Longitudinal Changes in Macular Optical Coherence Tomography Angiography Metrics in Primary Open-Angle Glaucoma With High Myopia: A Prospective Study

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Purpose. To characterize longitudinal changes in macular microvasculature as quantified from optical coherence tomography angiography (OCTA) metrics in primary open-angle glaucoma (POAG) eyes with and without high myopia.

Methods. In total, 63 and 61 POAG eyes with and without high myopia, respectively, underwent swept-source OCTA imaging in at least four follow-up visits at an ophthalmic center, with a scanning protocol of 3- × 3-mm centered at the fovea. The foveal avascular zone (FAZ) area, FAZ circularity, and vessel density (VD) in both the superficial (SCP) and deep capillary plexuses (DCP) were measured. The rate of change in macular OCTA metrics over time was estimated using linear mixed-effects models in both groups of POAG eyes.

Results. The mean follow-up time and number of visits were 27.72 ± 8.57 months and 8.5 (8 to 13) times, and 30.95 ± 10.19 months and 10 (8–13) times in POAG eyes with and without high myopia, respectively. VD in the DCP reduced significantly more quickly in POAG eyes with high myopia than in those without high myopia (−5.14%/year vs. −3.71%/year, $P = 0.008$). Moreover, lower baseline VD in the DCP was significantly associated with faster VD reduction in POAG with high myopia eyes ($P < 0.001$). Conversely, the VD reduction rate in the SCP, FAZ area, and FAZ circularity in both the SCP and DCP were similar in both groups (all $Ps > 0.05$).

Conclusions. VD in DCP reduced significantly more quickly in POAG eyes with high myopia over time. Density in the DCP reduced more quickly when baseline VD was low.

Keywords: primary open-angle glaucoma, high myopia, optical coherence tomography angiography, longitudinal study

Myopia is a risk factor for primary open-angle glaucoma (POAG).[1–4] Population-based studies have revealed that individuals with myopia have twice the risk of developing POAG than those without myopia; high myopia increases the risk to nearly six times.[1,5] Moreover, previous studies have reported that high myopia is associated with glaucoma progression.[6,7] However, the underlying pathophysiology and effects of high myopia in POAG eyes remain poorly understood.

Impaired ocular blood flow may play an important role in the pathogenesis of POAG with high myopia. Previous studies using fluorescein angiography, laser Doppler flowmetry, and the Heidelberg retinal flowmeter to measure ocular blood flow reported that retinal blood flow was decreased in both eyes with high myopia and POAG.[8–11] However, because of the poor segmentation of the retinal layers and reproducibility of these methods, quantification of ocular blood flow in vivo has been unsatisfactory.

Optical coherence tomography (OCT) angiography (OCTA) allows non-invasive imaging of retinal vessels in vivo, and quantitative assessment of the macular microvasculature (i.e., vessel density [VD] and foveal avascular zone [FAZ][12]) in the superficial (SCP) and deep capillary plexuses (DCP).[13–15] Moreover, quantitative OCTA measurements have high repeatability.[16,17] Studies using OCTA have shown that glaucoma patients have significantly lower ocular perfusion than healthy subjects,[18] and decreased VD was correlated with axial length (AL) elongation.[19,20] Furthermore, lower VD, measured by OCTA, was associated with more severe glaucomatous visual field (VF) damage in highly myopic eyes,[21,22] and a larger FAZ area was associated with both glaucoma and high myopia.[23,24] However, little

is known about whether changes in these OCTA metrics are detectable over time in POAG eyes with high myopia.

Early glaucomatous damage could affect the macula; macular VD was shown to have better discriminative performance than peripapillary VD in glaucomatous eyes with high myopia.[25,26] This study aimed to evaluate the longitudinal changes in the macular OCTA metrics in the SCP and DCP of POAG eyes with and without high myopia, and to investigate whether baseline structural and functional measurements were related to subsequent changes in macular OCTA metrics.

Methods

Participants

This prospective, longitudinal study was performed in Zhongshan Ophthalmic Center, Sun Yat-sen University, from June 2016 to November 2019. The study adhered to the tenets of the Declaration of Helsinki. Ethical approval was granted by the ethics committee of the Zhongshan Ophthalmic Center, Sun Yat-sen University, China. All subjects provided written informed consent.

We applied the following inclusion criteria: (1) clinical diagnosis of POAG; (2) age >18 years; (3) best corrected visual acuity (BCVA) ≥20/40; (4) at least four visits. Exclusion criteria were (1) previous laser peripheral iridotomy, selective laser trabeculoplasty or intraocular pressure (IOP)–lowering surgery in the study eye; (2) presence of other intraocular diseases, such as severe cataracts, diabetic retinopathy, retinal detachment, optic neuritis, and uveitis in the study eye, which could affect VF sensitivity; (3) poor-quality OCTA images or OCT scans; (4) classification of myopic maculopathy > category 1 or with "plus" lesions[27]; (5) comorbid systemic hypertension or diabetes. Eyes that underwent laser treatment or IOP-lowering surgery during follow-up visits were also excluded.

POAG was defined as the presence of glaucomatous optic disc changes (i.e., vertical cup-to-disc ratio >0.7, neuroretinal rim notching, wedge-shaped retinal nerve fiber layer [RNFL] defects, or disc hemorrhage) with corresponding glaucomatous VF defects, an open angle confirmed by gonioscopy examination, and IOP ≥21 mm Hg, as measured by Goldmann applanation tonometry, at least twice previously.[28,29] POAG progression was determined by VF progression analysis. VF progression was defined as at least three test points showing significant decreases in visual sensitivity compared with two baseline tests (separated by approximately three months in this study), at the same locations on three consecutive glaucoma change probability maps and were detected in all follow-up visits.[28,29] Eyes with POAG that met the eligibility criteria were divided into two groups according to the level of axial elongation: POAG with (AL ≥26.0 mm) and without (AL <26.0 mm) high myopia groups. Classification and progression of myopic maculopathy in POAG eyes with high myopia was evaluated at baseline and during follow-up.[27,30]

Subjects underwent a comprehensive ophthalmic examination at baseline and each follow-up visit (every three months); this included slit-lamp biomicroscopy, gonioscopy, BCVA, refractive error measured with an autorefractometer (KR800; Topcon, Tokyo, Japan), IOP measurement using Goldmann applanation tonometry (AT900; Haag Streit, Koeniz, Switzerland), AL and central corneal thickness (CCT) measurement using an IOL master (IOL master 700; Carl Zeiss Meditec, Jena, Germany), fundus photography using a fundus stereo camera (Nonmyd WX3D; Kowa, Nagoya, Japan), VF testing (Humphrey Field Analyzer Mark 3, with Swedish Interactive Threshold Algorithm standard 30-2 program; Carl Zeiss Meditec), as well as OCT scans. IOP at examination was defined as the IOP at the time when OCTA images were obtained. Reliable VF tests were those with fixation losses <20%, false-positive error <15%, and false-negative error <33%.

OCTA Imaging

All subjects underwent OCTA with a commercial swept-source OCT (Atlantis, DRI-OCT 1; Topcon), which contains a swept-source with a wavelength of 1050 nm and a speed of 100,000 A-scans per second. Macular 3- × 3-mm volumetric scans, centered at the fovea, each consisting 320 × 320 A-scans were obtained from each eye. We used the built-in software (IMAGEnet6, Version 1.23.15008, Basic License 1) to automate and segment the slabs of the SCP and DCP. The SCP was delineated as 2.6 µm below the internal limiting membrane to 15.6 µm below the junction between the inner plexiform and the inner nuclear layers. The DCP was delineated as 15.6 µm below the inner plexiform and the inner nuclear layers to 70.2 µm below them.[31] Littman and the modified Bennett formulae were used to correct the magnification of OCAT images based on the AL.[32–34] All OCTA images were reviewed by trained graders (F Lin, F Li, and W He) and passed image quality control, using the following exclusion criteria[35]: (1) quality score <40; (2) motion artifacts (i.e., significant residual motion lines); (3) blurry images (i.e., due to axial movement or media opacity); (4) inaccurate segmentation of retinal layers or slabs; (5) poor centration (i.e., fovea not at center); and (6) projection artifacts in the DCP. Eligible images were then imported into a customized MATLAB (MathWorks, Natick, MA, USA) program. A series of OCTA metrics of SCP and DCP, including FAZ area, FAZ circularity, whole image vessel density (wiVD), and VD within the ETDRS sectors were automatically analyzed (Fig. 1).[31,35] Repeatability and reproducibility of these measurements have been reported in our previous study.[35]

OCT Imaging

Ganglion cell-inner plexiform layer (GC-IPL) images were obtained using macular cube scans of the swept-source OCT (Atlantis, DRI-OCT 1; Topcon). The macular cube scans generated GC-IPL thickness images that covered a 6- × 6-mm macular region centered at the fovea (three-dimensional volume, 256 × 256 axial scans). GC-IPL thickness was measured within an annulus with inner vertical and horizontal diameters of 1 and 1.2 mm, respectively, and outer vertical and horizontal diameters of 4 and 4.8 mm, respectively.[36] Only eligible images (i.e., scan quality [SSI] >50, without artifacts, without segmentation failure, and without eye movement) were included in the analysis. Two trained graders (F Lin and F Li) reviewed all three-dimensional images.

Statistical Analysis

Each eligible eye in this study was regarded as a unit of analysis. A generalized estimated equation was used to adjust for inter-eye correlation of the same subject. Continuous

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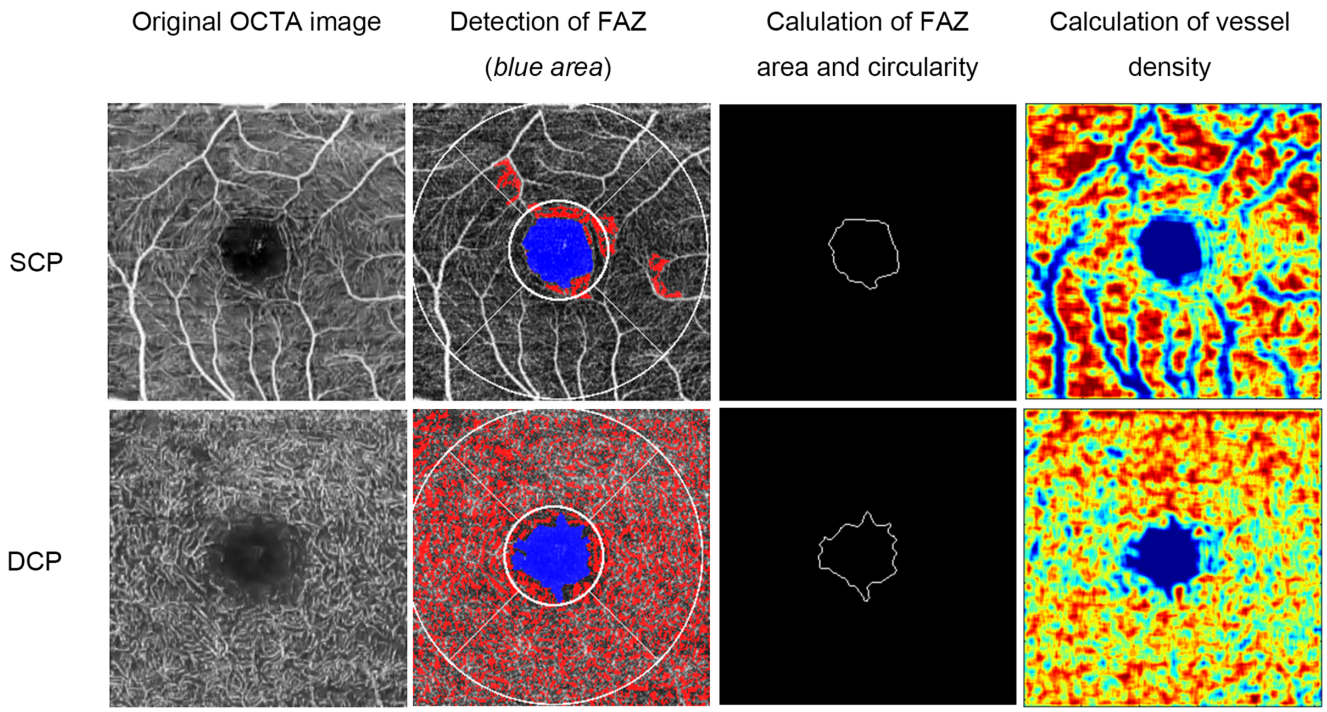

Figure 1. Quantification of retinal capillary network from OCTA images. A series of OCTA metrics, including parafoveal VD, FAZ area, and FAZ circularity of the SCP and DCP, can be calculated automatically by a customized MATLAB program.

and categorical data were descripted as mean ± standardized deviation (SD) and frequency (percentage), respectively. The independent *t* test was used to compare the baseline characteristics and ocular parameters between the two groups when data was normally distributed. Pearson's χ^2 test was used for categorical variables. The linear mixed-effects models were used to estimate the rate of reduction in macular OCTA metrics and the difference in the macular OCTA metrics reduction over time between POAG eyes with and without high myopia. Linear mixed models were also used to determine the factors associated with changes in VD in POAG eyes with and without high myopia. Univariate analysis was first performed; predictive variables with a *P* value <0.1 were entered in the multivariate equation. These models included fixed effects for follow-up duration, baseline age, sex, IOP at examination, AL at baseline, diagnosis group, and interaction between diagnosis group and duration. Statistical analyses were performed using R version 3.5.0 software (R Foundation for Statistical Computing, Vienna, Austria) and SPSS version 24.0 software (IBM Corporation, Armonk, NY, USA). A *P* value < 0.05 was considered statistically significant.

Results

Overall, 134 eyes of 86 subjects were initially enrolled. Eight eyes were excluded due to poor quality OCTA (5 eyes) or OCT (3 eyes) images, 2 eyes were excluded because of IOP-lowering surgery performed during the follow-up period. The remaining 124 eyes (63 POAG eyes with high myopia in 38 subjects and 61 POAG eyes without high myopia in 42 subjects) were included in the final analysis. Baseline demographic and ocular characteristics are summarized in Table 1. The mean follow-up time was 27.72 ± 8.57 months for POAG eyes with high myopia and 30.95 ± 10.19 months for POAG eyes without high myopia. All eyes were treated with at least one type of anti-glaucoma eye drop. The follow-up period, number of visits, number of topical anti-glaucoma medications, baseline age, and sex were not significantly different between the POAG eyes with and without high myopia (all *Ps* >0.05). There were also no statistically significant differences between baseline BCVA, IOP at examination, mean IOP during follow-up, mean deviation and pattern standard deviation of VF, and disc hemorrhage during follow-up (all *Ps* >0.05). The groups differed significantly in terms of baseline spherical equivalent, AL, CCT, and average GC-IPL thickness (all *Ps* <0.05). For baseline macular OCTA metrics, the FAZ area of the SCP and DCP was significantly smaller in POAG eyes with high myopia than in those without ($P < 0.001$), other OCTA metrics were not significantly different between the groups (all *Ps* >0.05). Of the 63 eyes with POAG with high myopia, 12 eyes showed no macular lesions (category 0) and 51 eyes had a tessellated fundus (category 1) at baseline. Myopic maculopathy progression and "plus" lesions were not found during the study period. During the follow-up time, 13 (20.63%) and 4 (6.56%) eyes were determined to have VF progression in POAG with and without high myopia, respectively.

Rate of Change of Macular OCTA Metrics

Follow-up duration, baseline age, sex, IOP at examination, baseline AL, diagnosis group, and interaction between diagnosis group and duration-adjusted rates of macular OCTA metrics changes are presented in Table 2. The mean rate of change of VD in the DCP was significantly faster in POAG eyes with high myopia than in those without (−5.14 %/year vs. −3.71 %/year, $P = 0.008$). In both the inferior and nasal

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Table 1. Demographic and Ocular Characteristics of POAG Eyes With And Without High Myopia

Characteristics	POAG With High Myopia	POAG Without High Myopia	*P* Value
By subject, no	38	42	—
Baseline age, year	37 ± 12	41 ± 15	0.167*
Sex, male	28	33	0.608†
Self-reported history of Diabetes, no	0	0	—
Self-reported history of Hypertension, no	0	0	—
Follow-up period, month	27.72 ± 8.57	30.95 ± 10.19	0.130*
Number of visits, median (IQR)	8.5 (8, 13)	10 (8, 13)	0.910*
By eye, no	63	61	—
Topical anti-glaucoma medication, no			
Total	2.24 ± 0.64	2.31 ± 0.73	0.587*
Beta-blockers	0.80 ± 0.41	0.81 ± 0.40	0.786*
Adrenalin agonist	0.48 ± 0.50	0.53 ± 0.50	0.583*
Prostaglandin analogs	0.92 ± 0.27	0.83 ± 0.38	0.135*
Carbonic anhydrase inhibitor	0.05 ± 0.22	0.14 ± 0.35	0.096*
Baseline BCVA, logMAR	0.04 ± 0.10	0.06 ± 0.12	0.553*
IOP at examination, mmHg	15.16 ± 3.93	15.41 ± 3.39	0.706*
Mean follow up IOP, mmHg	14.76 ± 2.44	15.40 ± 3.31	0.226*
Baseline spherical equivalent, diopter	−6.79 ± 2.79	−2.05 ± 2.51	**<0.001***
Baseline axial length, mm	27.11 ± 0.79	24.68 ± 1.01	**<0.001***
Baseline central corneal thickness, um	533.79 ± 32.04	549.48 ± 33.89	**0.009***
Baseline MD of VF, dB	−5.52 ± 5.04	−5.99 ± 8.05	0.700*
Baseline PSD of VF, dB	5.62 ± 4.35	4.54 ± 4.46	0.177*
Baseline average GC-IPL thickness, um	58.92 ± 6.74	63.53 ± 8.66	**0.001***
Disc hemorrhage during follow-up, n (%)	9 (14.28)	6 (9.84)	0.588*
Baseline Macular OCTA Metrics			
Superficial Capillary Plexus			
FAZ area, mm^2	0.29 ± 0.11	0.37 ± 0.12	**<0.001***
FAZ circularity	0.55 ± 0.12	0.58 ± 0.11	0.203*
Vessel density within whole image, %	76.76 ± 7.64	77.14 ± 8.13	0.793*
Deep Capillary Plexus			
FAZ area, mm^2	0.34 ± 0.15	0.53 ± 0.17	**<0.001***
FAZ circularity	0.54 ± 0.12	0.51 ± 0.10	0.068*
Vessel density within whole image, %	57.28 ± 6.28	56.55 ± 6.35	0.522*

Boldface values indicate statistical significance.
IQR, interquartile range; MD, mean deviation; PSD, pattern standard deviation.
* Two-sample *t* test.
† Pearson χ^2 test.

Table 2. Change Rates In Macular OCTA Metrics In POAG Eyes With And Without High Myopia

Characteristics	POAG With High Myopia (Mean, 95% CI)	POAG Without High Myopia (Mean, 95% CI)	*P* Value*
Superficial capillary plexus			
FAZ area, mm^2/year	−0.00 (−0.02, 0.01)	−0.02 (−0.11, 0.06)	0.654
FAZ circularity, per year	−0.00 (−0.02, 0.02)	−0.01 (−0.02, 0.01)	0.402
Vessel density, %/year			
Whole image	−2.58 (−3.62, −1.53)	−1.64 (−2.64, −0.64)	0.200
Superior	−1.17 (−2.47, 0.12)	−1.25 (−2.42, −0.08)	0.939
Temporal	−2.32 (−4.16, −0.48)	−0.10 (−1.96, 1.76)	0.099
Nasal	−3.41 (−5.30, −1.52)	−2.28 (−3.82, −0.74)	0.393
Inferior	−3.57 (−5.56, −1.58)	−1.66 (−3.46, 0.15)	0.151
Deep capillary plexus			
FAZ area, mm^2/year	0.03 (−0.00, 0.07)	0.02 (−0.13, 0.17)	0.843
FAZ circularity, per year	−0.04 (−0.08, 0.01)	0.08 (−0.09, 0.24)	0.190
Vessel density, %/year			
Whole image	−5.14 (−5.91, −4.38)	−3.71 (−4.43, −2.98)	**0.008**
Superior	−5.90 (−6.98, −4.81)	−4.60 (−5.60, −3.59)	0.074
Inferior	−5.95 (−7.10, −4.80)	−4.23 (−5.38, −3.08)	**0.042**
Nasal	−4.84 (−5.80, −3.88)	−3.34 (−4.32, −2.36)	**0.045**
Temporal	−5.30 (−6.39, −4.21)	−3.94 (−5.03, −2.85)	0.092

Boldface values indicate statistical significance.
* P value in linear mixed-effects model.

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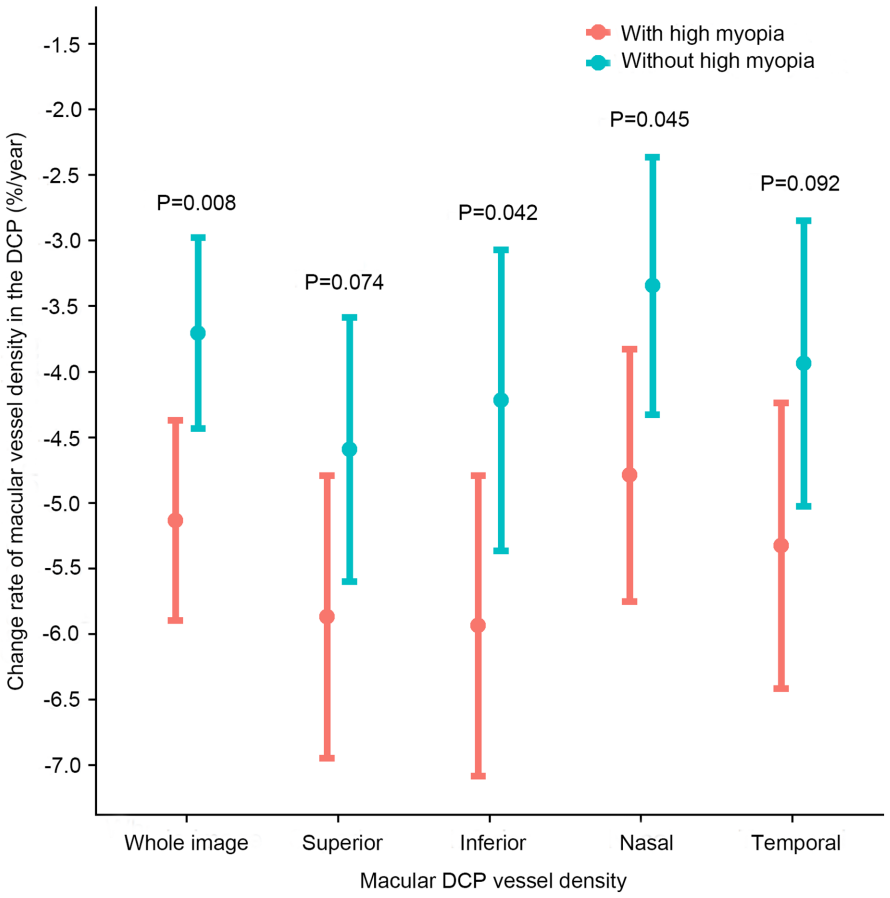

Figure 2. Interval plots of rate of change of macular VD in the DCP in POAG eyes with and without high myopia. POAG eyes with high myopia showed faster rates of reduction of the whole image, inferior and nasal sectoral VD of the macular DCP, than POAG eyes without high myopia (*dot*, mean; *line*, 95% CI).

sectors, the mean rate of VD decrease in the DCP was significantly faster in POAG eyes with high myopia than in those without (both *Ps* <0.05). In contrast, the macular VD in the SCP, FAZ area, and FAZ circularity in both the SCP and DCP were not significantly different between the two groups (all *Ps* >0.05). After excluding POAG eyes with VF progression, a similar trend of faster decrease in VD in the DCP in POAG eyes with high myopia compared to those without high myopia was observed (−4.84 %/year vs. −3.71 %/year, $P = 0.045$) (Supplemental Table S1). Figure 2 shows the rate of change in VD maps in the DCP over time in POAG eyes with and without high myopia. Supplemental Figure S1, as an example, shows a subject had a rapid reduction of VD in the DCP due to irregular antiglaucoma medication using. We did not exclude him so as to mimic real clinical challenges.

Risk Factors Associated with Rate of Change in DCP Vessel Density

The relationships between baseline patient and ocular characteristics and macular OCTA metrics to the rate of decrease in wiVD in DCP in POAG eyes with and without high myopia are summarized in Table 3 and Supplemental Table S2, respectively. Baseline wiVD in the DCP was significantly associated with wiVD decrease over time in the DCP in POAG eyes with high myopia (whole image; Estimate, −4.03; 95% confidence interval [CI], −6.06 to −2.00; $P < 0.001$). Each 1% reduction in baseline VD in the DCP contributed to a 4.03% faster VD reduction in the DCP (Table 3). No baseline variables demonstrated significant associations with the rate of decrease in VD in the DCP in POAG eyes without high myopia (Supplemental Table S2).

The relationships between baseline sectoral VD analysis in the DCP to the rate of decrease in wiVD in DCP in POAG eyes with and without myopia was further analyzed. Significant associations were observed between the rate of decrease in wiVD in DCP and baseline superior and inferior sectoral VD in DCP in POAG eyes with high myopia in both univariate (Estimate, −2.95; 95% CI, −5.37 to −0.53; $P = 0.022$ and Estimate, −2.69; 95% CI, −4.74 to −0.65; $P = 0.014$, respectively) and multivariate analysis (Estimate, −5.11; 95% CI, −8.16 to −2.05; $P = 0.002$ and Estimate, −5.12; 95% CI, −8.69 to −1.55; $P = 0.008$, respectively) (Supplemental Table S3). Figure 3 shows the effects of baseline whole image and sectoral VD in the DCP to the slope of change of the wiVD in the DCP over time. Lower baseline whole image, superior and inferior sectoral VD in the DCP were associated with a faster reduction of wiVD in the DCP over time (whole image $R^2 = 31.1\%$, $P < 0.001$; superior sector $R^2 = 11.0\%$, $P = 0.032$; inferior sector $R^2 = 18.8\%$, $P = 0.004$).

Table 3. Univariate Linear Mixed Model Determination of Factors Associated with Changes in Whole-Image Vessel Density in the DCP in POAG Eyes with High Myopia

Characteristics	Estimate	(95% CI) Lower	Upper	*P* Value
Baseline age, year	0.02	−0.12	0.16	0.751
Sex, male	−1.93	−6.27	2.40	0.386
IOP at examination, mm Hg	−0.10	−0.59	0.40	0.707
Baseline axial length, mm	0.12	−2.07	2.31	0.918
Baseline MD of VF, dB	−0.20	−0.54	0.14	0.244
Baseline average GC-IPL thickness, um	0.01	−0.26	0.29	0.919
Baseline superficial capillary plexus				
FAZ area, mm^2	−1.14	−2.49	0.21	0.106
FAZ circularity	0.54	−1.48	2.55	0.605
Vessel density within whole image, %	−0.62	−2.66	1.42	0.554
Baseline deep capillary plexus				
FAZ area, mm^2	−1.31	−3.11	0.48	0.161
FAZ circularity	−0.65	−2.54	1.24	0.507
Vessel density within whole image, %	−4.03	−6.06	−2.00	**<0.001**

Boldface values indicate statistical significance.
CI, confidence interval; MD, mean deviation.

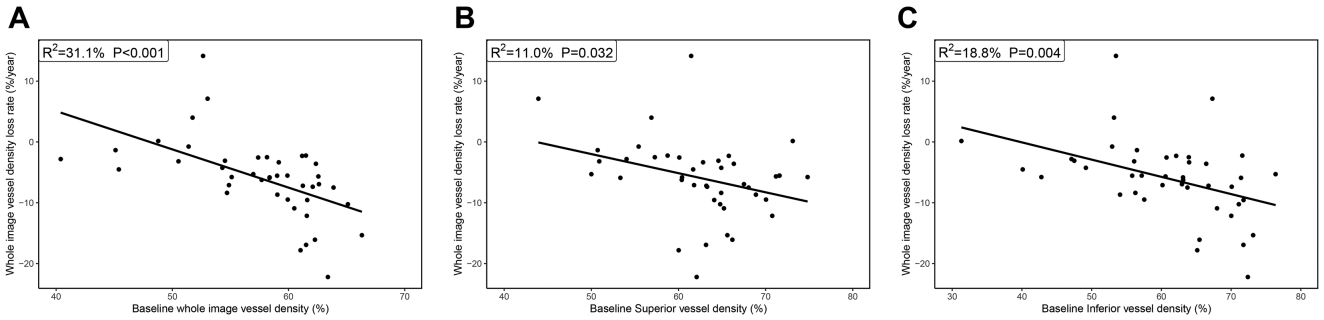

Figure 3. Scatterplots illustrating the linear association between the change rate of VD in the DCP and baseline VD in the DCP in POAG eyes with high myopia. VD reduction over time in the DCP was associated with baseline VD, particularly baseline superior and inferior VD in the DCP.

Discussion

We found that the rate of macular VD loss in the DCP in POAG eyes with high myopia was significantly faster than that in those without high myopia, over a mean 2-year follow-up period. Moreover, lower baseline total, superior and inferior sectoral VD in the DCP were associated with faster rate of total VD loss in the DCP in POAG eyes with high myopia. We did not observe any significant differences in the rates of changes in the FAZ area and circularity in both the SCP and DCP, and macular VD in the SCP over time between POAG eyes with and without high myopia.

This study provides new longitudinal data to characterize the change of macular OCTA metrics over time in POAG eyes with and without high myopia. Our findings support previous cross-sectional studies in high myopia, which observed retinal blood flow reduction in highly myopic eyes using laser Doppler velocimetry and OCTA.[10,37] Our results are consistent with previous longitudinal studies that observed macular VD loss in glaucoma without myopia. The mean rate of change of VD in the SCP was between −2.23%/year and −1.35%/year in those studies.[38,39] In this study, the rates of VD loss of SCP were −2.58%/year and −1.64%/year in POAG eyes with and without high myopia, respectively.

Notably, only the rate of VD reduction in the DCP was significantly faster in POAG eyes with high myopia than in those without high myopia, whereas the rate of VD reduction in the SCP was similar between the two groups. A possible explanation is that the DCP is more related to high myopia than the SCP. Growing evidence supports the different roles of distinct retinal capillary layers in high myopia. Cheng et al.[20] observed that a decreasing perifoveal VD in DCP was associated with high myopia. He et al.[40] reported a significant correlation of AL with parafoveal VD in DCP, but not in the SCP. Ye et al.[19] also indicated that decreased VD in DCP correlated with outer retinal layer thinning in eyes with high myopia. The SCP is located near the large retinal vessels in the RNFL; hence, its density might be less sensitive to alterations associated with axial elongation and thinning of the retina in high myopia.[41–44] Our findings indicated that the deep retina is more vulnerable to microvascular changes over time than the SCP in POAG eyes with high myopia. These findings remained significant after exclusion of all POAG eyes that developed VF deterioration. Thus such reduction in VD in the DCP over time would most likely be attributed to the effect of high myopia on the retinal microvasculature per se.

Regarding factors associated with the rate of VD reduction, a lower baseline VD in the DCP was a significant factor in POAG eyes with high myopia. Hence, highly myopic

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POAG eyes with lower baseline VD in the DCP were more susceptible to experience a faster rate of VD loss. According to previous studies, the deep retinal vascular plexus comprises small-diameter vessels[45,46] that become smaller as the AL elongates.[10] Thus the deep retinal layer microvasculature in highly myopic eyes may have decreased retinal function and oxygen consumption and is then more vulnerable to blood flow reduction. Because glaucoma mainly affects macular VD in the superior and inferior sectors,[25] the baseline superior and inferior VD showed closer correlation with the rate of change in VD.

Vascular dysfunction and circulatory insufficiency have been increasingly recognized for their potential roles in POAG development and progression.[47,48] Various cross-sectional studies in using OCTA to assess the microvasculature in POAG provided mounting evidence to support the associations between rarefaction of macular VD and glaucoma.[49–51] A recent longitudinal study showed that worse baseline macular VD was associated with an increased rate of RNFL thinning in POAG eyes.[52] Nevertheless, currently, there is limited utility of OCTA in the risk assessment of POAG progression and the prognostic value of the macular OCTA metrics in POAG remains unknown. Our findings suggest that the macular OCTA metrics may offer more value in highly myopic eyes, because worse baseline macular VD in the DCP was associated with subsequent rapid reduction of VD, which further predicted POAG progression. Further studies to evaluate the role of macular metrics in this group of patients are warranted.

Our study strength was its prospective design with longitudinal data of macular OCTA metrics in both the SCP and DCP obtained in POAG eyes with and without high myopia, which provided novel information on the temporal relationships between baseline macular OCTA metrics to subsequent changes in such measurements in myopic POAG eyes. There were several limitations to this study. First, use of topical ocular hypotensive medications was not an exclusion criterion. Some antiglaucoma eyedrops are reported to affect retinal vascular autoregulation and ocular blood flow.[53,54] However, because the number of medications were not significantly different between the POAG eyes with and without high myopia, the effect caused by medications would be insignificant. Second, 3- × 3-mm macular scans were used in this study. According to previous studies,[26,55] the macular areas most vulnerable to glaucoma lie mostly outside the central 3- × 3-mm area. Thus further longitudinal data on larger scanning areas in more POAG eyes are required to ascertain our findings. Third, only high-quality images were included in our study, which may have introduced selection bias and limited the generalizability of results. Fourth, our subjects were relatively younger than those in previous studies,[16,38] which might not be representative of all ages. Finally, this study could not rescale the images according to AL before OCTA scanning. However, we had corrected the magnification of OCTA images on the basis of acquired images to minimize the effect of AL on image magnification.

In conclusion, POAG eyes with high myopia had a significantly faster decrease in macular VD in the DCP than those without high myopia. Additionally, a lower baseline VD in the DCP is associated with a faster decrease in VD in POAG eyes with high myopia. These findings provided insights into the longitudinal effects of high myopia in retinal microvasculature, which can potentially be used in future clinical practice for risk assessment of myopic POAG progression by means of OCTA and contribute to understanding POAG development and progression in the presence of high myopia.

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