

Initial Stages of Posterior Vitreous Detachment in Healthy Eyes of Older Persons Evaluated by Optical Coherence Tomography

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Objective: To promote understanding of the development of posterior vitreous detachment (PVD) in healthy eyes using optical coherence tomography (OCT).

Methods: We studied 209 eyes of 209 healthy volunteers (165 men and 44 women; mean age, 52.3 years [range, 31-74 years]). In addition to biomicroscopy and ophthalmoscopy, OCT was performed to obtain high-resolution cross-sectional images of the vitreoretinal interface in the posterior fundus.

Results: The condition of the posterior vitreoretinal interface was classified as 1 of 5 stages, according to biomicroscopic findings and OCT images relative to discrete linear signals indicating a detached posterior vitreous face: stage 0, no PVD (61 eyes [29.2%]); stage 1, incomplete perifoveal PVD in up to 3 quadrants (100 eyes [47.8%]); stage 2, incomplete perifoveal PVD in all quadrants, with residual attachment to the fovea and optic disc (26 eyes [12.4%]); stage 3, incomplete PVD over the posterior pole, with residual attachment to the optic disc

(4 eyes [1.9%]); or stage 4, complete PVD identified with biomicroscopy, but not with OCT because of instrument limitations (18 eyes [8.6%]). Stage 1, 2, and 3 incomplete PVD without subjective symptoms was not recognizable on contact lens biomicroscopy. There was a significant age-related progression in the condition of the vitreoretinal interface from stage 0 to stage 4. The superior quadrant was usually the initial site of incomplete PVD.

Conclusions: Optical coherence tomography demonstrates that healthy human eyes have incomplete or partial PVD beginning as early as the fourth decade of life. Age-related PVD occurs initially as a focal detachment in the perifovea of 1 quadrant, with persistent attachment to the fovea and optic nerve head, with a predilection for the superior quadrant. It extends its range slowly for years and eventually results in complete PVD, associated with release of vitreopapillary adhesion.

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POSTERIOR vitreous detachment (PVD) is one of the most striking age-related changes in the human eye. According to autopsy studies,^{1,2} PVD is present in fewer than 10% of persons younger than 50 years, but has been found in at least one eye in 27% of individuals aged 60 to 69 and in 63% of subjects aged 70 and older. Clinical studies³⁻⁸ also reveal a low incidence of PVD in individuals younger than 50. Posterior vitreous detachment is believed to develop after liquefied vitreous passes abruptly into the subhyaloid space and separates the posterior hyaloid from the retina.^{9,10} However, the actual process in older persons with healthy eyes remains unknown, because of the difficulty in identifying its initial stage.¹¹ Optical coherence tomography (OCT) provides high-resolution cross-sectional images of the posterior vitreous cavity and the retina.¹²⁻¹⁴ In this prospective study, we

used commercially available OCT equipment to improve our understanding of the process of PVD in older persons with healthy eyes.

RESULTS

Optical coherence tomography of the posterior vitreous cortex in 209 healthy eyes of 209 adults with healthy eyes showed either optically empty space or a discrete linear signal (**Figure 2**). The discrete linear signal was blue or blue-green, sharply defined, and localized up to about 800 μm from the retinal surface, forming a convexoconvex or planoconvex clear space by attachment to the posterior and mid-peripheral retina. The discrete linear signal was reproducible. Based on the location and extent of the signal, the condition of the posterior vitreous was classified as 1 of 5 stages: no PVD (stage 0), incomplete PVD (stages 1, 2, and 3), or complete PVD (stage 4).

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SUBJECTS AND METHODS

A prospective study using biomicroscopy and OCT was designed to evaluate the relationship of the posterior vitreous face relative to the retina in older persons with healthy eyes. Subjects were recruited on a voluntary basis and gave informed consent to the study purpose and examinations. A complete medical and ophthalmic examination included measurement of best-corrected visual acuity and refraction, slitlamp biomicroscopy with a +90 diopter (D) lens, and indirect ophthalmoscopy. Individuals were excluded if they had corrected visual acuity of less than 20/20, intraocular pressure of 22 mm Hg or higher, a remarkable eye disorder such as cataract or retinal detachment, or systemic diseases such as diabetes mellitus or systemic hypertension. Therefore, 209 subjects (165 men and 44 women) were enrolled in the study. The mean age was 52.3 years (range, 31-74 years). Only the right eye of each subject was examined by OCT. The mean refractive error was -1.42 D (range, $+5.0$ D to -10.75 D). One hundred ninety-three eyes (92.3%) had refractive errors between $+3.0$ D and -3.0 D; 16 eyes (7.7%) with larger refractive errors were included in the study because they had corrected visual acuity of 20/20 or better.

Optical coherence tomography was performed in all eyes by a single operator (E.U.), using commercially available equipment (Humphrey Instruments, Division of Carl Zeiss; San Leandro, Calif) to obtain axial views of the vitreoretinal interface in the posterior fundus. After pupillary dilation with a mixture of 0.5% phenylephrine hydrochloride and 0.5% tropicamide (Mydrin-P; Santen Pharmaceuticals, Osaka, Japan), we obtained a series of at least 6 images of 7 mm in length through the center of the fovea along the horizontal and vertical axes, each overlapped to evaluate the widest possible area of the posterior fundus, as illustrated in **Figure 1**. To assess the faint reflectivity of the posterior hyaloid, the incident light was set at its maximum (750 μ W), and the focal plane and polarization of the instrument were adjusted to provide the highest possible signal. Optical coherence tomographic digital images of the posterior fundus were processed using commercial software (Adobe Photoshop; Adobe Systems Inc, San Jose, Calif) to obtain a composite of overlapped images. All images were assessed independently by 2 of us (E.U. and A.U.) relative to the vitreoretinal interface and, in particular, the discrete linear signals in the posterior vitreous cavity, believed to represent the posterior hyaloid face separated from the retina.^{14,15} In addition, the extent of PVD was evaluated by measuring the distance between the detached posterior vitreous face and the retina. Data were analyzed using χ^2 test and analysis of variance.

Stage 0 was defined by the absence of PVD (Figure 2A). At this stage, there was no discrete linear signal on any images along the horizontal or vertical axis. Some eyes at this stage had random signals over the retinal surface, presumably representing the posterior vitreous face firmly attached to the retina.

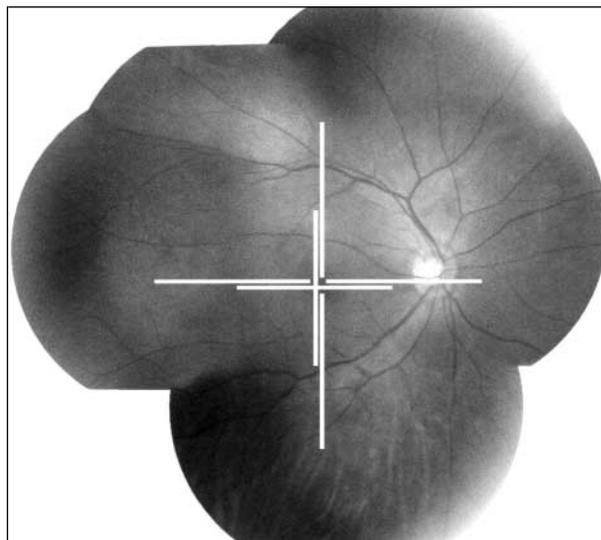


Figure 1. The area of optical coherence tomographic scanning. A series of images 7 mm in length was obtained in each subject through the fovea along the horizontal and vertical axes; each overlapped to evaluate the widest possible area of the posterior fundus.

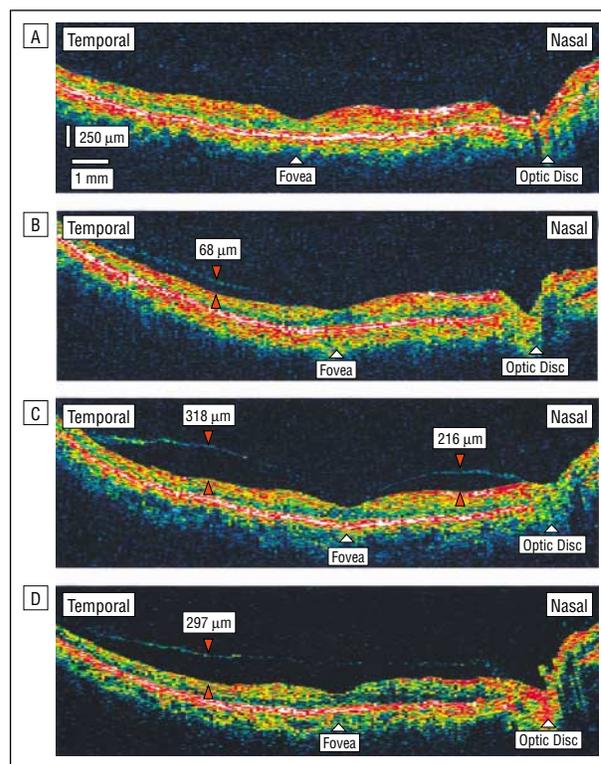


Figure 2. Optical coherence tomographic images illustrating various stages of posterior vitreous detachment (PVD). A, Stage 0, no PVD. B, Stage 1, incomplete PVD in the temporal periphery, with a definite discrete linear signal (68 μ m from the retinal surface), with attachment to the fovea, optic nerve head, and midperipheral retina. C, Stage 2, incomplete PVD in the temporal and nasal periphery, with convex retrovitreous spaces associated with attachment of the posterior vitreous face to the fovea and midperipheral retina. D, Stage 3, incomplete PVD over the posterior pole, with persistent attachment to the optic nerve head.

Stage 1 was defined by focal perifoveal PVD (Figure 2B). This stage showed incomplete PVD that was localized in the perifovea, with persistent attachment to the fovea, optic nerve head, and midperipheral retina. In-

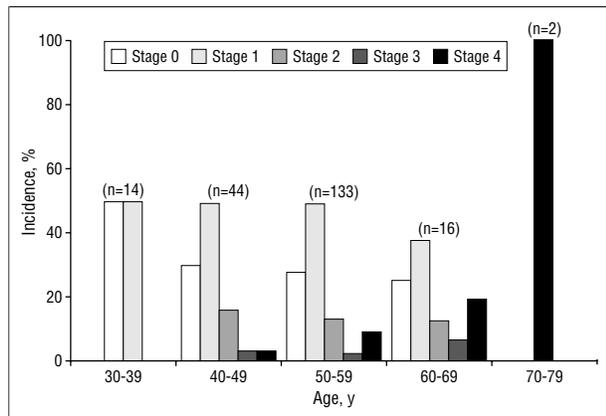


Figure 3. Incidence of stages of the vitreoretinal interface relative to the subjects' age by decade, as seen by optical coherence tomography. Stage 0, no posterior vitreous detachment (PVD); stages 1, 2, and 3, incomplete PVD; and stage 4, complete PVD. A χ^2 test of data grouped by stage (stages 0, 1-3, and 4) and age (30-49, 50-59, and 60-79 years) shows a significant age-related increase in the number of advanced stages ($\chi^2_4=12.31$, $P=.02$).

complete PVD occurring in 1 to 3 quadrants was classified as stage 1.

Stage 2 was defined by perifoveal PVD across all quadrants, with persistent attachment to the fovea, optic nerve head, and midperipheral retina (Figure 2C).

Stage 3 was defined by detachment of the posterior vitreous face from the fovea, with persistent attachment to the optic nerve head and midperipheral retina (Figure 2D).

Stage 4 was defined by complete PVD, with biomicroscopically identified detachment of the posterior vitreous face with Weiss ring. However, OCT at this stage failed to detect any discrete linear signal because the distance from the retina was outside of the range of OCT.

Of the 209 eyes, 61 (29.2%) were stage 0; 100 (47.8%), stage 1; 26 (12.4%), stage 2; 4 (1.9%), stage 3; and 18 (8.6%), stage 4, with complete PVD. One hundred thirty eyes (62.2%) with incomplete PVD (stages 1-3) were asymptomatic, and none had any biomicroscopic evidence of PVD or Weiss ring. All eyes with complete PVD showed Weiss ring on biomicroscopy.

Figure 3 illustrates the incidence of incomplete or complete PVD relative to the subjects' age decade. Stage 1 PVD was found in half of subjects in their fourth decade. With age, the number of subjects with no PVD decreased, while the number with incomplete or complete PVD increased. Although the number of subjects older than 60 years was small, an age-related progression from no PVD through incomplete PVD to complete PVD was significant.

The site and extent of incomplete PVD were variable among eyes. Of 100 stage 1 eyes, 46 had incomplete PVD in 1 quadrant, 26 in 2 quadrants, and 28 in 3 quadrants. Twenty-six stage 2 eyes had, by definition, incomplete PVD in all quadrants. The extent of PVD in these eyes was determined with OCT by measuring the maximum distance (in micrometers) between the discrete linear signals and the retina (Figure 2). Among stage 1 eyes, the mean (SD) distance was 97.6 (47.9) μm in 46 eyes involving 1 quadrant, 115.0 (69.4) μm in 26 eyes involving 2 quadrants, 122 (89.6) μm in 28 eyes involving 3 quadrants, and among 26 stage 2 eyes, the mean distance was 143.8 (100.4) μm . A statistically significant in-

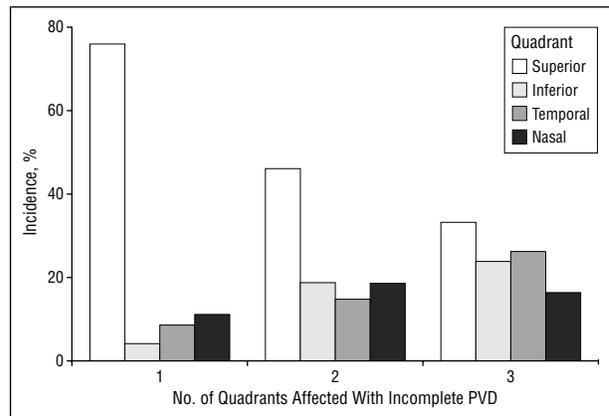


Figure 4. Geographical distribution of stage 1 incomplete posterior vitreous detachment (PVD). The incidence is shown in 3 groups: 46 regions of 46 eyes involving 1 quadrant, 52 regions of 26 eyes involving 2 quadrants, and 84 regions in 28 eyes involving 3 quadrants. Involvement of the superior quadrant is significantly frequent in all groups (χ^2 test, $P<.001$ for all groups).

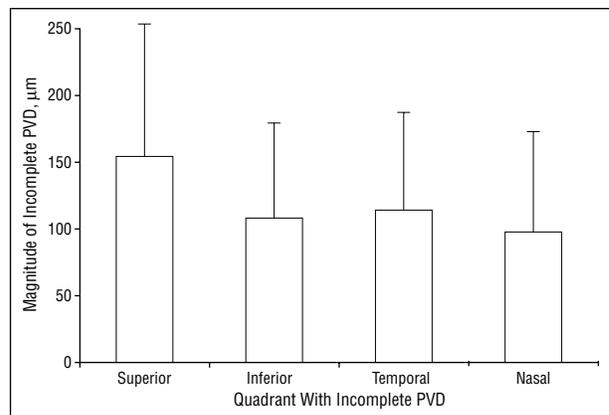


Figure 5. Quadrants of incomplete posterior vitreous detachment (PVD) and distance in micrometers between the discrete linear signal and retina. Data were collected from 100 eyes with incomplete PVD: superior quadrant, mean (SD), 152.1 (99.9) μm , measured in 167 sites in 87 eyes; inferior quadrant, 107.9 (68.6) μm , in 87 sites in 32 eyes; temporal quadrant, 113.6 (74.6) μm , in 86 sites in 34 eyes; and nasal quadrant, 98 (73.0) μm , in 67 sites in 29 eyes. The magnitude of incomplete PVD was significantly greater in the superior quadrant (1-way analysis of variance, $P<.001$).

crease in magnitude was noted between the stages of incomplete PVD (1-way analysis of variance, $P=.02$). The magnitude of incomplete PVD increased significantly from stage 1 involving 1 quadrant to stage 2 ($P=.002$), and from stage 1 involving 2 quadrants to stage 2 ($P=.048$).

To determine whether there is any geographic predilection for the initial development of PVD, a series of OCT images through the fovea along the horizontal and vertical axes was evaluated for the quadrant affected with stage-1 incomplete PVD. The results are shown in **Figure 4**. There was a statistically significant predilection for the superior quadrant. Furthermore, the extent of incomplete PVD was significantly greater in the superior quadrant, as shown in **Figure 5**.

COMMENT

These results elucidate the anatomical properties and evolution of PVD in adults with healthy eyes. A reproduc-

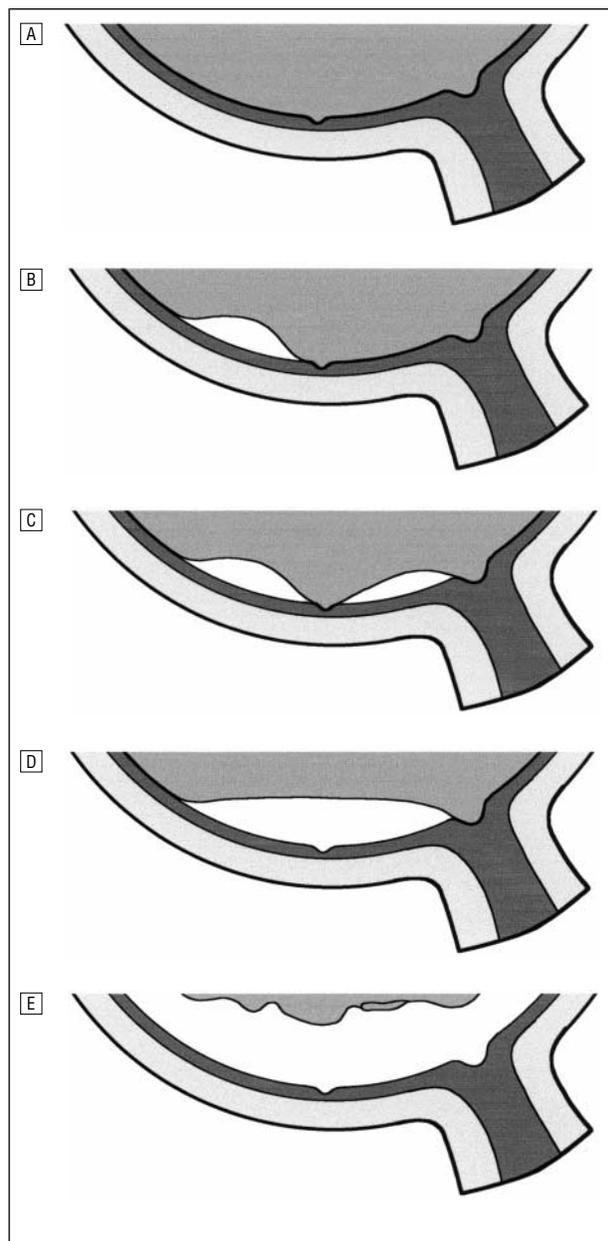


Figure 6. A schematic portrayal of the development of age-related posterior vitreous detachment (PVD), as seen by optical coherence tomography. A, Vitreoretinal interface without PVD. B, Posterior vitreous detachment initially occurs in the perifovea, with a predilection for the superior quadrant. C, Detachment extends widely in the perifovea, with persistent attachment to the fovea and optic nerve head. D, Detachment occurs in the fovea, with persistent attachment of the posterior vitreous face to the optic nerve head. E, Detachment is completed in association with release of the vitreopapillary adhesion.

ibly observed, remarkable finding was a discrete linear signal in the posterior vitreous cavity, characterized by a blue or blue-green weak intensity in the false-color display system of the OCT instrument and distinguished from random noise signals in the vitreous cavity. Similar characteristic vitreous signals on OCT have been described previously, termed *posterior hyaloid membrane* or *discrete linear signals*, and are believed to represent a detached posterior vitreous face.¹³⁻¹⁵

The condition of the vitreoretinal interface is staged according to OCT findings. In this study, many healthy

eyes without biomicroscopic identification of PVD had shallow vitreous detachment in the macular area in varying degrees. In addition, PVD begins at younger ages than previously thought, with more than half of individuals younger than 50 years showing asymptomatic, initial PVD localized in the perifovea, with a significant age-dependent, slow progression to advanced stages in subsequent decades. Subclinical or occult PVD, as observed by OCT, has also been reported in the healthy fellow eyes of patients with macular holes.^{14,15} Gaudric et al¹⁴ detected initial stages of vitreous separation in 45 of 61 eyes: 26 with perifoveal hyaloid detachment, corresponding to stage 1 or stage 2 in this study, and 19 with central hyaloid detachment, corresponding to stage 3. The present study is the first, to our knowledge, to evaluate the initial occurrence and progressive development of PVD in a large number of older persons with healthy eyes, as seen by OCT.

Previous studies³⁻⁸ have reported age-dependent PVD in older populations with or without vitreoretinal disease, describing a prevalence of 50% or more in individuals aged 70 years and older. Posterior vitreous detachment is usually subdivided into partial and complete forms.^{16,17} However, most data concern complete PVD, with little information available about the prevalence of the earlier phase of PVD in eyes without vitreoretinal disease, presumably because of the difficulties in obtaining biomicroscopic evidence of partial or incomplete PVD. Recently, Kakehashi et al¹⁷ examined a large cohort of eyes with and without vitreoretinal disease using biomicroscopy and photography and reported that partial PVD without thickened vitreous cortex was found in 44% of eyes without any ocular disease. They speculated that this type of PVD might be a transition phase to complete PVD. In our study, obvious partial PVD without thickened vitreous cortex was not detected on biomicroscopy. A reason for the discrepancy may be that the mean age of the subjects in the present study was younger than that of the patients described in the report by Kakehashi et al (52.3 years vs 62.5 years). Incomplete or subclinical PVD, as seen on OCT, is considered a form of partial PVD without thickened vitreous cortex. Stage 3 incomplete PVD may be visible on biomicroscopy when extensive, but we found no biomicroscopic abnormalities in those eyes.

The pathophysiologic mechanism of the development of PVD is beyond the scope of this study. However, some aspects warrant discussion. Aging of the vitreous and vitreoretinal interface, with liquefaction of the vitreous and weakened adhesion of the internal limiting membrane, is thought to be responsible for the development of PVD.^{11,18} We believe that subclinical PVD is also caused by other age-dependent changes of the vitreous, such as vitreous shrinkage and weakening of vitreoretinal adhesion, which may pull the posterior vitreous forward and result in its slight detachment. Morphologic changes of the vitreous body, as visualized by OCT, may begin in most individuals before age 50.

Age-related PVD is believed to occur as an acute event. Lindner⁴ and Eisner⁹ described such precipitating events as a tear formed in the posterior cortical vitreous in the region of the macula, through which lique-

fied vitreous passes to the vitreous cortex, followed by separation of the surrounding cortical vitreous from the retina. Eisner referred to this as *rhegmatogenous PVD*. Acute PVD usually results in extensive separation of the vitreous gel from the retina posterior to the vitreous base, in particular the superior quadrants. However, our results indicate that age-related PVD is not acute but insidious, so that it occurs initially in the perifovea as a focal, shallow PVD, extends slowly as subclinical PVD for years without any visual symptoms, and eventually results in complete PVD on acute release of the vitreopapillary adhesion of the posterior vitreous face.

The OCT images in this study provide new information about the evolutionary process of PVD in healthy eyes. It has been suggested that age-related PVD begins in the posterior pole.^{1,2,19,20} Optical coherence tomography images by Gaudric et al⁴ of healthy fellow eyes of patients with idiopathic macular hole showed partial posterior hyaloid detachment beginning around the macula, usually on its nasal side. The present results demonstrate that the initial occurrence of occult PVD is predominantly in the perifovea of the superior quadrant. In addition, the extent is initially small and becomes larger with progressive extension of the PVD.

Based on the present findings, a schema of the age-related evolution of PVD in otherwise healthy eyes is presented in **Figure 6**. The initial site of PVD is the perifovea, seen as a shallow, convexoconvex or planoconvex retrohyaloid space in a single quadrant, predominantly its upper site, followed by a gradual progression over many years to involve all quadrants, with persistent attachment to the fovea and to the margin of the optic disc. Throughout these stages, the separation of the posterior vitreous face remains focal in the posterior pole of the fundus, corresponding to partial PVD in the classification system, although midperipheral and peripheral conditions are not informative with OCT because of instrument limitations. Eventually, the evolution of PVD results in separation from the optic disc margin and leads to clinically identifiable PVD, with acute signs and symptoms.

This study assessed the evolution of PVD in healthy adults. Separation of the posterior vitreous face plays a role in the underlying cause of age-related vitreoretinal disorders, such as idiopathic macular hole and vitreomacular traction syndrome.¹⁵ None of our subjects with OCT-observed separation of the posterior vitreous face showed any disruptive change in the high-resolution cross-sectional images of the retina. Optical coherence tomographic images of healthy-appearing fellow eyes of patients with idiopathic macular hole sometimes demonstrate minimal macular change, associated with in-

complete PVD.^{14,15} High-resolution evaluation of the vitreoretinal interface using OCT may provide useful information about the pathogenesis of various vitreoretinal disorders.

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