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Research Article

Increased Choroidal Blood Flow in Eyes with Macular Edema is Associated with Branch Retinal Vein Occlusion on Laser Speckle Flowgraphy

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Abstract

Purpose: To examine the choroidal blood flow (CBF) and vascular resistance (CVR) in eyes with treatment-naive non-ischemic branch retinal vein occlusion (BRVO).

Methods: We included 52 patients with BRVO (29 patients with major BRVO and 23 patients with macular BRVO) attending a university-related medical center. The CBF and CVR in the subfovea were measured via laser speckle flowgraphy (LSFG) and were compared between affected and fellow eyes of patients with major and macular BRVO.

Results: The mean CBF in the subfovea was significantly higher in affected (9.35 ± 4.65) than in fellow eyes (7.91 ± 3.07 P = 0.031) in the major BRVO group, whereas mean CBF was similar between affected (9.07 ± 2.92) and fellow eyes (8.56 ± 3.11, P = 0.649) in the macular BRVO group. The CVR in the subfovea was significantly lower in affected (7.28 ± 2.93) than in fellow eyes (8.32 ± 3.70, P = 0.020) in the major BRVO group. In contrast, there was no significant difference in the mean CVR between affected (6.97 ± 2.72) and fellow eyes (7.58 ± 2.89, P = 0.520) in the macular BRVO group. The CBF in the subfovea of the affected eye was significantly associated with the central retinal thickness (R = -0.307, P = 0.027).

Conclusion: Our data showed that the CBF in the subfovea is increased in eyes with major BRVO due to reduced CVR. An increase in CBF might compensate for the ischemic retina in patients with major BRVO.

Keywords: *Branch Retinal Vein Occlusion; Choroidal Blood Flow; Choroidal Thickness; Vascular Resistance; Laser Speckle Flowgraphy*

Abbreviations

BRVO: Branch Retinal Vein Occlusion; ME: Macular Edema; OCT: Optical Coherence Tomography; LSFG: Laser Speckle Flowgraphy; CBF: Choroidal Blood Flow; CVR: Choroidal Vascular Resistance; MBR: Mean Blur Rate; CCT: Central Choroidal Thickness; CRT: Central Retinal Thickness; FA: Fluorescein Angiography; OPP: Ocular Perfusion Pressure; BCVA: Best Corrected Visual Acuity; IOP: Intraocular Pressure; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MBP: Mean Blood Pressure

Introduction

Branch retinal vein occlusion (BRVO) is a common retinal vascular disorder and can induce macular edema (ME), subretinal hemorrhage, and retinal ischemia [1,2], causing subsequent damage to the foveal photoreceptor. Previous clinical and angiographic findings of BRVO

using several imaging techniques, such as scanning laser ophthalmoscopy, laser Doppler flowmetry, optical coherence tomography (OCT) angiography, and laser speckle flowgraphy (LSFG), have confirmed disturbances in retinal blood flow [3-8]. One of these studies also reported that total retinal blood flow in eyes with BRVO was significantly decreased compared with normal eyes, based on laser Doppler OCT [4].

The retinal blood vessels supply the inner retina, such as the nerve fiber layer, ganglion cell layer, and inner plexiform layer [9]. On the other hand, the choroidal vasculature supplies the outer regions of the human retina; this vasculature diffuses across Bruch's membrane through the retinal pigment epithelium and into the outer neural layers of the retina [9]. However, compensation for the decreased retinal blood flow by choroidal blood flow (CBF) is not fully understood, particularly in acute BRVO patients.

In terms of the relationship between choroidal circulation and BRVO, several techniques have been used. Luksch and associates reported that the fundus pulsation amplitude obtained by laser interferometry, which indicates pulsatile CBF, was increased in eyes with BRVO [10]. However, that previous study did not include eyes with macular involvement, because the fundus pulsation amplitude cannot be adequately analyzed in such cases. Therefore, we considered that it is important to evaluate CBF in eyes with ME associated with BRVO using a different noninvasive method, to assess the increase in CBF in eyes with BRVO as compared to fellow eyes. In addition to CBF, choroidal vascular resistance (CVR) is another important parameter to evaluate, because sufficient CBF is, at least in part, related to low vascular resistance in the choriocapillaris [11].

Laser speckle flowgraphy (LSFG-NAVITM, Softcare Co., Ltd., Fukuoka, Japan) is useful for measuring the optic nerve head and choroidal circulation noninvasively throughout the cardiac cycle, for a period of 4 seconds. It yields a speckle pattern due to the interference of the light scattered by the movements of the erythrocytes [12-18]. LSFG was used to measure the mean blur rate (MBR) as an indicator of blood flow [14]. In an animal model, there was a correlation between LSFG measurements of the MBR and hydrogen gas clearance measurement of ocular blood flow, which showed differences in fundus pigmentation [19]. Therefore, LSFG measurement is usable for interindividual and intergroup comparisons.

To the best of our knowledge, the CBF and CVR have not yet been evaluated using LSFG in patients with major and macular BRVO. The primary purpose of the present study was to investigate CBF in the subfovea of eyes with ME associated with either macular or major BRVO, as well as in the contralateral fellow eye using LSFG. In addition to CBF, we examined the central choroidal thickness (CCT) in the subfovea of eyes with BRVO and in the corresponding fellow eye, to assess the relationship between CBF and CCT.

Materials and Methods

Participants

The study was conducted at Toho University Sakura Medical Center from October 2015 to September 2017. All procedures adhered to the tenets of the Declaration of Helsinki and were approved by the Institutional Review Board/Ethics Committee of Toho University Sakura Medical Center (number: 2015056).

Fifty-two eyes of 52 subjects (26 males and 26 females, mean age 66.1 ± 10.8 years) with treatment-naïve non-ischemic BRVO were enrolled consecutively in this retrospective analysis study. Patients were included if patients had ME associated with treatment-naive non-ischemic BRVO and were enrolled within 12 weeks of BRVO onset, if the BRVO eye had a central retinal thickness (CRT) > 300 μm, if central fovea involvement was apparent via optical coherence tomography (OCT; Spectralis OCT®, Heidelberg Engineering Inc., Heidelberg, Germany) at the initial visit, and if symptom duration was < 6 months prior to examination. Hayreh reported that BRVO consists of 2 distinct clinical entities, including major BRVO and macular BRVO [20], and that there are differences in the initial visual status and final visual outcome, after long-term observations, between major and macular BRVO [21]. Therefore, we investigated major and macular

BRVOs separately in accordance with the above-mentioned clinical criteria in all 52 subjects. We diagnosed major and macular BRVO based on the fundus examination by retinal specialists (R.H., K.Y.., and T.M.).

Patients were excluded if they had glaucoma, other vitreoretinal disease (e.g. epiretinal membrane, macular hole, diabetic retinopathy, uveitis, or age-related macular degeneration), a history of previous vitreous surgery or photocoagulation, a history of intravitreal injection of anti-VEGF or triamcinolone acetonide, or a history of taking anticoagulants, antiplatelet agents, or corticosteroids, or had high myopia (axial length > 26 mm). At the initial visit, we performed fluorescein angiography (FA). In cases where the non-perfusion area was greater than 6 optic disc areas, we defined the case as ischemic BRVO; these patients were excluded.

Eye examinations

All patients underwent ocular examinations at the initial visit. Eye examinations included best corrected visual acuity (BCVA), intraocular pressure (IOP) and axial length measurements, slit-lamp assessment, fundus photography, OCT, EDI-OCT, and LSFG. BCVA was measured as a decimal VA using a Landolt C chart and was converted to the logarithm of the minimal angle of resolution (logMAR).

Choroidal blood flow measured using laser speckle flowgraphy

LSFG was used to examine CBF in patients with treatment-naive non-ischemic BRVO, and was used to measure the MBR as an indicator of blood flow [22]. To investigate the CBF in the subfovea using LSFG Analyzer software (Softcare Co., Ltd., Fukuoka, Japan), we set a measurement circle on the subfovea on the LSFG color composite map (Figure 1). The circle's position was manually determined by comparing fundus photographs and LSFG color composite map images. To determine the size of the circle within the foveal avascular zone so as to measure CBF exclusively, we overlaid the LSFG image on the FA image using LSFG Analyzer software (Ver. 3.5.0.0, Softcare Co., Ltd.) (Figure 1).

Approximately 30 minutes before CBF measurement, we induced mydriasis via eye drops containing 0.5% tropicamide and 0.5% phenylephrine hydrochloride (Mydrin-P ophthalmic solution, Santen Pharmaceutical Co., Ltd., Osaka, Japan), and CBF was measured using LSFG after the patients had rested for 10 minutes in a quiet room, maintained at 24°C.

Choroidal and retinal thickness measurements

In addition to CBF, CCT was assessed via enhanced depth imaging (EDI)-OCT [23]. The CRT and CCT were measured by three independent examiners (S.I., M.O., and M.I.) (Figure 1A). CCT was determined via EDI-OCT (Figure 1, bottom). All examinations were performed between 12:00 noon and 3:00 p.m. in order to avoid circadian variations in choroidal thickness [24].

Vascular resistance

The vascular resistance was determined by the formula Vascular resistance = ocular perfusion pressure (OPP)/blood flow, as shown in a previous report [25]. We used the OPP (mmHg)/MBR (arbitrary units, AU) as an indicator of vascular resistance and calculated this in the subfovea.

Ocular hemodynamics

We measured IOP using a non-contact tonometer (Canon TX-F; Canon Inc., Tokyo, Japan). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using an automated sphygmomanometer (HBP-9020; OMRON Healthcare, Kyoto, Japan), in the

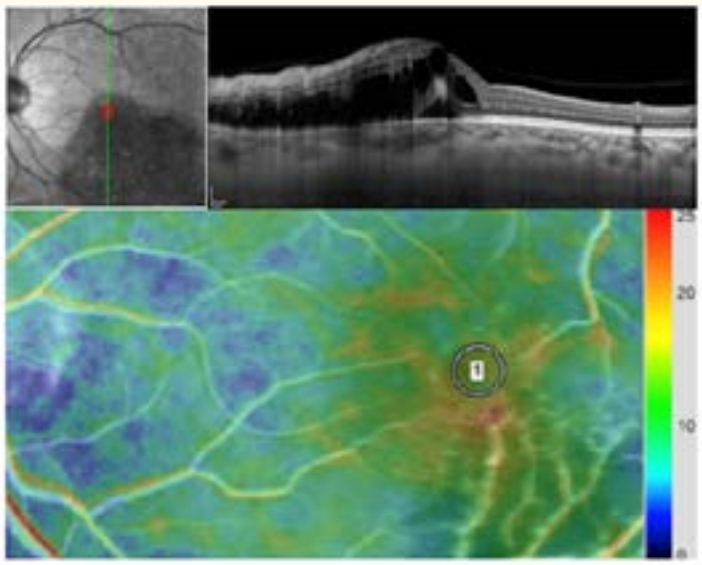

Figure 1: *Choroidal thickness and choroidal blood flow, measured using enhanced depth-imaging optical coherence tomography and laser speckle flowgraphy, in eyes with branch retinal vein occlusion.*

Enhanced depth imaging-optical coherence tomography (EDI-OCT) image of an affected eye. (Top) The central choroidal thickness was manually determined by measuring the distance from the outer border of the hyper-reflective line, corresponding to the retinal pigment epithelium, to the outer border of the choroid beneath the fovea, in a horizontal EDI-OCT image.

Laser speckle flowgraphy (LSFG) color image. (Bottom) The measurement circle was set to macular regions to measure and analyze the choroidal blood flow (CBF). The position of the circle was manually determined by comparing the fundus photograph, and scanning laser ophthalmoscopy and fluorescein angiography (FA) images. To determine the size of each circle within the foveal avascular zone to measure exclusively CBF, we overlaid the LSFG image on the FA image using LSFG Analyzer software (Ver. 7.5.0.0, Softcare Co., Ltd., Fukuoka, Japan).

sitting position, at the same time as measuring CBF, because there is a linear relationship between CBF and OPP [26]. Mean blood pressure (MBP) was calculated from the SBP and DBP values using the following equation: MBP = 1/3 (SBP - DBP) + DBP [27,28].

The following equation was used to calculate OPP: OPP (sitting position) = (2/3 × MBP) - IOP [27,28].

Statistical analysis

All results are expressed as the mean ± standard deviation (SD), and $P < 0.05$ was deemed to indicate statistical significance. We performed the Shapiro–Wilk test to assess the normality of distributions. CBF, CRT, and CCT in the affected eyes were compared with those in the contralateral fellow eyes using the Wilcoxon t-test. We used Spearman correlation coefficients to assess the relationship between the variables. All statistical analyses were performed using GraphPad Prism version 8.0.1 for macOS (GraphPad Software, San Diego, CA, USA).

Results

Table 1 summarizes the clinical characteristics of the 52 patients enrolled in the present study (26 males and 26 females, mean age 66.1 ± 10.8 years) (Table 1). Thirty-five patients had a superior occlusive region, while 17 patients had an inferior occlusive region. Systemic diseases were present among the patients, and included hypertension (34/52, 65.4%), hyperlipidemia (16/52, 30.8%), and type 2 diabetes mellitus (4/52, 7.69%).

Among the 52 BRVO patients, 29 patients were diagnosed with major BRVO and 23 with macular BRVO (Table 1). In both macular and major BRVO groups, there was no significant difference in mean OPPs between the affected eyes and the fellow eyes (P = 0.126 and 0.063, Wilcoxon t-test). Axial length was only significantly different between the affected eyes and fellow eyes in the major BRVO group (P = 0.045), whereas there was no significant difference in the macular BRVO group (P = 0.170, Wilcoxson t-test).

	Total (N = 52)	Macular BRVO (N = 23)	Major BRVO (N = 29)
Male: Female	26: 26	14:9	12:17
Age (years)	66.1 ± 10.8	67.6 ± 9.61	64.9 ± 11.7
Superior: Inferior (Occlusive region)	35: 17	15:8	20:9
Axial length (mm) Affected eye Fellow eye	 23.6 ± 1.09 23.8 ± 1.19	 23.6 ± 1.21 23.7 ± 1.26	 23.7 ± 1.01 23.8 ± 1.14
LogMAR VA Affected eye Fellow eye	 0.38 ± 0.30 -0.038 ± 0.087	 0.39 ± 0.28 -0.050 ± 0.069	 0.37 ± 0.33 -0.028 ± 0.098
IOP (mmHg) Affected eye Fellow eye	 13.7 ± 3.65 14.0 ± 3.76	 13.5 ± 3.90 13.3 ± 3.95	 13.9 ± 3.51 14.4 ± 3.65
SBP (mmHg)	148 ± 17.1	147 ± 19.3	148 ± 15.6
DBP (mmHg)	84.9 ± 11.0	84.4 ± 12.0	85.2 ± 10.3
MBP (mmHg)	106 ± 11.4	105 ± 12.8	106 ± 10.4
OPP (mmHg) Affected eye Fellow eye	 56.9 ± 7.13 56.5 ± 7.00	 56.7 ± 7.06 56.9 ± 7.16	 57.0 ± 7.30 56.5 ± 6.93
Hypertension	34/52	15/22	19/30
Hyperlipidemia	16/52	6/22	10/30
Type 2 Diabetes	4/52	3/22	1/30

Table 1: *Clinical characteristics of study participants.*

Data are expressed as the mean ± standard deviation.

Log MAR VA: Logarithm of the Minimum Angle of Resolution Visual Acuity; IOP: Intraocular Pressure; SBP: Systemic Blood Pressure; DBP: Diastolic Blood Pressure; MBP: Mean Blood Pressure; OPP: Ocular Perfusion Pressure.

Choroidal blood flow and vascular resistance in branch retinal vein occlusion eyes and contralateral fellow eyes

A comparison of mean CBFs and CVRs between the affected eyes and the fellow eyes is shown in figure 2. There was no significant difference in mean CBF between the affected eyes (9.07 ± 2.92) and fellow eyes (8.56 ± 3.11, P = 0.649) in the macular BRVO group. On the other hand, in the major BRVO group, mean CBF in the subfovea was significantly higher in the affected eyes (9.35 ± 4.65) than in the fellow eyes (7.91 ± 3.07 P = 0.031).

There was no significant difference in the mean CVRs between the affected eyes (6.97 ± 2.72) and the fellow eyes (7.58 ± 2.89, P = 0.520) in the macular BRVO group. On the other hand, the mean CVR in the subfovea was significantly lower in the affected eyes (7.28 ± 2.93) than in the fellow eyes (8.32 ± 3.70, P = 0.020) in the major BRVO group.

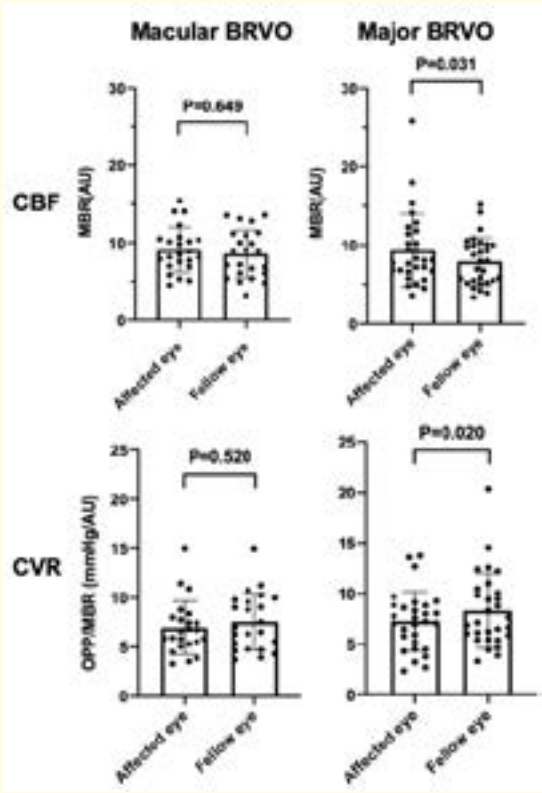

Figure 2: *Choroidal blood flow and vascular resistance in eyes with branch retinal vein occlusion.*

Mean choroidal blood flow (CBF) of the affected eye and fellow eye in major and macular branch retinal vein occlusion (BRVO) groups. (Top) The mean CBF in the subfovea was significantly higher in the affected eye (9.35 ± 4.65) than in the fellow eye (7.91 ± 3.07 P = 0.031) in the major BRVO group, whereas there was no significant difference in mean CBF between the affected eye (9.07 ± 2.92) and fellow eye (8.56 ± 3.11, P= 0.649) in the macular BRVO group.

Mean choroidal vascular resistance (CVR) in the affected eye and fellow eye in major and macular BRVO groups. (Bottom) The mean CVR in the subfovea was significantly lower in the affected eye (7.28 ± 2.93) than in the fellow eye (8.32 ± 3.70, P = 0.020) in the major BRVO group, whereas there was no significant difference of the mean CVRs between in the affected eye (6.97 ± 2.72) and fellow eye (7.58 ± 2.89, P = 0.520) in the macular BRVO group.

Retinal and choroidal thickness in branch retinal vein occlusion eyes and contralateral fellow eyes

A comparison of mean CRTs and CCTs between the affected eye and the fellow eye is shown in figure 3.

In the macular and major BRVO groups, the mean CRTs in the affected eyes (471 ± 150 μm and 533 ± 186 μm) were significantly greater than that in the fellow eyes (226 ± 23.1 μm and 215 ± 29.5 μm; P < 0.001, respectively).

In the macular and major BRVO groups, the mean CCT in the affected eyes (269 ± 92.1 μm and 277 ± 84.8 μm) were significantly greater than that in the fellow eyes (235 ± 103 μm and 247 ± 73.0 μm; P= 0.021 and P = 0.001, respectively).

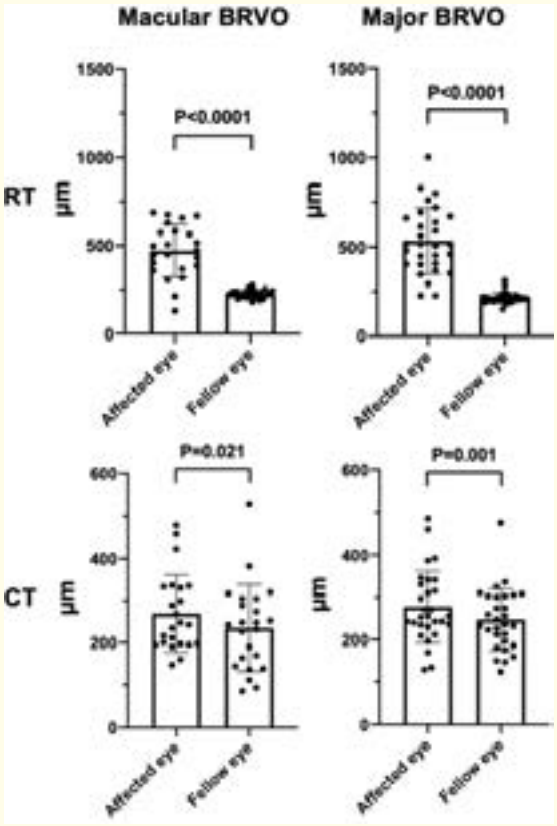

Figure 3: *Retinal and choroidal thicknesses in eyes with branch retinal vein occlusion.*

The mean central retinal thickness (CRT) of the affected eye and the fellow eye in the major and macular branch retinal vein occlusion (BRVO) group. (Top) In both the macular and the major BRVO group, the mean CRT in the affected eye (471 ± 150 μm and 533 ± 186 μm) was significantly greater than that in the fellow eye (226 ± 23.1 μm and 215 ± 29.5 μm; P < 0.001, respectively). The mean central choroidal thickness (CCT) of the affected eye and fellow eye in major and macular branch retinal vein occlusion (BRVO) group. (Bottom) In both the macular and the major BRVO group, the mean CCT in the affected eye (269 ± 92.1 μm and 277 ± 84.8 μm) was significantly greater than that in the fellow eye (235 ± 103 μm and 247 ± 73.0 μm; P < 0.001, P = 0.021, and P = 0.001, respectively).

Factors related to choroidal blood flow in the subfovea in eyes with branch retinal vein occlusion

We analyzed the relationships between the CBF in the subfovea and the other variables investigated (Table 2). In a Spearman's correlational analysis of the dependent variables, the CBF in the subfovea was significantly and negatively correlated with CRT in the affected eyes (r = -0.266, P = 0.016). Although there was no statistically significant difference, CBF in the subfovea tended to correlate negatively with LogMAR VA (r = -0.266, P = 0.057). There was no significant correlation between CBF and CCT in the affected eye (P = 0.199).

	CBF in the subfovea	
	r or mean ± SD	P-value
Male: Female	9.66 ± 4.60: 8.80 ± 3.20	0.727†
Superior: Inferior (Occlusive region)	9.25 ± 4.03: 9.18 ± 3.90	0.988†
Age	-0.159	0.260*
Log MAR VA in the affected eye	-0.266	0.057*
Axial length in the affected eye	0.214	0.128*
IOP in the affected eye	-0.077	0.589*
SBP	-0.086	0.546*
DBP	0.002	0.986*
MBP	-0.038	0.792*
OPP in the affected eye	-0.168	0.269*
CRT in the affected eye	-0.307	0.027*
CCT in the affected eye	-0.181	0.199*

Table 2: *Association between choroidal blood flow in the subfovea in the affected eye and clinical characteristics.*

Data are expressed as the mean ± standard deviation for 52 eyes.

*†Mann-Whitney test, *Spearman r coefficient.*

CBF: Choroidal Blood Flow; Log MAR VA: Logarithm of the Minimum Angle of Resolution Visual Acuity; SBP: Systemic Blood Pressure, DBP: Diastolic Blood Pressure; MBP: Mean Blood Pressure; OPP: Ocular Perfusion Pressure; CRT: Central Retinal Thickness; CCT: Central Choroidal Thickness.

Figure 4 showed a representative photograph of a fundus photo combined with an LSFG color map, LSFG color composite map, and EDI-OCT images in patients with major BRVO. The OPP was 54.2 mm Hg and 52.8 mm Hg in the affected eye and the fellow eye. Mean axial lengths in the affected eyes and fellow eyes were 23.2 mm and 23.3 mm. The CRTs and CCTs in the affected eyes and fellow eyes were 408 μm and 297 μm, and 199 μm and 289 μm, respectively. LSFG colors were warmer in the affected eyes than the fellow eyes, and the CBF in the affected eyes (6.73) was higher than that in the fellow eyes (5.03). On the other hand, the CVR in the affected eyes (8.05) was lower than that in the fellow eyes (10.5).

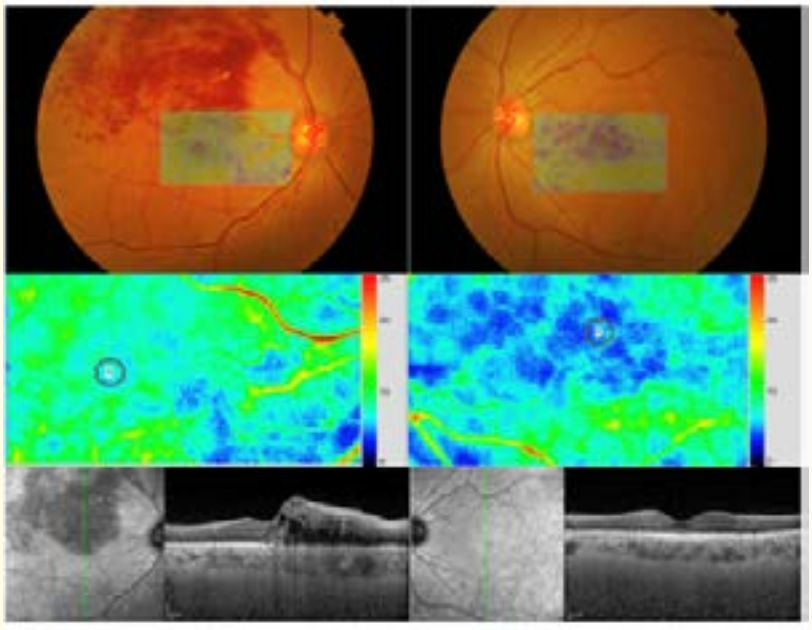

Figure 4: *Representative laser speckle flowgraphy images in a patient with major branch retinal vein occlusion. The case is a 70-year-old female with a major branch retinal vein occlusion in the right eye. Her best-corrected visual acuity is 20/40 and 20/20. Fundus photographs combined with laser speckle (LSFG) color composite map in the affected eye and fellow eye. (Top left, Top right) LSFG color composite map in the affected and fellow eye with circles in the subfovea. (Middle left, Middle right) Choroidal blood flow (CBF) values in the subfovea were 6.73, and 5.03 in the affected and fellow eye, respectively. Central retinal and choroidal thickness (CRT and CCT) in the affected and fellow eye using enhanced depth imaging-optical coherence tomography (EDI-OCT) (Bottom left, Bottom right). The EDI-OCT findings show that the CRTs and CCTs were 408 μm and 289 μm, 199 μm and 289 μm, respectively.*

Discussion

In the current study, we found that the mean CBF in the subfovea, determined by LSFG, was significantly higher in the affected eyes than in the contralateral fellow eyes, particularly in major BRVO eyes; this has not been reported previously. On the other hand, the mean CVR was significantly lower in the affected eye than that in fellow eye in major BRVO. Secondly, our data also showed that mean CRTs and CCTs in the affected eyes were significantly greater than those in the fellow eyes in macular and major BRVO. Lastly, the CBF in the subfovea was significantly and negatively correlated with the CRT, and tended to correlate negatively with the LogMAR VA in the affected eye.

Our data showed an increase in the CBF in the subfovea of eyes with major BRVO, but not those with macular BRVO. There was no significant difference in OPP between affected eyes and fellow eyes in both macular and major BRVO groups. Luksch and associates previously reported that fundus pulsation amplitude, which indicates CBF, was higher in BRVO eyes without macular involvement than in the fellow eye [10]. A previous animal study, using a hydrogen gas clearance method, demonstrated that the CBF is increased after a

decrease in retinal blood flow induced by endothelin-1, and they concluded that an increase in the CBF resulted from compensation for the decrease in retinal blood flow [29]. Additionally, the inner region of the retina was oxygenated by diffusion from the choroid under ischemic conditions in the animal model [9].

In terms of differences in clinical features between major and macular BRVO, the levels of vascular endothelial growth factor (VEGF) in the aqueous humor were significantly higher in cases with major BRVO than in those with macular BRVO [30]. The level of VEGF in the vitreous fluid was reported to correlate with the nonperfused retinal area in eyes with BRVO [31]. Based on these clinical findings, it is understandable that an increase in CBF may play an important role in compensating for the decrease in retinal blood flow in eyes with major BRVO.

Our data also showed that CVR in the affected eye was significantly lower than that in the fellow eye in cases with major BRVO. Foulds reported that the high CBF is, at least in part, related to low vascular resistance in the choriocapillaris, which has a comparatively wide bore [11]. VEGF induces the release of nitric oxide [32], which leads to the dilation of retinal arterioles and veins [33-35]. VEGF levels are higher in the vitreous fluid of BRVO eyes than in that of control eyes [36,37]. Moreover, VEGF levels in the aqueous humor are significantly higher in cases with major BRVO than in those with macular BRVO [30]. Considering the above findings and that overexpression of VEGF affects both the outer retina and choroidal vascular tissues produced by ischemic regions [38,39], the CVR might be decreased due to an increase in nitric oxide in eyes with major BRVO. Additionally, greater CCT and CRT in the affected eye in this study might have been due to elevated VEGF levels, similar to previous reports [40-42].

Lastly, our data showed that the CBF in the subfovea of the affected eyes was associated with the CRT of the affected eyes. Generally, a high CBF rate ensures that the metabolic demand of the photoreceptors is satisfied [43]. Photoreceptor function in the fovea of eyes with ME is diminished as compared to that in eyes without ME [44]. We found that the CBF in the subfovea was negatively correlated with the CRT, and it also tended to correlate negatively with LogMAR VA. Given that greater CRT indicates severe ME, a negative correlation between CBF and CRT may reflect the decrease in metabolic demand of the photoreceptors in eyes with ME associated with BRVO. In contrast, our study also showed that there was no significant correlation between the CBF and CCT in the affected eye. This finding might be due to the wavelengths used by LSFG. The CBF measured by LSFG-NAVI reflects the blood flow in both the choriocapillaris and the large choroidal vessels in Sattler's or Haller's layer, because the fundus camera of the LSFG device is equipped with a diode laser with a wavelength of 830 nm [22]. Future studies with longitudinal data are required to elucidate the correlation between changes in CCT and changes in CBF after anti-VEGF injection.

The present study had several limitations. First, we did not investigate retinal blood flow in eyes with BRVO. Further studies will be required to assess the relationship between retinal blood flow and CBF in patients with BRVO. Second, we did not include patients with ischemic-type BRVO. In order to evaluate the relationship between the ischemic retina and changes in CBF, further studies with ischemic-type BRVO are required to elucidate the mechanism by which CBF compensates for retinal ischemia. Third, the present study did not include the history of administrated drugs, such as antihypertensive or antihyperlipidemic drugs, which might influence ocular hemodynamics [45-47].

Lastly, we did not measure the foveal avascular zone area using OCT angiography. In order to elucidate the relationship between fovea avascular zone area and CBF in macular region, further investigations will be needed.

Conclusion

In conclusion, CBF in the subfovea is increased in eyes with major BRVO, due to a decrease in the vascular resistance. An increase in CBF in the subfovea may compensate for the reduced retinal blood flow in eyes with BRVO. Further research will be needed to elucidate whether increase in CBF in eyes with BRVO become a predictive factor of the recurrence of ME after injection of anti-VEGF drugs.

Conflict of Interest

None.

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