Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Comparison of Choriocapillary Flow Density Between Fellow eyes of Polypoidal Choroidal Vasculopathy and Neovascular Age-Related Macular Degeneration

Mingyue Luo
PUMCH
Xinyu Zhao
Chinese Academy of Medical Sciences & Peking Union Medical College Hospital of Skin Diseases and Institute of Dermatology
Nan Zhao
Peking Union Medical College Hospital
Mingzhen Yuan
Peking Union Medical College Hospital
Jingyuan Yang
Peking Union Medical College Hospital
Rongping Dai
Peking Union Medical College Hospital
Youxin Chen (chenyouxinpumch@163.com)
Peking Union Medical College Hospital

Research article

Keywords: polypoidal choroidal vasculopathy, age-related macular degeneration, optical coherence tomography angiography, contralateral eye, choriocapillary flow density

Posted Date: March 5th, 2020

DOI: https://doi.org/10.21203/rs.2.21264/v2

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Version of Record: A version of this preprint was published at BMC Ophthalmology on April 22nd, 2020.
See the published version at https://doi.org/10.1186/s12886-020-01386-0.

Abstract

Purpose: To compare the choriocapillary flow density (CFD) among the fellow eyes of polypoidal choroidal vasculopathy (PCV), neovascular age-related macular degeneration (nAMD) and healthy controls with spectral-domain optical coherence angiography tomography (SD-OCTA).

Methods: This is a cross-sectional study, including the fellow eyes of 38 patients with unilateral PCV, 36 patients with unilateral nAMD, and 36 eyes from 36 healthy volunteers. PCV group was further classified into polypoidal CNV (P-CNV) and typical PCV (T-PCV) for subgroup analysis. Age, subfoveal choroidal thickness (SFCT), Age-Related Eye Disease Study (AREDS) classification and fellow eye diagnosis were acquired. All subjects underwent 6.0 mm scan pattern of SD-OCTA. Circles with radius of 1.00, 1.50 and 3.00 mm were manually selected in choriocapillaris (CC) slab, and CFD was calculated as the percentage of flow area to the whole selected area as CFD-1.00, 1.50, 3.00 respectively. Univariate and multivariate analysis were performed to study correlation between aforementioned factors with CFD,

Results: Mean CFD-1.00, 1.50, 3.00 of nAMD group were 61.51, 63.18 and 66.20, significantly lower than PCV group (65.90, 66.89, 67.94, P<0.001 , <0.001, and 0.010, respectively) and control (66.28, 66.96, 68.42, P<0.001 , <0.001, and 0.001, respectively), while no difference were detected between PCV group and control or between PCV subtypes. AREDS classification and fellow eye diagnosis were correlated with CFD in univariate analysis, but only fellow eye diagnosis remained significantly correlated after multiple linear regression.

Conclusions: CFD of nAMD fellow eyes were significantly lower than that of PCV and control eyes, while no difference was detected between PCV and control group, indicating different role of CC loss in early pathogenesis of nAMD and PCV.

Background

Polypoidal choroidal vasculopathy (PCV) is characterized by orange-red nodules in fundus examinations, polypoidal lesions during indocyanine green angiography (ICGA) and tremendous bleeding of posterior pole. It has raised many controversies since first described by Yannuzi in 1980s[1], especially its pathogenesis and whether it is a subtype of neovascular age-related macular degeneration (nAMD), or a distinct disease within pachychoroid disease spectrum[2], due to obvious heterogeneity that lies in their clinical, pathophysiological and epidemiological features and treatment responses to anti-vascular endothelium growth factor (VEGF) agents[3].

The pathogenesis and nature of PCV remains to be elucidated, so is its characteristic lesions, namely polyps and branching vascular network (BVN). In recent years, multimodal imaging technologies allows more precise view of polypoidal lesions and PCV choroid. Specifically, with optical coherence tomography angiography (OCTA), a novel imaging modality reflecting choroid flow with higher accuracy and resolution compared to traditional dye-based ophthalmic angiography[4], emerging evidence suggests the classical polypoidal lesions manifest as tangled vessels at the edge of BVN[5]. This finding further

complicates our knowledge that whether there is actual difference between PCV and nAMD, since the characteristic lesions of PCV and choroidal neovascularization (CNV) in nAMD are essentially both vascularization in nature and there might be actually no “polyps” or “aneurysmal vessels”[6].

Despite various rates of bilateral presentation[3], substantial studies identified asymptomatic lesions in fellow eyes of both PCV and nAMD patients. For example, non-exudative neovascularization of the fellow eye was found associated with pachychoroid pigment epitheliopathy in PCV and nAMD patients[7], and an increased trend of choriocapillaris (CC) nonperfusion was detected in the fellow eyes of nAMD using OCTA[8]. Additionally, retinal pigmented epithelium (RPE) and outer retinal abnormalities were observed in 84% of a cohort of unilateral PCV patients, and CNV formation was observed more if these abnormalities were accompanied with pachyvessels [9]. These studies, among other fellow eye studies, may shed light on the pathogenesis, especially in the early phases. It remains to be clarified whether there is a direct causal effect between pachychoroid and the pathogenesis of PCV, yet RPE alterations seems a secondary downstream event occurring in later stage of the disease. This differs from nAMD, in which the interplay between RPE and CC[10, 11] plays a central role in the early phase, and finally elevated VEGF gives rise to CNV.

CC flow deficits (CFD) detected with OCTA has emerged as a potential metrics to evaluate inner choroid vasculature with fast non-invasive imaging, which has been extensively utilized in various retinal diseases [12-15]. However, there has not been a comparison between PCV and nAMD in their fellow eyes with OCTA. This study aimed to compare the fellow eyes of PCV and AMD in terms of CFD at an early stage without signs of neovascularization.

Methods

This is a cross-sectional, observational study of unilateral PCV and nAMD patients recruited from June 2017 to July 2019 at Peking Union Medical College Hospital. Healthy controls were also included. The study was approved by the institutional review board (S-K631) and was conducted in accordance with the tenets of the Declaration of Helsinki. Written informed consent was waived because of the study’s retrospective design.

PCV and nAMD were diagnosed according to published criteria[1, 16]. Two masked ophthalmologists (M.L. and M.Y.) reviewed the early to late phases of the angiography images, verified the diagnosis and classified PCV cases into polypoidal CNV (P-CNV) or typical PCV (T-PCV)[17]. A third retinal consultant (Y.C.) arbitrated in case of any discrepancy. The inclusion criteria for patients were unilateral PCV or nAMD cases with complete medical records. Patients and controls were excluded if (1) any signs of neovascularization in the included eyes, namely exudation in FFA or ICGA for patients, and BVN or blood flow signal between RPE and Bruch’s membrane in OCTA for all; (2) comorbid with other ophthalmic diseases except for myopia less than -3.0D and mild cataract; (3) cloudy refractory media impedes examination of the posterior pole (4) OCTA scan quality was lower than 7.

All patients received comprehensive ophthalmologic examinations, including Snellen best-corrected visual acuity (BCVA), and SD-OCTA (RTVue XR Avanti AngioVue; Optovue, Inc., Fremont, CA, USA) and simultaneous fluorescein angiography ICGA and enhanced depth imaging (EDI) SD-OCT (Heidelberg Retina Angiography 2, HRA2, Heidelberg Engineering, Heidelberg, Germany). For statistical analysis, the Snellen BCVA was converted to a logarithm of the minimal angle of resolution (logMAR).

All included eyes were stratified according to Age-Related Eye Disease Study (AREDS) classification[18] into: (1) No apparent aging changes or normal aging changes; (2) Early AMD; (3) Intermediate AMD; and (4) Late AMD, according to drusen size and pigmentary abnormalities (AREDS category 1-4, respectively). Subfoveal choroidal thickness (SFCT) was measured using EDI-OCT horizontal B-scans as the distance between the Bruch membrane and choroid-scleral border. HD Angio Retina 6.0 mm scan pattern of each subject was acquired and used for further analysis. Motion correction technology and 3D projection artifact reduction was automatically employed. Circles centered at the fovea with radius of 1.00, 1.50 and 3.00 mm were manually adjusted in CC slab using built-in software, and CFD was calculated as the percentage of flow area to the whole selected area, which were generated automatically, as CFD-1.00, 1.50, and 3.00 respectively.

Statistical analysis

Statistical analyses were performed using SPSS 22 (IBM, Inc, Chicago, IL). Normally distributed continuous data were presented in mean and standard deviation (SD), otherwise in median and interquartile range (IQR). A *P* value less than 0.05 was considered significant in all aforementioned analysis. Categorical and continuous variables were assessed using chi-square test and one-way analysis of variance (ANOVA) respectively with post-hoc Bonferroni correction. Bivariate relationships were assessed with Spearman correlation coefficient analysis to evaluate potential correlating factors of CFD. Multivariate linear regression analysis was performed with age, SFCT and other factors with significance from univariate analysis as dependent factors.

Results

The fellow eyes of 38 patients with unilateral PCV (mean age: 63.8±8.8 years), 36 patients with unilateral nAMD (mean age: 67.1±8.4 years), and 36 eyes from 36 healthy volunteers (mean age: 63.4±7.1 years) were included. Subjects were matched in terms of age, gender, BCVA, smoking status, hypertension, and diabetes mellitus (DM) among the groups. Basic demographic and clinical characteristics of the subjects are summarized in Table1.

AREDS category of AMD group were more advanced, compared to PCV and control group (*P*=0.012 and 0.001, respectively), with 7 and 8 subjects classified as AREDS category 2 and 3, respectively. SFCT of PCV group was significantly greater than that of AMD and control group (242.97±53.59 vs 196.61±45.58 and 209.94±46.22 μm, *P*<0.001 and =0.013, respectively). Mean CFD-1.00, 1.50, 3.00 (SDs) of nAMD group were 61.51, 63.18 and 66.20, significantly lower than PCV group (65.90, 66.89, 67.94, P<0.001,

<0.001, and 0.010, respectively) and control (66.28, 66.96, 68.42, P<0.001, <0.001, and 0.001, respectively), while no difference was detected between PCV group and control.

Univariate analysis (Table 2) indicated that CFD-1.00, CFD-1.50 and CFD-3.00 were all correlated with AREDS classification (*P*=0.001, 0.006 and 0.049, respectively) and fellow eye diagnosis (*P*<0.001, <0.001 and =0.001, respectively). Multiple linear regression (Table 3) revealed that in this study cohort, fellow eye diagnosis was the only factor strongly correlated with CFD (*P*<0.001, <0.001 and =0.001, respectively).

There were 13 P-CNV and 25 T-PCV patients in PCV group. SFCT of T-PCV group was significantly greater than P-CNV, wAMD and control group (265.08±43.68 μm vs 200.46±45.44μm, 196.61±45.58μm and 209.94 46.22μm, all *P*<0.001). CFD-1.00 and CFD-1.50 of P-CNV and T-PCV were significantly higher than that of wAMD, but not significantly different from control (Supplementary files, Table 4). CFD-3.00 of wAMD group was significantly lower than T-PCV and control, but not P-CNV. All CFD values were not significantly different between PCV subtypes (Supplementary files, Table 4). Univariate analysis and multiple linear regression results were similar. (Supplementary files, Table 5-6)

Discussion

In this study, we evaluated the CFD of fellow eyes of nAMD and PCV with OCTA, and found fellow eyes of nAMD had significantly lower CFD compared with PCV and control group, while the difference was not statistically significant between PCV group and control or between PCV subtypes. Although CFD was found negatively correlates with aging[19], it is unlikely that aging itself can account for the difference, since PCV, AMD and control group were age-matched. Another important factor is the existence of drusen, which is considered a hallmark of dry AMD. In this study, all included eyes were stratified according AREDS classification, and more subjects with advanced category were observed in nAMD group. But this index was not statistically significant in multivariate linear regression analysis. Although there is a myriad of overlap between PCV and nAMD, the difference of CFD in their fellow eyes may serve as a proof of their heterogeneity.

The interplay of RPE and CC loss has always been a hotspot in the pathogenesis of AMD[20-23], although the sequential order remains controversial. Indeed, PCV is a well-recognized disease within pachychoroid disease spectrum, characterized by dilation of Haller layer and attenuation of choriocapillaires and Sattler layer. Engorgement of vortex vein is often observed in PCV, with correlating choroidal hyperpermeability[24], also confirmed by the pathology showing atherosclerotic change of choroid vessel wall, massive exudation of fibrin and blood plasma at polypoidal lesion[25, 26]. Apoptosis of smooth muscle cells and choroidal endothelial cells were also observed[25]. Chen *et al* induced polyp-like structures by ligating vortex veins in cynomolgus monkeys[27] These findings above suggest a role of choroidal hemodynamics in PCV pathogenesis[28]. While the CFD of fellow eyes of PCV was not significantly different from control, indicating RPE-Bruch's membrane-CC complex may not be involved in the preclinical stage of PCV and may be a downstream effect secondary to primary pathology. Specifically, near normal CFD of fellow eyes of PCV is not a contradiction to the vital role of CC flow

deficit and RPE changes in pachychoroid pathogenesis, which may be a downstream event secondary to dilation of Haller layer. Thus, in the relatively healthy contralateral eyes of PCV, CFD may be near normal, possibly accompanied with some pachychoroid features. Alternatively, this might be associated with lower bilaterality of PCV eyes. Further studies regarding PCV laterality and sequential order of choroidal changes in PCV are necessary for elaboration.

A plethora of studies investigated the difference of choroidal morphology between PCV and nAMD. SFCT is often used as an index, but it fluctuates with circadian rhythm and correlates with age and refractive errors[29]. Bakthavatsalam *et al.* [29] found that choroidal vascular index (CVI) of nAMD was lower than that in PCV (64.94 vs 62.54), but the difference was not statistically significant (P=0.10). Pachyvessels especially diffuse pattern were observed more commonly in thick-choroid PCV[30], and vascular area of typical PCV was significantly larger than nAMD[31]. All aforementioned results indicate the two diseases are heterogeneous in terms of choroidal morphology.

Our study had the limitations that are inherent as a retrospective cross-sectional study. Besides, the sample size is relatively small. Lastly, DM, hypertension and smoking status was collected from patients' past medical records which were recorded in a self-report manner, thus not accurate enough to be included into multivariate analysis. Nevertheless, to the best of our knowledge, this is the first study that provided quantitative analysis of CC among the fellow eyes of PCV, nAMD, and healthy eyes. Our study may provide evidence for the heterogeneity of nAMD and PCV.

Conclusions

In conclusion, our findings suggest that CFD of nAMD fellow eyes were significantly lower than that of PCV and control eyes, while no difference was detected between PCV and control group or between PCV subgroups, indicating a different role CC loss plays in the early pathogenesis of nAMD and PCV.

Abbreviations

polypoidal choroidal vasculopathy, PCV

indocyanine green angiography, ICGA

neovascular age-related macular degeneration, nAMD

vascular endothelium growth factor, VEGF

branching vascular network, BVN

optical coherence tomography angiography, OCTA

choroidal neovascularization, CNV

choriocapillaris, CC

retinal pigmented epithelium, RPE

CC flow deficits, CFD

polypoidal CNV, P-CNV

typical PCV, T-PCV

best-corrected visual acuity, BCVA

enhanced depth imaging, EDI

logarithm of the minimal angle of resolution, logMAR

Age-Related Eye Disease Study, AREDS

standard deviation, SD

interquartile range, IQR

analysis of variance, ANOVA

diabetes mellitus, DM

Declarations

Ethics approval and consent to participate

The study was approved by the institutional review board (S-K631) and was conducted in accordance with the tenets of the Declaration of Helsinki. Written informed consent was waived because of the study's retrospective design.

Consent to publish

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by The Non-profit Central Research Institute Fund of Chinese Academy of Medical Sciences (2018PT32029).

Authors' contributions

ML: collection of medical records, image evaluation, statistical analysis, drafting the manuscript and manuscript revision. **XZ:** modification of study design, data collection and manuscript revision. **NZ**: statistical analysis. **MY and JY**: data collection. **RD**: manuscript revision. **YC:** conceived of the study, coordinated and participated in the entire process of drafting and revised the manuscript. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

References

1. Yannuzzi, L.A., et al., *Idiopathic polypoidal choroidal vasculopathy (IPCV).* Retina, 1990. **10**(1): p. 1-8.
2. Balaratnasingam, C., et al., *Polypoidal Choroidal Vasculopathy: A Distinct Disease or Manifestation of Many?* Retina, 2016. **36**(1): p. 1-8.
3. Laude, A., et al., *Polypoidal choroidal vasculopathy and neovascular age-related macular degeneration: same or different disease?* Prog Retin Eye Res, 2010. **29**(1): p. 19-29.
4. Jia, Y., et al., *Quantitative optical coherence tomography angiography of vascular abnormalities in the living human eye.* Proc Natl Acad Sci U S A, 2015. **112**(18): p. E2395-402.
5. Bo, Q., et al., *Appearance of Polypoidal Lesions in Patients With Polypoidal Choroidal Vasculopathy Using Swept-Source Optical Coherence Tomographic Angiography.* JAMA Ophthalmol, 2019.
6. Dansingani, K.K., et al., *Understanding aneurysmal type 1 neovascularization (polypoidal choroidal vasculopathy): a lesson in the taxonomy of 'expanded spectra' - a review.* Clin Exp Ophthalmol, 2018. **46**(2): p. 189-200.
7. Yanagi, Y., et al., *Prevalence and Risk Factors for Nonexudative Neovascularization in Fellow Eyes of Patients With Unilateral Age-Related Macular Degeneration and Polypoidal Choroidal Vasculopathy.* Invest Ophthalmol Vis Sci, 2017. **58**(9): p. 3488-3495.
8. Treister, A.D., et al., *Prevalence of Subclinical CNV and Choriocapillaris Nonperfusion in Fellow Eyes of Unilateral Exudative AMD on OCT Angiography.* Transl Vis Sci Technol, 2018. **7**(5): p. 19.
9. Baek, J., et al., *Polypoidal Choroidal Vasculopathy: Outer Retinal and Choroidal Changes and Neovascularization Development in the Fellow Eye.* Invest Ophthalmol Vis Sci, 2019. **60**(2): p. 590-598.
10. Alagorie, A.R., et al., *Quantitative Assessment of Choriocapillaris Flow Deficits in Eyes with Advanced Age-Related Macular Degeneration Versus Healthy Eyes.* Am J Ophthalmol, 2019.

11. Boltz, A., et al., *Choroidal blood flow and progression of age-related macular degeneration in the fellow eye in patients with unilateral choroidal neovascularization.* Invest Ophthalmol Vis Sci, 2010. **51**(8): p. 4220-5.
12. Arya, M., et al., *Choriocapillaris changes in dry age-related macular degeneration and geographic atrophy: a review.* Eye Vis (Lond), 2018. **5**: p. 22.
13. Borrelli, E., et al., *Topographic Analysis of the Choriocapillaris in Intermediate Age-related Macular Degeneration.* Am J Ophthalmol, 2018. **196**: p. 34-43.
14. Yang, J., et al., *Optical coherence tomography angiography analysis of the choriocapillary layer in treatment-naive diabetic eyes.* Graefes Arch Clin Exp Ophthalmol, 2019. **257**(7): p. 1393-1399.
15. Wang, Q., et al., *Optical coherence tomography angiography in retinal vein occlusions.* Graefes Arch Clin Exp Ophthalmol, 2018. **256**(9): p. 1615-1622.
16. Miyake, M., et al., *Pachychoroid neovasculopathy and age-related macular degeneration.* Scientific reports, 2015. **5**: p. 16204-16204.
17. Kawamura, A., et al., *Indocyanine green angiographic and optical coherence tomographic findings support classification of polypoidal choroidal vasculopathy into two types.* Acta Ophthalmol, 2013. **91**(6): p. e474-81.
18. Ferris, F.L., 3rd, et al., *Clinical classification of age-related macular degeneration.* Ophthalmology, 2013. **120**(4): p. 844-851.
19. Pettenkofer, M., et al., *Choriocapillaris Flow Density Negatively Correlates With Advancing Age on Spectral-Domain Optical Coherence Tomography Angiography.* Ophthalmic Surg Lasers Imaging Retina, 2019. **50**(5): p. 302-308.
20. Biesemeier, A., et al., *Choriocapillaris breakdown precedes retinal degeneration in age-related macular degeneration.* Neurobiol Aging, 2014. **35**(11): p. 2562-2573.
21. Seddon, J.M., et al., *Histopathological Insights Into Choroidal Vascular Loss in Clinically Documented Cases of Age-Related Macular Degeneration.* JAMA Ophthalmol, 2016. **134**(11): p. 1272-1280.
22. Saint-Geniez, M., et al., *An essential role for RPE-derived soluble VEGF in the maintenance of the choriocapillaris.* Proc Natl Acad Sci U S A, 2009. **106**(44): p. 18751-6.
23. McLeod, D.S., et al., *Relationship between RPE and choriocapillaris in age-related macular degeneration.* Invest Ophthalmol Vis Sci, 2009. **50**(10): p. 4982-91.
24. Chung, S.E., et al., *Engorgement of vortex vein and polypoidal choroidal vasculopathy.* Retina, 2013. **33**(4): p. 834-40.
25. Nakashizuka, H., et al., *Clinicopathologic findings in polypoidal choroidal vasculopathy.* Invest Ophthalmol Vis Sci, 2008. **49**(11): p. 4729-37.
26. Okubo, A., et al., *Clinicopathological correlation of polypoidal choroidal vasculopathy revealed by ultrastructural study.* Br J Ophthalmol, 2002. **86**(10): p. 1093-8.
27. Chen, L.L., et al., *Choroid changes in vortex vein-occluded monkeys.* Int J Ophthalmol, 2018. **11**(10): p. 1588-1593.

28. Ng, D.S., et al., *Classification of Exudative Age-Related Macular Degeneration With Pachyvessels on En Face Swept-Source Optical Coherence Tomography.* Invest Ophthalmol Vis Sci, 2017. **58**(2): p. 1054-1062.
29. Bakthavatsalam, M., et al., *Choroidal structures in polypoidal choroidal vasculopathy, neovascular age-related maculopathy, and healthy eyes determined by binarization of swept source optical coherence tomographic images.* Graefes Arch Clin Exp Ophthalmol, 2017. **255**(5): p. 935-943.
30. Baek, J., et al., *Morphologic features of large choroidal vessel layer: age-related macular degeneration, polypoidal choroidal vasculopathy, and central serous chorioretinopathy.* Graefe's Archive for Clinical and Experimental Ophthalmology, 2018. **256**(12): p. 2309-2317.
31. Gupta, P., et al., *DETAILED CHARACTERIZATION OF CHOROIDAL MORPHOLOGIC AND VASCULAR FEATURES IN AGE-RELATED MACULAR DEGENERATION AND POLYPOIDAL CHOROIDAL VASCULOPATHY.* Retina, 2017. **37**(12): p. 2269-2280.

Tables

Table 1. Baseline Demographics and Clinical Characteristics of Subjects

.....	PCV ($N = 38$)	nAMD ($N = 36$)	Control ($N = 36$)	*P* value (PCV vs. AMD)	*P* value (PCV vs. control)	*P* value (AMD vs. control)
Age, y mean (SD)	63.8 (8.8)	67.1 (8.4)	63.4 (7.1)	0.270	1.000	0.171
Gender, female (N) (%)	20 (52.6)	12 (33.3)	22 (61.1)	0.282	1.000	0.054
BCVA (logMAR) (IQR)	0.09 (0.00-0.10)	0.12 (0.00-0.22)	0.08 (0.00-0.10)	0.676 [a]	0.942 [a]	0.344 [a]
Smoker/non-smoker	4/34	5/31	3/33	1.000 [b]	1.000 [b]	1.000 [b]
Hypertention (%)	4 (10.5)	9 (25.0)	5 (13.9%)	0.306	1.000	0.702
DM (%)	4 (10.5)	4 (11.1)	1 (2.8)	1.000 [b]	0.507 [b]	0.453 [b]
AREDS Category 1/2/3/4	34/3/1/0	21/7/8/0	36/0/0/0	0.012 [b]*	0.186 [b]	0.001[b]*
SFCT (μm)	242.97 (53.59)	196.61 (45.58)	209.94 (46.22)	<0.001*	0.013*	0.744
CFD-1.00 (%)	65.90 (3.47)	61.51 (3.90)	66.28 (3.39)	<0.001*	1.000	<0.001*
CFD-1.50 (%)	66.89 (3.30)	63.18 (3.42)	66.96 (2.96)	<0.001*	1.000	<0.001*
CFD-3.00 (%)	67.94 (2.52)	66.02 (3.10)	68.42 (2.59)	0.010*	1.000	0.001*

SD: standard deviation;BCVA: best-corrected visual acuity; logMAR, logarithm of the minimal angle of resolution; IQR: interquartile range; DM: diabetes mellitus; AREDS: Age-Related Eye Disease Study; SFCT: subfoveal choroidal thickness; CFD: choriocapillaris flow deficit;

PCV: polypoidal choroidal vasculopathy; nAMD: neovascular age-related macular degeneration.

*Statistically significant *P* value. [a] Post-hoc Tambane correction. [b] Fischer's exact test.

Table 2. Univariate Analysis of Potential Correlation Factors (Age, gender, BCVA, smoking status, hypertension, DM, AREDS classification, and SFCT) With CFD-1.00, CFD-1.50, and CFD-3.00 as dependent variable.

	CFD-1.00		CFD-1.50		CFD-3.00	
Characteristic	Correlation Coefficient	*P* value [a]	Correlation Coefficient	*P* value [a]	Correlation Coefficient	*P* value [a]
Age	-0.06	0.537	0.01	0.921	-0.05	0.617
Gender	-0.07	0.483	-0.06	0.563	-0.13	0.895
BCVA	-0.01	0.902	0.03	0.750	0.05	0.581
Smoking status	-0.08	0.388	-0.07	0.478	-0.09	0.340
Hypertension	-0.07	0.453	-0.063	0.515	<0.01	0.974
DM	-0.08	0.428	-0.06	0.519	-0.12	0.221
AREDS classification	-0.30	0.001*	-0.26	0.006*	-0.19	0.049*
SFCT	0.11	0.244	0.10	0.284	0.06	0.520
Fellow eye diagnosis	-0.46	<0.001*	-0.42	<0.001*	-0.32	0.001*

DM: diabetes mellitus; AREDS: Age-Related Eye Disease Study; SFCT: subfoveal choroidal thickness; CFD: choriocapillaris flow deficit.

*Statistically significant *P* value. [a] Spearman correlation analysis.

Table 3. Multiple linear regression analysis of Correlation Factors with CFD-1.00, CFD-1.50 and CFD-3.00 as Dependent Variables

	CFD-1.00		CFD-1.50		CFD-3.00	
	β	*P* value	β	*P* value	β	*P* value
Yellow eye diagnosis	-0.443	<0.001*	-0.437	<0.001*	-0.334	0.002*
AREDS Classification	-0.166	0.082	-0.399	0.691	-0.059	0.572
Age	0.059	0.518	0.109	0.249	-0.007	0.947
SFCT	-0.038	0.671	-0.037	0.691	-0.055	0.576

AREDS: Age-Related Eye Disease Study; SFCT: subfoveal choroidal thickness; CFD: choriocapillaris flow deficit.

*Statistically significant *P* value.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementarytables.xlsx