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Reduction of retinal blood flow in high myopia

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Abstract *Purpose:* To investigate changes in retinal vessel diameter and blood velocity in high myopia using laser Doppler velocimetry. *Methods:* Thirty-nine subjects (39 eyes) were enrolled in the study. The subjects were divided into three groups according to their refractive status; 15 eyes (15 patients) with emmetropia (within ± 3.0 diopters), 14 eyes (14 patients) with mild myopia (between -3.0 and -8.0 diopters), and 10 eyes (10 patients) with high myopia (> -8.0 diopters). Patient age was matched between groups. Blood velocity and vessel diameter of the upper or lower temporal retinal artery were measured using laser Doppler velocimetry with an eye-tracking system, and measurements were compared between

groups. *Results:* The average retinal blood flow and vessel diameter in highly myopic eyes were significantly decreased compared with emmetropic eyes or mild myopic eyes (Mann-Whitney U test, $p < 0.05$). Also, there was significant difference regarding retinal blood flow and vessel diameter between eyes with mild myopia and the other groups. In addition, there was no significant difference in blood velocity between the three groups. *Conclusions:* Retinal blood flow was decreased in high myopia, mainly due to the narrowing of the retinal vessel diameter. Impaired retinal blood flow might have a role in the development of chorioretinal atrophy in high myopia.

Introduction

High myopia is a major cause of legal blindness in many developed countries [7, 18, 21]. The prevalence of high myopia with a refractive error greater than -7.9 diopters is 0.2–0.4% in the general population of the United States [18]. High myopia is especially common in Asia and the Middle East [4]. In Japan, the number of cases of myopia is unknown, but pathologic or high myopia affects 6–18% of the myopic population and 1% of the general population [22].

Previous studies reported a reduced choroidal or retinal blood flow in highly myopic patients. Akyol et al. [1] reported reduced choroidal blood flow in patients with myopic retinopathy using a color Doppler ultrasonography technique. James et al. [10] reported that choroidal

blood flow was decreased as the axial length increased using Langham ocular blood flow computerized tonometry. A fluorescein angiography study indicated that fluorescein transit times were delayed in high myopia [2]. To our knowledge, however, retinal circulation has not been studied in highly myopic eyes using quantitative methods.

The Canon laser blood flowmeter (CLBF-100, Canon, Tokyo, Japan) is a new, objective, quantitative, and non-invasive machine that measures retinal blood circulation with an eye-tracking system. This machine utilizes the bidirectional laser Doppler velocimetry technique pioneered by Feke and Riva [5] and Riva et al. [14].

The purpose of the present study was to measure retinal blood flow using the CLBF and to quantitatively investigate the retinal arterial blood flow to determine

whether retinal blood flow is altered in highly myopic eyes.

Patients and methods

The study followed the tenets of the Declaration of Helsinki and was performed in accordance with the standards of the ethics committee of Tokyo Medical and Dental University. Thirty-nine human subjects participated in the study. The subjects underwent assessment of refraction, best corrected visual acuity with the Snellen visual acuity chart, slit-lamp biomicroscopy, axial length, and fundus photography. They were then categorized into three groups according to their refractive status (Table 1). In the present study, we defined emmetropia as a refractive error within ± 3 diopters, mild myopia as myopia between -3 and -8 diopters, and high myopia as myopia greater than -8 diopters.

Patients with other ocular diseases possibly affecting ocular circulation, such as diabetic retinopathy and glaucoma, and those with a history of laser treatment, ocular injury, or intraocular surgery were excluded from the study. Also, patients with hypertension, diabetes mellitus, or other systemic diseases that involve the circulation were excluded from the study. Patients who had taken any medications within 2 weeks of the measurements were also excluded.

In addition, various chorioretinal atrophy lesions in the posterior fundus could secondarily affect retinal blood flow in highly myopic eyes. To exclude the influence of myopic retinopathy, the degree of background myopic chorioretinal changes was first categorized in each patient, according to Avila et al. [3]. The myopic fundus changes (M) were graded retrospectively on a scale of increasing severity from 0 to 5, as follows: grade M₀, normal-appearing posterior pole; grade M₁, choroidal pallor and tessellation; grade M₂, choroidal pallor and tessellation, with posterior pole staphyloma; grade M₃, choroidal pallor and tessellation, with posterior staphyloma and lacquer cracks; grade M₄, choroidal pallor and tessellation, with posterior pole staphyloma, lacquer cracks, and focal areas of deep choroidal atrophy; and grade M₅, posterior pole showing large geographic areas of deep choroidal atrophy ("bare sclera"). Highly myopic eyes with myopic chorioretinal atrophy more severe than M₃ by Avila et al.'s [3] classifications were excluded from the study. Only eyes with fundus changes of M₀, M₁, and M₂ were included.

Measurement and estimation of retinal arterial blood flow

We measured retinal arterial velocity and vessel diameter using laser Doppler velocimetry with an eye-tracking system. The pupils were dilated with 1% tropicamide before the measurements were taken. Laser Doppler velocimetry is a noninvasive measurement of retinal circulation [15, 16, 19, 24], based on a bi-directional method. A pair of Doppler signals is acquired along two directions simultaneously by the device, so that the angular parameters of the

vessel in the eye are canceled. Moreover, CLBF is designed to repeat a series of two measurements in 2 s (called Path1 and Path2) for one reading of the target vessel [20] to avoid the special adjustment of the two apertures for Doppler detection that is required using Riva et al.'s instrument [15]. The probing laser is a low-power red diode laser that is emitted from a fundus-camera-like measuring head. A retinal laser Doppler instrument quantifies the maximum velocity in a retinal vessel from scattered laser light from the blood cells flowing in the target vessel, and a computer analyzes the signals received. Retinal blood flow is calculated automatically by simultaneous measurement of blood velocity and vessel diameter as $RBF = 1/2 \cdot \pi D^2 / 4 \cdot 1/T \cdot \int V_{max}(t) dt$, where $V_{max}(t)$ is maximum RBC velocity, D is vessel diameter, T is the observation period, and $1/T \cdot \int V_{max}(t) dt$ is the average of V_{max} during T . This formula assumes (a) that the velocity distribution is according to Poiseuille flow, and (b) that the vessel columns have a circular cross section; therefore, retinal blood flow RBF should be calculated from vessels larger than 50 μm in diameter. Vessel diameter measurements were performed before and after each of two velocity measurements, and the final diameter reading was determined from the four results of each session. In the session, a linear imaging sensor takes 15 vessel profiles of the target vessel, which is illuminated by a green laser beam. The data were adjusted on the basis of the eye's axial length and refractive error; the latter is measured by the CLBF itself, which has an auto-correction function for refractive error. The refractive error of the eye is detected based on the position of the focusing lens of the device, and the eye axial length is manually input into the PC. The software compensates for the diameter using Littman's formula. The magnification change of the optics is calculated from the lens data of the device. Certain assumptions were made:

1. All thickness and refractive indexes of the eye segments were not changed by the refractive error and were derived from the value of Gullstrand's model eye.
2. Rear curvature of the cornea was proportional to the front curvature of the cornea.
3. The corneal curvatures were the only parameters to change and were calculated from the refractive error and the eye axial length.
4. After calculation of the corneal curvatures, the total magnification was determined. The same vessel images were used for the auto-tracking to lock the red laser onto the target vessel.

Briefly, eye tracking was performed when a green stripe from a 544-nm He-Ne laser is projected through a beam-steering galvanometer system onto a particular retinal vessel. The stripe is projected perpendicular to the vessel axis. The stripe reflected from the retinal vessel is incident on an array sensor that detects lateral vessel movement and controls the galvanometer system to stabilize the center of the vessel. The laser Doppler measuring source is the beam from a red 675-nm diode laser that is centered on the stripe. When the center of the stripe is stabilized on the target, the red beam on the target is also stabilized.

We measured retinal arterial velocity and diameter five times at the same site of a major superotemporal or inferotemporal ar-

Table 1 Baseline clinical data of the patients in the three groups. *D* diopters

Characteristics	Emmetropia (refraction within ± 3.0 D)	Mild myopia (refraction < -3.0 and > -8.0 D)	High myopia (refraction < -8.0 D)
No. of patients	15	14	10
Gender (M/F)	8/7	7/7	5/5
Age (years; SD)	43.1 (16.7)	40.3 (14.7)	44.6 (15.3)
Refraction (diopter; mean SD)	-0.80 (0.76)	-4.74 (1.82)	-10.25 (1.55)
Axial length (mm; mean SD)	23.9 (0.7)	25.9 (0.7)	28.3 (0.6)

tery before the first branching at a distance of 1–2 disc diameters from the optic nerve head over a diameter of approximately 100 μm . The superotemporal artery was measured in 8 of 15 patients with emmetropia, 6 of 14 patients with mild myopia, and 5 of 10 patients with high myopia, respectively. Several studies [9, 23] evaluating the reproducibility of measurements reported that repeated measurements are more reliable; therefore, five measurements were performed for each vessel and were averaged.

Statistical analysis

Data were expressed as mean \pm standard deviation. Group comparisons were performed using the ANOVA. Pairwise comparisons were performed using the Mann-Whitney U test when the results of the ANOVA were significant. A p value of <0.05 was considered to be statistically significant.

Results

Thirty-nine patients were consecutively enrolled into the study. According to the definition of refractive status described in the Patients and methods, 15 patients with emmetropia, 14 with mild myopia, and 10 with high myopia were included in the study. Only the right eye was examined in each patient. Table 1 shows the baseline clinical data of the patients in the three groups. There was no significant difference in patient age between groups. Of the 10 highly myopic eyes, 6 eyes had a tessellated fundus only (M_1), and 4 had slight diffuse atrophy (M_2).

The reproducibility of measurements was evaluated in all subjects. The averages of the coefficient of variation for vessel diameter, velocity, and blood flow were 4.9, 10.5, and 11.8%, respectively. Figure 1 shows the retinal arterial diameter in the three groups. The average retinal arterial diameter was 128.1 μm in eyes with emmetropia, 118.1 μm in eyes with mild myopia, and 103.9 μm in eyes with high myopia. Statistical analysis revealed that eyes with high myopia had a significantly smaller retinal arterial diameter compared with emmetropic eyes or mild myopic eyes ($p<0.05$; ANOVA and Mann-Whitney U test). There was also a significant difference in the retinal arterial diameter between eyes with mild myopia and eyes with emmetropia. Figure 2 shows the retinal arterial velocity in the three groups. The mean retinal arterial velocity was 39.5 mm/s in eyes with emmetropia, 38.6 mm/s in eyes with mild myopia, and 38.6 mm/s in eyes with high myopia. There was no significant difference in retinal blood velocity among the three groups.

Figure 3 shows the retinal arterial blood flow in the three groups. The mean retinal arterial blood flow was 15.5 $\mu\text{l/min}$ in eyes with emmetropia, 12.6 $\mu\text{l/min}$ in eyes with mild myopia, and 9.8 $\mu\text{l/min}$ in eyes with high myopia. The retinal blood flow was significantly decreased in highly myopic eyes compared with eyes with emmetropia or eyes with mild myopia ($p<0.05$; ANOVA and Mann-Whitney U test). Also, there was significant difference between eyes with mild myopia and eyes with

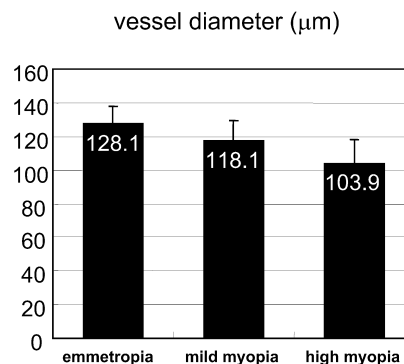


Fig. 1 Mean retinal arterial diameter in the three groups (in μm , mean \pm standard deviation). Statistical analysis revealed that eyes with high myopia had a significantly smaller retinal arterial diameter compared with emmetropic eyes and eyes with mild myopia ($p<0.05$; Mann-Whitney U test)

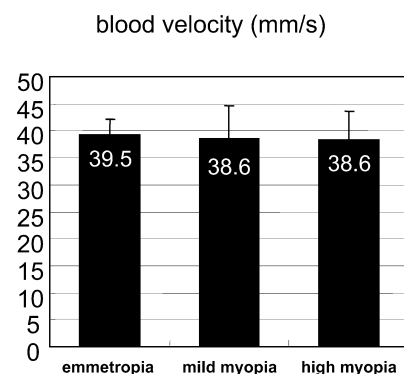


Fig. 2 Mean retinal blood velocity (in mm/s, mean \pm standard deviation). There was no significant difference in retinal blood velocity among the three groups

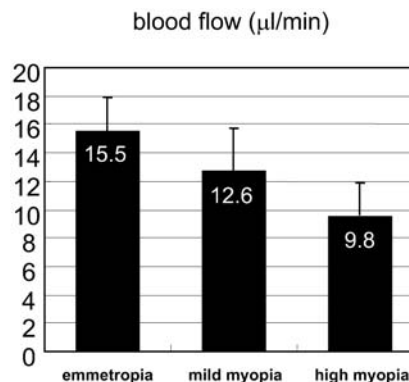


Fig. 3 Mean retinal arterial blood flow volume (in $\mu\text{l/min}$, mean \pm standard deviation). Retinal blood flow was significantly decreased in highly myopic eyes compared with eyes with emmetropia and eyes with mild myopia ($p<0.05$; Mann-Whitney U test)

emmetropia. Retinal blood flow averaged 15.3 $\mu\text{l}/\text{min}$ superiorly and 15.8 $\mu\text{l}/\text{min}$ inferiorly in emmetropia, 12.4 $\mu\text{l}/\text{min}$ superiorly and 12.5 $\mu\text{l}/\text{min}$ inferiorly in mild myopia, and 9.8 $\mu\text{l}/\text{min}$ superiorly and 9.7 $\mu\text{l}/\text{min}$ inferiorly in high myopia. Although statistical analysis is difficult because of the small sample size, the values did not appear to be different between the different measurement locations (superiorly and inferiorly).

Discussion

The present study demonstrates for the first time a significant reduction in retinal blood flow in eyes with high myopia using quantitative methods and laser Doppler velocimetry.

In previous studies that examined ocular blood flow in high myopia, mainly choroidal blood flow, there was a negative correlation between the axial length and choroidal blood flow using pulsatile ocular blood flow (POBF) [20] or color Doppler imaging (CDI) techniques [1, 6]. Akyol et al. [1] reported that the central retinal artery blood velocity was lower in highly myopic eyes using the CDI technique. Retinal blood flow has not previously been measured in highly myopic eyes using quantitative techniques; therefore, it has been uncertain whether retinal blood flow was affected in highly myopic eyes.

Laser Doppler velocimetry reported first by Tokoro [22] is a noninvasive, quantitative measurement of retinal circulation. The CLBF can measure retinal vessel diameter and blood velocity using laser Doppler velocimetry. With the CLBF, the retinal blood flow in highly myopic eyes was significantly decreased compared with eyes with emmetropia or eyes with mild myopia. The present study also demonstrated that the decreased retinal blood flow in high myopia was due mainly to the narrowing of vessel diameter. Blood velocity did not differ among groups.

What causes the narrowing of retinal vessel diameter in highly myopic eyes? One possible mechanism is that excessive elongation of the eyeball in high myopia causes mechanical expansion and thinning of the retina, which might result in the straightening and decreased di-

ameter of the retinal vessels. Also, the thinning and atrophy of the retinal tissues might decrease the need for oxygen and consequently decrease blood circulation. Another explanation for our findings is that increased diffusion of oxygen from the choroid because of thinning of the retina might cause a secondary narrowing of retinal vessels. Sullivan et al. [19] reported a decrease in retinal blood flow and retinal vessel diameter after panretinal photocoagulation in eyes with proliferative diabetic retinopathy using laser Doppler velocimetry [2]. Sullivan et al. [19] suggested that the decrease in retinal vessel diameter in these patients is most likely due to an improvement in retinal oxygenation following photocoagulation. Although the mechanism of the decreased retinal vessel diameter in highly myopic eyes is not known, similar mechanisms might underlie the decreased retinal blood flow in highly myopic eyes with thinning of the retina. This requires further investigation.

Whether the reduced retinal blood flow in high myopia is a result of axial elongation of the eyeball or could possibly be involved in the development of high myopia is not known. Shih et al. [17] reported a greatly reduced ocular blood flow in chick eyes in which myopia was induced by visual deprivation (by means of wearing goggles for 14 days after hatching), and examined a possible link between decreased ocular blood flow and ocular enlargement. The exact mechanisms underlying the development of myopia and myopic retinopathy are largely unknown; however, the altered retinal blood flow in high myopia demonstrated in the present study could also have a role in the retinopathy that occurs in high myopia. In addition, decreased retinal blood flow might also have a role in the higher incidence of glaucoma [11, 12, 25] in highly myopic patients.

In conclusion, the present study demonstrates reduced retinal blood flow in highly myopic eyes using laser Doppler velocimetry. This reduced retinal blood flow might be involved in the development of chorioretinal atrophy in high myopia.

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