Posterior Vitreous Detachment in Highly Myopic Patients

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Received: November 12, 2019
Accepted: March 4, 2020
Published: April 25, 2020

Citation: Hayashi K, Manabe S, Hirata A, Yoshimura K. Posterior vitreous detachment in highly myopic patients. *Invest Ophthalmol Vis Sci.* 2020;61(4):33. https://doi.org/10.1167/iovs.61.4.33

Purpose. We compared the change in the state of posterior vitreous detachment (PVD) between highly myopic eyes and non-highly myopic eyes using age- and sex-matched patients.

Methods. Six hundred eyes of 600 patients with high myopia (axial length > 26.0 mm) or without high myopia were enrolled into each of six age categories with 50 eyes each: (1) 20 to 29 years, (2) 30 to 39 years, (3) 40 to 49 years, (4) 50 to 59 years, (5) 60 to 69 years, and (6) 70 to 79 years. The PVD status was evaluated using swept-source optical coherence tomography and classified into five stages: 0 (no PVD), 1 (paramacular PVD), 2 (perifoveal PVD), 3 (peripapillary PVD), and 4 (complete PVD).

Results. In the high myopia and non-high myopia groups, the mean PVD stage increased significantly with the age category ($P < 0.0001$). The PVD stage was significantly greater in the high myopia group than in the non-high myopia group in all age categories ($P \leq 0.0395$). In the age groups of patients 50 to 59 years old and 60 to 69 years old, complete PVD was detected in 54.0% and 73.9% of eyes, respectively, in the high myopia group and in 14.0% and 44.0% of eyes, respectively,in the non-high myopia group. Abnormal PVD characteristics of pathologic myopia were detected in 1.7% of eyes in the high myopia group.

Conclusions. We precisely revealed, using age- and sex-matched patients, that partial PVD, including paramacular, perifoveal, and peripapillary PVD, and complete PVD develop at a significantly younger age in highly myopic eyes compared with non-highly myopic eyes, suggesting that PVD-related retinal pathologies occur younger in highly myopic patients.

Keywords: posterior vitreous detachment, high myopia, age, swept source-optical coherence tomography

Posterior vitreous detachment (PVD) is associated with serious ocular pathologies, including retinal tears, rhegmatogenous retinal detachment, vitreous hemorrhage, macular holes, and macular traction syndrome.[1–8] These PVD-related retinal pathologies occur more frequently in patients with high myopia than in patients without high myopia.[9–16] Accordingly, it is assumed that the progression of PVD also differs between highly myopic eyes and non-highly myopic eyes.

Previous studies using various methods to examine the posterior vitreous showed that PVD occurs at an earlier age in highly myopic patients compared with non-highly myopic patients.[17–20] Precise visualization of the posterior vitreous, however, was not possible before the improvement of optical coherence tomography (OCT), specifically by the advent of swept-source OCT (SS-OCT).[21–23] Using SS-OCT, Itakura et al.[20] showed that partial PVD and complete PVD occur earlier in highly myopic patients than in non-highly myopic patients, but they did not classify the minute progression of partial PVD in that study, despite their group's three-stage classification system of partial PVD, including paramacular, perifoveal, and peripapillary PVD.[24] Furthermore, using ultra-widefield SS-OCT, Takahashi et al.[25] reported various abnormal PVDs that are specific to pathologic myopia. More recently, however, it was reported that PVD occurs at a younger age in women compared with men among highly myopic patients 60 years of age and older.[26] Accordingly, it is necessary to compare the state of PVD between patients with and without high myopia using age- and sex-matched cohorts and to classify the stage of partial PVD in a more detailed manner.

The purpose of the present study was to precisely compare the stage of PVD around the posterior retina in association with age between highly myopic patients and non-highly myopic patients. Because we enrolled age- and sex-matched cohorts, the findings obtained in this study reflect the actual clinical difference in the PVD stage between highly myopic patients and non-highly myopic patients. Furthermore, the present study classified the development of partial PVD into three stages (paramacular, perifoveal, and peripapillary) in eyes with high myopia.

Methods

Study Design

This study was designed as a prospective cross-sectional study and was conducted at the Hayashi Eye Hospital, Fukuoka, Japan, between April 5, 2019, and September 20, 2019. The study protocol was approved by the Institutional Review Board of the Hayashi Eye Hospital on March 30, 2019. Informed consent was obtained from all patients. The

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study protocol adhered to the tenets of the Declaration of Helsinki.

Participants

All consecutive patients who newly visited the clinic of the Hayashi Eye Hospital were screened for inclusion in the study by ophthalmic technicians beginning on April 5, 2019. One eye of each patient with better corrected distance visual acuity (CDVA), or the right eye when both eyes had the same CDVA, was enrolled in the study. Eyes with an axial length greater than 26.0 mm were recruited into the high myopia group. Age- (within ±5 years) and sex-matched eyes with an axial length of 26.0 mm or less were selected to serve as controls (non-high myopia group). A total of 600 eyes of 600 patients were enrolled; 300 patients in each of the high myopia and non-high myopia groups were enrolled in six age categories (50 eyes in each age category; 25 men and 25 women): (1) 20 to 29 years, (2) 30 to 39 years, (3) 40 to 49 years, (4) 50 to 59 years, (5) 60 to 69 years, and (6) 70 to 79 years. The exclusion criteria for both groups were (1) aphakic or pseudophakic eyes; (2) eyes with corneal or optic nerve pathology; (3) eyes with clinically significant cataracts interfering with visualization of the posterior vitreous; (4) eyes with marked retinal disease around the macula, including epiretinal membrane, macular hole, vitreoretinal traction syndrome, foveoschisis, and myopic retinochoroidal atrophy; (5) patients with diabetes; (6) eyes with a history of ocular surgery or inflammation; (7) patients who refused to participate in the study; and (8) patients who had any difficulties undergoing the examinations. Eyes with abnormal PVDs characteristic of pathologic myopia, such as residual vitreous cortex after complete PVD, multiple PVDs, multilayered PVDs (vitreoschisis), and thickened vitreous cortex adhering to retinal vessels at multiple points were not excluded from the study. Patient screening was continued until 50 eyes of 50 patients (25 men and 25 women) were included in each of the six age categories for both the high myopia and non-high myopia groups; the last eye was enrolled on September 20, 2019.

Outcome Measures

The states of the posterior vitreous and retina were evaluated in all enrolled patients by SS-OCT (PLEX Elite 9000 Version 1.7; Carl Zeiss Meditec, Jena, Germany). The SS-OCT procedure is described elsewhere.[26] In the present study, we used the HD Spotlight 1 protocol, which covers a 16-mm-wide section centered on the fovea. Using this protocol, we obtained a horizontal image centered on the fovea and disc and a vertical image centered on the fovea. The scans were repeated 100 times in enhanced depth imaging mode and were averaged to create the OCT image. FastTrac motion correction software (Carl Zeiss Meditec) was also used during image acquisition. Experienced ophthalmic technicians enhanced the visualization of the posterior vitreous by manually changing the image contrast and brightness without using a specific imaging protocol.

The PVD stage was classified according to the five-stage classification system described by Itakura and Kishi:[24] stage 0 (no PVD), stage 1 (paramacular PVD), stage 2 (perifoveal PVD), stage 3 (vitreofoveal separation or peripapillary PVD), and stage 4 (complete PVD). One of the two experienced technicians involved in the study acquired high-quality (16-mm wide) images of the posterior vitreous and retina from each patient in the outpatient clinic using SS-OCT, and the images were then stored on a computer. Afterward, the same technician determined the PVD stage and consulted the two ophthalmologists involved in the study (SM, AH) when classification was difficult. When the PVD stage determined using the horizontal and vertical scans differed, the more advanced stage was regarded as the representative stage of each eye. The examiner also manually determined the foveal thickness of each eye using SS-OCT.

Inter- and intra-examiner reproducibility for determining the PVD stage was assessed using the kappa coefficient for 40 eyes of 40 randomly selected patients (20 eyes with high myopia and 20 eyes without high myopia). To assess the inter-examiner reproducibility, the two examiners independently obtained SS-OCT images and then determined the PVD stage. To assess the intra-observer reproducibility, both examiners obtained SS-OCT images three times to determine the PVD stage. The kappa coefficient between the two examiners was 0.9650 (95% confidence interval [CI], 0.8975–1.000), and among the three examinations it was 1.000 (95% CI, 1.000–1.000). Thus, the PVD stage agreed almost perfectly between the two examiners and among the three examinations of both examiners, indicating that the PVD stage determined by each examiner was essentially correct.

The refractive spherical and cylindrical powers were measured without cycloplegia using an autorefractometer (KR-7100; Topcon, Tokyo, Japan). The manifest spherical equivalent value was determined as the spherical power plus half the cylindrical power. The axial length of each eye was examined by the SS-OCT (IOLMaster 700 Version 1.14; Carl Zeiss Meditec). Corrected distance decimal visual acuity was evaluated, and the decimal visual acuity was converted to the logarithm of minimal angle of resolution (logMAR) scale for statistical analysis. The grade of nuclear opalescence was determined by the ophthalmologists according to the Lens Opacities Classification System III.[27] Ophthalmic technicians who were unaware of the purpose of the study performed all examinations.

Statistical Analysis

Because the PVD stage is a rank categorical variable, it was compared using the Mann–Whitney *U* test between the high myopia and non-high myopia groups. Changes in the PVD stage with age were compared among age categories using the Kruskal–Wallis test. The normality of the data distribution of continuous variables was assessed by inspecting histograms. We compared the data of continuous variables that were normally distributed using Student's *t*-test and those that were not normally distributed using the Mann–Whitney *U* test. Categorical variables were compared between groups using the χ^2 test or Fisher's exact probability test where applicable. The correlation between the axial length and PVD stage, which was converted to a rank variable, was determined using the Spearman rank correlation coefficient. Any difference with a *P* value less than 0.05 was considered statistically significant.

Results

The patient characteristics of the two groups are shown in Table 1. Mean age and central retinal (foveal) thickness did not differ significantly between the high myopia and

Table 1. Comparison of Patient Characteristics for Eyes with High Myopia and Eyes Without High Myopia in Six Age Categories

Characteristic	Mean ± SD: High Myopia Group (n = 295 eyes)	Mean ± SD: Non-High Myopia Group (n = 300 eyes)	*P*
Age, y			
20–29 y	24.4 ± 2.8	24.7 ± 2.9	0.6800
30–39 y	34.9 ± 2.9	34.9 ± 2.5	0.9945
40–49 y	45.6 ± 2.6	45.4 ± 2.8	0.6903
50–59 y	55.7 ± 3.0	54.8 ± 2.7	0.1218
60–69 y	64.4 ± 2.9	64.2 ± 2.8	0.8450
70–79 y	72.9 ± 2.4	73.4 ± 2.5	0.3130
Manifest spherical equivalent value, diopter			
20–29 y	−8.1 ± 3.0	−2.9 ± 2.5	<0.0001*
30–39 y	−8.2 ± 4.0	−2.7 ± 2.2	<0.0001*
40–49 y	−9.3 ± 6.0	−1.8 ± 2.7	<0.0001*
50–59 y	−10.3 ± 5.8	−1.6 ± 1.9	<0.0001*
60–69 y	−10.6 ± 7.3	−1.4 ± 2.4	<0.0001*
70–79 y	−7.5 ± 3.3	−1.1 ± 2.5	<0.0001*
Axial length, mm			
20–29 y	27.2 ± 0.9	24.6 ± 1.1	<0.0001*
30–39 y	27.4 ± 1.2	24.6 ± 0.9	<0.0001*
40–49 y	27.7 ± 1.2	24.2 ± 1.1	<0.0001*
50–59 y	27.1 ± 0.9	24.3 ± 0.9	<0.0001*
60–69 y	27.8 ± 1.4	24.0 ± 1.0	<0.0001*
70–79 y	27.2 ± 1.2	23.7 ± 0.9	<0.0001*
Nuclear opalescence			
20–29 y	1.1 ± 0.3	1.1 ± 0.2	0.2969
30–39 y	1.2 ± 0.5	1.1 ± 0.3	0.1331
40–49 y	1.8 ± 1.0	1.4 ± 0.6	0.0882
50–59 y	2.4 ± 0.7	1.5 ± 0.7	<0.0001*
60–69 y	2.6 ± 0.7	2.3 ± 0.8	0.0675
70–79 y	2.7 ± 0.8	2.4 ± 0.6	0.0613
Central retinal thickness, µm			
20–29 y	213.6 ± 10.3	211.3 ± 15.0	0.3239
30–39 y	222.2 ± 24.3	217.3 ± 21.4	0.2020
40–49 y	218.1 ± 21.2	217.5 ± 17.9	0.8721
50–59 y	219.3 ± 23.6	223.1 ± 21.2	0.5485
60–69 y	225.0 ± 33.3	220.1 ± 18.2	0.2586
70–79 y	216.1 ± 24.3	219.3 ± 20.8	0.2523
LogMAR CDVA			
20–29 y	−0.03 ± 0.08	−0.05 ± 0.04	0.2420
30–39 y	0.01 ± 0.15	0.00 ± 0.21	0.9636
40–49 y	0.18 ± 0.42	0.15 ± 0.39	0.7305
50–59 y	0.31 ± 0.30	0.15 ± 0.44	0.0370*
60–69 y	0.37 ± 0.30	0.27 ± 0.42	0.1420
70–79 y	0.25 ± 0.21	0.28 ± 0.22	0.3623

* Statistically significant difference between the two groups.

non-high myopia groups in any age category. Foveal thickness and PVD stage were not significantly correlated. Mean CDVA was significantly worse in the high myopia group than in the non-high myopia group at 50 to 59 years of age ($P = 0.0370$), but it did not differ significantly among groups in the other age categories. The mean grade of nuclear opalescence was significantly greater in the high myopia group than in the non-high myopia group at 50 to 59 years ($P < 0.0001$) but did not differ significantly among groups in the other age categories.

Of the 300 eyes of 300 patients enrolled in each of the two groups, the PVD stage could be classified in all but five eyes (1.7%) in the high myopia group and in all eyes in the non-high myopia group according to the classification system of Itakura and Kishi.[24] The five eyes for which the PVD stage could not be classified presented with abnormal PVDs that are characteristic of pathologic myopia; therefore, 295 eyes remained in the high myopia group for analysis of the PVD stage. Residual vitreous cortex was detected after complete PVD in four eyes (1.3%) in the high myopia group and in no eyes in the non-high myopia group.

Table 2. Clinical Characteristics of the Five Eyes with Abnormal Posterior Vitreous Detachments Specific to High Myopia

Cases	Characteristics
Case 1	
Type of PVD	Multiple PVDs (vitreous adhesion at multiple points) Multilayered PVDs (vitreoschisis)
Status of retina	Tessellated fundus
Posterior staphyloma	Present
Axial length, mm	28.6
Foveal thickness (µm)	198
LogMAR CDVA	0.10
Case 2	
Type of PVD	Long strands of vitreous cortex adhering to the retinal vessel
Status of retina	Tessellated fundus
Posterior staphyloma	Present
Axial length, mm	31.3
Foveal thickness, µm	216
LogMAR CDVA	0.30
Case 3	
Type of PVD	Thickened vitreous cortex adhered to the inner surface of the retinal vessels at multiple points
Status of retina	Tessellated fundus
Posterior staphyloma	Present
Axial length, mm	30.0
Foveal thickness, µm	183
LogMAR CDVA	0.15
Case 4	
Type of PVD	Long strands of vitreous cortex adhering to the retinal vessel
Status of retina	Tessellated fundus
Posterior staphyloma	Present
Axial length, mm	29.5
Foveal thickness, µm	259
LogMAR CDVA	1.70
Case 5	
Type of PVD	Multiple PVDs (vitreous adhesion at multiple points)
Status of retina	Tessellated fundus
Posterior staphyloma	Present
Axial length, mm	26.6
Foveal thickness, µm	268
LogMAR CDVA	1.70

The clinical characteristics of the five eyes with abnormal PVDs specific to pathologic myopia in the high myopia group are shown in Table 2. The SS-OCT images included multiple PVDs with multilayered PVDs in one eye, multiple PVDs in one eye, thickened vitreous cortex adhered to the retinal vessels in one eye, and long strands of vitreous cortex adhering to the retinal vessels in two eyes. All of these eyes had a tessellated fundus with posterior

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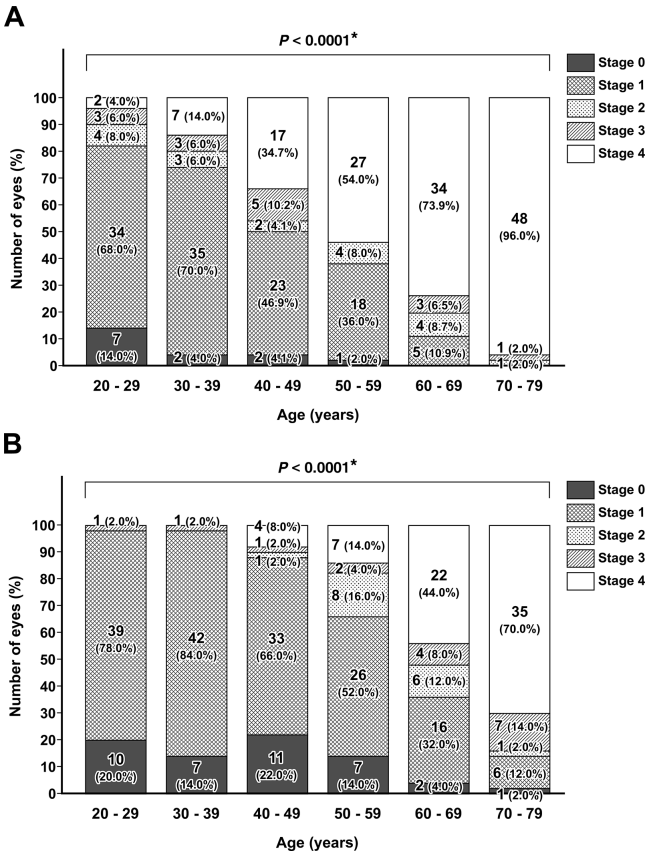

Figure 1. Comparison of the stage of PVD among the six age categories in eyes with high myopia (**A**) and in eyes without high myopia (**B**). In both the high myopia and non-high myopia groups, the mean stage of PVD was significantly progressed in association with the age category. *Statistically significant difference among age categories.

staphyloma, but retinochoroidal atrophy was not detected around the macula.

Stage 4 PVD (complete PVD) was detected in 34 eyes (68.2%) in the high myopia group and in 22 eyes (44.0%) in the non-high myopia group at 60 to 69 years. In both groups, the mean PVD stage significantly increased in association with age ($P < 0.0001$) (Fig. 1). In the high myopia group, complete PVD was detected in two eyes (6.7%) at 20 to 29 years and in 34 eyes (68.2%) at 60 to 69 years. In the non-high myopia group, complete PVD was not detected at 20 to 29 years but was detected in 22 eyes (44.0%) at 60 to 69 years.

The mean PVD stage was significantly greater in the high myopia group than in the non-high myopia group in all age categories evaluated ($P \leq 0.0395$) (Fig. 2). At 30 to 39 years, complete PVD was found in seven eyes (14.0%) in the high myopia group and in no eyes in the non-high myopia group ($P = 0.0003$). At 70 to 79 years, complete PVD was detected in 44 eyes (93.6%) in the high myopia group and in 36 eyes (70.0%) in the non-high myopia group ($P = 0.0005$).

The PVD stage correlated with axial length in both groups Table 3. In the high myopia group, axial length significantly correlated with the PVD stage both overall and in eyes at 30 to 39 years and 40 to 49 years of age ($P \leq 0.0219$), but there was no significant correlation between axial length and PVD stage in the other age categories. In the non-high myopia group, no significant correlation was detected between the axial length and PVD stage in any age category.

Table 3. Spearman Correlation Coefficient Between Stages of PVD and Axial Length in Eyes with High Myopia and in Eyes without High Myopia in Six Age Categories

Group	Spearman Correlation Coefficient	*P*
High myopia group		
Overall	0.201	0.0219*
20–29 y	0.305	0.2165
30–39 y	0.531	0.0019*
40–49 y	0.622	<0.0001*
50–59 y	0.143	0.7481
60–69 y	0.159	0.7002
70–79 y	0.445	0.9530
Non-high myopia group		
Overall	0.015	0.1805
20–29 y	0.426	0.0716
30–39 y	0.449	0.0955
40–49 y	0.269	0.3182
50–59 y	0.196	0.3582
60–69 y	0.168	0.4199
70–79 y	0.240	0.5639

* Statistically significant correlation.

The SS-OCT images of abnormal PVDs specific to pathologic myopia of representative eyes are shown in Figure 3. They include SS-OCT images of multiple PVD with multilayered PVD (vitreoschisis), thickened vitreous cortex adhering to the retinal vessels, and long strands of posterior vitreous cortex.

Discussion

The findings of the present study using age- and sex-matched cohorts revealed that the mean PVD stage was significantly greater in eyes with high myopia than in eyes without high myopia in all age categories. For example, at 50 to 59 years and 60 to 69 years, complete PVD was detected in 54.0% and 73.9% of eyes, respectively, in the high myopia group and 14.0% and 44.0% of eyes, respectively, in the non-high myopia group. These findings indicate that PVD develops at a younger age in eyes with high myopia than in eyes without high myopia.

The axial length significantly correlated with the PVD stage overall and in eyes at 30 to 39 years and 40 to 49 years in the high myopia group, but the correlation was not significant in the other age categories. No significant correlation was detected between the axial length and PVD stage in the non-high myopia group. Thus, longer axial length tended to correlate with advanced PVD stage in highly myopic eyes. This finding suggests that the increase in PVD occurrence at a younger age in eyes with high myopia may be partly attributed to earlier vitreous liquefaction due to a longer axial length.[20,28]

Our previous study demonstrated that PVD occurred at a younger age in women compared with men among patients without high myopia.[26] This finding suggests that the PVD stage should be compared using sex-matched patients. Accordingly, to strictly compare the difference in the PVD stage between eyes with and without high myopia, we enrolled an equal number of men and women in all age categories in the present study.

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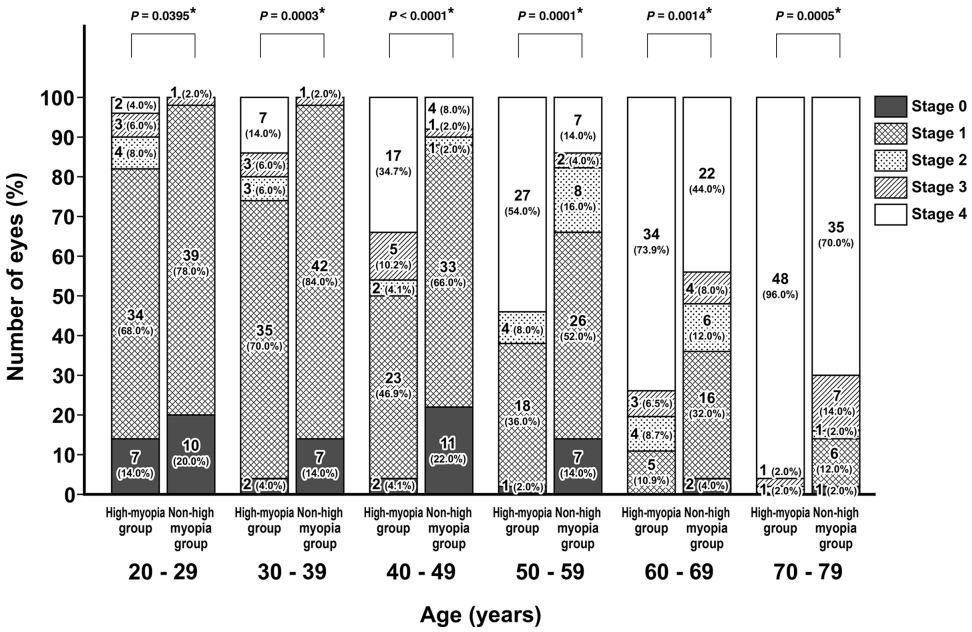

Figure 2. Comparison of the stage of PVD between eyes with high myopia and eyes without high myopia. The PVD stage was significantly more progressed in the high myopia group than in the non-high myopia group in all age categories. *Statistically significant difference between the high myopia and non-high myopia groups.

Mean CDVA was significantly worse in the high myopia group than in the non-high myopia group at 50 to 59 years. Mean CDVA worsened with age in both groups, but this worsening began at 50 years of age in the high myopia group and at 60 years of age in the non-high myopia group. Because cataracts, primarily nuclear sclerosis, develop at a younger age in patients with high myopia than in patients without high myopia, the cataract grade was significantly greater in the high myopia group at 50 to 59 years. Thus, cataract formation is thought to be a predominant cause of impaired visual acuity. The earlier cataract formation in patients with high myopia results in a significant difference in mean visual acuity at 50 years of age.

On the basis of various examination methods of the posterior vitreous, partial PVD and complete PVD occur earlier in eyes with high myopia than in eyes without high myopia.[17–20] Prior to the development of advanced OCT such as SS-OCT, however, complete visualization of the posterior vitreous was difficult.[21–23] Using SS-OCT, Itakura et al.[20] revealed that partial PVD and complete PVD occur at a younger age in eyes with high myopia than in eyes without high myopia. In that study, however, they did not classify the detailed progression of partial PVD, despite their group's classification system of partial PVD,[24] and differences in the PVD development between men and women were not considered. Additionally, Takahashi et al.[25] used ultra-widefield SS-OCT to evaluate various types of PVDs that are specific to pathologic myopia, including multiple PVD, vitreoschisis, and thickened vitreous cortex adhering to retinal vessels. Furthermore, Song et al.[29] also reported a high frequency of vitreoretinal abnormalities in highly myopic eyes with retinoschisis. Taking all these findings into consideration, the present study precisely revealed, using sex-matched cohorts, that the development of PVD stages, including the three stages of partial PVD, is significantly faster in highly myopic eyes than in non-highly myopic eyes.

The present study has several limitations. First, the sample size of each age category may not be sufficient for performing a subgroup analysis, including the correlation between axial length and the PVD stage in highly myopic eyes. Indeed, although axial length correlated significantly with the PVD stage overall and in eyes at 30 to 39 years and 40 to 49 years of age, there was no significant correlation in the other age categories. Elucidating the relationship between axial length and the development of PVD will require further studies with a larger sample size. Second, the frequency of abnormal PVDs specific to pathologic myopia was low in our cohorts,[29] because eyes with marked retinal disease were excluded. Accordingly, it was not possible to classify the PVD stage in eyes with pathologic myopia. Further studies are necessary to examine the PVD in eyes with pathologic myopia.

In conclusion, the present study demonstrated, using age- and sex-matched cohorts, that the three stages of partial PVD and complete PVD develop at a younger age in eyes with high myopia than in eyes without high myopia. Complete PVD occurred in highly myopic eyes of patients as young as 20 years of age. Thus, ophthalmologists should be aware that PVD-related retinal pathologies, including retinal tears, retinal detachment, macular holes, and macular traction syndrome, begin to develop at a younger age (about 20 years of age) in eyes with high myopia compared with non-highly myopic eyes. Although it is known that PVD-associated pathologies are likely to develop immediately or early after ocular surgery because PVD may occur in the immediate or early postoperative periods, controversy remains as to when and how PVD progresses after surgery, specifically in eyes with high myopia. Further studies are necessary to evaluate the beginning of PVD and its progression after ocular surgery.

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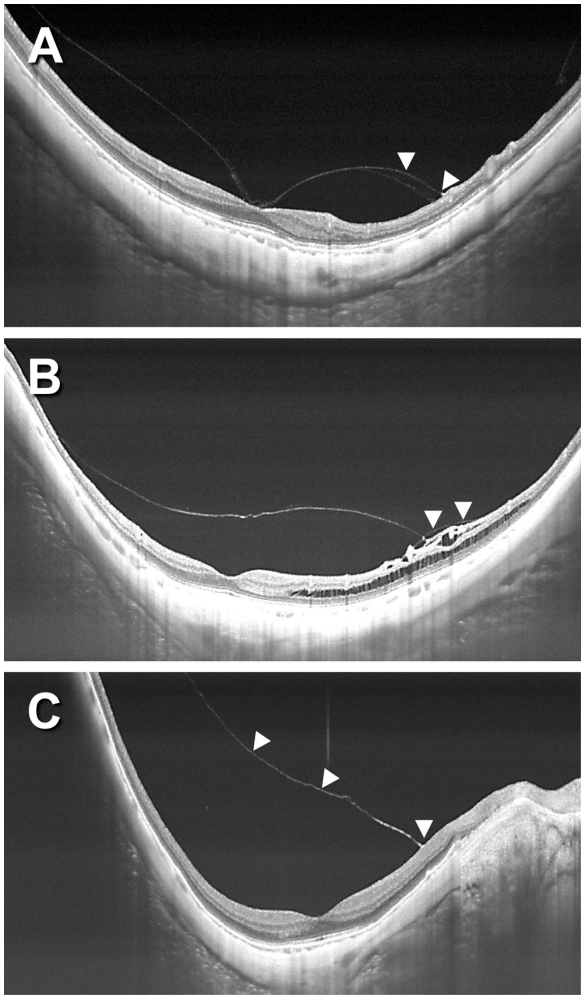

Figure 3. Swept-source OCT and fundus images of representative eyes with abnormal PVDs that are specific to pathologic myopia. The SS-OCT images show multiple PVDs with vitreoschisis (**A**, arrowheads), thickened vitreous cortex adhering to the retinal vessels (**B**, arrowheads), and long strands of posterior vitreous cortex (**C**, arrowheads). All eyes had a tessellated fundus without myopic retinochoroidal atrophy.

Acknowledgments

The authors thank Koji Yonemoto (Ryukyu University, Naha, Japan) for assistance with the statistical analysis.

The authors alone are responsible for the content and writing of the paper.

Disclosure: **K. Hayashi,** None; **S. Manabe,** None; **A. Hirata**, None; **K. Yoshimura,** None

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