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ORIGINAL PAPER

# The comparison of spectral domain optical coherence tomography and indocyanine green angiography in the diagnosis of polypoidal choroidal vasculopathy

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**Abstract**
*Objectives* To evaluate the diagnostic capability of spectral domain optical coherence tomography (SD-OCT) in patients with potential diagnostic findings for polypoidal choroidal vasculopathy (PCV).
*Materials and methods* Ninety-three eyes with potential diagnostic findings for PCV were prospectively evaluated. Patients with multiple retinal pigment epithelial detachment (RPED), sharp RPED peak, RPED notch, hyporeflective lumen representing polyps, double-layer sign and the presence of hyperreflective intraretinal hard exudate were considered as PCV in SD-OCT. The sensitivity and specificity of SD-OCT in the diagnosis of PCV were determined by comparing SD-OCT-based diagnosis with indocyanine green angiography (ICGA).
*Results* Sixty-nine (74.2%) of 93 eyes included in the study were confirmed with ICGA and diagnosed as PCV. The sensitivity and specificity of SD-OCT for the diagnosis of PCV were 75.3% and 75%, respectively.
*Conclusion* The SD-OCT-based method helps clinicians to develop appropriate diagnostic and treatment strategies for patients in whom ICGA cannot be used.

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**Keywords** Polypoidal choroidal vasculopathy · SD-OCT · ICGA

## Introduction

Polypoidal choroidal vasculopathy (PCV) is a clinical entity characterised by multiple recurrent serosanguineous detachments of the retinal pigment epithelium and neurosensory retina secondary to leakage and bleeding from choroidal vascular lesions [1]. The disease usually presents with orange subretinal nodules in the macula or peripapillary region [2]. PCV has a higher prevalence in the Asian population, and it is frequently observed in men and unilateral [3].

While many studies have argued that PCV is a subgroup of neovascular age-related macular degeneration (n-AMD), there are also studies advocating that PCV is a different choroidal vasculopathy than n-AMD [4–6]. Furthermore, optical coherence tomography (OCT)-based imaging studies of PCV suggest that PCV may be included in the pachychoroid spectrum caused by pathology in the choroidal circulation [7]. Clinical manifestations of patients with PCV, overall visual prognosis, the natural history of the disease and evaluation of the group of patients at risk support that PCV is different from n-AMD [6, 8]. In addition, the differentiation of PCV from n-AMD is important because of the different management and treatment responses of these two diseases [9].

In many cases, the co-use of OCT and fluorescein angiography (FA) is considered sufficient for the diagnosis of n-AMD, while misdiagnosis of PCV as n-AMD is common in current clinical practice. Given the common clinical scenarios for both diseases, it would be useful to know the diagnostic values of other multimodal imaging features in the diagnosis of PCV. Multimodal imaging is important for the definitive diagnosis of PCV and n-AMD, which share some common imaging features.

Indocyanine green angiography (ICGA) is the most valuable method for the diagnosis of PCV [10]. Two prominent choroidal vascular changes have been described for PCV: branching vascular network and polypoidal vascular dilatation [11]. However, the lack of active use of ICGA in many centres, long shooting time, high costs and deficiencies in evaluation lead to some uncertainty in the diagnosis of PCV.

With the development of spectral domain-OCT (SD-OCT) and high-resolution cross-sectional images, high sensitivity and specificity have been achieved in distinguishing PCV from neovascular AMD. In addition several reports have described characteristic features like multiple retinal pigment epithelial detachment (RPED), sharp RPED peak, RPED notch, hyporeflective lumen representing polyps, double-layer sign and the presence of hyperreflective intraretinal hard exudate for the diagnosis of PCV [12, 13]. In our study, clinical evaluation of patients with potential diagnostic findings for PCV was performed and SD-OCT, FA and ICGA findings were evaluated. The study aimed to evaluate the sensitivity and specificity of SD-OCT in the diagnosis of PCV confirmed with ICGA.

## Materials and methods

The study was conducted prospectively in the Ondokuz Mayıs University Hospital between January 2017 and May 2018 and included previously untreated patients with serous or serosanguineous maculopathy. The study adhered to the principles of the Declaration of Helsinki and was approved by the Institutional Review Board and Ethics Committee of the Ondokuz Mayıs University (Date 2017/No 409). Consecutive patients with serous or serosanguineous maculopathy and patients with potential diagnostic findings for PCV in SD-OCT were evaluated. Patients with other retinal diseases, myopia of $\geq -6.0$ D, axial length of $\geq 26.0$ mm, presenting with massive subretinal haemorrhage or media opacity to prevent OCT imaging, history of visual trauma, infection or surgery and systemic diseases that may constitute contraindications for ICGA and FA were excluded from the study.

Each patient underwent clinical ophthalmologic assessment, colour fundus photography, SD-OCT (Spectralis HRA + OCT, Heidelberg Engineering, Heidelberg, Germany) with viewing module version 1.9.13.0, FA and ICGA (Heidelberg Spectralis Retinal Angiography, Spectralis HRA + OCT, Heidelberg Engineering, Heidelberg, Germany). SD-OCT images were acquired by high-speed mode with 25 horizontal linear B-scans aligned at 30 degrees field in lesion area. Enhanced depth-imaging OCT (EDI-OCT) was used to evaluate the mean choroidal thickness measured at the lesion site, and choroidal thickness of $\geq 200$ μm was considered as a thick choroid. All images were consecutively evaluated by two authors (H.B and B.E) masked to the patient characteristics and ICGA imaging.

The presence of multiple RPED, sharp RPED peak, RPED notch, hyporeflective lumen representing polyps, double-layer sign and intraretinal hard exudate were evaluated by SD-OCT. SD-OCT-based PCV was diagnosed with at least three of these findings [14]. ICGA was considered to be the gold-standard method in our study and was performed to all patients who had any of the OCT findings mentioned above and serous or serosanguineous maculopathy. The results of the SD-OCT-based diagnosis were compared with those of the ICGA-based analysis.

Diagnosis of PCV based on EVEREST criteria; choroidal polypoidal lesions in the form of subretinal hyperfluorescence seen in the early stage of ICGA with dilated branched choroidal vascular network, hypofluorescent halo around the polyp, massive subretinal haemorrhage and fundus examination revealed at least one red–orange subretinal nodule.

### Statistical analyses

Data were analysed with Statistical Package for the Social Sciences (SPSS) software (v23.0 for Windows; SPSS Inc., Chicago, IL, USA). Quantitative data were presented as mean ± standard deviation, and qualitative data were presented as frequency (percentage). Shapiro–Wilk test was used for the normal distribution

of data, independent samples $t$ test was used for comparing normal distribution data, and Pearson's Chi-square test was used for comparison of categorical data. Independent risk factors on diagnosis were examined by dual-logistic regression analysis. The significance level was taken as $p < 0.05$.

## Results

Ninety-three eyes of 58 patients with suspected PCV diagnoses were included in the study. Twenty-one (36.2%) of the patients were females, and 37 (63.8%) were males. The mean age was 58.2 ± 13.7 years. Twenty-three (39.6%) patients had unilateral involvement, and 35 (60.4%) patients had bilateral involvement. Sixty-nine (74.2%) of 93 eyes were diagnosed as PCV by confirmed with ICGA. Unilateral involvement was observed in 19 patients (43.2%) and bilateral involvement was observed in 25 patients (56.8%), whose diagnosis was confirmed by ICGA. Of the 24 patients who were not evaluated as PCV by ICGA, 7 patients had dry-type AMD, 13 patients had n-AMD, and 4 patients had central serous chorioretinopathy (CSCR).

RPED was the most common finding in SD-OCT, and 64 of 69 eyes (92.7%) diagnosed with PCV had multiple RPED. The mean number of RPED was 2.9 ± 2.7 (minimum 0 and maximum 16). RPED notch findings in 27 eyes (39.1%), sharp RPED peaks on which was believed to correspond to polyps in 48 eyes (69.5%), and round hyporeflective lesions representing polyp lumen in hyperreflective lesions under RPE in 36 eyes (52.1%) were detected (Figs. 1, 2). Thirty-two eyes (46.3%) had intraretinal hard exudate, 53 eyes (76.8%) had double-layer sign, and 25 eyes (36.2%) had choroidal neovascular membrane in SD-OCT. The mean central macular thickness was 299 ± 163.8 μm, and the mean choroidal thickness measured from the lesion site by EDI-OCT was 373.1 ± 99.5 μm (Table 1).

While occult-type CNVM was observed in 25 (36.2%) of 69 eyes, classical-type CNVM was not observed in any patient diagnosed with PCV. Window defects, RPED-related filling defects and scar staining due to fibrous scars were detected in the remaining eyes without occult CNVM. In 12 eyes (17.3%), the polyp itself could be observed in FA.

For the diagnosis of PCV, multiple RPEDs, sharp RPED peak, RPED notch, hyporeflective area representing the polyp lumen and double-layer sign variables were determined as independent risk factors in SD-OCT. The potential diagnostic value was determined for each SD-OCT parameter used for PCV diagnosis (Table 2).

While focal hyperfluorescence lesions (polyp appearance) were observed in all patients, single polyps were observed in 6 eyes (8.7%) and multiple polyps were observed in 63 eyes (91.3%) in ICGA. Branching vascular network was observed prominently in 51 eyes (73.9%) (Fig. 3), hypofluorescent halo image in 12 eyes (17.4%) and late geographic hyperfluorescence in 15 eyes (12.9%).

In our study, PCV was diagnosed based on the coexistence of at least three of the SD-OCT findings,

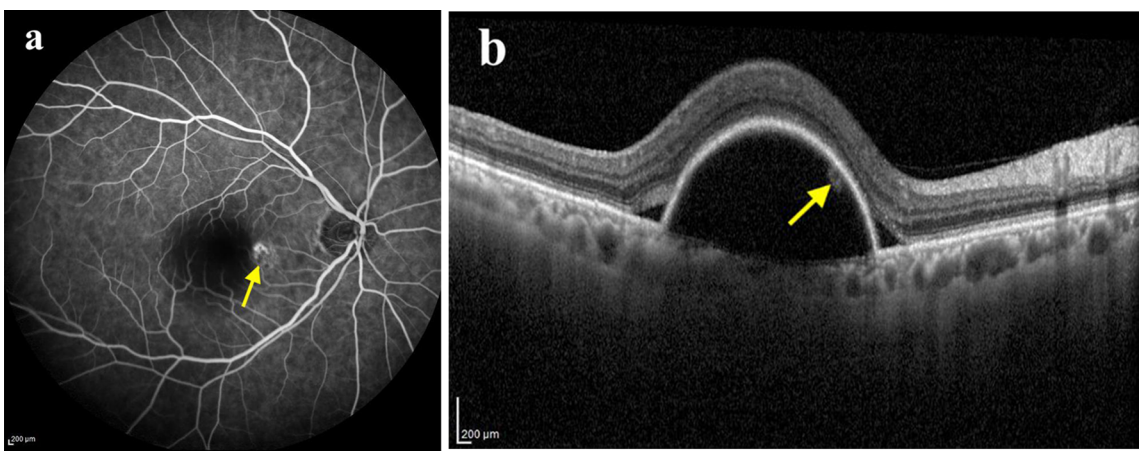


**Fig. 1** The appearance of the polyp displayed in FA (left) in the SD-OCT scan (right) as a hyporeflective area (arrow) surrounded by a hyperreflective ring representing the polyp lesion at the edge of the PED

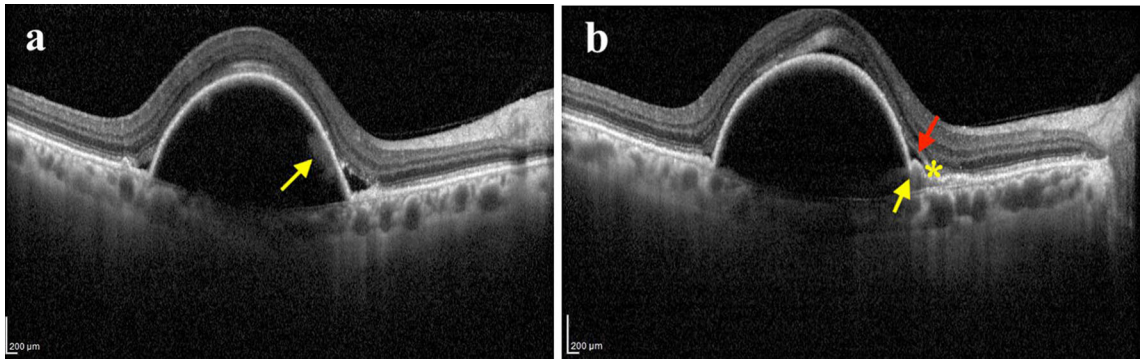


**Fig. 2** **a** Image of sharp RPED peak, polypoidal lesion and lumen under peak in OCT section. **b** Image of sharp peak and peak on RPED in OCT section and under lumen (yellow arrow), RPED notch (red arrow) double-layer sign appearance (star)

**Table 1** Spectral domain optical coherence tomography features of polypoidal choroidal vasculopathy

| | PCV ($n$ = 69) |
|---|---|
| Multiple RPEDs, $n$ (%) | 64 (92.7%) |
| Sharp RPED peak, $n$ (%) | 48 (69.5%) |
| RPED notch, $n$ (%) | 27 (39.1%) |
| Hyporeflective area representing the polyp lumen, $n$ (%) | 36 (52.1%) |
| Double layer sign, $n$ (%) | 53 (76.8%) |
| Intraretinal hard exudate, $n$ (%) | 32 (46.3%) |
| Choroidal thickness (ort ± SD) | 373.1 ± 99.5 µm |

*RPED* retinal pigment epithelial detachment

and the diagnosis of these patients was confirmed by ICGA. Sixty-nine eyes were confirmed with ICGA and diagnosed as PCV. While 52/69 eyes were diagnosed as true positive by SD-OCT, 17 eyes evaluated as PCV in ICGA did not meet the adequacy of SD-OCT parameters. Six eyes were evaluated as false-positive by SD-OCT. The sensitivity and specificity of SD-OCT for diagnosis of PCV were 75.3% and 75%, respectively (Table 3). When the effect of choroidal thickness on the diagnosis was added, SD-OCT had a sensitivity of 71.67% and a specificity of 78.95% in the diagnosis of PCV.

## Discussion

PCV is characterised by recurrent serosanguineous retinal pigment epithelial detachments and polypoidal dilatations of the choroidal vessels. The distinction between PCV and AMD is important because the treatment responses of the two diseases are different. Therefore, the differential diagnosis from AMD should be well known. However, due to the lack of routine use of ICGA in exudative AMD patients, its use as an expensive and invasive test led ophthalmologists to search for imaging methods and evaluation criteria that can be used to diagnose PCV even without ICGA. Therefore, knowing the characteristics of PCV detected in colour fundus photography, SD-OCT and FA may help to define PCV in the absence of ICGA.

De Salvo et al. compared the accuracy of SD-OCT with ICGA in diagnosing PCV in a selected clinical population with one or more serous or haemorrhagic RPEDs and excluding other retinal diseases. Thirty-five of 37 eyes with PCV confirmed by ICGA, were found to have PCV with SD-OCT. Sensitivity and specificity were found as 94.6% and 92.9%, respectively, for the SD-OCT features in identifying PCV lesions [13].

In the study performed by Chang et al., 263 patients with exudative AMD were examined, and SD-OCT and ICGA findings of all patients were evaluated. In total, 126 (85.7%) of 147 patients diagnosed with PCV with three or more SD-OCT findings and 16 of 116 patients with exudative AMD were confirmed as PCV. It was reported that the sensitivity value was determined as 89.8% and specificity value was determined as 84.5% by adding the choroidal thickness parameter to SD-OCT findings [14].

When choroidal thicknesses are evaluated, another important point is that the mean choroidal thickness is below 200 µm and the negative predictive value is 100%. In a more detailed analysis of a subset of

**Table 2** Sensitivity, specificity and predictive values of spectral domain optical coherence tomography findings

| | Sensitivity (%) | Specifity (%) | Positive predictive value (%) | Negative predictive value (%) |
|---|---|---|---|---|
| Multiple RPEDs | 92.8 | 48.9 | 72.7 | 82.1 |
| Double-layer sign | 76.8 | 74.5 | 81.5 | 68.6 |
| Sharp RPED peak | 69.6 | 80.9 | 84.2 | 64.4 |
| Hyporeflective area representing the polyp lumen | 52.2 | 85.1 | 83.7 | 54.8 |
| Intraretinal hard exudate | 46.4 | 93.5 | 91.4 | 53.8 |
| RPED notch | 39.1 | 83.0 | 77.1 | 48.1 |

*RPED* retinal pigment epithelial detachment

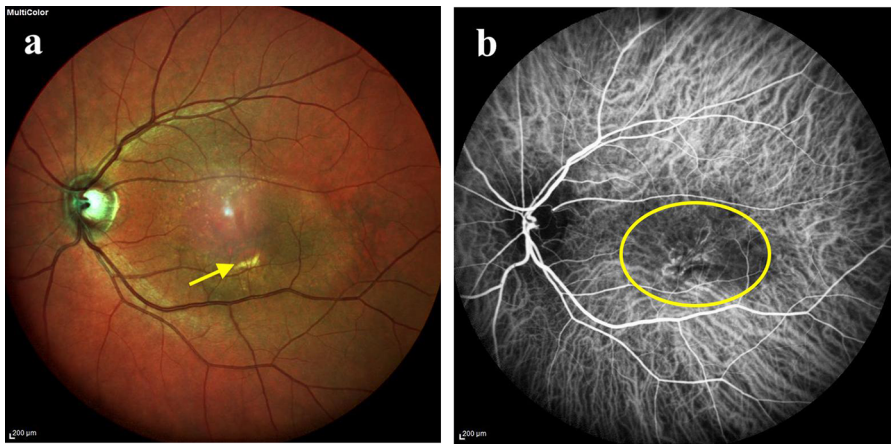


**Fig. 3** **a** Multicolour fundus photography with lipid exudation and orange nodules around it (arrow). **b** Branching vascular network with polypoidal dilatation in ICGA

patients with choroidal thickness < 200 µm, they found an increased rate of Haller layer thickness over total choroidal thickness; this supports the classification of PCV as a disorder driven by the pachychoroid mechanism, even in cases where the choroidal thickness is relatively low, and it should be borne in mind that contrary to the results of our study, the disease may also appear at a low choroidal thickness (Fig. 4) [15].

Chaikitmongkol et al. reported that the sensitivity, specificity and predictive values of fundus photography, OCT and FA findings were investigated for the diagnosis of PCV, and major and minor criteria that could be used in the diagnosis of PCV were determined [16]. Notched or haemorrhagic RPED appearance, sharp RPED peak at OCT, presence of hyperreflective ring under notched multilobulated RPED and RPED, especially in fundus photography, were classified as major criteria, and the presence of at least two criteria for the diagnosis of PCV without ICGA showed high sensitivity and specificity.

The use of FA in PCV is relatively limited because FA cannot visualise sub-RPE structures, including polyps. Most of the cases have findings similar to occult CNVM. Therefore, the diagnosis of PCV should be kept in mind in cases with occult CNVM in FA and ICGA should be performed in cases that cause clinical suspicion. Window defects due to RPE atrophy, and in some cases, hyperfluorescent spots may be observed in areas with polypoidal structures [17]. In our study, occult-type CNVM was detected in 25 (36.2%) out of 69 eyes diagnosed with PCV, whereas there was no CNVM image in FA in 44 eyes (63.8%). Classical-type CNVM was not observed in any patient. In these eyes, there were window defects, filling defects due to RPED and scar staining due to fibrous scarring.

We believe that the main reasons for these different study results are due to the difference in the inclusion criteria of the patients. In the study by De Salvo et al., while at least one or more RPEDs were required, classical exudative AMD was excluded from the study, and in the study by Chang et al., patients were included regardless of FA and OCT findings [13, 14].

**Table 3** Detection of eyes with polypoidal choroidal vasculopathy using spectral domain optical coherence tomography compared to indocyanine green angiography

| | Indocyanine green angiography | | |
|---|---|---|---|
| | Positive | Negative | Total |
| *Spectral domain optical coherence tomography* | | | |
| Positive | 52 | 6 | 58 |
| % within SD-OCT group | 89.7 | 10.3 | 100 |
| % within ICGA group | 75.4 | 25 | 62.4 |
| % of total | 55.9 | 6.5 | 62.4 |
| Negative | 17 | 18 | 35 |
| % within SD-OCT group | 48.6 | 51.4 | 100 |
| % within ICGA group | 24.6 | 75 | 37.6 |
| % of total | 18.3 | 19.3 | 37.6 |
| Total | 69 | 24 | 93 |
| % within SD-OCT group | 74.2 | 25.8 | 100 |
| % within ICGA group | 100 | 100 | 100 |
| % of total | 74.2 | 25.8 | 100 |

*SD-OCT* spectral domain optical coherence tomography, *ICGA* indocyanine green angiography

In addition, it should be kept in mind that sensitivity and specificity values that we detected may be seen in higher rates in populations with a higher prevalence of PCV. Another important point is the need to use a standardised OCT scanning strategy, such as a certain number of average frames and number of scan lines, to achieve consistent results. The best image for OCT analysis can be obtained using the maximum number of average frames, maximum scans and number of lines in random scans. This strategy cannot be used in patients with discordant and medium concentration as it requires significantly longer screening time. Future investigations will be required to determine the most appropriate OCT screening strategy that produces satisfactory image quality.

The limited number of patients, the lack of standardised diagnostic criteria for PCV in OCT and the absence of a single OCT screening protocol are the limitations of our study. Patients were included taking into consideration to the fundus examination findings regardless of whether they met at least three SD-OCT findings. When evaluating OCT findings, it is thought that at least three of these findings may increase their effectiveness in diagnosis by searching for coexistence.

As a result, when the qualitative analysis of SD-OCT findings that can be used in the diagnosis and follow-up of patients with PCV was evaluated in a selected clinical population, SD-OCT had high sensitivity and specificity in the diagnosis of PCV. Our results suggest that the use of SD-OCT in the

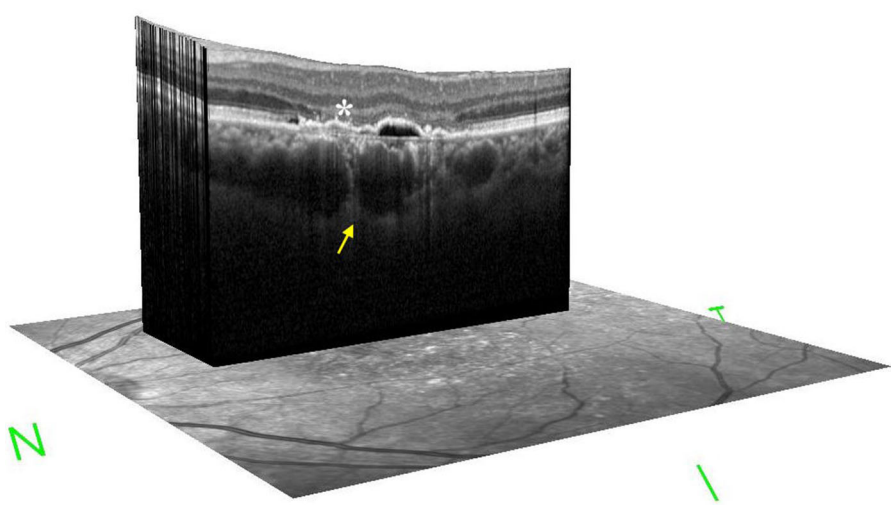


**Fig. 4** Weak choriocapillaris and Sattler layers in SD-OCT, significant dilatation of Haller veins (arrow), double-layer sign appearance (star)

differential diagnosis of serous or serosanguineous maculopathy may be a useful and noninvasive alternative. Based on previous reports describing the possible anatomical features of PCV, it was found that SD-OCT showed high sensitivity and specificity in the diagnosis of PCV.

## Conclusion

High sensitivity and specificity were obtained with SD-OCT in the diagnosis of PCV. The examination of the effect of choroidal thickness increased the specificity of this method. The diagnostic method based on SD-OCT is considered helpful for clinicians to develop appropriate diagnostic and therapeutic strategies for patients in whom ICGA cannot be used. Further studies are needed to further assess by experts and establish more precise criteria for the diagnosis of PCV.

## References

1. Yannuzzi LA, Sorenson J, Spaide RF, Lipson B (1990) Idiopathic polypoidal choroidal vasculopathy (IPCV). Retina 10(1):1–8
2. Yannuzzi LA, Sorenson J, Spaide RF, Lipson B (2012) Idiopathic polypoidal choroidal vasculopathy (IPCV). Retina 32(1):1–8
3. Imamura Y, Engelbert M, Iida T, Freund KB, Yannuzzi LA (2010) Polypoidal choroidal vasculopathy: a review. Surv Ophthalmol 55(6):501–515
4. Lim TH, Laude A, Tan CS (2010) Polypoidal choroidal vasculopathy: an angiographic discussion. Eye (Lond) 24(3):483–490
5. Yannuzzi LA, Wong DW, Sforzolini BS et al (1999) Polypoidal choroidal vasculopathy and neovascularized age-related macular degeneration. Arch Ophthalmol 117(11):1503–1510
6. Laude A, Cackett PD, Vithana EN et al (2010) Polypoidal choroidal vasculopathy and neovascular age related macular degeneration: same or different disease? Prog Retin Eye Res 29(1):19–29
7. Manayath GJ, Shah VS, Saravanan VR, Narendran V (2018) Polypoidal choroidal vasculopathy associated with central serous chorioretinopathy: Pachychoroid spectrum of diseases. Retina 38(6):1195–1204
8. Lim LS, Cheung CM, Wong TY (2013) Asian age-related macular degeneration: current concepts and gaps in knowledge. Asia Pac J Ophthalmol (Phila) 2(1):32–41
9. Cheung CMG, Lai TYY, Ruamviboonsuk P et al (2018) Polypoidal choroidal vasculopathy: definition, pathogenesis, diagnosis, and management. Ophthalmology 125(5):708–724
10. Spaide RF, Yannuzzi LA, Slakter JS, Sorenson J, Orlach DA (1995) Indocyanine green videoangiography of idiopathic polypoidal choroidal vasculopathy. Retina 15(2):100–110
11. Japanese Study Group of Polypoidal Choroidal Vasculopathy (2005) Criteria for diagnosis of polypoidal choroidal vasculopathy. Zasshi Nippon Ganka Gakkai 109(7):417–427
12. Liu R, Li J, Li Z et al (2016) Distinguishing polypoidal choroidal vasculopathy from typical neovascular age-related macular degeneration based on spectral domain optical coherence tomography. Retina 36(4):778–786
13. DeSalvo G, Vaz-Pereira S, Keane PA et al (2014) Sensitivity and specificity of spectral-domain optical coherence tomography in detecting idiopathic polypoidal choroidal vasculopathy. Am J Ophthalmol 158(6):1228–1238
14. Chang YS, Kim JH, Kim JW et al (2016) Optical coherence tomography based diagnosis of polypoidal choroidal vasculopathy in Korean patients. Korean J Ophthalmol 30(3):198–205
15. Lee WK, Baek J, Dansingani KK et al (2016) Choroidal morphology in eyes with polypoidal choroidal vasculopathy and normal or subnormal subfoveal choroidal thickness. Retina 36(1):73–82
16. Chaikitmongkol V, Kong J, Khunsongkiet P et al (2019) Sensitivity and specificity of potential diagnostic features detected using fundus photography, optical coherence tomography, and fluorescein angiography for polypoidal choroidal vasculopathy. JAMA Ophthalmol 137(6):661–667
17. Honda S, Matsumiya W, Negi A (2014) Polypoidal choroidal vasculopathy: clinical features and genetic predisposition. Ophthalmologica 231(2):59–74