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Original article

Correlations between Optical Coherence Tomography Angiography Parameters and the Visual Acuity in Patients with Central Retinal Vein Occlusion

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Abstract

Background: Central retinal vein occlusion (CRVO) is the second most common retinal vascular disorder next to diabetic retinopathy. **This study aimed to** study the optical coherence tomography angiography (OCTA) findings in patients with central retinal vein occlusion (CRVO) and their relationship to the best correct visual acuity (BCVA) at presentation. **Subject and Methods:** A total of 40 cases with CRVO were evaluated. Patients were grouped into 2 groups according to BCVA at presentation, group I with BCVA≤ of 1.0 logMAR and group II with BCVA > 1.0 logMAR. OCTA studies were performed after resolution of the cystoid macular edema (CME) following a serial of intravitreal anti vascular endothelial growth factors (VEGF) injections to ensure reliability of the data. OCTA findings were recorded and correlated to BCVA. **Result:** Regarding FAZ diameter it was significantly larger in cases with BCVA > 1.0 LogMAR (0.71) than study group with BCVA ≤ 1.0 LogMAR (0.39) (P<0.001). Regarding SVD, SFVD, SPFVD, DVD, DFVD, DPFVD, it was significantly lower in study group with BCVA > 1.0 than study group with BCVA ≤ 1.0. **Conclusion:** OCTA is a fast, noninvasive, and effective examination for CRVO that can display the vascular density and the FAZ area quantitatively and distinctly. An enlarged FAZ area and disruption of the foveal avascular zone correlated significantly with poorer visual outcomes.

Keywords: Optical Coherence Tomography Angiography; Visual Acuity; Central Retinal Vein Occlusion

Introduction

Central retinal vein occlusion (CRVO) is the second most common retinal vascular disorder next to diabetic retinopathy. It can

be divided into ischemic and non-ischemic CRVO according to the non-perfusion (NP) area of retinal capillaries caused by obstruction. Retinal ischemia is the main complication of CRVO and may result in macular ischemia which limits visual recovery and/or in anterior segment neovascularization and neovascular glaucoma (NVG) [1].

OCTA is a recently developed non-invasive technology that allows analysis of retinal microvasculature without the need for dye injection [2]. A variety of vascular illnesses may benefit from OCTA's non-invasive imaging of the superficial and deep retinal capillary network, as well as its ability to show the FAZ and measure vessel density in great detail [3]The deep capillary plexus can scarcely be seen on FA, but with the advent of OCTA, it is feasible to analyze this layer in separate from the superficial vascular plexuses [4].

To study the vascular changes in eyes with CRVO using OCTA, it is important to look at the retina layer by layer. Retinal histology shows four different retinal vascular layer that are split into 2 complexes, but in clinical practice it is best to look at the superficial and deep capillary plexuses [5].

Even though people's vision often gets better after a serial of intravitreal anti vascular endothelial growth factors (VEGF) injections, morphological signs that can be seen by OCTA stay the same over time in the occlusion area. The use of OCTA made it possible to watch how macular ischemia developed and changed over time [6].

The aim of the current study was to assess the correlation between best corrected visual acuity (BCVA) and different OCTA parameters in patients with CRVO.

Patients and methods:

This is a prospective observational clinical study which was conducted on 40 patients with the diagnosis of CRVO at Banha University Hospital from the period June 2022 to June 2023 who were grouped into 2 groups according to BCVA at presentation, group I with BCVA of >1.0 LogMAR and group II with BCVA ≤ 1.0 LogMAR. Inclusion criteria included patients with age ≥ 18 years old with confirmed ophthalmologic diagnosis of CRVO in less than 6 months prior to screening. All patients received multiple intravitreal injections with anti-VEGF to treat resultant cystoid macular edema. We excluded eyes with prior history of laser treatment, eyes with coexisting macular disease as diabetic retinopathy and age-related macular degeneration, eyes with glaucoma, uveitis or pathological optic nerve diseases, and eyes with significant media opacities interfering with OCTA imaging.

Ophthalmological examination:

All patients underwent a full ophthalmological examination including

slit-lamp examination, refraction, BCVA using Snellen chart (expressed as LogMAR for statistical analysis), IOP measurement by applanation tonometry, and dilated fundus examination. OCTA scans were performed for all subjects using the RTVue XR OCT Avanti System with AngioVue version 2018.0.0.18 (Optovue, Fremont, CA, USA). Scan acquisition protocol including AngioVue HD imaging retinal scan size 6×6 mm^2, 400×400 pixels (two repeats/B-scan), scan time 3s, axial resolution 5 µm and transversal resolution 15 µm. En face, A-scan and B-scan angiography images of both the superficial vascular plexus (SVP) and deep vascular plexus (DVP) were used for analysis. The automated measured OCTA parameters were the foveal avascular zone (FAZ) area in mm^2, the superficial vascular density (SVD), the superficial foveal vascular density (SFVD), the superficial parafoveal vascular density (SPFVD), the deep vascular density (DVD), the deep foveal vascular density (DFVD) and the deep parafoveal vascular density (DPFVD). The vessel density was automatically calculated in two circular rings after excluding the FAZ area, the parafoveal area in a circular zone of 3 mm diameter and the whole area in a circular zone of 6 mm diameter. The vessel density was demonstrated as a percentage by taking the ratio of the total vessel area to the total area of analyzed region. The central retinal thickness was recorded from a 6×6 mm^2 area on the B-scan map.

Approval code: All Patients were recruited from the Medical Retina subspeciality outpatient clinic in the Ophthalmology department at Banha University Hospital. Every patient signed an informed consent, and all procedures were carried out in accordance with the Declaration of Helsinki, and the study was approved by the local ethics committee, Benha Faculty of Medicine Research Ethics Committee (approval number Ms 29-11-2020) from the period June 2022 to June 2023.

Statistical analysis:

Clinical data were recorded in a report form. These data were tabulated and analyzed using the SPSS (Statistical package for social science) version 20 software. Descriptive statistics were calculated for the data in the form of:

1. Mean and standard deviation (± SD) for quantitative data.
2. Frequency and distribution for qualitative data.

In the statistical comparison between different groups, the significance of difference was tested using Student's t-test which was used to compare mean of two groups of quantitative data. A P value <0.05 was considered statistically significant (*) while > 0.05 was considered statistically insignificant. P value of <0.01 was considered highly significant (**) in all analyses.

Results

40 patients with CRVO were divided into two groups:

Group (I): 15 patients with BCVA> 1.0 LogMAR at 1st presentation.

Group (II): 25 patients with BCVA≤ 1.0 LogMAR at 1st presentation.

The patients' age ranged from 43 to 64 years with a mean of 56.23 (± 6.5). The study included 18 male patients (45%) and 22 female patients (55%) female. 45% of patients were diabetics, 60% of patients were hypertensive and 45% of patients had hyperlipidemia **(Table 1)**.

There was less improvement in BCVA in study group with BCVA>1.0 LOGMAR **(Table 2).**

All patients received serial intravitreal anti-VEGF injections to allow consistent OCTA measurements after resolution of cystoid macular edema. Range of monthly intravitreal injection frequency was 2-6 injections with an average of (5) injections in Group I and (3) injections in Group II **(Table 3)**.

Regarding FAZ diameter it was significantly larger in cases with BCVA > 1.0 LogMAR (0.71) than study group with BCVA ≤ 1.0 LogMAR (0.39) (P<0.001). Regarding SVD it was significantly lower in study group with BCVA > 1.0 LogMAR (36.5%) than study group with BCVA ≤ 1.0 LogMAR (44.46%) (P<0.001). Regarding SFVD it was significantly lower in study group with BCVA > 1.0 LogMAR (14.84%) than study group with BCVA ≤ 1.0 LogMAR (17.70%) (P<0.001). Regarding SPFVD it was significantly lower in study group with BCVA > 1.0 LogMAR (39.79%) than study group with BCVA ≤1.0 LogMAR (44.91%) (P<0.001). Regarding DVD it was significantly lower in study group with BCVA > 1.0 LogMAR (32.03%) than study group with BCVA ≤ 1.0 LogMAR (45.62%) (P<0.001). Regarding DFVD it was significantly lower in study group with BCVA > 1.0 LogMAR (24.24%) than study group with BCVA ≤ 1.0 LogMAR (29.48%) (P<0.001). Regarding DPFVD it was significantly lower in study group with BCVA > 1.0 LogMAR (32.76%) than study group with BCVA ≤ 1.0 LogMAR (47.42%) (P<0.001). Regarding CRT there was no significant difference between study group with BCVA > 1.0 LogMAR (225.38) and study group with BCVA ≤ 1.0 LogMAR (234.33) (P<0.460). Regarding IOP there were no statistically significant difference between study group BCVA > 1.0 LogMAR (13.8) and study group with BCVA ≤ 1.0 LogMAR (13.4) (P<0.79) **(Table 4).**

OCTA of CRVO in a 45-year-old female with BCVA at time of presentation 1.4 (logMAR), underwent previous 5 intravitreal anti VEGF injection **(Figure 1)**.

OCTA of CRVO in a 56 years old female with BCVA at time of presentation 0.8 (logMAR), underwent previous 2 intravitreal anti VEGF injection **(Figure 2)**.

Table (1): Distribution of the studied group according to personal data:

	No (40)	%
Age (yrs)		
mean ± SD	56.23±6.5	
Range	43-64	
Sex		
Male	18	45.0
Female	22	55.0
Side		
Right	20	50.0
Left	20	50.0
Diabetes		
Yes	18	45.0
No	22	55.0
Hypertension		
Yes	24	60.0
No	16	40.0
Hyperlipidemia		
Yes	18	45.0
No	22	55.0

Table (2): Distribution of the studied group according to BCVA.

	No (40)	%
BCVA		
> 1.0 LogMAR	15	37.5
≤1.0 LogMAR	25	62.5

Table (3): Distribution of studied groups according to numbers of IVI, and BCVA at time of presentation and BCVA at time of OCTA examination after intravitreal injection of anti-VEGF (IVI).

		Group I (> 1.0 LogMAR N=15)	Group II (≤1.0 LogMAR N=25)	P value
Numbers of IVI	**M±SD**	4.93±0.70	2.96±0.54	<0.001*
	Median(Range)	5(4-6)	3(2-4)	

LogMAR	**BCVA at time of presentation (40)**		**BCVA at time of OCTA after IVI (40)**	
	No	**%**	**No**	**%**
1.5	3	7.5	1	2.5
1.4	3	7.5	5	12.5
1.3	6	15.0	5	12.5
1.2	0	0.0	2	5.0
1.1	3	7.5	2	5.0
1.0	2	5.0	0	0.0
0.5	3	7.5	7	17.5
0.6	10	25.0	8	20.0
0.8	10	25.0	10	25.0

Table (4): Comparison between the studied groups according to OCTA parameters.

	BCVA > 1.0 LogMAR (15)		**BCVA ≤1.0 LogMAR (25)**		**P value**
	Mean	±SD	Mean	±SD	
FAZ diameter (mm)	0.71	0.32	0.39	0.13	<0.001**
SVD	36.5	2.08	44.46	1.83	<0.001**
SFVD	14.84	2.24	17.70	2.95	<0.001**
SPFVD	39.79	2.14	44.91	2.21	<0.001**
DVD	32.03	1.85	45.62	2.03	<0.001**
DFVD	24.24	2.89	29.48	2.71	<0.001**
DPFVD	32.76	2.37	47.42	2.42	<0.001**
CRT	225.38	39.49	234.33	45.45	0.460
IOP	13.8	1.9	13.4	2.0	0.79

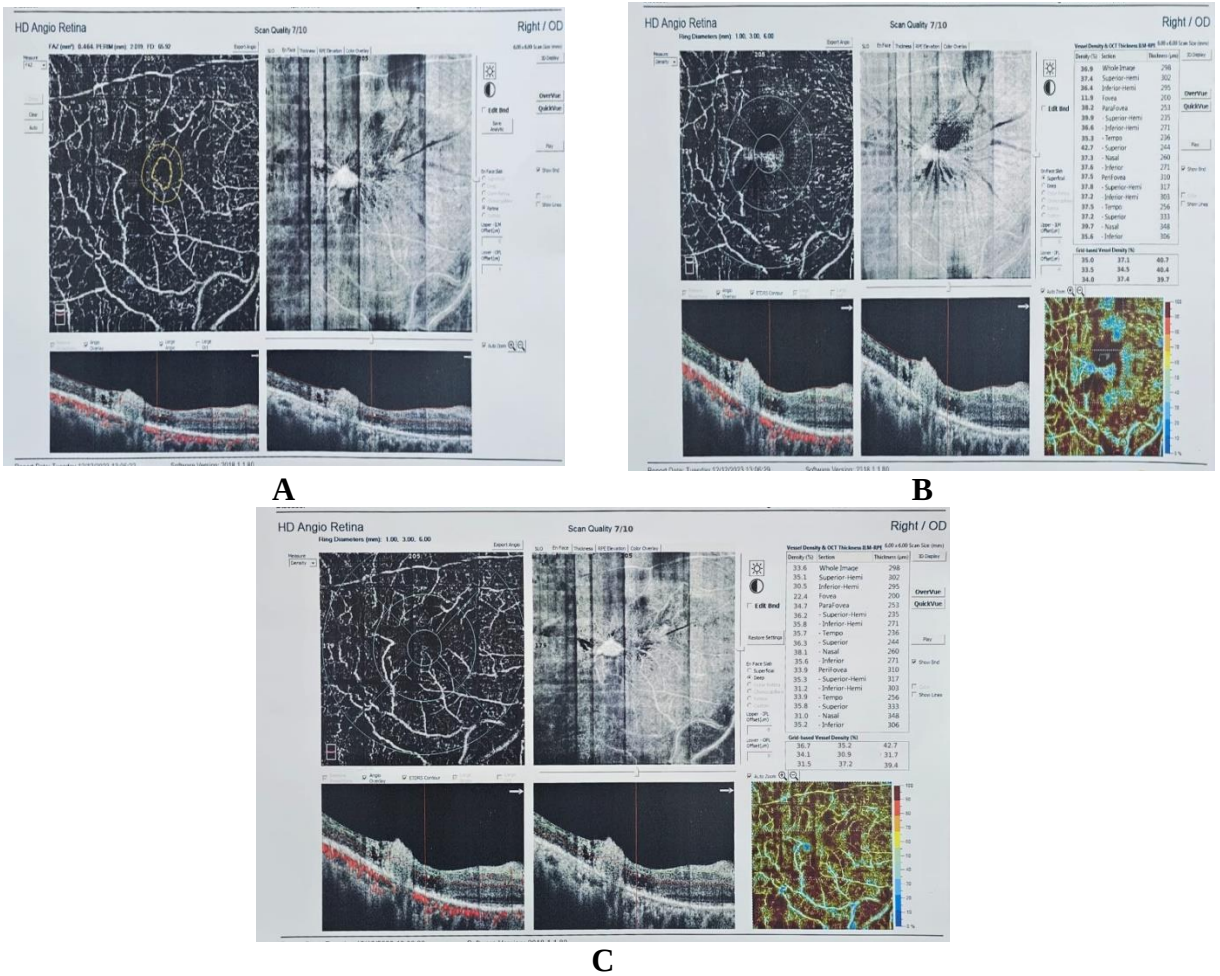

Figure 1: (A) OCT angiogram (6 x 6 mm^2)demonstrating FAZ area (0.464 mm^2), (B)OCT angiogram (6 x 6 mm^2) showing vascular density in SCP, SVD (36.9%), SFVD (11.9%)and SPFVD (38.2%), and (C) OCT angiogram (6 x 6 mm2) showing vascular density in DCP, DVD (33.6 %),DFVD (22.4%)and DPFVD (34.7%)

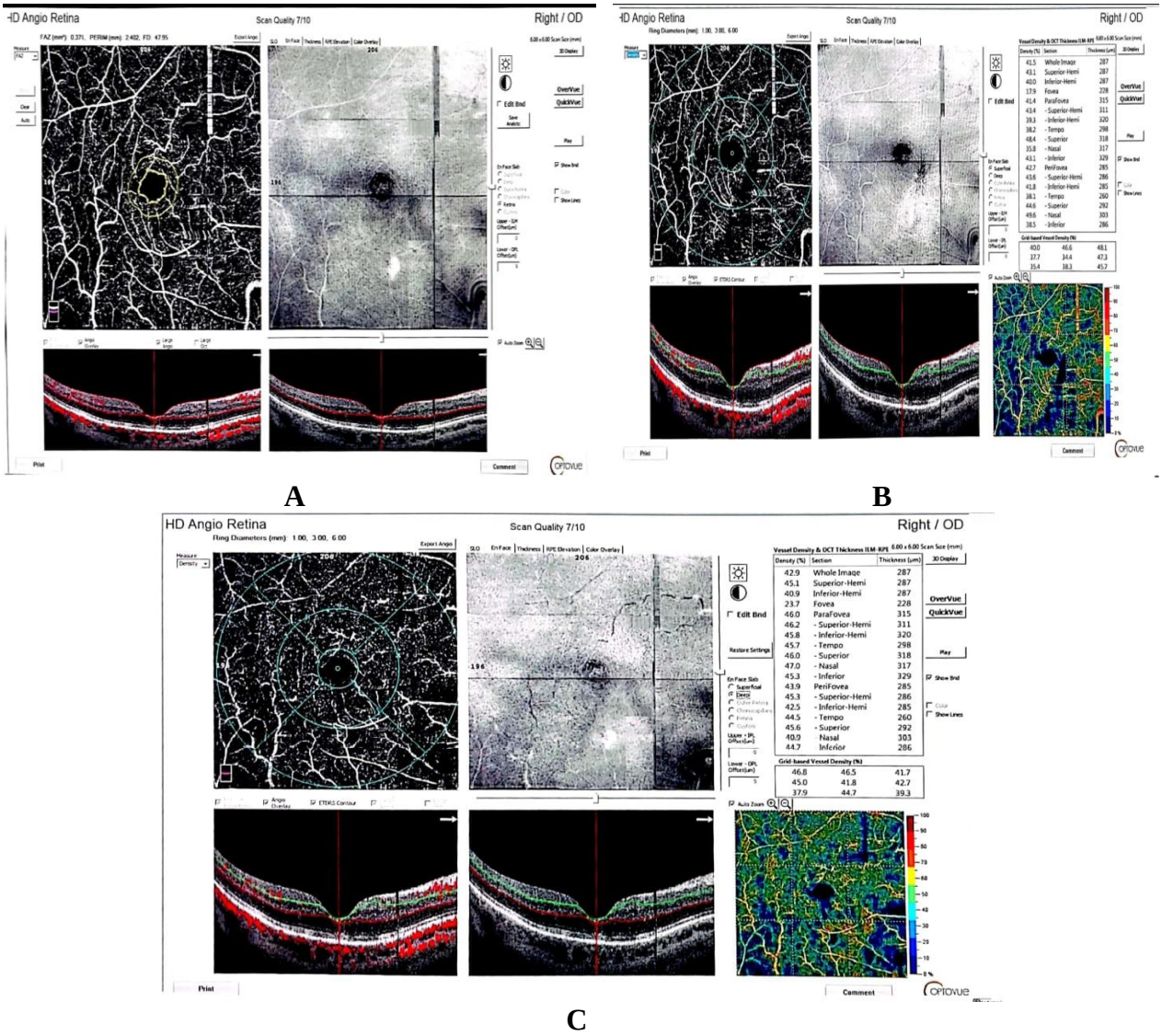

Figure 2: (A) OCT angiogram (6 x 6 mm^2)demonstrating FAZ area (0.371mm^2), (B) OCT angiogram (6 x 6 mm^2) showing vascular density in SCP .SVD (41.5%) , SFVD (17.9%) and SPFVD (41.4%), and (C) OCT angiogram (6 x 6 mm^2) showing vascular density in DCP. DVD (42.9%), DFVD (23.7%) and DPFVD (46%).

Discussion

Optical coherence tomography angiography (OCTA) is a new imaging modality for both choroidal and retinal microvasculature. It allows demonstration of the blood flow in both superficial and deep retinal capillary layers and hence can delineate microvascular changes in case of CRVO, such as FAZ irregularity, areas of capillary dropout and neovascularization, all of which have serious effects on visual acuity [7].

The main advantages of OCTA over other imaging techniques are the shorter acquisition time and being non-invasive and safe process. Fluorescein and indocyanine-green angiography, on the other hand, require an injectable dye which takes time to

reach retinal vessels, and may be associated with systemic adverse effects and even anaphylactic reaction. OCTA technology uses motion contrast to visualizes both the retinal and choroidal vasculature and shows structural and blood flow information in tandem. OCTA scans can be segmented to specific depths and provides accurate size and localization information. It can be obtained within seconds, so scanning is rapid without any side effect with easier follow up and assessment of treatment than any other techniques else [8].

Macular edema is the most common complication of CRVO. It interferes with the automatic segmentation of SCP and DCP, and also affects the automatic quantification of VD and thus accurate analysis of OCTA image [9]. It was divided RVO patients into two groups according to CRT and researched the factors affecting the reproducibility of VD measured by OCTA. They found that the coefficient of variation of VD in the first group (CRT > 400 μm) was much greater than that of the second group (CRT < 400 μm), indicating the increase of CRT caused by macular edema would significantly affect the accuracy of VD measurement. Therefore, in our study, all patients received multiple intravitreal anti-VEGF injections until resolution of macular edema to avoid errors caused by macular edema as much as possible and ensure the reliability of the data [10].

The aim of our study was to demonstrate the impact of the OCTA-detected microvascular changes on the visual outcome in patients with CRVO by analyzing the correlation between best corrected visual acuity and retinal vessel density, as well as the area of FAZ.

In our study, the patient's mean age was 56.23 ± 6.5 years, 45% of patients were males and 55% were females, 45% of patients were diabetic, 60% of them were hypertensive and 45% of the patients had hyperlipidemia. In his study on CRVO cases, It was reported a higher mean age of 68.4 ± 16.3 years with comparable male : female ratio of 57:43% [11]. It was showed a lower mean age compared to our study with an average of 52.47 ± 11.26 years [12].

Adhi et al. [13] used OCTA to measure the FAZ area of normal people in comparison to eyes with retinal vein occlusion, which was 0.30±0.09 mm^2, suggesting that the FAZ area of both groups in our study was larger than that of normal eyes. It also used OCTA to measure the VD of normal people in the SCP and DCP, which were 49.00±2.72 and 53.05±3.26, respectively, suggesting that the VD in the SCP and DCP were decreased in the two groups in this study [14].

This current study showed enlargement of the FAZ area in both study groups. The FAZ area was significantly higher in group (I) with BCVA > 1.0 logMAR (0.71±0.32 mm^2) in comparison to group (II) with BCVA ≤ 1.0 LogMAR (0.39±0.13 mm^2) (P<0.001). This was found to be parallel to the study by Weiting An et al. [14] who found an enlarged FAZ area and significant differences between ischemic CRVO group (0.81±0.47) and non-ischemic CRVO group (0.44±0.16) (P<0.001).

Our study illustrated a positive correlation between FAZ area and BCVA (logMAR). This was found to be consistent with the study that have shown that an enlarged FAZ area correlated significantly with poorer visual outcome [11].

In the present study we found reduction of SVD and DVD. SVD was significantly lower in group (I) with BCVA > 1.0 LogMAR (36.5±2.08) than group (II) with BCVA ≤1.0 LogMAR (44.46±1.83) (P<0.001). DVD was significantly lower in group (I) (32.03±1.85) than group (II) (45.62±2.03) (P<0.001).

Similar results were reported in which, they showed significant decrease in SVD in ischemic group (36.58±5.64) than non-ischemic group (42.50±4.25), and significant decrease in DVD in ischemic group (32.65±4.73) than non-ischemic group (43.98±5.01) [14].

It was showed that eyes with CRVO as compared with fellow eyes and control group showed significant reduction of vascular density in superficial (45.92 ± 4.2 vs. 50.99 ± 4.35 vs. 52.85 ± 2.99) and deep (48.03 ± 4.71 vs. 55.86 ± 3.81 vs. 58.2 ± 2.65) capillary plexuses [15].

In the present study, DFVD was significantly lower in group (I) with BCVA > 1.0 LogMAR (24.24%) than group (II) with BCVA ≤1.0 LogMAR (29.48%) (P<0.001). DPFVD was significantly lower in group (I) (32.76%) than group (II) (47.42%) (P<0.001).

It was showed decrease in SVD (39.79±5.08), SPFVD (41.78±5.50), DVD (38.99±6.82) and DPFVD (40.38±7.43), but showed that SFVD and DFVD were slightly higher in CRVO eyes (20.44±4.85 and 28.20±8.79) this is in contrast to our findings in this study that showed decrease of SFVD and DFVD which were (14.84± 2.24 and 24.24± 2.89) in group (I) and were (24.24± 2.89 and 29.48± 2.71) in group (II) **[16]**.

In previous work, they reported that deep capillary plexus was markedly influenced compared with superficial capillary plexus in RVO [17] and such result is in agreement with the study of two previous study [9, 18] showed that the DCP is more vulnerable to the ischemic change in RVO. This result suggests that ischemic damage by RVO in the DCP, resulting in decreased parafoveal VD, can cause visual acuity impairment.

In this current study we found that there were significant differences in SVD, DVD, SFVD, DFVD, SPFVD, DPFVD and FAZ area between study group (I) and group (II) (P<0.001). and no significant differences in CRT, age and IOP ($P > 0.05$). We found significant negative correlation between SVD, DVD, SFVD, DFVD, SPFVD, DPFVD and LogMAR BCVA.

It was showed that there were no significant differences in SFVD, DFVD and CRT between the ischemic and non-ischemic group ($P > 0.05$) and significant differences in SVD, SPFVD, DVD, DPFVD and FAZ area between the ischemic and non-ischemic group ($P < 0.05$).

Our study limitations were the lack of control group the small sample size. Future research involving bigger numbers and studying the correlation between microvascular OCTA parameters and the functional changes in macular area using other technologies, such as multifocal electroretinography, are needed to assess the relative sensitivity between microvascular damage and macular dysfunction [18].

Conclusion

In conclusion, we have shown that an enlarged FAZ area and disruption of the foveal avascular zone correlated significantly with poorer visual outcomes and that there was a statistically significant decrease in vessel density (VD) in the foveal and parafoveal area in both superficial and deep capillary plexus in eyes with CRVO that was obviously noted with poorer visual outcome. Optical coherence tomography angiography can supply additional information in the evaluation of patients with CRVO and can help us predict patient's long-term visual prognosis.

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