinning of the choroids and choriocapillaris loss. Chorioretinal atrophy was graded according to the classification proposed by Steidl et al.\(^2\) Grade 0 represented no atrophic change; grade 1, attenuated choroidal vasculature, limited lacquer cracks or retinal pigment epithelium mottling; grade 2, area of geographic atrophy less than 2 disc diameters (DD); grade 3, geographic atrophy more than 2 DD but less than 4 DD; grade 4, geographic atrophy more than 4 DD. The position (posterior pole, macular, peripapillary or others) of chorioretinal atrophy was also noted.

7. T-sign
Axial elongation of the myopic globe results in increased exposure of the central retinal vessels as they enter the eye via the lamina cribosa. This formed a “T-sign” as the central retinal vessels divide into the superior and inferior branches at least 0.5 mm from the lamina cribosa (Fig. 3).\(^2\)

8. Retinal tessellation
Retinal tessellation is characterised by “tigeroid” appearance of thinned retina and the increased visibility of the underlying choroidal vasculature (Fig. 4). This was classified according to the method described by Avila et al.\(^1\) on a grading scale of M0 to M5—grade M0 representing a normal appearance of the posterior pole; grade M1, choroidal pallor with tessellation; grade M2, features of grade M1 with posterior staphyloma; grade M3, features of grade M2 with lacquer cracks; grade M4, features of grade M3 and focal areas of deep choroidal atrophy; and grade M5, large

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Fig. 1. Fundal photos (A) showing optic tilt and (B) showing negligible optic disc tilt.

Fig. 2. Fundal photos (A) showing peripapillary atrophy and (B) showing absence of peripapillary atrophy.
geographic areas of choroidal atrophy at the posterior pole.

**Optical Coherence Tomography**

Stratus OCT was used to scan the retina after pupil dilation. Stratus OCT is a time-domain OCT whose detailed principles were described elsewhere. In this study, the Stratus OCT was used to measure RNFL thickness and to diagnose retinoschisis and macular holes. Standard and fast macular thickness scan programmes were used to assess the status of macular thickness, fast RNFL thickness programme to assess the RNFL thickness and fast optic disc scan to assess the optic disc status. The fovea depression was well centred for every image. Only images of good quality i.e. signal strength equal to or more than 7 were included for grading and analysis.

**Statistical Analysis**

Statistical analysis was performed using the statistical software, Statistical Package for Social Science (SPSS, version 17.0, Chicago, Illinois, USA). The ocular parameters between included and excluded eyes were compared using independent t-tests and chi square tests and statistical significance was defined as $P < 0.005$. If a subject’s both eyes were affected by spherical equivalent (SE) worse than $-10.00 \, \text{D}$, only 1 eye with the worse myopia was selected for multivariate regression analysis. Multivariate regression analysis adjusting for age, ethnicity, age of onset of myopia, body mass index and academic qualification was employed to examine for significant association between structural variables.

**Results**

Of the 20 selected male subjects, 16 (80%) agreed to participate in the study, with a mean age of 21.8 years, [standard deviation (SD) 1.3 years] and all were Chinese except 1 Indian. The mean age of onset of myopia and the mean duration of myopia were 8.1 years (SD, 1.0 years) and 13.7 years (SD, 1.5 years) respectively. Of these 16 subjects, 21 eyes had a SE worse than $-10.00 \, \text{D}$. There were 5 (31.3%) subjects with bilateral eyes and 11 (68.7%) subjects with unilateral eye affected by SE worse than $-10.00 \, \text{D}$. All 32 eyes had a best corrected visual acuity of at least 6/7.5 based on standard Snellen visual acuity chart, mean contrast acuity of 0.36 (SD, 0.07) and dark adaptation test of at least 102 seconds which was within the normal range. Table 1 showed the comparison of the main ocular parameters between eyes with SE worse than $-10.00 \, \text{D}$ and eyes equal to or better than $-10.00 \, \text{D}$.

All fundus photos were of sufficient quality and none were excluded from grading. Of the 21 eyes with SE worse than $-10.00 \, \text{D}$, 10 (47.6%) had optic disc tilt (Fig. 1), 17 (81.0%) had significant beta peripapillary atrophy (Fig. 2), 1 (4.8%) had positive T-sign (Fig. 3) and 18 (85.7%) had retinal tessellation (Fig. 4) consistent with M1 grading based on Avila classification. The location of all beta peripapillary atrophy was in the temporal aspect of the optic nerve head. Of the eyes with disc tilt, 15 discs were tilted temporally and 1 was tilted supero-temporally. There were no eyes which fulfill the criteria for myopic retinopathy i.e.
Pathologic Changes in Young Myopic Eyes—Victor TC Koh et al

lacquer cracks, posterior staphyloma, chorioretinal atrophy, choroidal neovascularisation or Fuchs’ spot. The mean cup-disc ratio was 0.41 (SD, 0.15) and the mean longest diameter-to-shortest diameter ratio was 0.89 (SD, 0.07). A dilated fundal examination of the peripheral retina showed that out of the 21 eyes (spherical equivalent worse than –10.00 D), 4 eyes (19.0%) had posterior vitreous detachment and 14 eyes (66.7%) had peripheral retina degeneration –6 eyes with lattice degeneration, 5 eyes with snail-tracks and 4 eyes with white-without-pressure. Table 2 showed the demographics and ocular parameters of the 16 subjects included in the study.

Table 3 showed the mean values of Stratus OCT measurements of the RNFL. When compared with the normative database of Stratus OCT, only 71.4% of the eyes were classified within the 95th percentile for global RNFL thickness. Comparing the 4 quadrants of the retina, the superior retina is the thickest and the nasal retina is

Table 1. Comparison of Ocular Parameters of Included and Excluded Eyes

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Eyes included (n = 21)</th>
<th>Eyes excluded (n = 11)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spherical equivalent (D)</td>
<td>–10.88 ± 1.28</td>
<td>–8.80 ± 0.82</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intra-ocular pressure (mmHg)</td>
<td>16.38 ± 3.19</td>
<td>15.36 ± 2.38</td>
<td>0.36</td>
</tr>
<tr>
<td>Axial length (mm)</td>
<td>27.43 ± 1.20</td>
<td>26.61 ± 0.58</td>
<td>0.011</td>
</tr>
<tr>
<td>Disc area (mm²)</td>
<td>2.39 ± 0.66</td>
<td>2.27 ± 0.34</td>
<td>0.57</td>
</tr>
<tr>
<td>Average RNFL thickness (µm)</td>
<td>92.48 ± 9.99</td>
<td>92.09 ± 10.37</td>
<td>0.91</td>
</tr>
<tr>
<td>Fovea volume (mm³)</td>
<td>0.16 ± 0.013</td>
<td>0.15 ± 0.012</td>
<td>0.28</td>
</tr>
<tr>
<td>Fovea thickness (µm)</td>
<td>174.62 ± 48.09</td>
<td>161.18 ± 48.50</td>
<td>0.46</td>
</tr>
<tr>
<td>Peripapillary atrophy (%)</td>
<td>17 (81.0%)</td>
<td>9 (81.8%)</td>
<td>0.67</td>
</tr>
<tr>
<td>Optic disc tilt (%)</td>
<td>10 (47.6%)</td>
<td>4 (36.4%)</td>
<td>0.41</td>
</tr>
<tr>
<td>Lattice degeneration (%)</td>
<td>6 (28.6%)</td>
<td>0 (0%)</td>
<td>0.06</td>
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Table 2. Demographics and Ocular Parameters of All Included Eyes

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (years)</th>
<th>Race</th>
<th>Age of onset of myopia</th>
<th>Eye</th>
<th>Spherical equivalent refraction (D)³</th>
<th>Axial length (mm)</th>
<th>Average RNFL thickness (µm)</th>
<th>Pathology</th>
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<td>1</td>
<td>23.00</td>
<td>Chinese</td>
<td>9.00</td>
<td>Right</td>
<td>–14.875</td>
<td>29.81</td>
<td>78.89</td>
<td>PPA, disc tilt, tessellated fundus, PVD, lattice, WWOP</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Left</td>
<td>–13.750</td>
<td>29.94</td>
<td>74.87</td>
<td>PPA, disc tilt, tessellated fundus, lattice, WWOP</td>
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<td>2</td>
<td>23.00</td>
<td>Indian</td>
<td>9.00</td>
<td>Right</td>
<td>–7.500</td>
<td>26.52</td>
<td>92.57</td>
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<td>26.73</td>
<td>103.54</td>
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<td>Chinese</td>
<td>8.00</td>
<td>Right</td>
<td>–11.750</td>
<td>26.73</td>
<td>103.54</td>
<td>PPA, disc tilt, tessellated fundus, snail-tracks</td>
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<tr>
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<td>8.00</td>
<td>Right</td>
<td>–11.375</td>
<td>27.94</td>
<td>101.91</td>
<td>PPA, disc tilt, tessellated fundus, PVD, lattice</td>
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<tr>
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<td>PPA, disc tilt, tessellated fundus</td>
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<tr>
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<td></td>
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<td>26.63</td>
<td>76.83</td>
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</table>

PPA: peripapillary atrophy; PVD: posterior vitreous detachment; WWOP: white without pressure
the thinnest (Table 3). The nasal retina showed the lowest proportion of eyes that fall within the 95th percentile range. However, the fovea thickness of all these 21 eyes was classified as within normal range. There was no evidence of macular hole or retinoschisis.

Using multivariate models adjusting for age, ethnicity, age of onset of myopia and body mass index, our results showed that increasing spherical equivalent refraction was associated with decreasing axial length ($P = 0.018$). However, there was no significant correlation between axial length or spherical equivalent refraction with average RNFL thickness. Increasing axial length was significantly associated with increased fovea thickness ($P = 0.036$) and fovea volume ($P = 0.001$).

### Discussion

Our study on highly myopic young eyes showed a high prevalence of optic disc tilt, beta peripapillary atrophy, retinal tesselation and peripheral retinal degeneration, which were associated with an abnormally thin RNFL layer. This provided insight to the baseline structural alterations of the retina in young Asian eyes with very high axial myopia which is at higher risk of further myopic progression. The nasal quadrant of the retina was found to be most frequently classified as abnormal and this may suggest that it is affected the earliest. However, it was important to note that the RNFL normative database of Stratus OCT comprised only Caucasian eyes and RNFL thickness had been shown to have ethnic-specific differences. The average RNFL thickness was 92.48 mm (SD, 9.99 mm) which was generally thinner compared to other Western and Asian population studies. The aforementioned studies had similar methodology to our study: Stratus OCT to measure RNFL thickness, young age group and comprised mainly Asian subjects. However, the mean RNFL thickness in our group of patients with SE of worse than $-10.00$ D was generally thinner.

The fundal examination of these 21 eyes revealed several myopia-specific vitreoretinal signs and suggested a high prevalence of such changes in severely myopic eyes, even at this young age group. We found that up to 47.6% of the eyes had tilted optic discs which were comparable to what was reported in 2 Singaporean studies based on children between 11 and 13 years old. This suggested that optic disc tilt appears early in the natural history of myopia and its severity remained stable for a long time. Optic disc tilt may pose a challenge in accurate characterisation of optic nerve hypoplasia (ONH) measurements in both clinical examination and interpretation of glaucoma imaging tools such as the confocal scanning laser ophthalmoscope. This is especially significant as glaucoma was shown to be associated with myopia. Up to 67% of these severely myopic eyes had peripheral retinal degeneration which was also higher than previous reports. The presence of lattice degeneration in these highly myopic eyes significantly increased the risk of rhegmatogenous retinal detachment in these participants from a very young age. The high prevalence of peripheral retinal degenerations in these young myopic eyes should also serve as a caution to ophthalmologist to actively examine for retinal tears and breaks which could lead to rhegmatogenous retinal detachment.

Overall, our findings suggest that tilted optic discs, peripapillary atrophy and peripheral retinal degeneration may be early signs of pathologic myopia in young myopic eyes. However, such changes may be mainly attributed to mechanical stretching of the elongated globe and require less time to develop compared to other characteristics of myopic maculopathy. Our findings were consistent with
another study which examined high myopia in young Japanese children [mean age 5.4 years, (SD, 2.1 years)]; mean refractive error –8.4 D, (SD, 3.8 D) and showed a lack of myopic maculopathy.45 In a recent follow-up study of SCORM which comprised of a younger participants aged between 12 and 16 years old, it was reported that myopic refraction is associated with tilted optic disc (49.2%) and peripapillary atrophy (76.1%). Interestingly, the study also reported only 1 case (0.1%) of myopic retinopathy.44 In comparison to a population study on myopic retinopathy in an older population (age 49 years or older) by Yongphanit et al,13 there was no detectable staphyloma, lacquer cracks, Fuch’s spot, chorioretinal atrophy in our study comprising of a younger age group. This may suggest that the aforementioned signs may be late presentations of myopic retinopathy as a consequence of tissue remodeling with time.46,47 Alternately, it was possible that the signs were younger and with better visual acuity compared to posterior staphyloma and lacquer cracks. The presence of early posterior staphyloma may be overlooked as the ectatic borders may be too shallow to be detected in the fundus photographs. The presence of lacquer cracks may also be partly masked by retinal tessellation, which was very common in our study. Lacquer cracks were also more easily detected by other forms of imaging which was not performed in this study such as fundus autofluorescence or indocyanine green angiography.

Our study comprised young Asian males (15 Chinese and 1 Indian) with a mean age of 21.8 years (SD, 1.3 years) and mean duration of myopia of 13.7 years (SD, 1.5 years). As such, these young subjects have not had high myopia for a long time and we do not expect to see myopic retinopathy in adults of a young age. Despite having high myopia, there seem to be minimal functional deficit and structural changes were also mild in severity. However, despite the absence of myopic retinopathy, these eyes were already showing early signs specific to axial elongation of the globe. Hayashi et al23 reported that up to 13.4% of myopic eyes (worse than –6.00 D) with tessellated fundus showed progression of myopic maculopathy in a longitudinal study. It was suggested that the presence of a tessellated fundus was one of the early signs and represented the start of a slow progression towards myopic maculopathy. The authors suggested, most tessellated fundus would progress to either diffuse chorioretinal atrophy or lacquer cracks, which in turn were at a much higher risk of further progression. It was also showed that eyes with only tessellated fundus were younger and with better visual acuity compared to the eyes with more advanced maculopathy. In our study, none of the eyes had chorioretinal atrophy or lacquer cracks at the time of examination. It may also be conceivable for highly myopic patients to be screened regularly with fundus photographs to detect myopic changes for early intervention.

Our study showed that the severity of myopia correlated with axial length. The finding that increased axial length was associated with increased fovea thickness was consistent with previous studies.48-50 This may be due to the axial elongation of the myopic globe resulting in vitreoretinal traction on the fovea. Whether this vitreoretinal traction will eventually lead to retinoschisis or macular hole is still unclear.

The strengths of our study included a young age group whose eyes did not have significant media opacity which would affect fundus visualisation and image quality. For each of the included subjects, all the structural and functional tests were performed within 1 week. There were limitations to our study. Firstly, this case series is small and follow-up data are needed. Ideally, to establish a normative database of RNFL thickness in subjects with high myopia requires a larger sample size. However, a larger prospective study is being conducted which will better quantify and stratify the risk of retinal complications and the functional limitations of this population. Secondly, our study was a descriptive study with no controls for comparison. Thirdly, as our subjects were all young males, the findings should be generalised with caution when applied to the general population as there were reports of higher prevalence of myopic retinopathy in women.51 Lastly, the imaging tool used in this study, Stratus OCT, is a time-domain OCT. However, more recently, with the introduction of Fourier-domain OCT, the retina can be imaged faster with better resolution and thus higher reproducibility.

In conclusion, our study showed that in these highly myopic eyes of adolescent males, the most common early abnormalities were optic disc tilt, beta peripapillary atrophy and retinal tessellation. Peripheral retinal degeneration was present in more than half of the eyes and generally, these highly myopic eyes have thinner RNFL. Although none of the eyes had myopic retinopathy, further longitudinal studies are required to investigate if these highly myopic eyes will develop complications of pathological myopia when they grow older.

REFERENCES


