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Optical coherence tomography angiography in myopic peripapillary intrachoroidal cavitation complicated by choroidal neovascularization

Chiara Comune[1], Daniela Montorio[1] and Gilda Cennamo[2]

Abstract

Purpose: To detect the vessel density (VD) of the radial peripapillary capillary (RPC) in eyes affected by pathological myopia with or without a peripapillary intrachoroidal cavitation (PICC) and in eyes with PICC complicated by choroidal neovascularization (CNV), using optical coherence tomography angiography (OCTA).

Methods: We prospectively enrolled highly myopic patients from January 2016 to December 2019 at the Eye Clinic of the University of Naples "Federico II." We divided included patients into three groups: group 1 including patients with PICC complicated by CNV; group 2 including patients with PICC without complications; group 3 including patients with high myopia without PICC and CNV. One-way analysis of variance (ANOVA) followed by Bonferroni post hoc analysis was used to evaluate differences in VD of radial peripapillary capillary (RPC) in papillary whole, peripapillary regions and its sectors among the three groups.

Results: We enrolled 12 highly myopic eyes with PICC complicated by CNV, 21 highly myopic eyes with PICC without CNV and 23 highly myopic eyes without PICC. The myopic eyes with PICC revealed a statistically significant reduction in VD of the RPC comparing to the other groups ($p < 0.001$), especially in eyes affected by myopic PICC complicated by CNV ($p < 0.001$). These results were similar analyzing the VD in different sectors of the peripapillary region among the three groups ($p < 0.001$).

Conclusion: OCTA detects the changes in peripapillary vascular density of highly myopic eyes. We demonstrated that the RPC vasculature is significantly influenced by the presence of PICC, especially in myopic eyes developing a CNV.

Keywords

Radial peripapillary capillary vessel density, peripapillary intrachoroidal cavitation, optical coherence tomography angiography

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Introduction

A peripapillary intrachoroidal cavitation (PICC) is a yellowish–orange lesion that can be found in 5% of eyes with pathologic myopia.[1] In most cases the PICC involved the area inferior to the optic disc which was invariably tilted.[1–3] The pathogenic mechanisms and the clinical impact of PICC are not well known yet. Wei et al. believed that PICC was due to a fluid accumulation, because they found defects of the retina overlying the intrachoroidal cavitation using optical coherence tomography (OCT),[4] while Spaide et al. theorized a novel mechanism of posterior scleral bowing that caused a mechanical choroid deformation. Macular choroidal neovascularization (CNV) is one of the main cause of central vision loss in pathologic myopia.[5] The discovery of risk factors of myopic CNV is considered

[1]Department of Neurosciences, Reproductive and Dentistry Sciences, University of Naples Federico II, Naples, Campania, Italy
[2]Eye Clinic, Public Health Department, University of Naples Federico II, Naples, Campania, Italy

Corresponding author:
Daniela Montorio, Department of Neurosciences, Reproductive Sciences and Dentistry, University of Naples Federico II, Via S. Pansini 5, Naples, Campania 80138, Italy.
Email: da.montorio@gmail.com

of fundamental importance to establish the correct follow-up of myopic patients and to allow early treatment of CNV. The best known precursor lesions of myopic CNV are large myopic conus, patchy retinal atrophy, and lacquer cracks at the posterior pole.[5]

Optical coherence tomography angiography (OCTA) had improved the diagnosis of myopic CNV in clinical practice. OCTA represents a useful, fast, and noninvasive method to distinguish myopic CNV from simple hemorrhage or other choroidopathies. CNV appears as a high flow hyperintense vascular anastomotic network at OCTA examination.[5] OCTA is able to identify two types of CNV complicating high myopia: an immature stage that appears as a small disorganized vascular network and a mature stage as a larger, highly structured, and interlacing network.[6] In this prospective study, we made use of OCTA to study peripapillary vessel density in eyes with PICC complicated or not by CNV to better understand the vascular changes underlying this disease and to evaluate a possible correlation between PICC and the development of a CNV in myopic retinopathy.

Methods

In this prospective, non-randomized, longitudinal study we enrolled 56 consecutive highly myopic patients from January 2016 to December 2019 at the Eye Clinic of the University "Federico II," Naples, Italy. Inclusion criteria were the presence of pathological myopia characterized by an axial length greater than 26 mm and by a refractive error greater than −6 D and retinal alterations at fundus related to the myopia. Exclusion criteria were: age less than 18 years, the presence of systemic vascular diseases (hypertension, diabetes, and heart diseases), clinically relevant lens opacities, low-quality images obtained with SD-OCT and OCTA, history of intraocular surgery and previous treatments for CNV (intravitreal injections of anti-vascular endothelial growth factor), vitreoretinal and retinal vascular diseases, uveitis, congenital eye disorders. We divided included patients into three groups: group 1 including patients with PICC complicated by CNV; group 2 including patients with PICC without complications; group 3 including patients with high myopia without PICC and CNV. The diagnosis of PICC was defined by typical features at SD-OCT: an intrachoroidal hyporeflective space located below the retinal pigment epithelium and adjacent to the optic disc.

Each patient underwent evaluation of best-corrected visual acuity (BCVA), according to the Early Treatment of Diabetic Retinopathy Study (ETDRS), slit-lamp biomicroscopy, fundus examination, multimodal imaging, namely multicolor imaging, fluorescein angiography (FA)/indocyanine green angiography (ICGA), spectral-domain (SD)-OCT (Spectralis, Heidelberg Engineering, Heidelberg, Germany), and OCTA (AngioVue, RTVue XR Avanti, Optovue, Inc., Freemont, CA). FA, SD-OCT, and OCTA were used to diagnose the presence of CNV. At FA, the active myopic CNV revealed a well-defined hyperfluorescence in the early phase with leakage in the late phase. On SD-OCT, the lesion appeared as a dome-shaped, hyperreflective elevation above the retinal pigment epithelium with blurred margins and minimal subretinal fluid and exudation. OCTA detected a dense, interlacing type vascular anastomotic network.

All observations and the OCTA measurements were performed by two masked examiners (C.C., D.M.) and a senior expert (G.C.) that confirmed the diagnosis of PICC and the presence of CNV.

In the study all investigations adhered to the tenets of the Declaration of Helsinki. Written informed consents were obtained from the patients enrolled in the study.

OCT angiography

OCTA images were obtained with the Optovue Angiovue System (software ReVue XR version 2017.1.0.151, Optovue Inc., Fremont, CA, USA) following a standardized protocol based on the split-spectrum amplitude decorrelation algorithm (SSADA), as previously described.[7] The Angio Vue disc mode automatically segmented the radial peripapillary capillary (RPC) vessel density (VD) analyzing the whole papillary region with an area scan of 4.5×4.5 mm. The VD of the RPC was analyzed in the superficial retinal layers and extended from the inner limiting membrane (ILM) to the retinal nerve fiber layer posterior boundary. Furthermore, the VD of the peripapillary region and of its sectors (nasal, inferior, superior, temporal) was analyzed by the software that automatically fits a 0.75 mm-wide elliptical annulus extending from the optic disc boundary.[8] Poor-quality images with a signal strength index less than 40 or registered image sets with residual motion artefacts were excluded from the analysis.

Statistical analysis

One-way analysis of variance (ANOVA) followed by Bonferroni post hoc analysis was used to evaluate differences in VD of radial peripapillary capillary (RPC) in papillary whole, peripapillary regions and its sectors among the three groups. Chi-squared test was used to determine differences among groups in terms of sex. A p value of <0.05 was considered statistically significant. Statistical analysis was performed using the Statistical Package for Social Sciences (Version 20.0 for Windows; SPSS Inc., Chicago, IL, USA).

Results

Sixty myopic eyes were initially enrolled in this study. Four eyes were excluded because the low quality of SD-OCT and OCTA images. We evaluated a total of 56 myopic eyes of 56 patients (30 female, 26 male; mean age 65.5 ± 6.1 years) divided in group 1 (12 myopic eyes of 12 patients with PICC complicated by CNV), the group 2

Table 1. Demographic and clinical characteristics of the three groups.

	Group 1	Group 2	Group 3	p value
Eyes (*n*)	12	21	23	
Gender (female/male)	5/7	12/9	13/10	0.646*
Age (years)	66.9 ± 4	64.8 ± 6	65.5 ± 8	0.602†
MSE (diopters)	9.47 ± 1.55	8.72 ± 1.92	9.34 ± 1.73	0.394*

MSE: mean spherical equivalent.
Data are expressed as mean ± SD.
*One-way analysis of variance (ANOVA) followed by Bonferroni post hoc analysis, statistical significance *p* value <0.05.
†Fisher's exact test, statistical significance *p* value <0.05.

Table 2. The vessel density of the radial peripapillary capillary in three groups.

Radial peripapillary capillary (%)	Group 1	Group 2	Group 3	ANOVA
				p value
Whole papillary region	38.16 ± 2.24	42.09 ± 1.22	45.26 ± 2.43	<0.001
Peripapillary region	41.5 ± 1.93	44.71 ± 2.79	48.08 ± 2.02	<0.001
Superior	42.08 ± 2.35	45.33 ± 2.90	49.65 ± 2.46	<0.001
Inferior	40.75 ± 2.17	43.04 ± 2.61	47.60 ± 2.08	<0.001
Nasal	42.58 ± 1.72	45.33 ± 2.98	48.69 ± 2.53	<0.001
Temporal	43.66 ± 1.66	44.42 ± 1.93	48.08 ± 2.04	<0.001

Data are expressed as mean ± SD; One-way analysis of variance (ANOVA) followed by Bonferroni post hoc analysis; Statistical significance $p < 0.05$.

(21 myopic eyes of 21 patients with PICC), and the group 3: (23 myopic eyes of 23 patients without PICC and CNV). There were no significant differences for age ($p = 0.602$), sex ($p = 0.646$) and mean spherical equivalent ($p = 0.394$) among the three groups. Table 1 reported the demographic and clinical characteristics of the three groups. SD-OCT B-scan identified PICC as an intrachoroidal space more frequently located on the inferior border of the optic disc in 32 eyes (58%) of the studied eyes. In four eyes (15%) SD-OCT detected an inner retinal defects overlying the intrachoroidal cavitation. The comparison in VD of the RPC among the three groups was shown in Table 2. There were statistically significant differences in VD of the RPC in peripapillary and whole papillary regions among the three groups of myopic patients ($p < 0.001$). We found that the mean VD of the whole papillary region was significantly reduced ($p < 0.001$) in group 1 (38.16% ± 2.24%) compared to groups 2 (42.09% ± 1.22%) and 3 (45.26% ± 2.43%). Eyes of group 1 had a lower retinal vessel density in the peripapillary region of the RPC layer (41.5% ± 1.93%) in comparing to group 2 (44.71% ± 2.79%) and group 3 (48.08% ± 2.02%) ($p < 0.001$). Likewise, the VD of the RPC in each peripapillary sector (superior, inferior, temporal, and nasal) was found decreased in group 1 compared to groups 2 and 3 ($p < 0.001$).

Furthermore, the comparison between groups 2 and 3 revealed that the mean VD of whole papillary region and peripapillary regions was significantly decreased in myopic eyes with PICC compared to ones without PICC (42.09% ± 1.22% vs 45.26% ± 2.43%; $p < 0.001$ and 44.71% ± 2.79% vs 48.08% ± 2.02%; $p < 0.001$). Likewise, the VD of the RPC in each peripapillary sector was found decreased in group 2 compared to group 3 ($p < 0.001$; Figure 1).

Discussion

To the best of our knowledge this is the first study that evaluated the correlation between PICC and the risk of the development of a myopic CNV. PICC is a disorder that can be detected in high myopic eyes. According to the literature PICC is more often located on the inferior border of the optic disc.[1,2] However, the pathogenetic mechanism of the PICC is still unclear. In 2007 Wei et al. hypothesized that the progression of staphyloma was responsible for stretch and subsequent tissue breaks at the edge of the myopic conus.[4] These breaks could lead to a communication between the vitreous cavity and the choroidal tissue creating a fluid pocket.[4] Furthermore, Spaide et al. noted in 2012 a posteriorly bowing of the sclera in these patients and hypothesized a mechanism of widening of the choroidal tissue at the inferior border of the optic nerve with the subsequent formation of an intrachoroidal cavitation.[3] We agree with the latter theory because in our study we found an inner retinal defects overlying the intrachoroidal cavitation on SD-OCT B-scan only in four eyes (15%). The deformation of the optic nerve associated with a complete ring of chorioretinal atrophy surrounded the optic disc better correlated with the theory of a posterior excursion of the sclera, which was already demonstrated by Dai et al. seen in 2015.[9] Our date showed a rate of PICC in highly

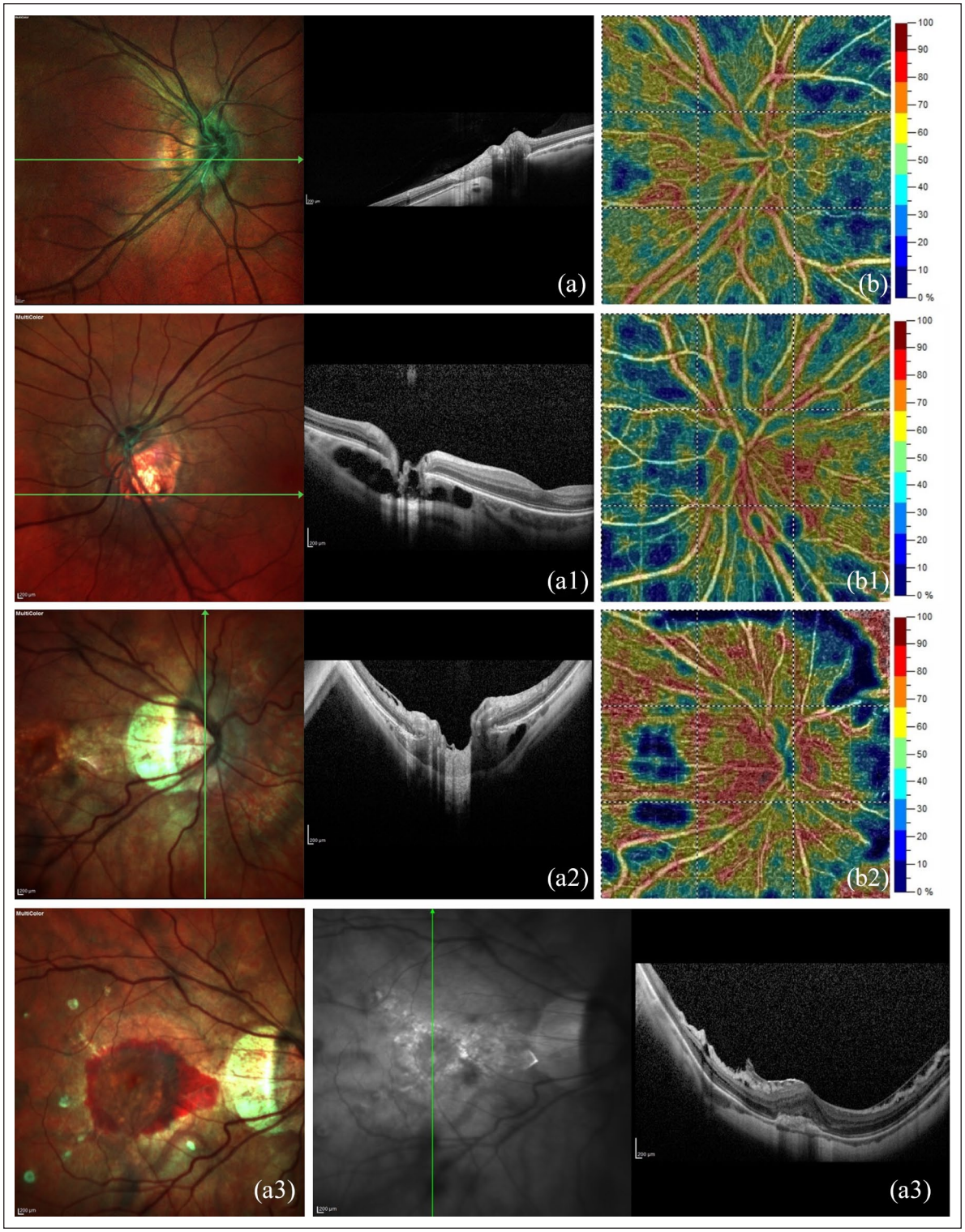

Figure 1. (a) SDOCT of right eye of a patient of group 3 demonstrated the absence of PICC; (b) OCTA image of the vessel density (VD) of radial peripapillary capillary plexus (RPC) of the eye in figure (a); (a1) SD-OCT of left eye of a patient of group 2 demonstrated the presence of a large PICC on the inferior border of the optic disc; (b1) VD of RPC of the eye in figure (a1) appeared lower than that in figure (b); (a2–a4) SD-OCT B-scans of right eye of a patient of group 1 passing respectively on optic disc and on macular region demonstrated the presence of PICC on the superior border of the optic disc and subretinal macular hemorrhage due to a CNV; (b2) the OCTA image of the eye in figure (a2) demonstrated a lower VD of RPC than figures (b) and (b1).

myopic eyes of 58%, which is similar to the PICC rate found by Venkatesh et al. (55.8%) in eyes with the presence of focal chorioretinal atrophy or myopic conus.[10]

OCTA was previously used to improve the diagnosis of myopic CNV[5] and also to evaluate the radial peripapillary capillaries not visible with traditional angiography. Performing the imaging of the peripapillary vasculature can be very helpful to better understand the anatomic features of PICC. Mazzaferro et al. using OCTA imaging demonstrated that PICC was characterized by the absence of choroidal and choriocapillary network.[11] In this study we analyzed the VD of RPC (whole papillary region and the four peripapillary sectors) in myopic eyes with PICC complicated by CNV, with PICC without CNV and in myopic eyes without PICC and CNV. We found that myopic eyes with PICC presented a statistically significant reduction in VD of whole papillary and peripapillary areas compared to myopic eyes without PICC. This reduction resulted greater in myopic eyes with PICC complicated by macular CNV compared to myopic eyes with PICC without CNV. Therefore, we hypothesize that the papillary and peripapillary hypoperfusion may be correlated to the development of the CNV. The pathogenesis of myopic CNV is not well known. The most recognized theory is that mechanical stretch due to ocular elongation leads to the development of lacquer cracks. Lacquer cracks are fissures in the retinal pigment epithelium–Bruch's membrane–choriocapillaris complex that could allow the growth of CNV.[5]

Chen et al. in a previous study proved that high myopic eyes with PICC had lower peripapillary vessel density, especially in the temporal area, than those without PICC or healthy controls.[12] According to the authors the lower VD in the temporal area was associated with a larger temporal β-zone peripapillary atrophy.[12] The authors suggested a possible correlation between low VD of papillary and peripapillary regions and the presence of a PICC. Our data showed that the reduced VD was present in all the peripapillary sectors, suggesting a widespread damage in groups with PICC, especially in eyes affected by CNV.

The main limitation of the study is the reduced number of included eyes, due to the small incidence of the PICC with or without CNV. In addition, such cases of myopic retinopathy can produce low-quality images or artifacts for the high ocular axial length, and for this reason they were excluded from this study.

Further longitudinal studies are needed to determine whether reduced VD of RPC is associated with PICC and with an increased risk of CNV development.

In conclusion the use of OCTA can improve our understanding of the pathogenic relationships between the optic disc perfusion and the formation of a CNV in myopic eyes with PICC.

Declaration of conflicting interests

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ORCID iDs

Daniela Montorio https://orcid.org/0000-0003-1423-9621
Gilda Cennamo https://orcid.org/0000-0003-4253-1929

References

1. Ohno-Matsui K, Shimada N, Akiba M, et al. Characteristics of intrachoroidal cavitation located temporal to optic disc in highly myopic eyes. *Eye* 2013; 27(5): 630–638.
2. Shimada N, Ohno-Matsui K, Yoshida T, et al. Characteristics of peripapillary detachment in pathologic myopia. *Arch Ophthalmol* 2006; 124(1): 46–52.
3. Spaide RF, Akiba M and Ohno-Matsui K. Evaluation of peripapillary intrachoroidal cavitation with swept source and enhanced depth imaging optical coherence tomography. *Retina* 2012; 32(6): 1037–1044.
4. Wei YH, Yang CM, Chen MS, et al. Peripapillary intrachoroidal cavitation in high myopia: reappraisal. *Eye* 2009; 23(1): 141–144.
5. Ohno-Matsui K, Ikuno Y, Lai TYY, et al. Diagnosis and treatment guideline for myopic choroidal neovascularization due to pathologic myopia. *Prog Retin Eye Res* 2018; 63: 92–106.
6. Bruyère E, Miere A, Cohen SY, et al. Neovascularization secondary to high myopia imaged by optical coherence tomography angiography. *Retina* 2017; 37(11): 2095–2101.
7. Jia Y, Tan O, Tokayer J, et al. Split-spectrum amplitude-decorrelation angiography with optical coherence tomography. *Biomed Opt Express* 2012; 20(4): 4710–4725.
8. Rao HL, Pradhan ZS, Weinreb RN, et al. Regional comparisons of optical coherence tomography angiography vessel density in primary open angle glaucoma. *Am J Opthahlomol* 2016; 171: 75–83.
9. Dai Y, Jonas JB, Ling Z, et al. Unilateral peripapillary intrachoroidal cavitation and optic disk rotation. *Retina* 2015; 35(4): 655–659.
10. Venkatesh R, Jain K, Aseem A, et al. Intrachoroidal cavitation in myopic eyes. *Int Ophthalmol* 2020; 40(1): 31–41.
11. Mazzaferro A, Carnevali A, Zucchiatti I, et al. Optical coherence tomography angiography features of intrachoroidal peripapillary cavitation. *Eur J Ophthalmol* 2017; 27(2): e32–e34.
12. Chen Q, He J, Hua Y, et al. Exploration of peripapillary vessel density in highly myopic eyes with peripapillary intrachoroidal cavitation and its relationship with ocular parameters using optical coherence tomography angiography. *Clin Exp Ophthalmol* 2017; 45(9): 884–893.