Evaluation of Microvascular Network with Optical Coherence Tomography Angiography (OCTA) in Branch Retinal vein Occlusion (BRVO)

CURRENT STATUS: UNDER REVISION

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DOI: 10.21203/rs.2.15193/v3

SUBJECT AREAS
Ophthalmology

KEYWORDS
optical coherence tomography angiography, retinal vasculature, foveal avascular zone, radial peripapillary capillary, branch retinal vein occlusion
Abstract

Purpose: To evaluate changes of microvascular network of macular and peripapillary regions and to provide a quantitative measurement of foveal avascular zone (FAZ) in unilateral BRVO patients. Methods: Forty-seven unilateral BRVO patients and forty-seven normal controls were enrolled. A 33 mm scan centered on fovea followed by a 4.5 mm scan centered on optic nerve head (ONH) were obtained in BRVO eyes, fellow eyes and control eyes of each individual using OCTA (Optovue Inc., Fremont, CA, USA). Vessel density (VD) in superficial (SVC) and deep vascular complex (DVC) of macula and radial peripapillary capillary (RPC) were automatically calculated. Parameters of FAZ region including size, perimeter, acircularity index (AI) and foveal vessel density 300 (FD-300) were measured. Results: VDs of SCV and DVC were significantly lower, especially in affected regions, in BRVO eyes compared with fellow eyes (P < 0.05). BRVO affected eyes has larger FAZ size, FAZ perimeter, AI and lower FD-300 compared with fellow eyes (all P < 0.05). VD of SVC and FD-300 were lower in fellow eyes compared with normal control eyes (P < 0.05). The average vessel density in whole area and peripapillary area in BRVO eyes were significantly lower compared with fellow eyes (P < 0.05). VD of inside disc in fellow eyes was lower than normal eyes (P < 0.05). Conclusions: OCTA provided quantitative information of vascular changes in BRVO. FAZ in BRVO eyes showed significant morphological alterations and decreases of VD in surrounding area. Decreases of VD existed not only in SVC and DVC in macular region but also in RPCs in BRVO eyes. Unaffected eyes of unilateral BRVO showed vascular abnormalities in superficial retinal layer, peri-FAZ area and also peripapillary regions. Key words: optical coherence tomography angiography, retinal vasculature, foveal avascular zone, radial peripapillary capillary, branch retinal vein occlusion
Background

Retinal vein occlusion (RVO) is the second most common retinal disease after diabetic retinopathy and is considered to be one of the major causes of vision loss[1]. Systemic conditions, especially hypertension, hyperlipidemia and diabetes mellitus have been considered to be the major risk factors to the development of RVO [2, 3]. Retinal vein occlusion was divided into central (CRVO), hemi-, and branch retinal vein occlusions (BRVO) based on the veins affected[4]. Fluorescein angiography (FA) is the gold standard for evaluating structural and functional status of retinal vasculature in retinal vascular diseases, especially in diabetic retinopathy and RVO. However, FA is an invasive procedure and it may lead to some side effects[5] such as allergic reaction and nausea. Details of retinal vessels may not be visualized because of dye leakage and pooling. It is also difficult to differentiate retinal vessels by layer, and deeper retinal vessels are not well presented in FA images. Spectral-domain optical coherence tomography (SD OCT) is a noninvasive method to evaluate retinal and choroidal structures because of its ability to provide high resolution images and has been widely used in clinical settings and research. Optical coherence tomography angiography (OCTA), a more recent imaging modality, has enabled us to visualize microvascular in different layers of retina and choroid, as well as quantify perfusion status of macular and peripapillary regions. Using OCTA, microvascular changes such as microaneurysms, telangiectasia, retinal capillary nonperfusion and disruption of the foveal avascular zone have been found in RVO[6-8]. Decreased microvascular density in different vessel layers of macula and peripapillary region was also reported with quantitative analysis[8-11]. Recent research about FAZ mainly focused on the enlargement of its size and perimeter in diseased eyes, however, acircularity index (AI) has been proved to be a useful parameter depicting the asymmetry of FAZ area in retinal vascular diseases especially in diabetic
retinopathy[12, 13]. Another quantitative parameter, foveal vessel density 300 (FD-300) is a new metric which evaluates vessel density of the area closely surrounding FAZ. To our knowledge, AI and FD-300 have not been used to evaluate FAZ asymmetry and perfusion states in BRVO patients.

The radial peripapillary capillary (RPC) layer is the most superficial capillary layer radiating from the optic nerve head (ONH). Cross sectional studies using OCTA has found a decreased RPC density in retinal vascular diseases such as branch and central retinal artery occlusions[14, 15]. Reports about RPC density from literature failed to differentiate RPCs and large retinal vessels around the disc[16], and quantitative data is currently not available on microvascular alterations in the peripapillary area in patients with unilateral BRVO.

In this study, we measured AI and FD-300 as well as RPC density in BRVO eyes and fellow eyes in unilateral BRVO patients and we also compared these parameters between fellow eyes in BRVO patients and normal eyes to present a thorough evaluation of microvascular changes in BRVO.

Methods

Patients

This retrospective observational study enrolled 47 eyes of 47 patients with unilateral BRVO who were examined at the Department of Ophthalmology of Peking Union Medical College Hospital (PUMCH), Beijing, China between January 2018 and December 2018. Treatment naïve patients and patients who have been treated with intravitreal medication were included. The exclusion criteria were patients with poor-quality images on OCTA (quality index lower than 5) because of significant eye movements, lens opacities, previous retinal surgery, pathologic myopia, ocular trauma, and the presence of other retinal diseases such as diabetic retinopathy or age-related macular degeneration. Eyes
with CRVO or hemicentral retinal vein occlusion (HRVO) were excluded.

The clinically unaffected fellow eyes of the patients with unilateral BRVOs served as one of the control groups if there was no history of any ocular disease or ocular surgery and with an unremarkable result of the ophthalmologic examination, including a normal appearance of both the anterior and posterior segment of the eye, a normal intraocular pressure. A second control group consisted of 47 normal individuals with no history of any ocular diseases or ocular surgery. The ophthalmic examination of the normal individuals was unremarkable. One eye of each normal individual was randomly chosen as the control eye.

The following data were obtained from the medical records of our enrolled patients: age, gender, best corrected visual acuity (BCVA, logMAR), slit lamp-assisted biomicroscopy of the anterior segment, intraocular pressure, fluorescein angiography (FA), SD-OCT (Spectralis Heidelberg Engineering, Heidelberg, Germany), and OCTA using the AngioVue OCTA system version 2017.1 (Optovue Inc., Fremont, CA, USA).

**Macular microvascular OCTA imaging**

Macular OCT angiograms were acquired using the AngioVue OCTA system version 2017.1 (Optovue Inc., Fremont, CA, USA) with the Angio Retina mode. A newly developed 3D projection artifact removal (PAR) algorithm was included in the software. With this algorithm, the software differentiates in situ OCTA signal from projection artifacts based on the information from OCT and OCTA volume and removes the projection artifacts.

For each eye, a 3 × 3-mm volume image centered on the fovea was obtained. The scan pattern was a 304 B-scan raster with 304 A-scans per B-scan. Two orthogonal volumes were acquired at each scanning location. The AngioVue software segmented the vascularized tissue into four layers based on the default settings: the superficial vascular complex (SVC), the deep vascular complex (DVC), the outer retinal layer, and the
choriocapillaris layer. The boundaries of the superficial network extended from the internal limiting membrane to 10 μm above the inner plexiform layer (IPL). The deep capillary network extended from 10 μm above the IPL to 10 μm below the outer plexiform layer (OPL) no overlap existed between the 2 slabs.

FAZ metrics including size, perimeter, foveal acircularity index (AI), and foveal vessel density 300 (FD-300) were evaluated with the software (Table 3). AI is the ratio between the measured perimeter and the perimeter of the same size circular area: the closer the shape is to the circle, the closer the value is to 1. FD-300 is the vessel density in a 300-mm wide area surrounding the FAZ, including both SVC and DVC. FAZ area is excluded in measurement of vessel density in this area, due to its high variability among different individuals. The value of FD-300 is a compliment to FAZ metrics and have been used to detect early signs of diabetic retinopathy in previous studies[17].

**Radial peripapillary capillary measurement**

A 4.5*4.5mm rectangle scan centered on ONH was obtained for each eye with AngioVue OCTA system using Angio-Disc mode. The software automatically fits a circle with a diameter of 2.0 mm, centered on ONH, and defines a circle 2.0 mm wide that extends from the optic disc as the peripapillary region. The peripapillary region was divided into eight regions automatically based on Garway-Heath method[18], designated as nasal superior (NS), nasal inferior (NI), inferior nasal (IN), inferior temporal (IT). Temporal inferior (TI), temporal superior (TS), superior temporal (ST) and superior nasal (SN). Vessel densities of the whole image, inside disc and each sector of peripapillary area were generated by the software automatically.

We divided our patients into two sub groups according to the location (superior or inferior) of the affected vein and compared vessel density in each sector of the superficial and deep vascular plexus and RPC in each group.
All scans were reviewed by two experts for correctness of automated layer segmentation, as well as for FAZ delineation. In case of segmentation errors, manual correction was performed by the examiners until agreement achieved.

**Statistical analysis**

Statistical analysis was performed using a commercially available statistical software program (SPSS for Mac, version 25.0; IBM/SPSS, Chicago, IL, USA). Continuous variables are presented as mean and SD. Paired t test was used to compare the demographics and evaluate the difference in macular metrics, FAZ parameters and peripapillary vessel densities between the eyes with BRVO and the clinically unaffected fellow eyes. Unpaired t test was used to evaluate difference between clinically unaffected contralateral eyes and normal control eyes. A two-tailed P value of < 0.05 was considered statistically significant.

**Results**

**Patients' Demographic and Clinical Characteristics**

Out of 57 primarily enrolled patients, 7 patients were excluded due to poor quality of the OCTA images, 1 patient was excluded due to lack of FAZ zones in both eyes, 2 patients were excluded due to diabetic retinopathy, so that the study eventually included 47 eyes of 47 patients (22 men) with a mean age of 55.0 ± 11.0 years (median, 55.0 years; range, 25–82 years). All patients had unilateral involvement. The right-eye to left-eye ratio was 30:17. The superior temporal branch vein was occluded in 38 patients, the inferior temporal branch vein was occluded in 8 patients, and the superior nasal branch vein was occluded in 1 patient. The mean presenting BCVA was logMAR 0.440 ± 0.324. The mean duration of the symptoms of BRVO was 8.3 ± 14.7 months (0.5–46 months). The mean BCVA for the contralateral eyes was logMAR 0.096 ± 0.143 (Table 1). The foveal retinal thickness was significantly (P < 0.001) thicker in eyes affected with BRVO than in the contralateral unaffected eyes. (Table 2). For the normal control group, the mean age was
53.9 ± 13.03 years (median, 56.0 years; range, 27–73 years). The mean BCVA was logMAR 0.040 ± 0.116. The foveal retinal thickness was 248 ± 19μm, not significantly differed from the contralateral unaffected eyes (P >0.05).(Table 3)

**Macular Vessel Density**

Eyes affected by BRVO had significantly lower vessel density in both the SVC (P < 0.05) and DVC (P < 0.05) compared with the contralateral unaffected eyes in OCTA images. In the BRVO group, the FAZ is more irregular in shape compared with that in the contralateral eyes. The size (P < 0.05) and perimeter of FAZ (P < 0.05) were significantly larger in BRVO eyes than fellow eyes. The AI was higher (P < 0.05) and foveal vessel density 300 was lower (P < 0.05) in BRVO eyes compared with the contralateral unaffected eyes[Table 2]. The contralateral eyes showed lower SVC in whole area, especially in temporal area and superior area of macular region (P < 0.05), compared with normal control eyes. FD-300 was significantly lower in contralateral unaffected eyes than in normal control eyes (P < 0.05). (Table 3)

In sub group analysis, we found vessel density was significantly lower in all sectors (P < 0.05) except foveal region in SVC and DVC in eyes with superior vein occlusion. Vessel density was significantly lower in inferior (P < 0.05) and nasal (P < 0.05) sectors in SVC and in all sectors except foveal region in DVC in eyes with inferior vein occlusion. (Fig. 1)

**Fig.1** Vessel density of SVC and DVC (a-b in macular region of superior vein occlusion group and c-d in inferior vein occlusion group. *, P<0.05; SVC, superficial vascular complex; DVC, deep vascular complex

**Peripapillary vessel density**

The average vessel density of the whole, inside disc and peripapillary region were 47.7±4.0 ±46.8±6.2 ±49.9±4.2 in BRVO eyes, and 49.9±2.3 ±47.7±5.6 ±52.7±3.0 in contralateral eyes. BRVO eyes has lower vessel density in whole area and peripapillary
area compared with contralateral eyes ($P<0.05$)(Table 4).

The average vessel density of the whole, inside disc and peripapillary region were 50.7±1.6, 50.7±5.3, 53.3±2.2 in normal control eyes. The contralateral unaffected eyes has lower VD in whole area and inside disc area of the peripapillary region ($P<0.05$)( Table 5) compared with normal eyes.

In eyes with superior vein occlusion, vessel density in inferior temporal, temporal superior, superior temporal and superior nasal sectors were significantly lower than contralateral eyes ($P<0.05$). In eyes with inferior vein occlusion, vessel density in inferior nasal, inferior temporal and temporal inferior sectors were significantly lower than contralateral eyes ($P<0.05$)(Fig. 2).

**Fig.2** Vessel density of RPC in (a) superior vein occlusion group and (b) inferior vein occlusion group. RPC, radial peripapillary capillary; s-hemi, superior -hemi; i-hemi, inferior-hemi TS, temporal superior; ST, superior temporal; SN, superior nasal; IT, inferior temporal; TI, temporal inferior; IN, inferior nasal; *, $P<0.05$

**Discussion**

In this study, we quantified vessel density in macular region using OCTA. Our study revealed that vessel density in BRVO eyes was significantly lower in affected and adjacent sectors in superficial retinal layer and in all regions except for the foveal region in deep retinal layer compared with contralateral unaffected eyes.

The decrease of vessel density in macular region was in accordance to previous studies that applied OCTA to measure vessel densities in retinal vein occlusion patients[7, 19-22].

In a previous BRVO study by Samara’s group, vessel densities in macular region were measured by sector and researchers found vessel density in affected sector of BRVO eyes was lower than fellow eyes in both superficial and deep network, while vessel density in the unaffected sector of BRVO eyes was also lower than fellow eye in deep network[23].
What’s more, affected sector was defined as superior or inferior quadrant of a circular grid in Samara’s study, so they only compared superior and inferior sectors in their research. Changes in nasal and temporal regions were not discussed in their work. Coscas et al. found that nonperfusion areas were more frequent in deep capillary plexus[7], suggesting that DCPs were more vulnerable to ischemic attack. Freund et al. discovered that collateral vessels mainly existed in deep vascular complex, supporting a continuous arrangement of superficial and deep vascular complexes and venous drainage through the deep vascular complex[24]. Agreed with previous study, our result suggested DCP was more vulnerable to ischemic changes and BRVO may cause a more extensive vascular alteration.

Recent studies found enlarged FAZ in superficial and deep retinal layer in BRVO eyes[23, 25, 26], which was negatively correlated with visual acuity[23, 25, 27]. In our study, FAZ area and perimeter were larger in BRVO eyes compared with fellow eyes, which agreed with previous reports. Besides, we also found a larger Al and lower FD-300 in BRVO affected eyes compared with fellow eyes. Wons et al. measured the angle between the maximum FAZ diameter and the papillomacular plane in RVO eyes and contralateral unaffected eyes and found a significant difference between the two groups. According to their research, eyes with RVO showed an asymmetrical FAZ and an unorganized capillary structure[28]. Previous studies has suggested that FAZ size may vary considerably in normal individual and causing a significant overlap among healthy and diseased individuals[29, 30], making it difficult to recognize difference between study groups. Recently, a new parameter Al was described by Tam et al. to quantify the irregularity of FAZ[13], which has been proved to be a useful parameter evaluating the asymmetry of the FAZ, providing information about the ischemic status of diseased eyes[12]. Our result agreed with Won’s study and showed that BRVO affected eyes are more irregular in shape.
compared with fellow eyes. This was the first study, to the best of our knowledge, to describe the asymmetry of FAZ in BRVO eyes with AI. Decrease in FD-300 reflects vascular drop out around foveal region and has been proved to be a useful parameter in diabetic retinopathy[17]. No significant difference was found in foveal vessel density in superficial or deep vessel complex in our study. This could be the caused by the scarcity of vessels in FAZ region. However, when the quantified area skipped FAZ and extend to 300μm area surrounding FAZ vascular drop out became obvious. A lower vessel density of SVC in contralateral unaffected eyes compared with normal control eyes was another discovery in our study, which agreed with Wang’s research[19]. This may suggest that BRVO may be the result of systemic changes in both eyes and vascular drop out may have happened prior to BRVO event. Interestingly, decrease of VD was only found in SVC in contralateral eyes, which also agrees with Wang’s result. This may indicate that the underlying mechanism of vascular drop out in contralateral eyes was different from the blockage of vessels in BRVO eyes. Besides, we also found that FD-300 in contralateral eyes was also lower compared with normal control eyes, while no difference was found regarding AI, FAZ size, and FAZ perimeter between the two groups. This may indicate that vascular drop out around FAZ is sensitive in the contralateral eyes.

Radial peripapillary capillary dropout was another important discovery in our study. Wang et al. measured flow velocity of veins merging from optic disc and found a slower flow velocity in the occluded hemisphere[31]. Recent studies found a reduction of peripapillary choroidal thickness in BRVO affected and nonaffected eyes in unilateral BRVO patients, suggesting BRVO may be associated with a hypoxic attack to the peripapillary choroid[11, 32]. Shin et al. found that the peripapillary vessel density and perfusion density were decreased in the fellow eyes of unilateral BRVO patients[16], indicating RVO may cause structural abnormality even in fellow unaffected eyes. However, Wang’s study only
measured large vessels around optic disc while Shin’s research measured both large vessels and radial peripapillary capillaries. In our study, we measured radial peripapillary capillaries around optic nerve head with the installed software and found a significant decrease of peripapillary radial peripapillary capillary density in the affected sectors of BRVO eyes. Similar to Shin’s research, we also found vascular drop out of peripapillary vessels in contralateral unaffected eyes. However, vascular drop out stands out in the inside disc region, which disagrees with Shin’s study. Since we use different apparatus and the area we measured was different, the result could be influenced by these factors. Further study is in need to reveal the most vulnerable area of vascular drop out in peripapillary regions. To our knowledge, this is the first report to quantify radial peripapillary capillary change in BRVO affected eyes.

In normal human eyes, ONH is supplied by the posterior ciliary artery and central retinal artery, which is also the blood supply of superficial RNFL layer of ONH. RPCs are straight, oriented superficial vessels that are paralleled to each other and arched to supply RNFL around the ONH[33-35]. Fluorescein angiography (FA) has been used to evaluate ONH perfusion for several decades. However, FA requires dye injection and it is difficult to observe RPCs with this traditional method. OCTA is advantageous for evaluating ONH perfusion because of its non-invasive nature. RPCs can be easily visualized and vascular perfusion status can be quantified within minutes with OCTA. RPC drop out has been reported in glaucoma[36] and diabetes mellitus[37] patients, and has been considered as a useful parameter evaluating vascular dysfunction. Current research has found a correlation between mean RPC density and mean RNFL thickness[34]. Decreasing of RNFL thickness was found with OCT in RVO eyes[32, 38, 39], suggesting retinal nerve fiber atrophy may be the result of RVO as the disease progressed. In our study, PRC was lower in BRVO eyes compared with fellow eyes, especially in the affected sectors. However, no
significant thinning of RNFL was observed in either the affected sector or the unaffected sector (data not shown), which disagreed with previous studies. This could be explained by the discrepancy of patients included in our research since we included both treatment naïve patients and those who has been treated. ONH swelling is usually observed in treatment naïve patients at the early stage of BRVO and this can influence the average RNFL thickness. However, the underlying swelling of RNFL may have little impact on RPC and the decrease of RPC density was prominent in our research.

There are a few limitations in this study. First, the study is a retrospective study and lacks longitudinal data. A longitudinal study is necessary to elucidate vascular changes with treatments. Besides, there is likely a selection bias due to the limited sample size. In addition, we did not measure vessel density of choriocapillaris in macular and ONH region. Artifacts such as projection and shadow may influence the accuracy of the measurement of choriocapillaris[40]. We scanned a 3*3mm² area of the foveal and 4.5*4.5mm² area of the ONH and these regions were relatively small. A larger scanning region with high accuracy may bring out more information of perfusion status. Future studies may be able to evaluate a thorough status of perfusion and vascular changes in a larger scale in BRVO eyes with the updated OCTA techniques.

Conclusions

In conclusion, our study demonstrated OCTA with upgraded software enhanced with 3D PAR provides high-resolution images and quantitative information of microvascular parameters of not only macular, but also peripapillary vascular in BRVO eyes. Vascular density of SVC and DVC in macular region was much lower in BRVO eyes compared with fellow eyes. SVC was significantly lower in affected sectors while all sectors in DVC were decreased in affected eyes. In addition to enlarged FAZ area and perimeter, larger AI and
lower FD-300 are prominent in BRVO eyes and can be used to evaluate the asymmetry and ischemic status of foveal region. More importantly, lower RPC density was another feature of BRVO affected eyes and RPC density can be a useful parameter to evaluate perfusion status of ONH in BRVO. Unaffected eyes of unilateral BRVO showed vascular abnormalities in superficial retinal layer, peri-FAZ area and also peripapillary regions.

List Of Abbreviations

RVO: Retinal vein occlusion; FAZ: foveal avascular zone; ONH: optic nerve head; VD: Vessel density; SVC: superficial vascular complex; DVC: deep vascular complex; RPC: radial peripapillary capillary; AI: acircularity index; FD-300: foveal vessel density 300; CRVO: central retinal vein occlusion; SD-OCT: spectral-domain optical coherence tomography; HRVO: hemicentral retinal vein occlusion; BCVA: best corrected visual acuity; FA: fluorescein angiography; IPL: inner plexiform layer; OPL: outer plexiform layer; NS: nasal superior; NI: nasal inferior; IN: inferior nasal; IT: inferior temporal; TI: temporal inferior; TS: temporal superior; ST: superior temporal; SN: superior nasal.

Declarations

**Ethics approval and consent to participate:**

The study adhered to the tenets of the Declaration of Helsinki and was approved by PUMCH. Written informed consent was obtained from all subjects (and the parents/guardians of any minors included as participants). The research was approved by the institutional review board of PUMCH (approval number: S-K631).

**Consent for publication:**

Written informed consents were obtained from all participants for the publication of clinical information and images.

**Availability of data and materials:**
The datasets presented in this study is available from the corresponding author upon request.

**Competing interests:**

The authors declare that they have no conflict of interest.

**Funding:**

Not applicable.

**Authors' contributions:**

CLL interpreted data, drafted this manuscript and reviewed the literature. YMZ and SL helped design the work. YMZ, WYL and SL collected the data. WYL and SL analyzed the data. YMZ and WYL revised the manuscript. CYX final approval. All authors have read and approved the final manuscript.

**Acknowledgements:**

Not applicable.

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Tables

Table 1 Demographics and clinical characteristics of patients with BRVO
| Variables                        | Mean ± Standard Deviation |
|---------------------------------|---------------------------|
| BRVO eyes                        | 47                        |
| Age, y, mean±SD                  | 55.0±11.0 (range, 25–82)  |
| Sex, male/female                 | 22/25                     |
| Affected eye, OD/OS              | 30/17                     |
| BCVA of BRVO eyes                | 0.440 ± 0.324             |
| BCVA of fellow eyes              | 0.096±0.143               |
| Symptom duration of BRVO         | 8.3 ± 14.7(range 0.5–46 months) |
| Superior/inferior, no            | 39/8                      |

Table 2 Macular measurements in BRVO eyes and fellow eyes
| Variables                        | Eyes with BRVO (n=47) | Contralateral unaffected eyes (n=47) | P value (paired t test) |
|---------------------------------|-----------------------|--------------------------------------|------------------------|
| BCVA                            | 0.440 ± 0.324         | 0.096 ± 0.143                       | <0.001                 |
| Foveal retinal thickness(μm)    | 321±113               | 248±20                               | <0.001                 |
| Vascular density in SVC (%)     |                       |                                      |                        |
| whole                           | 40.4±4.0              | 45.6±3.5                             | <0.001                 |
| foveal                          | 15.5±5.0              | 15.5±5.9                             | 0.960                  |
| temporal                        | 41.3±5.3              | 47.3±3.5                             | <0.001                 |
| superior                        | 42.2±7.5              | 50.1±3.9                             | <0.001                 |
| nasal                           | 42.7±6.0              | 47.5±4.0                             | <0.001                 |
| inferior                        | 44.6±5.5              | 49.8±4.0                             | <0.001                 |
| Vascular density in DVC (%)     |                       |                                      |                        |
| whole                           | 42.9±5.0              | 50.0±3.0                             | <0.001                 |
| foveal                          | 28.2±9.3              | 29.8±8.0                             | 0.158                  |
| temporal                        | 44.0±7.1              | 52.7±3.0                             | <0.001                 |
| superior                        | 41.1±8.8              | 52.0±3.6                             | <0.001                 |
| nasal                           | 46.2±6.4              | 52.8±3.2                             | <0.001                 |
| inferior                        | 46.0±7.4              | 52.2±3.8                             | <0.001                 |
| FAZmm2                          | 0.394±0.260           | 0.325±0.136                          | 0.046                  |
| FAZ perimetermm                 | 2.589±1.108           | 2.255±0.503                          | 0.031                  |
| AI                              | 1.23±0.13             | 1.14±0.04                            | <0.001                 |
| FD-300%                         | 45.66±6.04            | 49.21±4.46                           | <0.001                 |

Table 3 Macular measurements in contralateral eyes and normal control eyes
| Variables                        | Contralateral unaffected eyes (n=47) | Normal control eyes (n=47) | P value (unpaired t test) |
|---------------------------------|-------------------------------------|---------------------------|--------------------------|
| BCVA                            | 0.096±0.143                         | 0.040 ± 0.116             | 0.056                    |
| Foveal retinal thickness(μm)    | 248±20                              | 248±19                    | 0.954                    |
| Vascular density in SVC (%)     |                                     |                           |                          |
| whole                           | 45.6±3.5                            | 47.2±2.6                  | 0.015                    |
| foveal                          | 15.5±5.9                            | 15.6±6.6                  | 0.963                    |
| temporal                        | 47.3±3.5                            | 48.8±2.9                  | 0.022                    |
| superior                        | 50.1±3.9                            | 51.5±2.8                  | 0.047                    |
| nasal                           | 47.5±4.0                            | 48.7±5.3                  | 0.204                    |
| inferior                        | 49.8±4.0                            | 51.1±3.2                  | 0.094                    |
| Vascular density in DVC (%)     |                                     |                           |                          |
| whole                           | 50.0±3.0                            | 50.5±3.3                  | 0.451                    |
| foveal                          | 29.8±8.0                            | 28.7±5.5                  | 0.803                    |
| temporal                        | 52.7±3.0                            | 53.7±3.2                  | 0.141                    |
| superior                        | 52.0±3.6                            | 53.0±3.2                  | 0.142                    |
| nasal                           | 52.8±3.2                            | 53.9±2.9                  | 0.090                    |
| inferior                        | 52.2±3.8                            | 52.9±3.9                  | 0.340                    |
| FAZmm2                          | 0.325±0.136                         | 0.352±0.090               | 0.270                    |
| FAZ perimeter mm                | 2.255±0.503                         | 2.345±0.348               | 0.316                    |
| AI                              | 1.14±0.04                           | 1.14±0.04                 | 0.686                    |
| FD-300%                         | 49.21±4.46                          | 51.39±3.56                | 0.010                    |

Table 4 Peripapillary vessel density in BRVO eyes and fellow eyes
| Variables                  | Eyes with BRVO (n=47) | Contralateral unaffected eyes (n=47) | P value  |
|----------------------------|----------------------|-------------------------------------|----------|
| whole(%)                   | 44.7±4.0             | 49.9±2.3                            | <0.001   |
| Inside disc(%)             | 46.8±6.2             | 47.6±5.4                            | 0.390    |
| Peripapillary(%)           | 47.8±5.6             | 52.8±3.1                            | <0.001   |
| nasal superior(%)          | 44.1±5.6             | 48.9±4.7                            | 0.159    |
| nasal inferior(%)          | 47.2±5.8             | 47.9±4.8                            | 0.410    |
| inferior nasal(%)          | 49.4±9.1             | 52.5±4.2                            | 0.035    |
| inferior temporal(%)       | 52.9±9.3             | 58.4±4.5                            | <0.001   |
| temporal inferior(%)       | 52.4±6.4             | 53.3±5.0                            | 0.337    |
| temporal superior(%)       | 54.4±4.2             | 56.7±3.7                            | 0.005    |
| superior temporal(%)       | 49.0±7.9             | 56.6±4.1                            | <0.001   |
| superior nasal(%)          | 47.4±7.4             | 51.3±4.5                            | <0.001   |

Table 5 Peripapillary vessel density in contralateral unaffected eyes and normal control eyes.

| Variables                  | Contralateral unaffected eyes (n=47) | Normal control eyes (n=47) | P value  |
|----------------------------|-------------------------------------|---------------------------|----------|
| whole(%)                   | 49.9±2.3                            | 50.7±1.6                  | 0.040    |
| Inside disc(%)             | 47.6±5.4                            | 50.7±5.3                  | 0.007    |
| Peripapillary(%)           | 52.8±3.1                            | 53.2±2.2                  | 0.467    |
| nasal superior(%)          | 48.9±4.7                            | 49.1±4.0                  | 0.798    |
| nasal inferior(%)          | 47.9±4.8                            | 48.7±4.1                  | 0.394    |
| inferior nasal(%)          | 52.5±4.2                            | 53.0±3.6                  | 0.588    |
| inferior temporal(%)       | 58.4±4.5                            | 58.4±3.5                  | 0.953    |
| temporal inferior(%)       | 53.3±5.0                            | 53.7±3.3                  | 0.642    |
| temporal superior(%)       | 56.7±3.7                            | 57.6±2.6                  | 0.174    |
| superior temporal(%)       | 56.6±4.1                            | 56.9±3.1                  | 0.719    |
| superior nasal(%)          | 51.3±4.5                            | 51.2±4.2                  | 0.855    |

Figures
Figure 1

Vessel density of SVC and DVC in macular region of superior vein occlusion group and inferior vein occlusion group. *, P<0.05; SVC, superficial vascular complex; DVC, deep vascular complex

Figure 2

Vessel density of RPC in (a) superior vein occlusion group and (b) inferior vein occlusion group. RPC, radial peripapillary capillary; s-hemi, superior -hemi; i-hemi, inferior-hemi TS, tempo superior; ST, superior tempo; SN, superior nasal; IT, inferior tempo; TI, tempo inferior; IN, inferior nasal; *, P<0.05
