Special Focus on Uvea and Retina, Original Article

Microvascular and functional changes according to the fundus location of the affected arteriovenous crossing in patients with branch retinal vein occlusion

Gurcan Dogukan Arslan, Dilek Guven[1], Mehmet Demir[1], Abdurrahman Alpaslan Alkan[2], Delil Ozcan[1]

Purpose: The aim of this study was to evaluate the structural and functional changes occurring in patients with branch retinal vein occlusion (BRVO) according to the distance of the affected arteriovenous (AV) crossing to the centers of the fovea and optic disc by optic coherence tomography angiography (OCTA). **Methods:** Forty-five patients with unilateral BRVO and 45 age- and sex-matched healthy controls were included in this retrospective observational study. Images of the macula (3 mm × 3 mm) and affected AV crossing sites were obtained by OCTA. The fovea-AV crossing distance (FAVD), optic disc-AV crossing distance (DAVD), and optic disc-fovea distance (DFD) were measured. **Results:** The FAVD/DFD ratio was positively correlated with the vessel density in the superficial and deep affected hemifields ($r = 0.430$, $P < 0.05$ and $r = 0.308$, $P < 0.05$, respectively) and negatively correlated with the superficial foveal avascular zone and logarithm of the minimum angle of resolution (logMAR) visual acuity ($r = –0.412$, $P < 0.05$ and $r = –0.356$, $P < 0.05$, respectively). The DAVD/DFD ratio was not correlated with the logMAR visual acuity, superficial FAZ area or vessel densities in the affected hemifield (all $P > 0.05$). **Conclusion:** The affected AV crossing site that was further away from the fovea had better visual acuity and quantitative microvascular parameters in the affected hemifields. However, this correlation was not observed for the distance between the affected AV crossing site and the optic disc.

Access this article online

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_1018_20

Quick Response Code:

Key words: Arteriovenous crossing, branch retinal vein occlusion, optical coherence tomography angiography, visual function

Branch retinal vein occlusion (BRVO) is the most commonly encountered retinal vascular disease after diabetic retinopathy.[1-3] Various degrees of retinal hemorrhage, retinal ischemia, and macular edema may occur in patients with BRVO.[4,5] Vessel density in the superficial capillary plexus (SCP), deep capillary plexus (DCP), and foveal avascular zone (FAZ) has recently been evaluated by optical coherence tomography angiography (OCTA), and the ability of this imaging technique to reveal capillary vessel pathology has been assessed in these patients with BRVO.[6-8] Furthermore, the macula has been examined in healthy fellow eyes of patients to account for the effects of comorbid diseases.[9]

BRVO occurs most often at an arteriovenous (AV) crossing site and is described as first-degree or second-degree focal occlusion of a retinal vein.[5,10] Some researchers have suggested that venous flow is impaired because of mechanical compression of the vein by a rigid arterial wall.[11,12] AV crossings have been investigated in many studies and their role in the pathogenesis of BRVO has been examined.[10,13-15]

A previous study that investigated the pathophysiology of BRVO using fundus photography and intravenous fluorescein angiography identified one of the factors affecting visual function to be the extent and location of the venous drainage area involved.[16] Moreover, the extent of retinal ischemia in retinal vein occlusions has been associated with a worse prognosis.[17] Other important factors were reported to be the proportion of impaired perifoveal collaterals and the effectiveness of collateral drainage.[16] We already know that the extent of the venous drainage area affected, amount of cotton wool spots, and size of the edematous areas in the macula are greater when occlusions are closer to the optic disc (approaching the vascular root). On the other hand, damage to the perifoveal collaterals is enhanced in eyes with occlusions closer to the fovea. Nonetheless, to the best of our knowledge, there is no study in the literature that has investigated the relationship between the distances of the occlusion sites from the fovea and the optic disc using quantitative microvascular parameters, and visual function.

The aims of this study were (1) to evaluate the structural and functional changes that occur in patients with unilateral

Department of Ophthalmology, Tatvan State Hospital, Bitlis, [1]Department of Ophthalmology, University of Health Sciences Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, [2]Department of Ophthalmology, Ercis Sehit Ridvan Cevik State Hospital, Van, Turkey

Correspondence to: Dr. Gurcan Dogukan Arslan, Department of Ophthalmology, Tatvan State Hospital, 45 Hal Street, Tatvan, Bitlis, Turkey. E-mail: mr.dogukan2@gmail.com

Received: 17-Apr-2020 Revision: 26-Aug-2020
Accepted: 03-Dec-2020 Published: 30-Apr-2021

Cite this article as: Arslan GD, Guven D, Demir M, Alkan AA, Ozcan D. Microvascular and functional changes according to the fundus location of the affected arteriovenous crossing in patients with branch retinal vein occlusion. Indian J Ophthalmol 2021;69:1189-96.

BRVO according to the distance of the affected AV crossing sites from the centers of the fovea and optic disc using OCTA and (2) to compare the microvascular structures of the macula between eyes with BRVO, fellow eyes, and control eyes.

Methods

Participants and data collection

This retrospective observational study included patients admitted to our hospital with BRVO between April 2017 and May 2019. The study was approved by our institution's ethics committee and performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from each study participant after explanation of the nature and possible consequences of the study.

Forty-five eyes of 45 patients with BRVO and 45 eyes of 45 control subjects were enrolled in the study. Patients with major BRVO involving the temporal sector were included in the study if they had been followed for 1–3 years and had a foveal thickness of ≤ 300 μm without macular edema. The patients received 0.5 mg/0.05 ml intravitreal ranibizumab (Lucentis; Novartis, Basel, Switzerland and Genentech Inc., South San Francisco, California) injections if they had macular edema that exceeded 300 μm of central retinal thickness. Focal laser photocoagulation (532 nm) was performed only for closure of leaky microaneurysms causing macular edema that were located between 500 and 3000 microns from the center of the fovea (Carl Zeiss Meditec AG, Jena, Germany). The parameters for laser photocoagulation were as follows: duration, 100 ms; spot size diameter, 80-100 μm; sufficient power (70–120 mW) to produce a medium white burn. The exclusion criteria were as follows: Patients who received any other form of treatment (scatter laser photocoagulation, steroid therapy, surgical intervention, or intravitreal anti-vascular endothelial growth factor agent injections other than ranibizumab), co-existing ocular diseases (diabetic retinopathy, retinal arterial occlusion, glaucoma, or epiretinal membrane), serous retinal detachment, macular vein occlusion, a history of vitrectomy or glaucoma surgery, keratoconus, high myopia (more severe than –6 diopters), and an area of occlusion within the optic disc or its boundaries.

The control group consisted of 45 eyes of 45 patients matched for age and sex, without additional systemic or ocular pathology, who had attended the ophthalmology outpatient clinic and had a logarithm of the minimum angle of resolution (logMAR) best-corrected visual acuity of 0.05 (equivalent to 20/22 on a Snellen chart).

Complete ophthalmic examinations were performed for all participants. The best-corrected visual acuity was calculated as logMAR and Snellen chart values. Biomicroscopic anterior segment and fundus examinations were performed. Subsequently, fundus fluorescein angiography imaging was performed, and digitally colored fundus images were obtained (Kowa, VX-10-i, Kowa Optimed, Inc., Torrance, California). Red-free digital images of the fundus were recorded.

OCTA imaging

İmages of the macula (3 mm × 3 mm) were obtained by OCTA as previously described[18,19] using the AngioVue software of the RTVue XR Avanti spectral-domain OCT (SD-OCT) system (OptoVue, Fremont, California). The corresponding OCT B-scan images co-registered simultaneously with the OCTA data. Affected AV crossing sites were also identified by OCTA. The same experienced technician performed the OCTA data collection and processing for all study participants.

AngioVue uses a split-spectrum amplitude-decorrelation angiography algorithm (SSADA) to detect vascular density and capture the OCTA images.[20] This system has an A-scan repetition rate of 70 kHz, a wavelength of 840 nm, a tissue resolution of 5 μm axially, and a beam width of 15 μm. The device produces two optical coherence tomography units, each consisting of 304 × 304 A-scans, with two B-scans captured in 3 seconds. The software generates 3 × 3-mm² en face images of the microvascular plexuses centered on the fovea. As described previously,[21] the SCP in the macula was automatically measured by the device as the distance between 3 μm below the internal limiting membrane and 15 μm below the internal plexiform layer (IPL), whereas the DCP in the macula was automatically measured as the distance between 15 μm below the IPL and 70 μm below the IPL.

Vascular density was defined as the percentage area occupied by blood vessels. Vessel density in the macula was calculated for the whole field, the affected (superior or inferior) hemifield, and the unaffected hemifield. Non-flow function in the OCTA software was used for the FAZ area measurements. The FAZ area was calculated from the automated segmentation results using the automated OCTA algorithm with no manual adjustments. However, if the FAZ area differs from the expected value because of disease or normal variation, the segmentation may not be accurate. Automatic segmentation error might cause artifacts and contribute to abnormal findings. Therefore, caution is necessary when interpreting abnormalities detected on OCTA. Foveal thickness was evaluated in the central circle measuring 1 mm in diameter. Images with a low signal strength index (<70) were excluded, as were those with motion and blink artifacts.

The FAZ area and the vessel density in the SCP and DCP in the macula were examined. The whole field and the affected and unaffected hemifields of eyes with BRVO were compared with the corresponding quadrants in fellow eyes and control eyes.

Analysis of distances by OCTA

B-scan OCT imaging allows a detailed *in vivo* analysis of the interior of the retina, especially the fovea. The patients in our study did not have macular edema and had normal foveal contour. The foveal center in our patients was identified as the deepest point of the foveal pit and the thinnest position of the inner retinal layer.[22] The foveal center is marked on B-scan OCT images and automatically on their corresponding macula OCTA (3 mm × 3 mm) projection maps.

Fundus and OCTA images for each patient were combined by aligning the retinal vessels [Fig. 1]. Measurements on the processed images were obtained using ImageJ software (V.1.49, National Institutes of Health, Bethesda, MD, USA). Based on 3-mm distances at the edges of the OCTA image of the macula, the fovea-AV crossing distance (FAVD), optic disc-AV

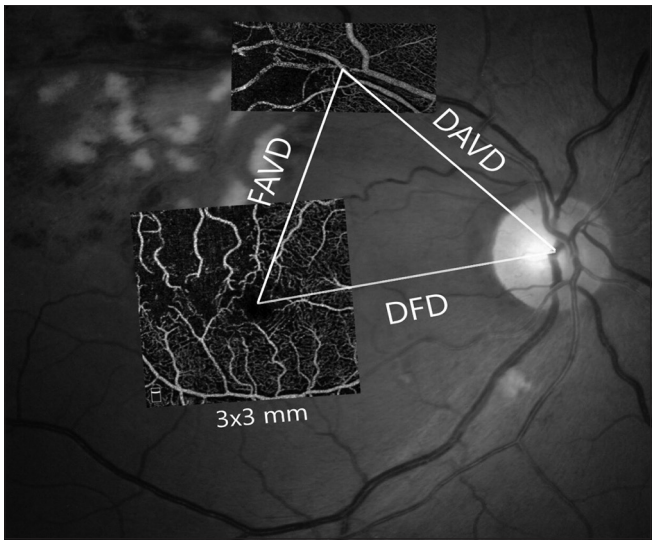

Figure 1: Optical coherence tomography angiography and fundus images combined by aligning the retinal vessels in a patient with right upper temporal branch retinal vein occlusion. DAVD, optic disc-arteriovenous crossing distance; DFD, optic disc-fovea distance; FAVD, fovea-arteriovenous crossing distance

crossing distance (DAVD), and optic disc-fovea distance (DFD) were measured [Fig. 1]. In view of interindividual variation in distances according to the macula size, the FAVD/DFD and DAVD/DFD ratios were calculated using the fixed DFD distance.

The FAVD/DFD ratio was used to show the distance to the fovea. The DAVD/DFD ratio was used to show the distance to the optic disc. Whether or not there were any correlations between the FAVD/DFD and DAVD/DFD ratios and the OCTA parameters (superficial FAZ area and vessel density in the SCP and DCP) was investigated.

Statistical analysis

The descriptive data are presented as the mean and standard deviation, range, frequency, or rate, as appropriate. Best corrected visual acuity values were converted to logMAR values for statistical analysis. The OCTA data for the BRVO and fellow eyes were compared using the Wilcoxon test. The Mann–Whitney *U* test was used to compare the OCTA data between the BRVO and control eyes and between the fellow eyes and control eyes. Pearson's correlation coefficient was used for the correlation analysis. All statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, New York). The values of $P < 0.05$ were considered reflective of statistical significance.

Results

Patient characteristics

The demographic and clinical characteristics of the participants are shown in Table 1. Twenty-three patients (51.5%) were female and 22 (48.9%) were male. The mean patient age was 64.3 ± 9.0 years. There was no difference in the age or sex distribution between patients with BRVO and controls (both $P > 0.05$). The BRVO was in the superior half of the retina in 35 patients and in the inferior half of the retina in 10 patients. Thirty-four patients (75.6%) had hypertension and the mean duration of follow-up was 20.4 ± 6.9 (range: 12–36) months.

Comparisons between eyes with BRVO, fellow eyes, and control eyes

Comparisons of OCTA data for the macula between eyes with BRVO and corresponding fields in fellow eyes and control eyes are shown in Table 2. The vessel density in the SCP and DCP was significantly lower in eyes with BRVO than in fellow eyes or control eyes in all fields of the macula (all $P < 0.05$). There was no significant difference in SCP vessel density in any of the fields between the fellow eyes and control eyes. However, the DCP vessel density was significantly lower in all fields in fellow eyes than in control eyes (all $P < 0.05$). The mean FAZ area was significantly larger in eyes with BRVO than in fellow eyes ($P < 0.05$) or control eyes ($P < 0.05$).

Changes according to the distance between the affected AV crossings and the fovea

The mean distance between the AV crossings and the fovea was 4.5 ± 0.6 mm. As shown in Fig. 2a, there was a significant negative correlation between logMAR visual acuity and FAVD/DFD values ($r = –0.356$, $P < 0.05$). The FAVD/DFD ratio was positively correlated with the vessel density in the superficial and deep affected hemifields ($r = 0.430$, $P < 0.05$, Fig. 2b, and $r = 0.308$, $P < 0.05$, Fig. 2c, respectively). However, the FAVD/DFD ratio was not correlated with vessel density in the superficial or deep unaffected hemifield [Fig. 2d and e]. There was a significant negative correlation between the FAZ area and the FAVD/DFD values ($r = –0.412$, $P < 0.05$; Fig. 2f).

Changes according to the distance between the affected AV crossings and the optic disc

The mean distance between the center of the optic disc and the AV crossing sites was 3.5 ± 1.4 mm and that between the center of the optic disc and the fovea was 4.9 ± 0.3 mm. As shown in Fig. 3a, there was no significant correlation between logMAR visual acuity and the DAVD/DFD values. The DAVD/DFD ratio was not correlated with vessel density in the superficial or deep affected hemifield [Fig. 3b and c]. However, the DAVD/DFD ratio was negatively correlated with vessel density in the superficial and deep unaffected hemifields ($r = –0.442$, $P < 0.05$, Fig. 3d, and $r = –0.313$, $P < 0.05$, Fig. 3e, respectively). There was no significant correlation between the FAZ area and the DAVD/DFD values [Fig. 3f].

Discussion

BRVO is a retinal vascular disease characterized by first-degree or second-degree focal occlusion. It is most frequently observed around the temporal vascular arcade. The upper temporal vascular arcade is more commonly affected than the lower temporal vascular arcade.[23,24] However, peripheral occlusions are relatively rarely encountered because of their tendency to have an asymptomatic course.[16] Occlusions are usually identified at AV crossings[25] and are associated with pathology such as macular edema and macular ischemia.[26,27] Therefore, in this study, we aimed to show the affected AV crossings, which are important in the pathogenesis of BRVO

Table 1: Demographic and clinical characteristics of the study participants

	BRVO group (*n*=45)	Control group (*n*=45)
Age in years, mean±SD (range)	64.3±8.4 (48-79)	62.4±9.2 (47-79)
Sex, *n* (%)		
Female	23 (51.1)	23 (51.1)
Male	22 (48.9)	22 (48.9)
Comorbidity, *n* (%)		
Hypertension	34 (75.6)	-
Previous treatment, *n*		
Intravitreal ranibizumab	25	-
Focal laser photocoagulation	4	-
Ranibizumab + focal laser	16	-
Follow-up duration in months, mean±SD (range)	20.4±6.9 (12.0-36.0)	-
Foveal thickness in µm, mean±SD (range)	254.5±29.2 (156-296)	231.8±18.5 (178-260)
BCVA in logMAR, mean±SD	0.26±0.16	0.01±0.02

BCVA, best-corrected visual acuity; BRVO, branch retinal vein occlusion; logMAR, logarithm of the minimum angle of resolution; SD, standard deviation

Table 2: Comparison of optical coherence tomography angiography data for the macula between eyes with BRVO and corresponding fields in fellow eyes and control eyes

	Mean±SD		*P*
	BRVO group	Control group	
SCP VD whole-field (%)			
BRVO eye	39.3±3.8	46.2±4.0	**<0.05***
Fellow eye	44.8±3.7	46.2±4.0	0.092†
P		**<0.05‡**	
SCP VD affected hemifield (%)			
BRVO eye	37.0±4.6	46.0±4.1	**<0.05***
Fellow eye	44.7±3.8	46.0±4.1	0.054†
P		**<0.05‡**	
SCP VD unaffected hemifield (%)			
BRVO eye	41.4±4.4	46.5±3.9	**<0.05***
Fellow eye	44.9±3.7	46.5±3.9	0.082†
P		**<0.05‡**	
DCP VD whole-field (%)			
BRVO eye	42.1±4.6	51.3±3.7	**<0.05***
Fellow eye	48.8±3.2	51.3±3.7	**<0.05†**
P		**<0.05‡**	
DCP VD affected hemifield (%)			
BRVO eye	39.9±5.5	51.4±3.9	**<0.05***
Fellow eye	48.8±3.3	51.4±3.9	**<0.05†**
P		**<0.05‡**	
DCP VD unaffected hemifield (%)			
BRVO eye	44.4±5.6	51.2±3.8	**<0.05***
Fellow eye	48.9±3.2	51.2±3.8	**<0.05†**
P		**<0.05‡**	
Superficial FAZ area (mm²)			
BRVO eye	0.39±0.18	0.28±0.09	**<0.05***
Fellow eye	0.29±0.10	0.28±0.09	0.6†
P		**<0.05‡**	

BRVO, branch retinal vein occlusion; DCP, deep capillary plexus; FAZ, foveal avascular zone; OCTA, optical coherence tomography angiography; SCP, superficial capillary plexus; SD, standard deviation; VD, vessel density. *Significance between BRVO eyes and control eyes (Mann-Whitney *U* test). †Significance between fellow eyes and control eyes (Mann-Whitney *U* test). ‡Significance between BRVO eyes and fellow eyes (Wilcoxon test). Bold values are statistically significant

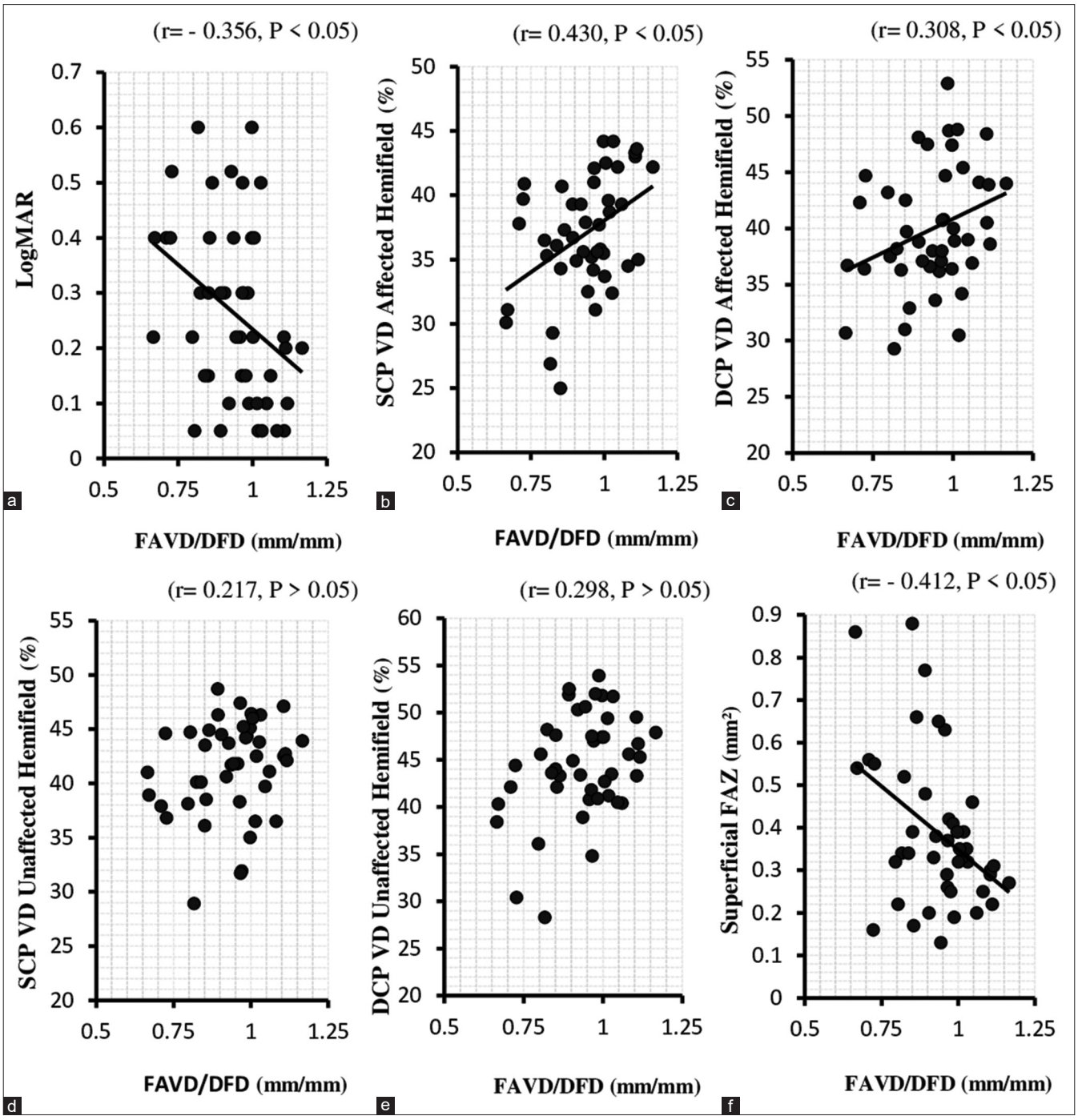

Figure 2: Correlations of FAVD/DFD values with visual acuity (logMAR) (a); SCP VD (b) and DCP VD (c) in the affected hemifield; SCP VD (d) and DCP VD (e) in the unaffected hemifield; and superficial FAZ area (f). DCP, deep capillary plexus; DFD, optic disc-fovea distance; FAVD, fovea-arteriovenous crossing distance, FAZ, foveal avascular zone; logMAR, logarithm of the minimum angle of resolution; SCP, superficial capillary plexus; VD, vessel density

and its prognosis. We measured the distances between the affected AV crossing sites and the centers of the fovea and optic disc identified by OCTA. We then compared these distances between the optic disc and fovea (using the FAVD/DFD and DAVD/DFD ratios) given that this distance is known to vary in healthy individuals.[28]

In this study, we found that the vessel density was greater in the superficial and deep plexuses of the affected hemifield, FAZ area was smaller (approached control group values), and visual acuity was better with greater fovea-affected AV crossing distances. Better visual acuity and quantitative vessel parameters were observed when the occlusion was more distant from the fovea. Our findings suggest that impairment of foveal vascularity and visual acuity were more prominent in eyes with occlusions closer to the fovea. Parodi *et al*.[29] found an irregular enlargement of the FAZ using fluorescein

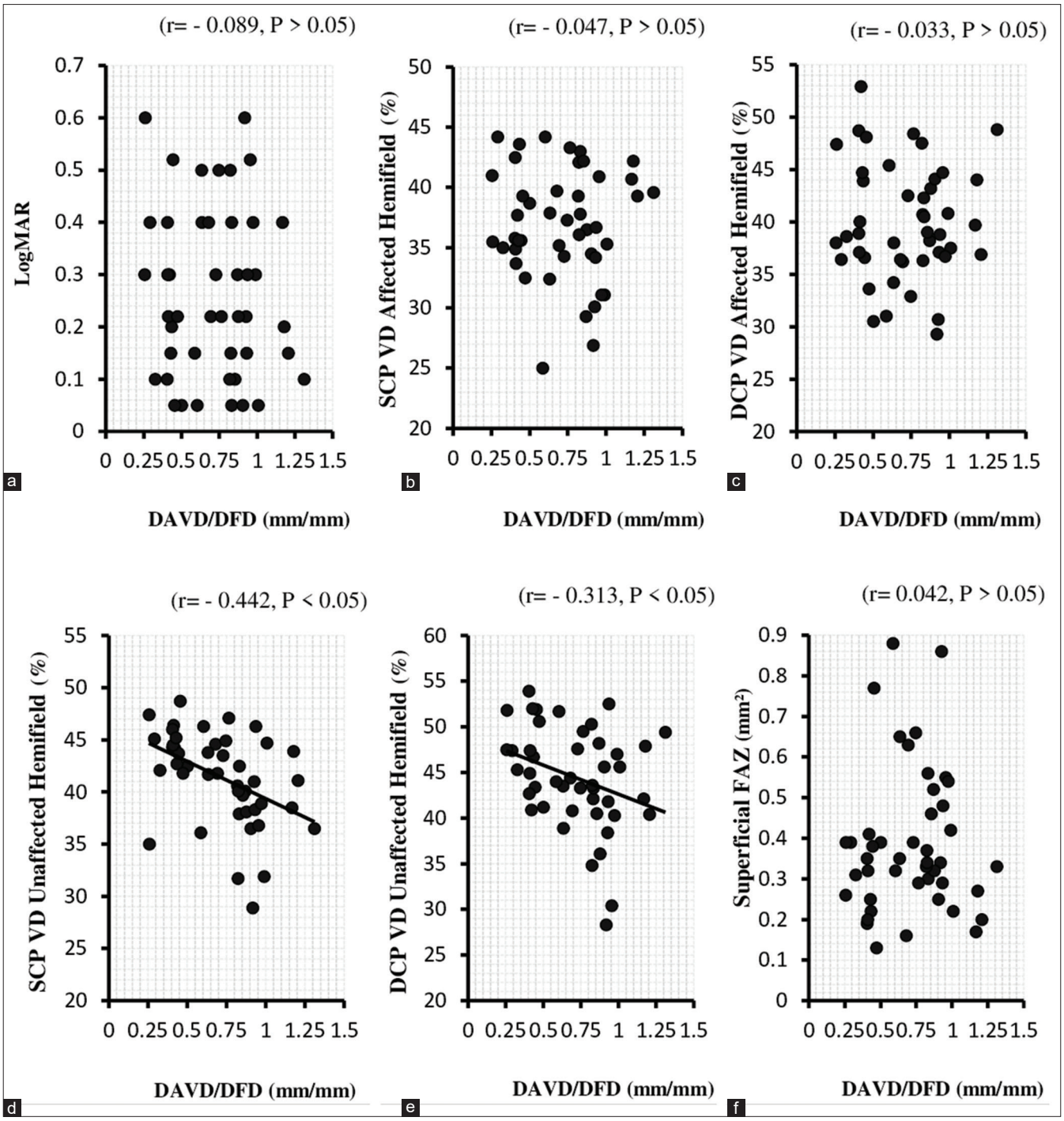

Figure 3: Correlations of DAVD/DFD values with visual acuity (logMAR) (a); SCP VD (b) and DCP VD (c) in the affected hemifield; SCP VD (d) and DCP VD (e) in the unaffected hemifield; and superficial FAZ area (f). DAVD, optic disc-arteriovenous crossing distance; DCP, deep capillary plexus; DFD, optic disc-fovea distance; FAZ, foveal avascular zone; logMAR, logarithm of the minimum angle of resolution; SCP, superficial capillary plexus; VD, vessel density

angiography in eyes with BRVO. Furthermore, the FAZ area correlated negatively with visual acuity in the eyes in that study. When looking at the capillary ring surrounding the FAZ, Hayreh *et al*. evaluated the association of capillary foveal ring (intact or broken) with improvement in visual acuity after macular edema had resolved. They found that visual acuity improved in 81% of eyes with an intact perifoveal capillary ring and in 58% of those with a broken ring.[30]

In previous studies, a short distance of occlusion from the disc margin was found to be associated with increased retinal hemorrhage and development of refractory macular edema.[31,32] Although it was expected that there would be more congestion and ischemic areas in occlusions located close to the vascular root, the FAZ area and visual acuity were not associated with the optic disc-affected AV crossing distance. However, the vessel density was greater in the

superficial and deep plexuses of the unaffected macular hemifield when the optic disc-affected AV crossing distance was smaller. The order of AV crossing at which the vein was occluded in BRVO was previously counted from the optic disc onwards as a first-order or second-order AV crossing.[5,33] In the study by Staurenghi *et al*.,[34] 26% of patients with BRVO had first-order occlusions and 74% had second-order occlusions. They argued that symptoms may be reduced because of the greater distance from the macula, causing underestimation of the prevalence of first-order occlusions. In this study, although the FAZ area and visual acuity values were significantly correlated with the distance between the affected AV crossings and the center of fovea, they were not significantly correlated with the distance of the AV crossings to the center of the optic disc. Feist *et al*. observed that occlusions of AV crossings were more common in the temporal quadrants than in the nasal quadrants and that temporal occlusions would be more likely to become symptomatic than would nasal occlusions distant from the macula.[35] In our study, we found better visual acuity and central macular quantitative vessel parameters when the affected AV crossing was more distant from the fovea in patients with BRVO.

In this study, we found that the vessel density was significantly lower in the superficial and deep whole fields in eyes with BRVO than in either fellow eyes or control eyes, which is consistent with the findings of previous studies.[8,36] In addition, the vessel density in the DCP was significantly lower in fellow eyes than in control eyes without any significant difference in vessel density in the SCP.

Hypertension is a known risk factor for BRVO and was present in 75% of our patients. Therefore, we suspect that the vessel density in the DCP was lower in the fellow eyes of patients because of vascular thinning that occurred as a result of chronic hypertension. This finding is consistent with that in a study performed in patients with hypertension by Donati *et al*.[37] who observed a significant reduction in vessel density in the deep DCP and attributed this change in the microvascular network to thinning of the retinal vessels and loss of capillaries as a result of endothelial injury. Moreover, Koulisis *et al*.[9] showed that the caliber of capillaries in the unaffected fellow eye was significantly lower in patients with retinal vein occlusion than in healthy control eyes. They suggested that this finding may represent a manifestation of chronic hypertension and attendant vascular attenuation.

This study has some limitations mainly because the study design was retrospective in nature, the duration of observation varied among patients and nonstandardized treatment protocol was used for treating macular edema. Moreover, measurements of the deep FAZ area could not be obtained (due to the OCTA software). Furthermore, we could only analyze a limited field (3 mm × 3 mm) in the macula, which is important for central vision but may not be representative of the vascular disorder overall. Finally, the study excluded patients with macular vein occlusion. Hence, our findings may not be generalizable to all types of BRVO.

Conclusion

Our study shows that quantitative vessel parameters and visual acuity values vary significantly according to the change in distance between the affected AV crossings and the fovea in eyes with BRVO. There was better visual acuity, greater capillary density in the affected macular hemifield, and a smaller FAZ area (approaching control values) as the distance between the affected AV crossing site and the fovea became greater. However, the proximity of affected AV crossings to the optic disc was not associated with visual acuity, the FAZ area, or vessel density in the affected hemifield. Therefore, we believe that our findings may permit clinicians to predict the prognosis of the disease based on the location of the occlusion determined via clinical examination. Further studies that include larger patient samples are needed to confirm the present findings.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Song P, Xu Y, Zha M, Zhang Y, Rudan I. Global epidemiology of retinal vein occlusion: A systematic review and meta-analysis of prevalence, incidence, and risk factors. J Glob Health 2019;9:010427. doi: 10.7189/jogh. 09.010427.
2. Klein R, Moss SE, Meuer SM, Klein BE. The 15-year cumulative incidence of retinal vein occlusion: The Beaver Dam eye study. Arch Ophthalmol 2008;126:513-8.
3. Rogers SL, McIntosh RL, Lim L, Mitchell P, Cheung N, Kowalski JW, *et al*. Natural history of branch retinal vein occlusion: An evidence-based systematic review. Ophthalmology 2010;117:1094-1101.e5.
4. Rehak J, Rehak M. Branch retinal vein occlusion: Pathogenesis, visual prognosis, and treatment modalities. Curr Eye Res 2008;33:111-31.
5. Hayreh SS, Zimmerman MB. Fundus changes in branch retinal vein occlusion. Retina 2015;35:1016-27.
6. Wakabayashi T, Sato T, Hara-Ueno C, Fukushima Y, Sayanagi K, Shiraki N, *et al*. Retinal microvasculature and visual acuity in eyes with branch retinal vein occlusion: Imaging analysis by optical coherence tomography angiography. Invest Ophthalmol Vis Sci 2017;58:2087-94.
7. Tsuboi K, Kamei M. Longitudinal vasculature changes in branch retinal vein occlusion with projection-resolved optical coherence tomography angiography. Graefes Arch Clin Exp Ophthalmol 2019;257:1831-40.
8. Samara WA, Shahlaee A, Sridhar J, Khan MA, Ho AC, Hsu J. Quantitative optical coherence tomography angiography features and visual function in eyes with branch retinal vein occlusion. Am J Ophthalmol 2016;166:76-83.
9. Koulisis N, Kim AY, Chu Z, Shahidzadeh A, Burkemper B, Olmos de Koo LC, *et al*. Quantitative microvascular analysis of retinal venous occlusions by spectral domain optical coherence tomography angiography. PLoS One 2017;12:e0176404. doi: 10.1371/journal.pone. 0176404.
10. Duker JS, Brown GC. Anterior location of the crossing artery in branch retinal vein obstruction. Arch Ophthalmol 1989;107:998-1000.
11. Opremcak EM, Bruce RA. Surgical decompression of branch

retinal vein occlusion via arteriovenous crossing sheathotomy: A prospective review of 15 cases. Retina 1999;19:1-5.

12. Yamamoto S, Saito W, Yagi F, Takeuchi S, Sato E, Mizunoya S. Vitrectomy with or without arteriovenous adventitial sheathotomy for macular edema associated with branch retinal vein occlusion. Am J Ophthalmol 2004;138:907-14.
13. Ascaso FJ, Padgett E, Núñez E, Villén L, Grzybowski A, Cristóbal JA. Branch retinal vein occlusion and vitreovascular traction: A preliminary spectral domain OCT case-control study. Graefes Arch Clin Exp Ophthalmol 2014;252:375-81.
14. Zhao J, Sastry SM, Sperduto RD, Chew EY, Remaley NA. Arteriovenous crossing patterns in branch retinal vein occlusion. The Eye Disease Case-Control Study Group. Ophthalmology 1993;100:423-8.
15. Hamid S, Mirza SA, Shokh I. Anatomic pattern of arteriovenous crossings in branch retinal vein occlusion. J Pak Med Assoc 2008;58:233-6.
16. Christoffersen NL, Larsen M. Pathophysiology and hemodynamics of branch retinal vein occlusion. Ophthalmology 1999;106:2054-62.
17. Khayat M, Williams M, Lois N. Ischemic retinal vein occlusion: Characterizing the more severe spectrum of retinal vein occlusion. Surv Ophthalmol 2018;63:816-50.
18. Ishibazawa A, Nagaoka T, Takahashi A, Omae T, Tani T, Sogawa K, *et al*. Optical coherence tomography angiography in diabetic retinopathy: A prospective pilot study. Am J Ophthalmol 2015;160:35-44.e1.
19. Tsuboi KH, Sasajima H, Kamei M. Collateral vessels in branch retinal vein occlusion: Anatomic and functional analyses by OCT angiography. Ophthalmol Retina 2019;3:767-76.
20. Jia Y, Tan O, Tokayer J, Potsaid B, Wang Y, Liu JJ, *et al*. Split-spectrum amplitude-decorrelation angiography with optical coherence tomography. Opt Express 2012;20:4710-25.
21. Casselholmde Salles M, Kvanta A, Amrén U, Epstein D. Optical coherence tomography angiography in central retinal vein occlusion: Correlation between the foveal avascular zone and visual acuity. Invest Ophthalmol Vis Sci 2016;57:OCT242-6.
22. Tick S, Rossant F, Ghorbel I, Gaudric A, Sahel JA, Chaumet-Riffaud P, *et al.* Foveal shape and structure in a normal population. Invest Ophthalmol Vis Sci 2011;52:5105-10.
23. Gutman FA, Zegarra H. The natural course of temporal retinal branch vein occlusion. Trans Am Acad Ophthalmol Otolaryngol 1974;78:OP178-92.
24. Blankenship GW, Okun E. Retinal tributary vein occlusion. History and management by photocoagulation. Arch Ophthalmol 1973;89:363-8.
25. Weinberg D, Dodwell DG, Fern SA. Anatomy of arteriovenous crossings in branch retinal vein occlusion. Am J Ophthalmol 1990;109:298-302.
26. Hayreh SS. Ocular vascular occlusive disorders: Natural history of visual outcome. Prog Retin Eye Res 2014;41:1-25.
27. Sekimoto M, Hayasaka S, Setogawa T. Type of arteriovenous crossing at site of branch retinal vein occlusion. Jpn J Ophthalmol 1992;36:192-6.
28. Qiu K, Chen B, Yang J, Zheng C, Chen H, Zhang M, *et al*. Effect of optic disc-fovea distance on the normative classifications of macular inner retinal layers as assessed with OCT in healthy subjects. Br J Ophthalmol 2019;103:821-5.
29. Parodi MB, Visintin F, Della Rupe P, Ravalico G. Foveal avascular zone in macular branch retinal vein occlusion. Int Ophthalmol 1995;19:25-8.
30. Hayreh SS, Zimmerman MB. Branch retinal vein occlusion: Natural history of visual outcome. JAMA Ophthalmol 2014;132:13-22.
31. Lee YH, Kim YC. Clinical characteristics of branch retinal vein occlusion with increased retinal haemorrhage during treatment for macular oedema. Sci Rep 2020;10:10272.
32. Moon BG, Cho AR, Kim YN, Kim JG. Predictors of refractory macular edema after branch retinal vein occlusion following intravitreal bevacizumab. Retina 2018;38:1166-74.
33. Kogo T, Muraoka Y, Iida Y, Ooto S, Murakami T, Kadomoto S, *et al*. Angiographic risk features of branch retinal vein occlusion onset as determined by optical coherence tomography angiography. Invest Ophthalmol Vis Sci 2020;61:8.
34. Staurenghi G, Lonati C, Aschero M, Orzalesi N. Arteriovenous crossing as a risk factor in branch retinal vein occlusion. Am J Ophthalmol 1994;117:211-3.
35. Feist RM, Ticho BH, Shapiro MJ, Farber M. Branch retinal vein occlusion and quadratic variation in arteriovenous crossings. Am J Ophthalmol 1992;113:664-8.
36. Kim JT, Chun YS, Lee JK, Moon NJ, Yi DY. Comparison of vessel density reduction in the deep and superficial capillary plexuses in branch retinal vein occlusion. Ophthalmologica 2020;243:66-74.
37. Donati S, Maresca AM, Cattaneo J, Grossi A, Mazzola M, Caprani SM, *et al*. Optical coherence tomography angiography and arterial hypertension: A role in identifying subclinical microvascular damage? Eur J Ophthalmol 2019:1120672119880390. doi: 10.1177/1120672119880390.