# Juxtapapillary Pigment Epithelium Detachment Observed in Asymptomatic Participants Using Optical Coherence Tomography

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**Purpose.** To use three-dimensional optical coherence tomography (3D-OCT) to assess the prevalence of juxtapapillary retinal pigment epithelial detachments (jPED) in an asymptomatic population.

**Methods.** Asymptomatic participants (i.e., family members of patients) were prospectively recruited over a 6-month period. Each subject completed a questionnaire prior to the acquisition of two undilated 45° fundus images and two undilated raster 3D-OCT scans (512 × 128) covering the macula and optic nerve from each eye using 3D-OCT-1000. Fundus images were graded for the presence of peripapillary atrophy (PPA), peripapillary pigment (PPP), drusen in the macula, and drusen elsewhere, whereas 3D-OCT scans were assessed for the presence of jPED, drusen in the macula, and drusen elsewhere.

**Results.** In all, 276 eyes from 138 participants were evaluated. Mean participant age was 37.6 years (range: 18–74 years; SD: 15.5 years). In all, 87 jPEDs were detected in 26.1% (36/138) of asymptomatic participants (25 bilateral and 11 unilateral) or 17.0% (47/276) of asymptomatic eyes (23 in the right eye and 24 in the left). The maximum height of jPED was 198.3 ± 53.8 (range: 101.8–376.0) μm. The minimum distance of jPED to the border of optic nerve head (OPN) was 2.6 ± 11.1 (range: 0–61.9) μm. The occurrence of jPEDs or drusen elsewhere by subjects increased statistically with increasing age ($P < 0.001$, respectively).

**Conclusions.** In this study, definite jPEDs were observed by OCT in asymptomatic participants, which were not seen with fundus photography. jPEDs were seen more commonly with increasing age, although it is not known whether these lesions represent deposition of drusen-like material or aborted choroidal neovascularization adjacent to the natural break in Bruch's membrane at the optic disc. (*Invest Ophthalmol Vis Sci.* 2013;54:1144–1149) DOI:10.1167/iovs.12-9903

Because of its central location connecting the optic nerve and the posterior termination of the retina, retinal pigment epithelium (RPE), Bruch's membrane, and choriocapillaris, the juxtapapillary region is of vital importance in clinical ophthalmology. This importance has been well recognized in the study of optic neuropathies such as glaucoma; as a result, extensive efforts have been made by glaucoma specialists to characterize the region's structure using imaging techniques such as optical coherence tomography (OCT). The juxtapapillary region is also important for a variety of chorioretinal diseases, such as peripapillary choroidal neovascularization (PPCNV) and serous retinal detachment secondary to optic disc pits.[1–3] Despite this, juxtapapillary anatomy has not been well studied by retina specialists, perhaps in large part due to its location away from the fovea, with lesions often remaining asymptomatic until they involve the macula. However, the insights afforded by such study may be applicable to macular pathologies, in particular, the deposition of drusenoid material in the juxtapapillary region, and the invasion of the potential space, between the termination of the RPE and Bruch's membrane, by choroidal neovascularization (CNV).

Previous histopathologic reports suggest a general underestimation of juxtapapillary lesions as reported in clinical studies.[1,2,4] In 1966, Gass[1] presented the histopathologic finding of large drusen deposition at the margin of the optic nerve head in a 60-year-old patient (a finding that was clinically unapparent) and considered the peripapillary deposit of sub-RPE eosinophilic material a common finding in older patients. This concept was in agreement with Hogan et al.,[5] who had previously proposed that drusen are frequently found at the posterior termination of Bruch's membrane. In the same study, Gass[1] also described histologic findings from an eye with peripapillary deposits invaded by new vessels from the margin of the optic nerve head, without clinical detection prior to eye dissection. Similarly, in 1973, Sarks[3] evaluated posterior pole histopathology in an older population, and found juxtapapil-

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**Table 1.** Grading Protocol

| | Image Used for Grading | | | |
|---|---|---|---|---|
| | FP (Centering at) | | 3D-OCT (Centering at) | |
| **Features Graded** | **Macula** | **OPN** | **Macula** | **OPN** |
| jPED | | | | X |
| Drusen elsewhere (OCT+FP) | X | X | X | X |
| Drusen in the macula (OCT+FP) | X | | X | |
| Peripapillary atrophy | X | | | |
| Peripapillary pigment | X | | | |

FP, fundus photography.

lary neovascularization in 16% of eyes with a normal fundal appearance, and without any visible break in Bruch's membrane. More recently, Curcio et al.[4] observed blood vessels at the peripapillary margin of Bruch's membrane and a high frequency of peripapillary drusen-like deposits in eyes without macular or peripapillary chorioretinal pathologic conditions.

In total, these studies suggest that, in older participants, small and asymptomatic PPCNV may occur with greater frequency than the large, asymptomatic peripapillary membranes that progress to involve the macular area.[3] It can also be inferred that, without the proper examination methodology and with this apparent lack of clinical manifestation, these abnormalities have been largely overlooked. Fortunately, however, OCT imaging is well suited to cross-sectional evaluation of the juxtapapillary region and, in particular, to the detection of juxtapapillary pigment epithelium detachment (jPED). In this study, we use spectral-domain OCT to evaluate the prevalence of jPED in an asymptomatic population, and to describe its clinical characteristics.

## Methods

### Data Collection

In this study, asymptomatic participants (i.e., family members of patients attending a retina subspecialty clinic of the Doheny Eye Institute) were prospectively recruited between June 5, 2009 and December 21, 2009. Written informed consent was obtained from all participants. Approval for data collection and analysis was obtained from the institutional review board of the University of Southern California. The research adhered to the tenets set forth in the Declaration of Helsinki.

Information about age, sex, race, history of systemic medical diseases or surgeries, history of ophthalmic diseases or surgeries, and family history of eye diseases was gathered before ophthalmic examination. Participants underwent examination of the optic nerve and retina with fundus and 3D-OCT imaging (3D OCT-1000; Topcon Corp., Tokyo, Japan), in the absence of pupillary dilatation. For each eye, two raster 3D-OCT scans ($512 \times 128$, one centering at the macula, one centering at the optic nerve head [OPN]) were obtained. Then, a pair of color images centering the optic disc and macula with a view angle of 45° was acquired with the same instrument as the OCT scans (OCT scans and color images were taken sequentially to maximize the quality of both).

Raw OCT data were exported from the imaging instruments and imported into validated custom image-grading software (3D-OCTOR; Doheny Image Reading Center [DIRC], Los Angeles, CA).[6] B-scans with the maximum height (MaxH) of each jPED were also exported and reviewed with free image and photo editing software (Paint.Net; dotPDN, LLC, Kirkland, WA) for measurement.

### Grading Methodology

Two graders (YO, ACW), certified for assessing color fundus and OCT images at the DIRC, independently evaluated each set of images for each eye (Table 1).

In color fundus photography (FP), the optic disc was defined as the area encompassed by the peripapillary sclera ring. Peripapillary atrophy (PPA) was characterized by depigmentation of RPE, clearly demarcated borders, and good visibility of large choroidal vessels and the sclera, adjacent to the peripapillary sclera ring of the optic nerve. Peripapillary hyperpigmentation (PPP) was defined as hyperpigmentary changes adjacent to the optic disc or PPA. For each eye, the grading from the optic nerve centered image and that from the macular centered image were combined to arrive at a single final grade. Using these criteria, PPA, PPP, "drusen in the macula (FP)," and "drusen elsewhere (FP)" (defined as drusen not adjacent to OPN seen by FP, including "drusen in the macula") were assessed as definite present (Y), questionable present (Q), absent (N), or cannot grade (CG).

Custom image-grading software (3D-OCTOR; DIRC)[6] was used to assess volume OCT scans in the study. It was specially adapted for this study to load and display the dense 3D-OCT data sets. It also allowed simultaneously point-to-point comparison of OCT B-scan with OCT projection map. On OCT B-scans, we defined jPED as elevation of the RPE, forming a detachment from the underlying Bruch's membrane, adjacent to the terminus of the optic disc (Fig. 1). "Drusen elsewhere (OCT)" was regarded as detachment of the RPE away from the terminus of the disc. "Drusen in the macula (OCT)" was "drusen elsewhere (OCT)" observed by using OCT images centered in the macula. For each eye, two sets of OCT images were assessed in combination before arriving at the final grading for drusen elsewhere (OCT). For each case, jPED, drusen in the macula (OCT), and drusen

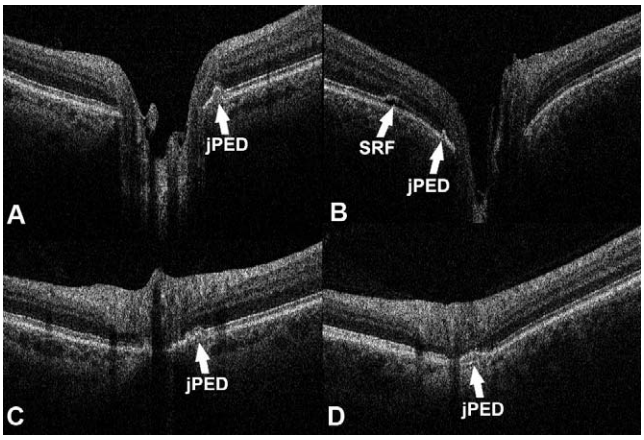


**Figure 1.** Case examples of jPED seen by 3D-OCT. (**A–D**) Examples of definite jPEDs in different locations. (**B**) jPED with adjacent subretinal fluid (SRF), suggesting that these are dynamic lesions.

**Table 2.** Patient Demographics

| Features | Age at Risk, y Mean ± SD (Range) | No. at Risk (Gradable) | | Positive Grading by Eye, No. (%) | | Positive Grading by Subjects, No. (%) | |
|---|---|---|---|---|---|---|---|
| | | Eyes | Subjects | Y | Q | Y | Q |
| jPED | 37.6 ± 15.5 (18–74) | 276 | 138 | 47 (17.0%) | 0 (0) | 36 (26.1%) | 0 (0) |
| Drusen elsewhere (OCT+FP) | 37.6 ± 15.5 (18–74) | 276 | 138 | 77 (27.9%) | 52 (18.8%) | 57 (41.3%) | 30 (21.7%) |
| Peripapillary atrophy | 35.8 ± 14.0 (18–69) | 247 | 130 | 67 (27.1%) | 0 (0) | 46 (35.4%) | 0 (0) |
| Peripapillary pigment | 36.0 ± 14.3 (18–69) | 245 | 129 | 70 (28.6%) | 0 (0) | 49 (38.0%) | 0 (0) |

elsewhere (OCT) were recorded as definite present (Y), questionable present (Q), absent (N), or cannot grade (CG). If the grading for jPED was positive ("Y" or "Q"), the location of the jPED relative to OPN was further assessed (using 3D-OCTOR). By clicking the jPED in OCT B-scan, the location of this jPED in the OCT projection map was also shown. They were documented as: temporal (T), superotemporal (ST), inferotemporal (IT), nasal (N), superonasal (SN), inferonasal (IN), superior (S), or inferior (I). When multiple lesions were present in the same sector, each location was counted only once for each eye. In addition, each positive jPED was given a unique identity. Then MaxH of jPED was measured (Paint.Net; dotPDN, LLC). The minimum distance of each jPED to the border of OPN was also measured by choosing the nearer end of the jPED to the closest border of OPN seen in OCT.

The final grading results for "drusen in the macula (OCT+FP)"/"drusen elsewhere (OCT+FP)" were then obtained by the combination of drusen in the macula/elsewhere (OCT) and drusen in the macula/elsewhere (FP) (Table 1).

## Statistical Analysis

Only gradable fundus photographic and OCT image sets were used for analyses in the study. For participant-specific analyses, when two eyes of a participant were discrepant in the severity of a lesion, the grade of the more severely affected eye was assigned to the participant. For example, if jPED was graded "Y" in one eye but "N" in the other eye, the participant was considered to have definite jPED. Participants with unknown sex or age were not included in the analyses of frequencies of lesions by sex and age, but included in all other analyses. For eye-specific analyses, the frequencies of lesions and their locations relative to the optic disc were obtained from all gradable records.

Commercially available software (SPSS, version 13; StataCorp LP, College Station, TX) was used for processing all statistical analysis. To evaluate the correlation of the presence of definite jPED/PPA/PPP/drusen in the macula (OCT+FP)/drusen elsewhere (OCT+FP) by participants with increasing age, logistic regression was used. Logistic regression measures the relationship between a categorical dependent variable (e.g., presence of definite jPED) and usually a continuous independent variable (e.g., age), by converting the dependent variable to probability scores.[7] Correlation analyses of the presence of jPED with PPP or PPA or drusen in the macula (OCT+FP) or drusen elsewhere (OCT+FP) by patients were also done. Since presence of each feature was graded as "Y," "Q," and "N" in our study, and was considered as ordinary or data, Kendall's tau-b correlation was used.[8]

All $P$ values were two-sided and were considered statistically significant at $P < 0.05$.

# Results

## Characteristics of the Study Population

In all, 158 participants signed the consent form for the study. Twenty-six eyes, from 14 participants, failed to complete OCT and/or color fundus examination. Two participants reported newly onset eye problems. Four eyes, from four participants, with ungradable OCT images were excluded. The remaining 282 eyes, from 144 participants, met the inclusion criteria for the study. Six of these participants had only one eye gradable for jPED; thus, for the purpose of analyzing the prevalence of jPED, a total of 276 eyes from 138 participants were evaluated.

The demographic characteristics of participants in the study are summarized in Table 2. Of all eligible participants, 81 (58.7%) were females. One subject with unknown sex and 5 with unknown age were documented. The mean age of patients was 37.6 years, with a range of 18 to 74 (SD = 15.5) years. In all, 50.7% participants identified themselves as Hispanic or Latino, 19.6% as White (non-Hispanic), 18.1% as Asian, 4.3% as Black or African American, and 7.3% as Other or Unknown Race. Nine subjects had claimed family history of age-related macular degeneration (AMD).

All OCT images included in the study met reading center criteria for sufficient image quality for both jPED, drusen in the macula (OCT) and drusen elsewhere (OCT) grading, including the absence of significant image artifacts or generalized reductions in signal strength. Color images were gradable in 247 eyes for PPA and 245 eyes for PPP.

## Detection of Juxtapapillary Pigment Epithelium Detachment

Grading outcomes for jPED are provided in Table 2. In all, 87 jPEDs were detected in 26.1% (36/138) of asymptomatic participants or 17.0% (47/276) of asymptomatic eyes (23 in the right eye and 24 in the left).The mean number of jPEDs per eye for eyes with positive jPED is 2.9 ± 2.0 (range, 1–7). The MaxH of jPED was 198.3 ± 53.8 (range: 101.8–376.0) μm. The minimum distance of jPED to the border of OPN was 2.6 ± 11.1 (range, 0–61.9) μm. In the juxtapapillary region where jPEDs were accessed, no other abnormalities were found either on FP or on OCT, although in the area adjacent to the juxtapapillary region, one eye with subretinal fluid (SRF) was seen on OCT next to jPED (Fig. 1). The regional distribution of

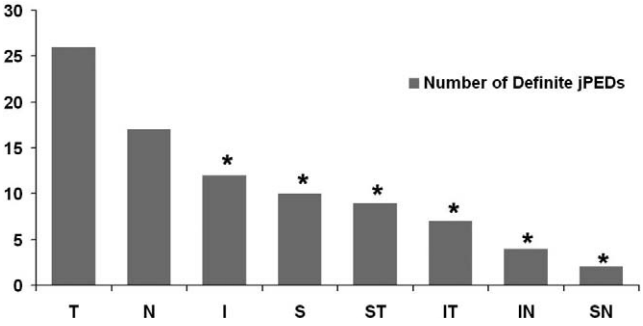


**Figure 2.** Regional distribution of jPEDs. *Asterisk* represents reduced visibility of the jPED under the large retinal vessels, which may have led to an artifactitious reduction in jPED prevalence in these areas.

**Table 3.** Percentage of Definite Juxtapapillary Features by Age and Sex, for Subjects with at Least One Eye Affected

| Age, y | No. at Risk | jPED No. (%) | PPA No. (%) | PPP No. (%) | Drusen Elsewhere (OCT+FP) No. (%) |
|---|---|---|---|---|---|
| Males | | | | | |
| <25 | 9 | 1 (11.1%) | 5 (55.6%) | 4 (44.4%) | 1 (11.1%) |
| 25 to 34 | 21 | 3 (14.3%) | 8 (38.1%) | 7 (33.3%) | 10 (47.6%) |
| 35 to 44 | 8 | 3 (37.5%) | 2 (25.0%) | 5 (62.5%) | 3 (37.5%) |
| 45 to 54 | 6 | 5 (83.3%) | 2 (33.3%) | 4 (66.7%) | 4 (66.7%) |
| 55 to 64 | 4 | 2 (50.0%) | 1 (25.0%) | 1 (25.0%) | 1 (25.0%) |
| 65 to 74 | 6 | 2 (33.3%) | 3 (50.0%) | 2 (33.3%) | 6 (100.0%) |
| Females | | | | | |
| <25 | 16 | 0 (0.0%) | 2 (12.5%) | 6 (37.5%) | 4 (25.0%) |
| 25 to 34 | 27 | 5 (18.5%) | 12 (44.4%) | 4 (14.8%) | 9 (33.3%) |
| 35 to 44 | 13 | 5 (38.5%) | 3 (23.1%) | 6 (46.2%) | 6 (46.2%) |
| 45 to 54 | 10 | 4 (40.0%) | 3 (30.0%) | 2 (20.0%) | 3 (30.0%) |
| 55 to 64 | 6 | 2 (33.3%) | 2 (33.3%) | 2 (33.3%) | 3 (50.0%) |
| 65 to 74 | 7 | 3 (42.9%) | 1 (14.3%) | 2 (28.6%) | 5 (71.4%) |
| Sexes combined | | | | | |
| <25 | 25 | 1 (4.0%) | 7 (28.0%) | 10 (40.0%) | 5 (20.0%) |
| 25 to 34 | 48 | 8 (16.7%) | 20 (41.7%) | 11 (22.9%) | 19 (39.6%) |
| 35 to 44 | 21 | 8 (38.1%) | 5 (23.8%) | 11 (52.4%) | 9 (42.9%) |
| 45 to 54 | 16 | 9 (56.3%) | 5 (31.3%) | 6 (37.5%) | 7 (43.8%) |
| 55 to 64 | 10 | 4 (40.0%) | 3 (30.0%) | 3 (30.0%) | 4 (40.0%) |
| 65 to 74 | 13 | 5 (38.5%) | 4 (30.8%) | 4 (30.8%) | 11 (84.6%) |
| Total combined | 133 | 35 (26.3%) | 44 (33.1%) | 45 (33.8%) | 55 (41.4%) |

jPEDs is shown in Figure 2 (fewer jPEDs were found superiorly and inferiorly).

The prevalence of jPED by paticipants and by age can be seen in Table 3. Eight percent participants (11/138) with evidence of jPED in both eyes and 18.1% participants (25/138) with jPED in one eye were observed. Of those with jPED in at least one eye, 52.8% (19/36) were females. Looking at more severely affected eyes, the prevalence of jPED among females was 23.5% (19/81) compared with 28.6% (16/56) among males. Among all the subjects with jPED in at least one eye, one had claimed family history of AMD. The proportion of subjects affected by positive jPED did not differ between subjects with and without a family history of AMD ($P = 0.441$, Fisher's exact test).

The frequency of participants with jPED in the more severely affected eye, by age, is shown in Figure 3. The mean age of participants with bilateral jPEDs was 54.5 years (SD = 10.3; range: 41–69 years), whereas it was 42.0 years (SD = 14.4; range: 23–74 years) for those with unilateral jPED. When compared with the age of participants with no observed jPED in either eye (34.8 ± 15.0; range: 18–71 years), those with jPED in at least one eye were statistically older ($P = 0.001$, independent samples *t*-test). Using logistic regression analysis, the presence of jPED by subject was statistically correlated with increasing age ($P < 0.001$).

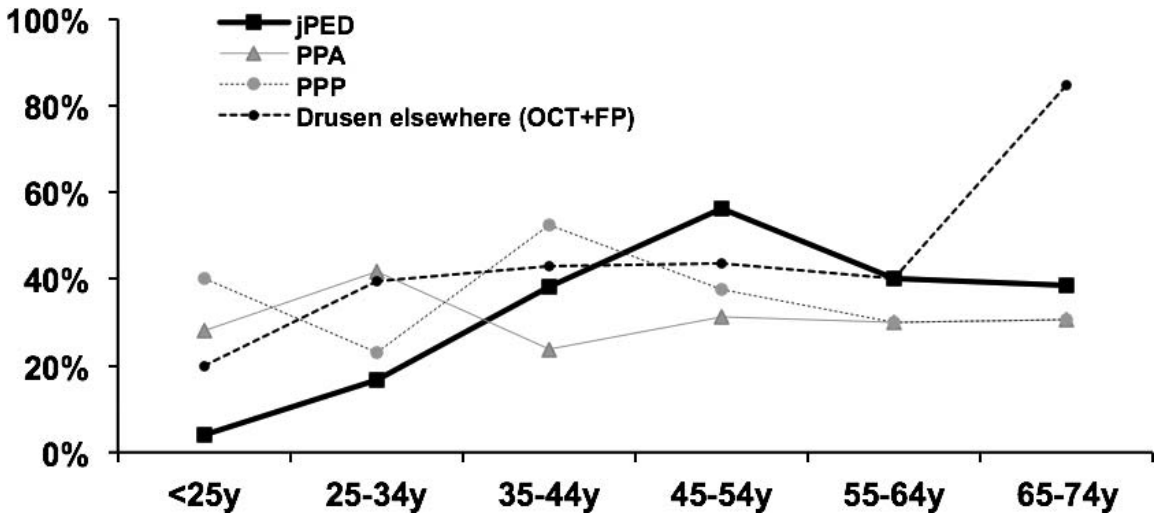


**Figure 3.** The frequencies of participants with definite jPED, PPA, PPP, and drusen elsewhere (OCT+FP), in the more severely affected eye, by age.

### Relationship of jPED with Other Juxtapapillary Features

Grading outcomes for drusen elsewhere (OCT+FP), PPA, and PPP are also shown in Table 2. In all, 22.5% (31/138) of subjects were affected with definite drusen in the macula (OCT+FP). Looking at the subjects with at least one eye affected for each feature, the presence of jPED by participants was not found statistically correlated with the presence of PPP ($P = 0.065$, $R^2 = 0.027$), or PPA ($P = 0.115$, $R^2 = 0.020$), or drusen in the macula (OCT+FP) ($P = 0.968$, $R^2 = 0.001$), or drusen elsewhere (OCT+FP) ($P = 0.219$, $R^2 = 0.011$). When both PPA and PPP were absent, jPED was still found in 20.6% (13/63) of participants or 15.4% (25/162) of eyes.

The frequency of participants with drusen elsewhere (OCT+FP), PPA, and PPP, in the more severely affected eye, by age is also shown in Figure 3. Using logistic regression analysis, the presence of drusen elsewhere (OCT+FP) ($P < 0.001$) by subjects was also found statistically significant with increasing age, although the presence of PPA ($P = 0.943$) or PPP ($P = 0.547$) by subjects did not correlate with age.

## Discussion

In this study, jPED was found in 26.1% of all study participants, and in 17.0% of all eligible eyes, with a strong association with increasing age, implying a disease progression rather than an inheritance variation. To our knowledge, this high prevalence of jPED in an asymptomatic population, and its clinical characteristics, have not been previously reported. Consideration of jPED structure and potential pathogenesis may provide insights applicable to future clinical and epidemiologic studies of macular disease (in particular, AMD).

What does the term "jPED" mean? A PED is defined as a separation of the RPE from Bruch's membrane.[9] The contents of the PED may consist entirely of fluid ("serous PED"), hemorrhage ("hemorrhagic PED"), sub-RPE deposits (drusen or drusen-like deposits: "drusenoid PED"), fibrovascularization ("fibrovascular PED"), or pseudovitelliform material. However, in many cases, a mixture of components is seen. In the present study, at the location where jPED was observed, no hemorrhage, drusen, or pseudovitelliform lesion was visible in either eye by careful color fundus grading. As a result, we considered serous fluid, drusen-like deposits, or fibrovascularization as candidates for jPED composition. On spectral-domain OCT raster scans, jPEDs usually appeared as an optically empty space. However, because the pigmented RPE monolayer is highly light reflective, visualization of the sub-RPE space is difficult on OCT without the use of specialized scanning protocols ("enhanced depth imaging"). Consequently, it may be difficult to differentiate a serous PED from a fibrovascular PED. Results from both histology and clinical studies also report a smaller proportion of patients with serous PED compared with fibrovascular PED.[10,11] In addition, progressive growth in size of serous PEDs is typically associated with vascularization of the PED.[11] The combination of these factors leads us to conclude that sub-RPE fibrovascularization (i.e., PPCNV) is the most likely feature of jPED in our study. This contention is somewhat supported by the finding in a single asymptomatic patient with SRF adjacent to a jPED in the study. However, irrespective of what the sub-RPE component proves to be, the space formed between Bruch's membrane and the RPE is associated with loss of normal adhesion between the two structures at the end of the optic nerve; such a space could facilitate neovascular ingrowth, particularly in areas with preexisting weakness or breaks in Bruch's membrane at its termination.

In a previous clinical study, PPCNV was considered to constitute only a small minority of cases of posterior pole CNV[2]; however, as discussed already, histopathologic reports suggest a higher prevalence, even in "normal" participants.[1,3,4] We conclude from our study that the frequency of PPCNV is higher than that previously described, although most such patients tend to be asymptomatic. Hence, we categorize PPCNV as symptomatic or asymptomatic. Symptomatic PPCNV is a well-recognized clinical feature of many pathologic conditions, most common in AMD and idiopathic cases. Idiopathic PPCNV is often described as occurring in patients between 60 and 70 years of age; however, many younger patients are also affected.[12,13] The natural course of untreated PPCNV ranges from spontaneous involution and stabilization to fulminant enlargement toward the fovea.[12] If it progresses toward the macula, it may result in disciform scar formation and significant visual loss. Thus, the importance of monitoring progression, and instigating appropriate treatment when necessary, is clear. For asymptomatic PPCNV, there is currently no evidence documenting its natural progression and the clinical risk of visual loss. In many patients, the growth factor milieu around the natural break in Bruch's membrane at the optic nerve may have an inhibitory effect on angiogenesis and counteract growth of neovascular tissue. With increasing age, however, degenerative changes accumulate in the RPE and choroid (as seen in patients with AMD), and the balance of growth factors may tip toward allowing vessel growth, with development of symptomatic PPCNV. This could explain why only a subset of patients would progress to symptomatic disease and the observed associations between jPED occurrence and age in this study.

Clinical detection of jPEDs, using biomicroscopy or FP, is made difficult by a number of factors. The anatomy of the optic nerve head and surrounding area is often highly variable, and jPEDs are often small (as was the case for most jPEDs in this study). The major vessels may obscure jPEDs in the superior and inferior quadrants. Juxtapapillary drusen deposition may also be obscured by proliferation or hyperpigmentation of the overlying pigment epithelium. PPCNV tissue is usually embedded in proteinaceous material and is partly covered by altered pigment epithelium, making clinical visualization difficult.[1] Even on angiography, during the initial stages of neovascularization, blood flow through the vascular network may be slow and accompanied by minimal or no exudation. During this preexudative, occult phase of neovascularization, the overlying RPE and retina may be anatomically and functionally minimally affected. Thus, biomicroscopic and angiographic clues to its presence are often missing.[10] Consequently, the results of our study suggest that volume OCT scans should be adopted for the detection and management of jPED and PPCNV.

Even OCT has limitations in the detection of jPED. The vast majority of jPEDs detected in this study with OCT were found in the nasal and temporal quadrants, with the fewer detected in the superior and inferior quadrants. Although an underlying anatomic explanation for this trend may be plausible, it is our contention that this represents an artifact of poor visualization in these quadrants due to obscuration of the outer retina, RPE, and choroid by the great vessels. If this is true, the actual frequency of jPED occurrence might be even greater than that found in this study.

In this study, we also sought to identify surrogate markers for jPED and thus aid clinicians in their choice of whether to perform OCT screening assessment of the juxtapapillary region. PPP or PPA or drusen in the macula (OCT+FP) or drusen elsewhere (OCT+FP) were the possibly coexisting

features; however, neither feature can be correlated with jPED. Even when both PPA and PPP were absent, jPED was still found in 15.4% of eyes. Thus, further studies may be required to identify better biomarkers.

It is noteworthy that a high prevalence of jPED was detected in the sample population (asymptomatic participants accompanying family members in an eye clinic waiting room) in the current study. In the case of retinal diseases of high prevalence, especially AMD, it was reported that for relatives of patients with late AMD, all manifestations of AMD occurred at an increased rate at a relatively young age.[14] Thus, selecting participants from family members of these patients could be a profound limitation of this study, although they considered themselves as "asymptomatic participants." In our study, the proportion of subjects affected by jPED in at least one eye was tested and did not differ between subjects with and without a family history of AMD; however, the participants were enrolled from all ophthalmology departments, with AMD a possible portion of the distribution, so the findings in our study may still not be representative. Further studies should be done to evaluate the prevalence of jPED in a larger and more representative population.

Our study has a number of other limitations. A relatively small number of participants was one major limitation, which potentially led to lower power for statistical analyses. For example, PPA was reported statistically significantly correlated with increasing age[15]; however, with our current data, this correlation was not found to be significant. Also as seen in Table 3, the number of subjects at risk in each age category had sizable variation. One other limitation was that color fundus images were obtained without mydriasis, possibly reducing the frequency of drusen detection and the accuracy of location and size determinations. In addition, information about medications related to systemic diseases and refractive error was not collected in the study. Future studies with more participants should be done.

In conclusion, jPEDs were found in 26.1% of asymptomatic participants, showing an increasing prevalence with age. The precise role of jPED in the pathogenesis of PPCNV and its value as a predictor of future damage remain to be determined. We speculate that jPEDs represent abortive attempts at neovascular invasion of the potential space between the RPE and Bruch's membrane; their exact nature is likely to be resolved with increased awareness of this feature, and improvement in advanced imaging techniques, such as OCT. The results of our study suggest that volume OCT scans should be adopted for the detection and management of jPED and PPCNV.

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