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Original Article

The Effect of Pathological Retinal Changes on Retinal Capillary Circulation in Myopic Patients

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Abstract

Objectives: Myopia is a common ocular disorder worldwide, leading to degenerative changes in the retina which is highly susceptible to vascular impairment. The aim of the study was to investigate the effects of pathological retinal changes on the retinal capillary structures using optical coherence tomography angiography (OCTA) in myopic patients.

Methods: Thirty-two patients with high myopia (HM), 29 patients with pathological myopia (PM), and 38 healthy subjects with emmetropia (EM) were enrolled in this study. OCTA was performed to measure the following parameters: Foveal avascular zone (FAZ) area; FAZ perimeter; FAZ acircularity index (AI); and superficial, deep, and radial peripapillary capillary (RPC) vessel densities. Axial length (AL), spherical equivalent, and anterior chamber depth were evaluated.

Results: Significant differences in the mean AL values were observed between the EM group and the other groups ($p<0.001$ for all); however, no significant differences were observed between the HM and PM groups ($p=0.135$). Significant differences in FAZ parameters, except for AI, were found among the three groups ($p<0.05$ for all). In all regions, except for the fovea and inside disc, the capillary plexus vessel densities were significantly lower in the PM group than in the other groups and were lower in the HM group than in the EM group ($p<0.05$ for all).

Conclusion: Significant differences identified in capillary densities between the HM and PM groups, both of which present similar AL measurements, suggest that pathological retinal findings have significant effects on retinal perfusion independent of the effect of AL.

Keywords: Axial length, high myopia, optical coherence tomography angiography, pathological myopia, retinal microcirculation

Introduction

Refractive status is a complex variable, determined by the balance between the optical power of ocular structures and the axial length (AL) of the eye (1). AL is a significant contributor to refractive status, and longer eyes tend to be myopic eyes (2). Myopia is a common cause of vision loss worldwide, especially in Asia, and the prevalence of myopia has increased rapidly over the past 50–60 years (3,4). Individuals with high myopia (HM) have increased risks of ocular complications, leading to visual impairment (5).

Pathological myopia (PM) is characterized by the excessive axial elongation of the globe and associated degenerative changes in the posterior segment of the eye, resulting in decreased best-corrected visual acuity (BCVA). PM is a major cause of legal blindness, globally, and the risk of PM

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development increases significantly among people with HM compared with the normal population (6,7). Recent studies have demonstrated vascular changes in patients with HM and PM, which may be correlated with axial elongation (8,9).

Different measurement strategies, such as fluorescein angiography, indocyanine green angiography, and laser Doppler velocimetry, have been used to determine ocular blood flow in myopic eyes (9-11). However, these techniques are not sufficient for a detailed assessment of macular and radial peripapillary capillary (RPC) microcirculation. Optical coherence tomography (OCT) angiography (OCTA) evaluates the retinal vascular tissues, in a non-invasive and quantitative manner, using a split-spectrum, amplitude-decorrelation angiography algorithm (12).

To date, many clinical studies have investigated retinal vascular changes in the posterior pole of patients with HM and PM, which have identified correlations between retinal vascular changes and AL (8,9). However, the present study focused on the effects of pathological myopic changes in retinal microcirculation by minimizing the effects associated with AL. The present study aimed to use OCTA to investigate differences in macular and RPC microcirculation among patients with HM and PM, who had similar AL values, and age- and gender-matched emmetropic control subjects.

Methods

This prospective study was performed by the department of ophthalmology at the tertiary hospital. The study was approved by the Ethics Committee (E-19-73) and conducted in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

The study included a series of 61 myopic patients and 37 emmetropic healthy controls, who were divided into three groups according to the results of a dilated fundus examination and color fundus photography. Thirty-two patients with HM (HM group), 29 patients with PM (PM group), and 37 emmetropic healthy controls (emmetropia [EM] group) were enrolled in this study. One eye from each patient was evaluated. Among those patients for whom both eyes met the study criteria, the right eye was used to select the studied eye. A total of 98 eyes from 98 patients were examined in this study.

The HM and PM study groups were constituted using the following three steps. First, patients with an AL ≥26.0 mm were included in the study. Second, these patients were divided according to the presence or absence of pathological retinal findings; patients without pathological findings were included in the HM group, whereas patients with pathological findings, including myopic maculopathy or myopic optic disc changes (optic disc tilt and peripapillary atrophy), were included in the PM group (Fig. 1) (13,14). Third, patients with an AL >28.0 mm were excluded from the study, to minimize the effects of AL on retinal microcirculation and OCTA image distortion. The presence of myopic maculopathy was classified according to the International Photographic Classification and Grading System for Myopic Maculopathy (Category 0, no macular lesions; Category 1, only tessellated fundus; Category 2, diffuse chorioretinal atrophy; Category 3, patchy chorioretinal atrophy; and Category 4, macular atrophy) (15). In addition, AL was verified to be between 22.0 mm and 24.0 mm for the EM group. The members of the control group were recruited from among subjects who had visited the ophthalmology clinic for a routine ocular examination. All of the control subjects had no ocular or systemic disorder.

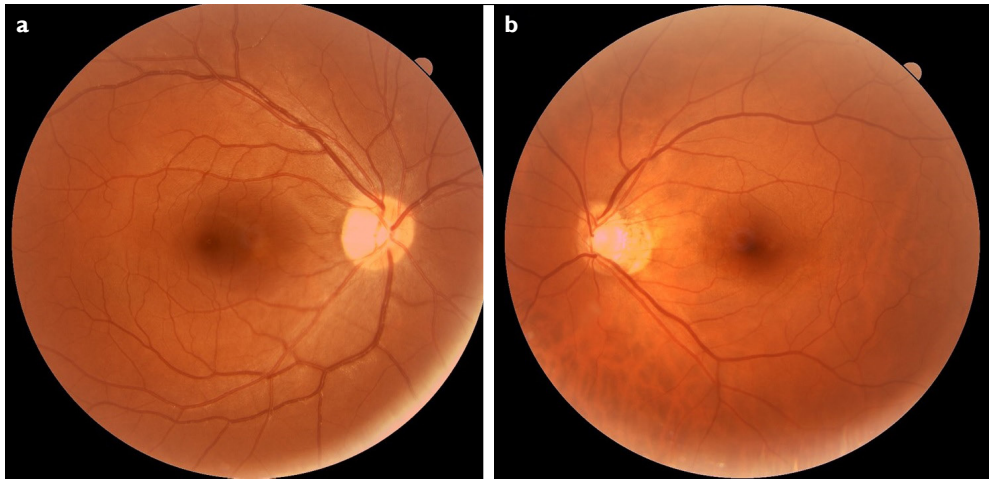

Figure 1. Fundus photographs of the right eye of a myopic patient without pathological fundus findings (**a**, High myopia group) and the left eye of another myopic patient with tilted optic disc and peripapillary atrophy (**b**, Pathological myopia group).

Participants with the following conditions were excluded from this study: Ocular disease other than HM or PM; any vascular systemic disease; the presence of choroidal neovascularisation (CNV), vitreomacular interface disorders, posterior staphyloma, or coloboma; a history of ocular trauma; any previous ocular surgery, retinal laser treatment, or intravitreal injection; intraocular pressure (IOP) measurements >21 mmHg; currently receiving any systemic or topical medical treatment; and smoking or any previous history of smoking. Participants with diseases that may affect OCTA measurements, such as amblyopia, cataract, vitreous hemorrhage, and dry eye, were also excluded from the study.

All participants underwent detailed ophthalmological examinations, including BCVA measurements using the Snellen chart, biomicroscopic anterior segment examinations, IOP measurements with non-contact tonometry, and dilated fundus examinations. Refractive error measurements were performed using the same automatic refractor-keratometer device (Canon RF-K2, Japan) for all patients. AL and anterior chamber depth (ACD) measurements were determined using a Lenstar LS 900 (Haag-Streit AG, Switzerland). The Humphrey 24–2 visual field (Carl Zeiss Meditec Inc., Dublin, CA) was applied to patients with suspected glaucoma. OCT (Spectralis OCT, Heidelberg Engineering, Heidelberg, Germany) was performed on all participants to detect macular hole, retinoschisis, epiretinal membrane, traction maculopathy, or posterior staphyloma. The presence of posterior staphyloma was defined as increased foveal depth (≥500 µm) than the periphery of the OCT scan (14).

After pupil dilation with topical 1% tropicamide eye drops, subjects were seated in front of the OCTA scanner, asked to fixate on an internal fixation target, and then examined with the XR Avanti AngioVue OCT-A (Optovue, Fremont, California, USA) (Version 2017.1.0.151). All scans performed on the individuals' eyes examined a 6 mm x 6 mm area, centered on the fovea. The OCTA device automatically inserted three fovea-centered circles on the macula, with density assessment tools for the superficial capillary plexus (SCP) and the deep capillary plexus (DCP; Fig. 2). The foveal zone vessel density was determined for the area of the small circle, which had a diameter of 1 mm; the parafoveal zone vessel density was determined for the area of the middle circle, which had a diameter of 3 mm; and the perifoveal zone vessel density was determined for the area of the outer circle, which had a diameter of 6 mm. In addition, the vessel density zones were automatically divided into four equal quadrants (temporal, nasal, inferior, and superior) and two equal hemispheres (superior and inferior). The foveal avascular zone (FAZ) area, FAZ perimeter, the acircularity index (AI) of the FAZ (defined as the ratio between the FAZ perimeter and the perimeter of a circle with an equal area), and the foveal density-300 (FD-300; the vessel density 300 mm around the FAZ) were also measured (Fig. 2).

All subjects underwent optic disc area measurements using the optic nerve head (ONH) scan protocol to measure the parameters of the disc angiogram. AngioVue disc mode was used to acquire optic disc OCTA images, in a 4.5 × 4.5 mm area. This device attaches two ONH-centered

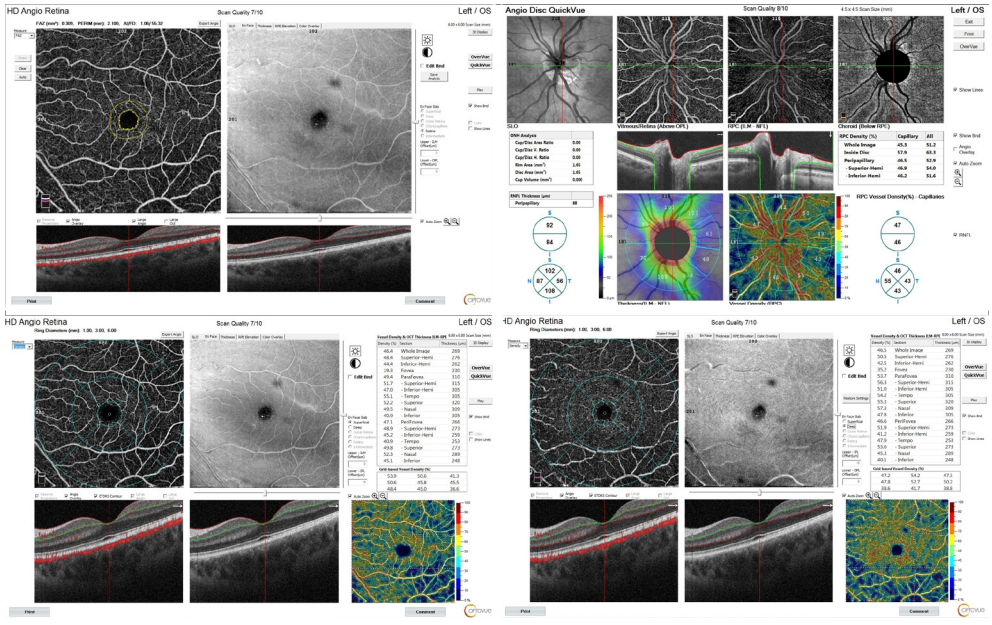

Figure 2. FAZ (upper-left), optic disc (upper-right), SCP vessel density (lower-left), and DCP vessel density (lower-right) assessment tools of optical coherence tomography angiography, in a patient with pathological myopia.

concentric circles (inner and outer), with diameters of 2 mm and 4 mm (ring width, 1 mm), and performs segmentation between the inner limiting membrane and the retinal nerve fiber layer, to calculate the RPC vessel density (RPCvd) (Fig. 2). The OCT-A device presents the data for these measurements, divided into eight equal, 45-degree sectors, and two equal hemispheres (superior and inferior hemispheres). In addition to the RPCvd, the vessel densities of the inside disc and the whole image were also calculated.

All OCTA scans were performed by the same specialist (A.M.K.), at the same time of day (between 1:00 PM and 2:00 PM), under the same environmental conditions. Three consecutive scans for each eye were captured, and the one with the best quality was enrolled in the statistical analysis. One experienced and independent grader (Y.S.G.) checked the reliability of all OCTA images then reviewed them. First, the grader checked the accuracy of the automated drawing FAZ area. Then, the conformity of fovea-centered circles on the macula was determined. Finally, correct segmentation of SCP (from the internal limiting membrane to the inner plexiform layer/inner nuclear layer interface) and DCP (from the inner plexiform layer/inner nuclear layer interface to the outer plexiform layer/outer nuclear layer interface) slabs were controlled. Any OCTA images with poor image characteristics, such as a low signal strength index (SSI <7), one or more blink artifacts, motion or doubling artifacts, or insufficient data for correct analysis were excluded from the study.

Statistical Analyses

To estimate the sample size for three independent groups, a statistical power analysis (G*Power 3.1) was performed. The estimated sample size required to detect a large effect size with 90% power (α=0.05) was 84 in total and 28 in each group.

For statistical analysis, SPSS 24.0 software for Windows (SPSS Inc., Chicago, IL) was used to analyze outcomes. Descriptive statistics are presented as the mean ± standard deviation, with the minimum and maximum values. The distribution patterns of the variables were tested by visual (histogram and probability graphs) and analytical (Kolmogorov–Smirnov/Shapiro–Wilk test) tools. The $\chi 2$ test was used to analyze categorical variables. One-way analysis of variance was used to compare the differences among the three groups, and the Dunnett T3 test was used for post hoc binary comparisons. Correlations between parameters were tested by Pearson's correlation test. P<0.05 was considered significant.

Results

Thirty-two patients with HM (15 females and 17 males), 29 patients with PM (17 females and 12 males), and 37 age- and sex-matched, healthy emmetropic subjects (20 females and 17 males) were enrolled in this study. The demographic and ocular characteristics of the study groups are shown in Table 1. The age and sex characteristics of study groups were similar (p=0.979 and p=0.648). Significant differences in AL and ACD were identified between the EM group and the other groups (p<0.001 for all); however, similar AL and ACD measurements were observed between the HM and PM groups (p=0.135 and p=0.515, respectively). The BCVA values in the PM group were lower than those in the EM and HM groups (p<0.001 for all). In addition, significant differences in the SE measurements were observed in the binary comparisons between all three groups, and more effect of astigmatism on SE was observed in the PM group compared to the HM group (p<0.001 for all). All participants in the HM and EM groups had no myopic macular lesions and no myopic optic disc changes. For the PM group, 21 patients (72.4%) had peripapillary atrophy and 19 patients (65.5%) had tilted optic disc. In addition, Category 0 and Category 1 myopic maculopathy were detected in 25 patients (86.2%) and 4 patients (13.7%) with PM, respectively. There were statistically significant dif-

Table 1. Demographic and ocular characteristics of the study groups

	Emmetropia Group (n=37) Mean±SD (min/max)	High Myopia Group (n=32) Mean±SD (min/max)	Pathological Myopia Group (n=29) Mean±SD (min/max)	p*
Age, years	33.2±12.2 (18.0/57.0)	33.6±13.7 (19.0/60.0)	33.8±13.3 (18.0/52.0)	0.979
BCVA, decimal units	0.9±0.1 (0.8-1.0)	0.9±0.1 (0.8/1.0)	0.6±0.1 (0.50/0.80)	<0.001
SE, D	-0.04±0.35 (-0.50/0.50)	-6.15±0.86 (-5.00/-7.25)	-8.27±1.45 (-5.50/-10.00)	<0.001
AL, mm	22.9±0.2 (22.5/23.7)	26.5±0.3 (26.0/27.6)	26.7±0.3 (26.1/27.8)	<0.001
ACD, mm	3.52±0.24 (3.20/3.86)	3.86±0.20 (3.48/4.09)	3.81±0.37 (3.05/4.37)	<0.001

BCVA: Best corrected visual acuity; SE: Spherical equivalent; AL: Axial length; ACD: Anterior chamber depth; SD: Standart deviation. *one-way ANOVA test. Significant p values are in bold.

ferences in myopic retinal changes including peripapillary atrophy, tilted optic disc, and myopic maculopathy for the PM group compared to the other groups (p<0.001, p<0.001, and p=0.007, respectively).

The FAZ parameters and vessel densities evaluated by OCTA, and the binary comparisons of these parameters between the study groups, are shown in Tables 2 and 3. Statistically significant differences among the three groups were observed for all FAZ parameters, including the vessel densities in the SCP, DCP, and RPC, but no significant differences were observed for AI. The PM group had decreased FAZ area with lower SCP, DCP, and RPC vessel densities than the EM and HM groups with the exception of foveal SCP (for the EM group), foveal DCP (for both groups), and inside disc RPC (for the HM group) vessel densities (p<0.05 for all). In addition, decreased FAZ area and lower capillary vessel densities were observed in the HM group compared to the EM group, excluding inside disc and superior-hemi RPC vessel densities (p<0.05 for all).

Table 4 shows the correlations between AL, SE, and ACD and the FAZ parameters and vessel densities evaluated by OCTA. Numerous significant negative correlations were identified between AL and SE with vessel densities, for all regions, except the fovea and inside disc. Significant negative correlations were also found between the area and perimeter of the FAZ with AL and SE.

Table 2. The parameters of FAZ and capillary vessel densities in study groups

	Emmetropia Group (n=37) Mean±SD (min-max)	**High Myopia Group (n=32) Mean±SD (min-max)**	**Pathological Myopia Group (n=29) Mean±SD (min-max)**	**p***
FAZ				
Area, mm^2	0.29±0.08 (0.08-0.42)	0.21±0.07 (0.08-0.33)	0.14±0.04 (0.07-0.20)	<0.001
Perimeter, mm	2.09±0.32 (1.12-2.58)	1.76±0.31 (1.19-2.22)	1.45±0.23 (1.11-1.78)	<0.001
Acircularity index	1.09±0.03 (1.06-1.21)	1.09±0.03 (1.05-1.15)	1.09±0.03 (1.04-1.18)	0.883
Foveal density-300, %	56.42±3.60 (45.10-64.90)	52.50±7.52 (30.40-64.20)	47.82±4.02 (38.56-55.43)	<0.001
SCP vessel density, %				
Whole image	51.9±2.2 (46.6-55.3)	48.7±3.1 (43.7-55.6)	44.3±3.8 (37.2-52.0)	<0.001
Superior-hemi	51.8±2.2 (46.8-55.7)	48.9±3.0 (43.7-55.4)	44.4±3.7 (28.2-51.0)	<0.001
Inferior-hemi	51.9±2.1 (46.5-56.1)	48.5±3.2 (43.7-55.8)	44.2±4.2 (35.5-53.1)	<0.001
Fovea	19.6±5.5 (10.0-30.2)	22.8±4.9 (14.6-30.8)	24.4±6.5 (13.9-33.1)	0.003
Parafovea	54.3±2.5 (48.3-57.6)	50.8±4.6 (39.7-59.6)	45.4±4.9 (36.7-54.4)	<0.001
Perifovea	52.6±2.3 (47.2-56.6)	49.2±3.3 (43.8-56.0)	45.2±3.5 (39.5-52.5)	<0.001
DCP vessel density, %				
Whole image	54.0±4.6 (43.5-62.2)	48.6±5.8 (36.5-57.7)	41.7±3.2 (36.0-51.5)	<0.001
Superior-hemi	54.3±4.6 (43.4-62.2)	48.8±6.1 (35.7-57.3)	42.2±2.9 (36.2-51.2)	<0.001
Inferior-hemi	53.7±4.7 (43.6-62.8)	48.3±5.6 (37.2-58.1)	41.2±4.1 (32.5-51.7)	<0.001
Fovea	37.9±7.5 (24.7-54.9)	41.9±5.7 (31.2-51.0)	41.3±5.5 (33.8-48.8)	0.024
Parafovea	57.5±3.5 (50.3-64.0)	55.1±3.4 (49.2-61.3)	49.6±3.8 (39.7-57.3)	<0.001
Perifovea	55.7±4.9 (44.3-64.6)	49.1±6.7 (34.8-59.7)	41.5±3.4 (35.4-52.0)	<0.001
RPC density, %				
Whole image	50.6±1.9 (46.0-53.8)	49.5±2.3 (45.1-55.0)	47.5±4.2 (39.7-52.0)	0.001
Inside-disc	50.0±4.8 (41.3-58.6)	50.7±4.5 (41.1-58.4)	55.7±6.9 (40.7-64.0)	0.001
Peripapillary	53.3±2.4 (47.7-56.6)	52.3±2.2 (49.5-58.6)	48.3±6.4 (35.9-55.6)	<0.001
Superior-hemi	53.0±2.5 (46.3-56.3)	53.0±2.1 (49.8-58.3)	48.5±6.9 (30.2-55.5)	<0.001
Inferior-hemi	53.5±2.5 (48.3-57.8)	51.5±3.1 (42.4-59.2)	48.0±7.3 (32.6-55.6)	<0.001

FAZ: Foveal avascular zone; SCP: Superficial capillary plexus; DCP: Deep capillary plexus; RPC: Radial peripapillary capillary; SD: Standart deviation. *one-way ANOVA test. Significant p values are in bold.

Table 3. Binary comparisons of FAZ and capillary vessel densities parameters between the study groups

	p*		
	EM Group vs HM Group	**EM Group vs PM Group**	**HM Group vs PM Group**
FAZ			
Area, mm^2	<0.001	<0.001	<0.001
Perimeter, mm	<0.001	<0.001	<0.001
Acircularity index	0.946	0.985	0.998
Foveal density-300, %	0.030	<0.001	0.011
SCP vessel density, %			
Whole image	<0.001	<0.001	<0.001
Superior-hemi	<0.001	<0.001	<0.001
Inferior-hemi	<0.001	<0.001	<0.001
Fovea	0.042	0.008	0.654
Parafovea	0.001	<0.001	<0.001
Perifovea	<0.001	<0.001	<0.001
DCP vessel density, %			
Whole image	<0.001	<0.001	<0.001
Superior-hemi	<0.001	<0.001	<0.001
Inferior-hemi	<0.001	<0.001	<0.001
Fovea	0.047	0.107	0.874
Parafovea	0.019	<0.001	<0.001
Perifovea	<0.001	<0.001	<0.001
RPC density, %			
Whole image	0.036	<0.001	0.002
Inside-disc	0.644	0.002	0.070
Peripapillary	0.017	<0.001	0.002
Superior-hemi	0.213	<0.001	0.001
Inferior-hemi	0.005	<0.001	0.039

FAZ, Foveal avascular zone; SCP, Superficial capillary plexus; DCP, Deep capillary plexus; RPC, Radial peripapillary capillary, EM, Emmetropia; HM, High myopia; PM, Pathological myopia. *Dunnett T3 test. Significant p values are in bold.

Discussion

Myopia is a public health problem, worldwide, especially in Asia (16). Myopia represents a major underlying cause of vision loss, due to uncorrected myopic refraction errors and secondary complications, including retinal detachment, myopic maculopathy, and CNV (1,17). Therefore, understanding the effects of pathological retinal changes on retinal capillary characteristics in myopic patients is important. In this study, the macular and peripapillary vascular features were quantitatively measured by OCTA in myopic patients with and without pathological retinal findings.

Various techniques, including laser Doppler velocimetry, color Doppler imaging, and dynamic vessel analysis, have been used to examine retinal vascular circulation in myopic patients (8,9,18,19). Decreased retinal artery blood flow was reported in patients with HM by Benavente-Pérez et al.(8) and Shimada et al.(9) In addition, reduced choroidal and retinal blood flow, with reduced retinal vessel diameters, were reported by previous studies (18,19). However, these techniques are not sufficient for detailed measurement of retinal capillary microcirculation. OCTA is an imaging technique that facilitates fast, reproducible, non-invasive, and quantitative assessments of the retinal vascular microcirculation and can be used to detect vascular changes in myopic patients.

A few previous studies have investigated the retinal vascular microcirculation using OCTA in patients with HM and

Table 4. The correlations between the AL, SE and ACD with OCTA parameters in all myopic patients

	AL, mm	SE, D	ACD, mm
FAZ			
Area, mm^2	-0.551**	-0.346**	-0.163
Perimeter, mm	-0.551**	-0.351**	-0.216
Acircularity index	-0.073	-0.039	-0.214
Foveal density-300, %	-0.499**	-0.304*	-0.157
SCP vessel density, %			
Whole image	-0.641**	-0.552**	-0.333*
Superior-hemi	-0.625**	-0.527**	-0.420*
Inferior-hemi	-0.635**	-0.553**	-0.220
Fovea	0.251*	-0.065	0.143
Parafovea	-0.597**	-0.531**	-0.249
Perifovea	-0.643**	-0.501**	-0.340*
DCP vessel density, %			
Whole image	-0.646**	-0.573**	-0.084
Superior-hemi	-0.635**	-0.538**	-0.088
Inferior-hemi	-0.642**	-0.599**	-0.078
Fovea	0.205*	0.223	0.261
Parafovea	-0.545**	-0.626**	0.032
Perifovea	-0.667**	-0.556**	-0.110
RPC density, %			
Whole image	-0.357**	-0.366*	0.277
Inside-disc	0.246*	0.240	-0.417**
Peripapillary	-0.349**	-0.401**	0.255
Superior-hemi	-0.256*	-0.549**	0.060
Inferior-hemi	-0.382**	-0.180*	0.197

FAZ, Foveal avascular zone; SCP, Superficial capillary plexus; DCP, Deep capillary plexus; RPC, Radial peripapillary capillary; AL, Axial length; ACD, Anterior chamber depth; SE, Spherical equivalent. Significant r values are in bold (Pearson's correlation coefficient). * $p<0.05$; ** $p<0.01$.

PM. Cennamo et al. (20) investigated the myopic CNV and found that the CNV area decreased after intravitreal ranibizumab injections. In myopic children, reduced superficial retinal vascular densities and enlarged FAZ areas were detected compared with those in emmetropic subjects (21). Wang et al. (22) investigated patients with various severe myopic refractive errors and determined that the HM group presented the lowest peripapillary vessel density compared to the mild and moderate myopia groups. In addition, a study presented by Mo et al. (23) showed decreased macular and RPC flow densities in the PM group compared with those in the EM and HM groups. In accordance with the previous studies, the PM group in the present study had lower capillary vessel densities in the SCP, DCP, and RPC than the EM and HM groups, for all studied regions, except the area of the fovea and the inside disc (Fig. 3). In addition, significant differences between the EM group and HM group were identified, with the lower vessel densities observed in the HM group, except in the fovea and inside disc (Fig. 3). The results for the fovea and inside disc found in the present study were similar to those reported by Mo et al. (23) The increased FAZ area observed in the EM group compared with the HM and PM groups and the negative correlation between AL and FAZ area identified in the present study may explain why foveal density was different from the densities of other regions; however, the results observed for the inside disc area are harder to explain. According to the results of this study, it can be thought that pathological myopic changes have detrimental effects on the retinal microvascular system. In addition, the presence of myopia seems to worsen the density of retinal capillaries regardless of pathological myopic changes. Therefore, myopic patients should be examined properly with dilated fundus examination, especially they have any vascular systemic diseases such as diabetes mellitus and hypertension. In addition, OCTA can be a beneficial imaging test to detect the progression of vascular changes in myopic patients.

Refractive errors and AL were used to define PM in most previous studies; however, currently, PM is defined as the presence of myopic retinal changes (13,15). In addition, PM differs from HM because PM causes compromised BCVA, whereas HM does not (1). Therefore, the presence of pathological fundus findings may be more indicative of retinal effects than the presence of high AL or refractive errors. However, the previous studies have reported that the prevalence of pathological retinal signs was significantly correlated with AL and refractive error, especially in patients with SE values higher than –5.00 to –6.00 D (24,25).

Correlations between AL and OCTA results have been investigated in a few previous studies. Venkatesh et al. (26) reported a positive correlation between DCP vessel densities and AL. In contrast, negative correlations between the peripapillary and macular flow densities and AL have been reported in recent studies (22,23). To the previous studies, it can be suggested that decreased vascular densities in myopic patients may occur due to both high AL and pathological retinal changes, but the exact effects of AL and pathological retinal changes on retinal microcirculation cannot be determined without elimination of one of these variables. Therefore, the present study aimed to minimize the effects of AL and focus on pathological retinal findings by only enrolling myopic patients with AL values between 26.0 mm and 28.0 mm. In accordance with the previous studies, the present study showed that increasing AL and SE (which is particularly

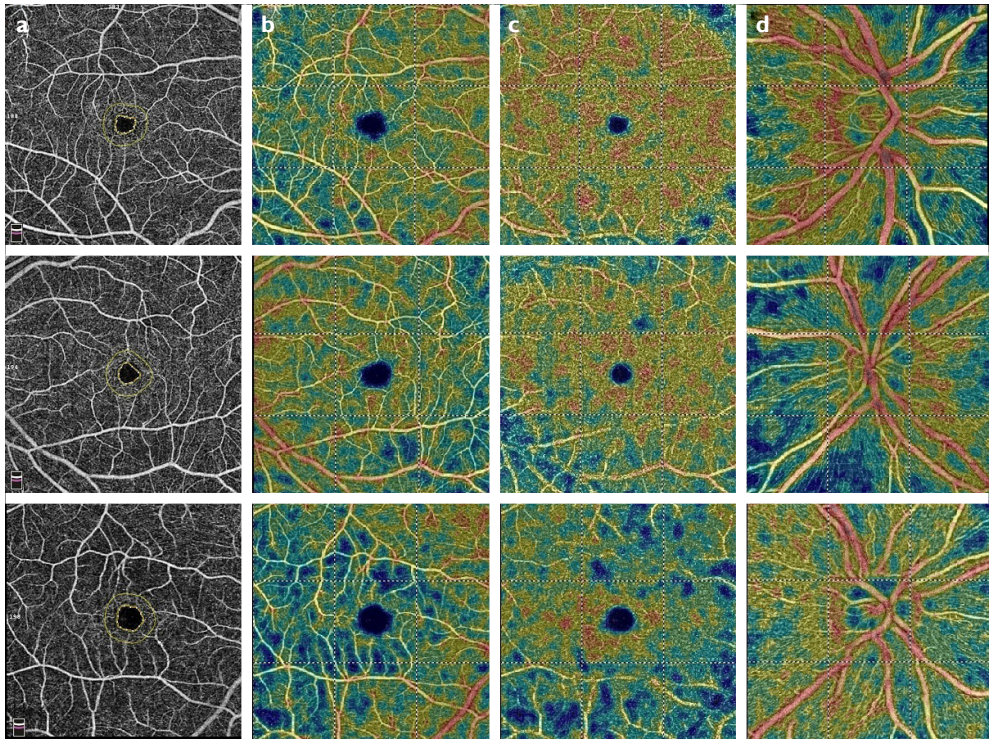

Figure 3. FAZ **(a)**, SCP vessel density **(b)**, DCP vessel density **(c)**, and RPC vessel density **(d)** images of an emmetropic subject (upper line), a patient with high myopia (middle line), and a patient with pathological myopia (bottom line). Prominently decreased vessel densities of SCP and DCP are seen in a patient with pathological myopia.

affected by AL) were correlated with decreasing SCP, DCP, and RPC vessel densities, which suggested that AL appears to be an important factor that affects the retinal vascular structure. Although there were some statistically significant correlations between vessel densities and ACD, the effect of ACD on retinal capillary densities was not as strong as the effects of AL and SE. In conclusion, this study revealed that macular and peripapillary retinal microcirculation was more strongly affected in the PM group than in the HM group, despite the two groups having similar AL values. The pathophysiology of decreased retinal vascular circulation in PM remains under investigation; (27) however, we hypothesize that atrophic areas in eyes with PM might result in decreased oxygen consumption compared with eyes with HM, and decreased oxygen requirements may result in reduced retinal vascular flow.

This study has several strengths and limitations. One strength of this study was the prospective nature of patient recruitment and the strict inclusion criteria, including the narrow AL range. However, the strict exclusion criteria also resulted in only a small number of participants in each study group, and the study population included a wide range of ages (although the age ranges were not significantly different among the groups), which represent limitations of this study. Therefore, longitudinal studies should be conducted in the future, to determine the relationship between myopia and retinal vascular structure. Another limitation is that OCTA cannot identify blood flow below a certain threshold; therefore, areas defined as capillary non-perfusion by OCTA may represent low blood flow, rather than a lack of blood flow. Finally, this study found that OCTA use was limited in myopic eyes due to significant image artifacts, poor image quality, abnormal patient fixation, and segmentation errors; however, this study investigated the participants with a narrow range AL to overcome these limitations. Because of this condition, the results of the present study are represented only a small part of myopic patients.

Conclusion

This study aimed to investigate the effects of pathological retinal changes on retinal capillary circulation, independent of AL, and determined that the macular and peripapillary vessel densities were more impaired in the eyes with PM than in eyes with HM. This study hypothesizes that atrophic areas may the cause of reduced vascular densities; however, further studies investigating the relationship between PM and retinal capillary structure remain necessary to understand the exact cause of impaired retinal capillary circulation.

Disclosures

Ethics Committee Approval: This prospective study was performed by the department of ophthalmology at the tertiary hospital. The study was approved by the Ethics Committee (E-19-73) and conducted in accordance with the ethical principles of the Declaration of Helsinki.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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