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ORIGINAL PAPER

Assessment of superficial retinal microvascular density in healthy myopia

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Abstract
Purpose To evaluate retinal microvasculature in healthy myopia and investigate the correlation between microvascular density and ocular factors.
Methods A total of 174 eyes from 174 healthy Korean subjects were included. The eyes were divided into four groups according to refraction: emmetropia [21 eyes, -1.00 D $\leq$ mean spherical equivalent (MSE) $< +0.75$ D], mild myopia (32 eyes, -3.00 D $\leq$ MSE < -1.00 D), moderate myopia (76 eyes, -6.00 D $\leq$ MSE < -3.00 D), and high myopia (45 eyes, MSE < -6.00 D). Images of retinal vasculature in parapapillary and parafoveal area were obtained using optical coherence tomography angiography. Superficial retinal microvascular density was measured for correlation analysis with ocular parameters.
Results High myopia was found to have a lower superficial parapapillary microvascular density compared with the other groups in total parapapillary area, and in sectors of nasal and inferonasal (all $p \leq 0.001$). The superficial parapapillary microvascular density showed a negative correlation with axial length (AL) and intraocular pressure (IOP) ($\beta = -0.479$, $p = 0.008$ and $\beta = -0.160$, $p = 0.048$, respectively), and a positive correlation with parapapillary retinal nerve fiber layer (RNFL) thickness ($\beta = 0.140$, $p < 0.001$). However, there was no significant difference in superficial parafoveal microvascular density among all groups ($p > 0.05$).
Conclusions This study reveals that superficial parapapillary microvascular density is lower in high myopia and has correlation with AL, IOP, and parapapillary RNFL thickness. It also indicates that superficial parafoveal microvascular density tends to be unaffected by healthy myopia. These retinal microvascular alterations may facilitate understanding the pathogenesis of glaucomatous optic nerve damage in high myopia.

Keywords Superficial retinal microvascular density · Optical coherence tomography angiography · Parapapillary · Parafoveal · Myopia

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Introduction

The prevalence of myopia, regarded as the most common type of refractive error, has shown an increase in recent years, especially in Asia [1–3]. Of note, several ocular complications including retinal

detachment, glaucoma, macular atrophy, and choroidal neovascularization occur more frequently in high myopia [4–6].

Earlier studies have found that high myopia is frequently associated with retinal vascular alterations, such as decreased retinal vessel density or increased vessel resistance, which can be detected by color doppler imaging (CDI) or fundus photography [7–11]. In myopia-related retinal disorders, much attention has been paid to the change in retinal microvasculature because it serves as the direct source of oxygen and nutrients for the neuroretinal layers.

Recently, the development of optical coherence tomography (OCT) angiography, a novel ocular blood imaging technology without using contrast agents, has made it possible to efficiently image and quantify retinal microcirculation in multiple layers by means of the split-spectrum amplitude-decorrelation angiography (SSADA) algorithm [12–16]. Previous studies have shown great intravisit repeatability and intervisit reproducibility of OCT angiography in the optic nerve head (ONH) and macular microvascular perfusion measurements [17–19].

However, studies using this technology have reported conflicting results. Wang et al. [20] evaluated the parapapillary and parafoveal microvascular perfusion using OCT angiography and found a decreased vessel density in the parapapillary area, but not in the parafoveal area, of eyes with high myopia in comparison with emmetropic eyes. Similar results were reported by Mo et al. [21]. Moreover, they observed a decreased macular flow density in pathological myopia compared with high myopia and emmetropia. On the contrary, Yang et al. [22] and Li et al. [23] showed a decreased parafoveal microvascular density in eyes with high myopia when compared to those with mild myopia and emmetropia.

To clarify the conflicting results of these reports mentioned above, we attempted to investigate the superficial retinal parapapillary and parafoveal microvasculature in healthy myopic individuals using OCT angiography and determine the potential relationship between microvascular density and other ocular factors in this study.

Materials and methods

Participants

A total of 174 eyes from 174 young healthy Korean subjects (83 men and 91 women) were recruited between January 2016 and December 2016 for this prospective, comparative clinical study. This study was approved by the Institutional Review Board of the Chonnam National University Hospital and was conducted in accordance with the tenets of the declaration of Helsinki. A written informed consent was obtained from each participant.

All subjects were required to provide a detailed medical history and undergo a thorough ophthalmic examination including measurement of refractive status, best corrected visual acuity (BCVA), intraocular pressure (IOP) measurement using Goldmann applanation tonometry, slit-lamp examination, anterior chamber angle examination by gonioscopy, axial length (AL) and central corneal thickness (CCT) measurement using optical low-coherence reflectometry (Lenstar; Haag-Streit AG, Koeniz, Switzerland), retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC, a summation of the RNFL, ganglion cell layer, and inner plexiform layer) thickness measurement using OCT (RTVue-XR Avanti; Optovue, Fremont, CA, USA), and visual field (VF) assessment using Swedish interactive thresholding algorithm 30-2 perimetry with a humphrey field analyzer (Carl Zeiss Meditec Inc., Dublin, CA).

The inclusion criteria were as follows: age between 18 and 35 years, astigmatism within $\pm$ 2.00 D, BCVA of 20/25 or better, IOP less than 21 mmHg, normal anterior chamber angles, no optic disk abnormalities, and absence of VF defects in both eyes. Participants with any sign of pathological myopia (chorioretinal atrophy, lacquer cracks, lattice degeneration, staphylomas, or choroidal neovascularization), history of ocular trauma or intraocular surgery, and any ocular or systemic disorders (such as glaucoma or diabetes mellitus) which might diminish the ocular circulation were excluded.

We selected one eye of each participant randomly for data analysis and divided the subjects into four groups depending on refractive status: emmetropia [21 eyes, $-$ 1.00 D $\leq$ mean spherical equivalent (MSE) $<$ + 0.75 D], mild myopia (32 eyes, $-$ 3.00 D $\leq$ MSE $<$ $-$ 1.00 D), moderate myopia (76 eyes,

$-$ 6.00 D $\leq$ MSE $<-$ 3.00 D), and high myopia (45 eyes, MSE $<-$ 6.00 D).

Retinal microvasculature imaging with OCT angiography

With a built-in AngioVue software, the Avanti spectral domain OCT (RTVue-XR Avanti; Optovue, Fremont, CA, USA) was used for retinal vessel imaging. Specifically, the signal for kinetic retinal blood was obtained using the SSADA algorithm, an amplitude-based OCT angiography method, which provided decorrelation values for each the vessel so that we could quantitatively evaluate the retinal vasculature. In this context, microvascular density, as one parameter of retinal perfusion, was calculated according to the ratio of a certain area occupied by small vessels.

We assumed the parapapillary area to be a 750-μm-wide elliptical annulus extending outward from the optic disk boundary; the parafoveal region was defined as a 1.9-mm-wide annulus surrounding the fovea with an inner diameter of 0.6 mm and an outer diameter of 2.5 mm. The entire en-face microvasculature was evaluated in the 4.5 $\times$ 4.5 mm area of the optic disk and 3 $\times$ 3 mm area of the parafoveal region.

The retina was automatically separated into various layers by the AngioVue software. It should be noted that we only used the superficial layer for further analysis. The superficial layer extended from the internal limiting membrane (ILM) to the RNFL in the parapapillary area, while in the parafoveal region it ranged from 3 μm below the ILM to 15 μm below the inner plexiform layer (IPL). Superficial retinal microvascular density was calculated separately in six sectors (superotemporal, inferotemporal, temporal, superonasal, inferonasal, and nasal) in the parapapillary area based on the Garway-Heath Map (Fig. 1a) and four sectors (superior, inferior, temporal, and nasal) in the parafoveal area based on the early treatment diabetic retinopathy study (ETDRS) contour (Fig. 1b). The average density of the total parapapillary and parafoveal area, together with the inside disk density and foveal density, was measured as well.

All OCT scans were performed by one proficient examiner who was unaware of the other ocular data of the participants. In addition, only OCT scans with a signal strength index $\geq$ 70, proper segmentation, and no evident motion artifact were included.

Examination of ocular parameters

To investigate the potential ocular factors that might affect the microvascular density, we examined RNFL thickness within both parapapillary and parafoveal areas and GCC thickness within an area of 6 $\times$ 6 mm centered on the fovea. Further, ovality index and cup-to-disk ratio (CDR) of the optic nerve head (ONH) were also determined. Ovality index was calculated by dividing the longest diameter of the optic disk by the shortest diameter [24, 25]. CDR was measured in the horizontal and vertical meridians of the optic disk.

Statistical analysis

All data were analyzed with SPSS software (version 18.0, SPSS, Inc., Chicago, IL, USA). The one-way analysis of variance (ANOVA) was used to compare the differences among the four groups. For control of type I error, post hoc test with Bonferroni adjustment was then used to determine significance between six pairs of relevant groups and only probability values $\leq$ 0.008 (0.05/6) were considered statistically significant. The effects of other independent ocular factors on microvascular density were detected by logistic regression analysis including the univariate and multivariate models. Ocular factors with $p < 0.1$ in the univariate model (including AL, IOP, horizontal CDR, vertical CDR, average GCC thickness, average parapapillary RNFL thickness, and ovality index) were included in the multivariable regression analysis. The coefficient of determination (R^2) was shown in the logistic regression analysis. Data were displayed as mean $\pm$ SD; $p < 0.05$ was considered statistically significant.

Results

Initially, 185 participants enrolled in this study. After examination, 11 were excluded due to poor image quality. A total of 174 participants were included in the following analysis. The demographics and ocular characteristics of all eligible subjects in the four groups are presented in Table 1. Significant differences were found in AL and SE ($p < 0.001$), but not in age, sex, IOP, CCT, and CDR ($p > 0.05$) among the four groups. The high myopia group had a larger ovality index in comparison with emmetropia

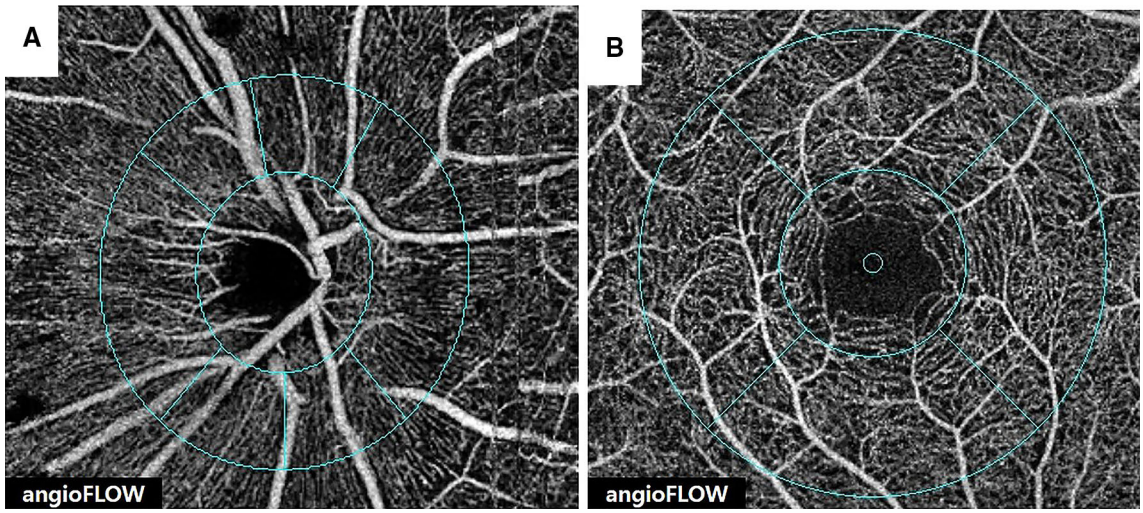

Fig. 1 **a** Parapapillary microvascular density was calculated separately in six sectors (superotemporal, inferotemporal, temporal, superonasal, inferonasal, and nasal) based on the Garway-Heath Map. The average density of the total parapapillary area and inside disk density were also measured. **b** Parafoveal microvascular density was calculated separately in four sectors (superior, inferior, temporal, and nasal) based on the ETDRS contour. The average density of the total parafoveal area and foveal density were also measured. *ETDRS* early treatment diabetic retinopathy study

Table 1 Demographic and ocular characteristics of the subjects in the four groups

Characteristics	Emmetropia (n = 21)	Mild myopia (n = 32)	Moderate myopia (n = 76)	High myopia (n = 45)	p value[a]	Post hoc[b]
Sex (male/female)	10:11	17:15	36:40	20:25	0.910	/
Age (years)	21.93 ± 2.93	24.05 ± 4.09	23.64 ± 3.82	23.64 ± 3.82	0.078	/
MSE (diopters)	− 0.76 ± 0.33	− 2.34 ± 0.75	− 4.68 ± 0.91	− 8.62 ± 1.67	<0.001	1 < 2 < 3 < 4
IOP (mmHg)	14.33 ± 2.74	14.26 ± 2.69	14.71 ± 2.36	15.00 ± 2.56	0.382	/
Axial length (mm)	23.58 ± 1.17	24.85 ± 0.83	25.87 ± 0.86	27.11 ± 1.02	<0.001	1 < 2 < 3 < 4
Central corneal thickness (μm)	560.27 ± 27.04	549.64 ± 40.21	558.77 ± 36.30	556.02 ± 27.90	0.765	/
Vertical CDR	0.51 ± 0.19	0.53 ± 0.15	0.49 ± 0.15	0.46 ± 0.16	0.176	/
Horizontal CDR	0.57 ± 0.19	0.65 ± 0.15	0.61 ± 0.15	0.58 ± 0.17	0.330	/
Ovality index	1.18 ± 0.64	1.23 ± 0.13	1.28 ± 1.51	1.31 ± 0.16	0.011	1 < 4

MSE mean spherical equivalent, *IOP* intraocular pressure, *CDR* cup-to-disk ratio, 1 emmetropia, 2 mild myopia, 3 moderate myopia, 4 high myopia

[a]Comparisons among the four groups using the one-way analysis of variance (ANOVA), except the sex was compared using $\chi 2$ test

[b]Multiple comparisons among the four groups

(1.18 ± 0.64 and 1.31 ± 0.16 in emmetropia and high myopia, respectively, $p < 0.05$).

There was a significant difference in parapapillary RNFL thickness between the high myopia and emmetropia groups. The average and all sectoral parapapillary RNFL thicknesses were significantly thinner in high myopia than in emmetropia (all $p < 0.05$); GCC thinning was also notable in high myopia compared with emmetropia (all $p < 0.001$). However, RNFL thickness in the parafoveal area was not significantly different for all sectors among the four groups (Table 2).

When evaluating the superficial retinal microvasculature, the high myopia group showed a lower

Table 2 Parapapillary and parafoveal RNFL thickness and GCC thickness of the four groups

Variables	Emmetropia (n = 21)	Mild myopia (n = 32)	Moderate myopia (n = 76)	High myopia (n = 45)	p value[a]	Post hoc[b]
Parapapillary RNFL thickness						
Superotemporal	150.62 ± 10.70	141.50 ± 14.28	141.13 ± 12.90	133.13 ± 16.57	< 0.001	1 > 2 = 3 = 4
Superonasal	121.62 ± 17.46	106.22 ± 14.96	105.08 ± 12.60	94.02 ± 11.67	< 0.001	1 > 2 = 3 > 4
Inferonasal	122.48 ± 18.23	113.53 ± 16.10	102.28 ± 14.48	90.13 ± 14.30	< 0.001	1 = 2 > 3 > 4
Inferotemporal	153.05 ± 14.65	147.00 ± 16.43	147.21 ± 15.43	140.58 ± 18.88	0.029	1 > 4
Average	110.07 ± 6.52	102.59 ± 7.07	100.14 ± 6.62	93.60 ± 7.15	< 0.001	1 > 2 = 3 > 4
Parafoveal RNFL thickness						
Fovea	247.67 ± 15.86	244.39 ± 16.65	251.39 ± 18.06	251.29 ± 22.93	0.296	/
Temporal	306.67 ± 18.50	304.66 ± 14.39	307.59 ± 13.60	302.73 ± 16.00	0.365	/
Superior	319.48 ± 14.31	317.94 ± 13.66	321.72 ± 13.65	315.58 ± 15.39	0.138	/
Nasal	316.29 ± 15.46	315.41 ± 14.77	317.49 ± 14.09	312.24 ± 17.53	0.343	/
Inferior	317.00 ± 16.60	314.88 ± 12.37	315.50 ± 13.21	312.02 ± 13.54	0.457	/
Average	316.93 ± 15.38	312.82 ± 13.31	315.54 ± 12.69	310.58 ± 15.10	0.269	/
GCC thickness						
Superior	100.19 ± 5.16	94.16 ± 6.38	96.74 ± 6.06	93.32 ± 4.46	< 0.001	1 > 2 = 4
Inferior	100.82 ± 5.51	94.48 ± 5.05	96.23 ± 6.06	93.01 ± 5.24	< 0.001	1 > 2 = 3 = 4
Average	101.23 ± 5.84	94.97 ± 5.33	96.47 ± 5.83	93.16 ± 4.57	< 0.001	1 > 2 = 3 = 4

RNFL retinal nerve fiber layer, *GCC* ganglion cell complex, 1 emmetropia, 2 mild myopia, 3 moderate myopia, 4 high myopia

[a]Comparisons among the four groups using the one-way analysis of variance (ANOVA)

[b]Multiple comparisons among the four groups

microvascular density in the total parapapillary area, and in the sectors of nasal and inferonasal (all $p \leq 0.001$) (Table 3). Figure 2 shows comparison of parapapillary microvasculature between emmetropic and high myopic eyes. The high myopic eye presented as much sparser distribution of microvasculature than that of emmetropic eye which supported the finding of microvascular density. However, there was no significant difference in parafoveal microvascular density overall and for each sector among the four groups (Table 3).

In the univariate linear regression analysis, the average parapapillary microvascular density reduction was associated with longer AL ($\beta = -0.846$, $p < 0.001$), thinner average parapapillary RNFL thickness ($\beta = 0.134$, $p < 0.001$), and larger ovality index ($\beta = -5.428$, $p = 0.001$) (Table 4). In the multivariate analysis, the average parapapillary microvascular density was negatively correlated with AL ($\beta = -0.479$, $p = 0.008$) and IOP ($\beta = -0.160$, $p = 0.048$), and positively correlated with average parapapillary RNFL thickness ($\beta = 0.140$, $p < 0.001$) (Table 5).

Discussion

Retinal perfusion in myopia has been an important issue for several decades because it may provide us insight into the pathophysiology of various myopia-related diseases which mainly damage the optic nerve and the macular region such as glaucoma, posterior staphyloma, macular atrophy, and choroidal neovascularization [4–6]. Previous studies have focused on large retinal vessels. An evident reduction in large retinal vascular perfusion was found to be related to high myopia by using various measuring techniques including fluorescein angiography (FA), CDI, fundus photography, ocular blood flow (OBF) analyzer, and laser Doppler velocimetry [7–11, 26, 27]. However, the alteration of retinal microvasculature was not fully understood due to the limitations of the measuring techniques used. Recently, OCT angiography, an

Table 3 Superficial parapapillary and parafoveal microvascular density of the four groups

Superficial microvascular density (%)	Emmetropia (n = 21)	Mild myopia (n = 32)	Moderate myopia (n = 76)	High myopia (n = 45)	p value[a]	Post hoc[b]
Parapapillary area						
Superotemporal	67.86 ± 3.79	67.35 ± 4.55	68.11 ± 3.46	66.45 ± 4.74	0.190	/
Superonasal	62.33 ± 5.50	60.81 ± 5.92	61.89 ± 4.84	60.44 ± 4.74	0.338	/
Inferonasal	65.22 ± 3.27	65.25 ± 4.05	64.04 ± 4.42	61.32 ± 5.70	0.001	1 = 2 = 3 > 4
Inferotemporal	68.12 ± 3.17	68.29 ± 3.36	68.08 ± 4.59	67.18 ± 4.64	0.624	/
Nasal	60.57 ± 3.66	59.00 ± 3.27	57.46 ± 4.39	52.80 ± 6.40	< 0.001	1 = 2 = 3 > 4
Temporal	65.62 ± 4.41	65.42 ± 2.77	65.35 ± 2.89	64.83 ± 3.90	0.778	/
Inside disk	43.08 ± 9.27	43.03 ± 9.29	46.76 ± 7.49	47.66 ± 9.61	0.041	/
Average	64.28 ± 2.95	63.60 ± 2.23	63.06 ± 2.60	60.80 ± 3.81	< 0.001	1 = 2 = 3 > 4
Parafoveal area						
Fovea	30.60 ± 3.54	31.08 ± 5.12	31.60 ± 4.25	31.63 ± 5.08	0.789	/
Temp	54.62 ± 2.62	54.28 ± 3.32	54.33 ± 3.07	54.36 ± 3.25	0.980	/
Superior	56.34 ± 2.87	55.98 ± 4.33	56.16 ± 3.19	56.60 ± 3.06	0.861	/
Nasal	54.55 ± 2.49	54.26 ± 3.10	54.58 ± 3.07	54.92 ± 3.49	0.835	/
Inferior	56.69 ± 3.22	55.80 ± 4.13	55.71 ± 3.48	55.51 ± 4.33	0.695	/
Average	55.55 ± 2.60	55.07 ± 3.49	55.19 ± 2.84	55.34 ± 3.17	0.945	/

1 emmetropia, 2 mild myopia, 3 moderate myopia, 4 high myopia

[a]Comparisons among the four groups using the one-way analysis of variance (ANOVA)

[b]Multiple comparisons among the four groups

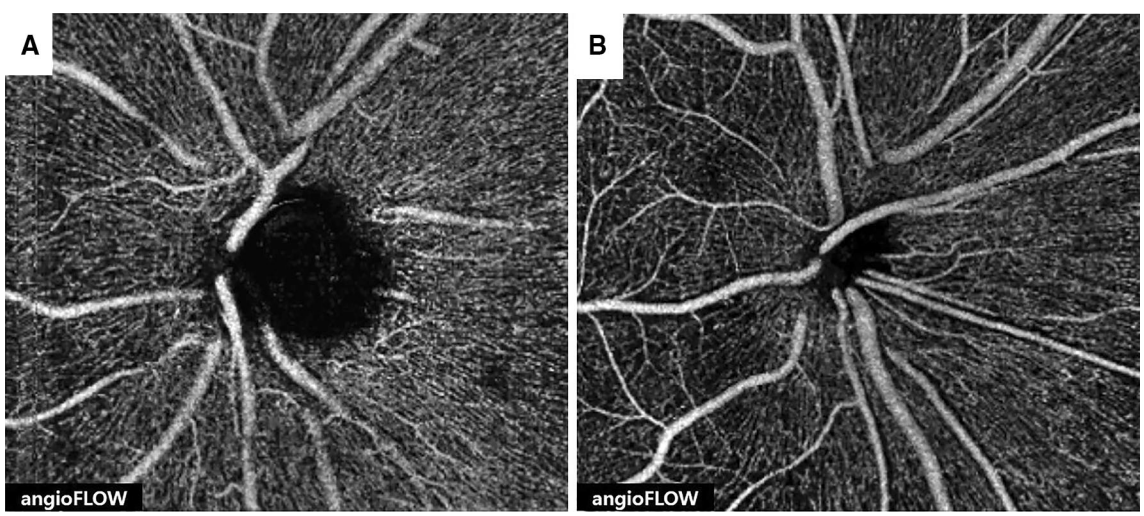

Fig. 2 **a, b** Representative images of parapapillary microvasculature measured by OCT angiography. **a** The image was from an emmetropic eye of a 21-year-old female with MSE of − 0.25 D, AL of 23.85 mm and superficial parapapillary microvascular density of 68.83%. **b** The image was from a high myopic eye of a 23-year-old female with MSE of − 10.80 D, AL of 29.19 mm and superficial parapapillary microvascular density of 52.43%. *OCT* optical coherence tomography, *MSE* mean spherical equivalent, *AL* axial length

advanced imaging technique characterized by noninvasiveness, quantification, and reliability, has been used to evaluate retinal vessels, including retinal microvasculature, in myopic eyes [12–16].

Table 4 Univariate regression analysis of ocular factors affecting average superficial parapapillary microvascular density

Variables	Average superficial parapapillary microvascular density		
	β	R^2	p value[a]
Age	0.003	0	0.956
IOP	− 0.177	0.019	0.071
Central corneal thickness	0.001	0	0.843
Horizontal CDR	7.366	0.135	0.095
Vertical CDR	7.364	0.136	0.084
Average GCC thickness	0.073	0.018	0.076
Axial length	− 0.846	0.142	< 0.001
Average parapapillary RNFL thickness	0.134	0.129	< 0.001
Ovality index	− 5.428	0.065	0.001

IOP intraocular pressure, *CDR* cup-to-disk ratio, *GCC* ganglion cell complex, *RNFL* retinal nerve fiber layer

[a]Ocular factors with $p < 0.1$ were included in the multivariable regression analysis

Table 5 Multivariable regression analysis of ocular factors affecting average superficial parapapillary microvascular density

Variables	Average superficial parapapillary microvascular density		
	β	R^2	P value
IOP	− 0.160		0.048
Horizontal CDR	2.408		0.479
Vertical CDR	2.161		0.385
Average GCC thickness	− 0.058	0.333	0.237
Axial length	− 0.479		0.008
Average parapapillary RNFL thickness	0.140		< 0.001
Ovality index	− 1.421		0.345

IOP intraocular pressure, *CDR* cup-to-disk ratio, *GCC* ganglion cell complex, *RNFL* retinal nerve fiber layer

In this present study, parapapillary and parafoveal microvascular densities were quantitatively measured using OCT angiography with SSADA in high myopia. We found that high myopia had a lower parapapillary microvascular density when compared with emmetropia, mild myopia, and moderate myopia. Furthermore, the parapapillary microvascular density showed a correlation with AL, IOP, and parapapillary RNFL thickness. However, no significant difference was found in parafoveal microvascular density among the four groups. Our findings are in agreement with those of Wang et al. [20] and Mo et al. [21], whereas the results regarding the parafoveal microvascular density are different from those of Yang et al. [22] and Li et al. [23] in which high myopia had a reduced parafoveal microvascular density. It is worth noting that vascular density was described as the fractal dimension which was quantified by fractal analysis using the box-counting technique [22, 23] in their studies. But in our study, vascular density was defined as the proportion of the total area occupied by vessels which has been previously described in detail [12, 20, 21]. Since vascular density was quantified in different ways, it may lead to the discrepancy in results. Therefore, consensus with respect to changes in retinal parafoveal microvascular density of high myopia is yet to be reached.

The ocular factors which may be correlated with retinal perfusion of high myopia have been previously discussed. It was commonly thought that high myopia was associated with elongation of the eyeball which would unavoidably stretch the ocular wall including

sclera, choroid, and retina. This stretching effect may play a critical role in RNFL thinning [28–30] and retinal perfusion alteration [9, 20–23, 31, 32]. This hypothesis seems to be plausible as we discovered the parapapillary microvascular density was negatively correlated with AL in univariate and multivariable regression analyses. Moreover, high myopia had a lower parapapillary microvascular density than those of the other three groups suggested that vascular density would decrease with the progression of axial myopia. Another reasonable explanation is that the retinal vessels tend to supply sufficient blood flow to satisfy the metabolic demands of the neuroretina through an intrinsic autoregulatory response [33–35], which means the supply would vary with the demand. In this case, the decreased metabolic demands in the local retinal region due to parapapillary RNFL thinning could conceivably lead to a diminished need of retinal blood supply, leading to a reduced parapapillary microvascular density. However, it is still difficult to illuminate whether the decreased vascular density was cause or consequence of the ocular structural changes based on this cross-sectional study. Future longitudinal studies are required to broaden our understanding on this.

It should also be noted that only the nasal and inferonasal sectors of the parapapillary region in high myopia had a significantly decreased microvascular density compared with the other three groups, whereas the other sectors did not. This was similar to the results reported by Mo et al. [21]. They speculated that the parapapillary capillary density was preserved to maintain the metabolic demands of the extensive retinal nerve fibers from the arcuate fiber region. However, they did not evaluate the RNFL parameters in their study. As described in our results, the thickness of all sectoral parapapillary RNFL was significantly thinner in high myopia, suggesting that the metabolic demands of parapapillary RNFL as well as microvascular density were reduced in all sectors. Hence, this explanation might be farfetched given our current knowledge. The underlying mechanisms require further study.

There was a negative correlation between ovality index and superficial parapapillary microvascular density in the univariate analysis, but this correlation was not noted in the multivariate analysis. This result was partly in accordance with our recent research in which we reported that myopic optic disk characteristics such as ovality index and optic disk rotation were associated with the deep parapapillary microvascular density rather than the superficial microvascular density [36].

We observed that a higher IOP was associated with lower superficial parapapillary microvascular density. It could be interpreted as follows: firstly, previous studies have shown that the superficial parapapillary capillary network was characterized by consistent vascular caliber and absence of anastomoses [37, 38], indicating poor compensatory capability in case of vascular impairment; secondly, the supporting effect of neuroretina that might protect the vasculature from being directly compressed by a raised IOP was compromised due to parapapillary RNFL thinning. Thus, the parapapillary microvasculature might be more susceptible to the damaging effects of IOP and not able to compensate effectively. This might be a risk factor for eyes with high myopia to develop glaucoma, especially normal tension glaucoma.

Surprisingly, no difference was found in parafoveal microvascular density between eyes with myopia and emmetropia. How can we attempt to explain this phenomenon? This might be because the anatomical configuration of neuroretina is not uniform over the entire retina, and the neural axons of parapapillary area are much denser than that of parafoveal area [39]. Consequently, the vascular autoregulatory response in the parafoveal area is less sensitive to the alteration of neural metabolic demand. Additionally, the macular RNFL thickness was well maintained in high myopia, as shown in the results, suggesting that the neural metabolic demand was less affected and the stretching effect by elongated eyeball was minimal in parafoveal area. Furthermore, it has been reported that macular flow density significantly decreased in pathological myopia and was positively correlated with BCVA [21]. Taken together, such a relative preservation of neural tissues and microvascular density in the macular area could also explain the normal central vision in healthy high myopia.

In summary, we demonstrated that the superficial parapapillary microvascular density significantly decreased in high myopia, which may contribute to the vulnerability of the eye to glaucomatous optic nerve damage. The superficial parapapillary microvascular density showed correlation with AL, IOP, and parapapillary RNFL thickness. The mechanical stretching effect of eyeball elongation along with

decreased metabolic demand by the thinned neuroretina and attenuate resistance to relative high IOP is three major possible mechanisms for parapapillary microvasculature deficiency. No significant difference was found in parafoveal microvascular density between myopia and emmetropia, indicating that normal visual function was preserved in healthy high myopia. A longitudinal study for retinal vascular alteration in myopia needs to be performed in the future.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interests to disclose regarding any material discussed in this article.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all participants included in the study.

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