# Vascular Density of Optic Nerve Head among Patients Who Had Central Retinal Vein Occlusion Using Optical Coherence Tomography Angiography

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# ABSTRACT

**Background**: There are a lot of potential benefits and drawbacks of optical coherence tomography angiography (OCTA), one of the most useful retinal imaging procedures, which may detect and diagnose a variety of diseases affecting the retina's blood vessels and optic nerve.

**Objective:** To reveal the effect of central retinal vein occlusion on the vascular density of the optic nerve head using (OCTA) aiming at better understanding the pathophysiology of vein occlusion and providing a guide for management. **Subjects and methods**: Our study was carried out as an observational, case control study, 33 subjects who underwent OCTA at Suez Canal University Hospital, Ismailia, Egypt, were included and were divided according to OCTA findings into 3 groups; ischemic central retinal vein occlusion (CRVO) patients group consisted of 11 patients, non-ischemic CRVO patients group consisted of 11 patients and normal group consisted of 11 subjects.

**Results**: Area under the curve = 1.000, sensitivity = 100%, and specificity = 100% were the results of a very effective discriminative capacity of RPC vessel density in the upper and lower quadrants to distinguish between ischemic and non-ischemic CRVO. Area under the curve = 0.979, sensitivity = 90.9%, and specificity = 100% were achieved when the RPC vessel density cutoff value in the nasal quadrant was 37. This significantly distinguished between ischemic and non-ischemic CRVO. Additionally, the ROC curve showed that macular thickness could not successfully distinguish between ischemic CRVO.

**Conclusion**: Early accurate diagnosis of central retinal vein occlusion (CRVO) must be the major goal of the ophthalmologist while facing these cases from the first second to avoid the probable dangerous sequences.

Keywords: Optic Nerve Head, Central Retinal Vein Occlusion, Optical Coherence Tomography Angiography.

# **INTRODUCTION**

The prevalence of diabetic retinopathy is first, with retinal vein blockage ranking second. Individuals suffering from systemic disorders including diabetes, hypertension, or high cholesterol may develop retinal vein blockage. Fundus fluorescein angiography shed light on the pathogenic mechanisms behind this condition's blindness by revealing the retinal circulation <sup>(1)</sup>. Anaphylaxis and mortality are among the severe adverse effects that might occur as a result of injecting a time-insensitive fluorescein dye during a fundus fluorescein angiography (FFA). Although optical coherence tomography angiography (OCTA) has reduced the invasiveness and speed of this procedure, it is not without its drawbacks, such as the difficulty in differentiating between layers of retinal vessels and the poor presentation of deep vasculature tissues in FFA images <sup>(2)</sup>.

We can also get quantitative data regarding the macular and peripapillary region's perfusion state via OCTA. Retinal vein blockage has been associated with microvascular abnormalities including telangiectasia, microaneurysms, avascular zones, and non-perfusion of retinal capillaries <sup>(3)</sup>.

Quantitative results also showed a reduction in microvascular density across the macula and peripapillary vascular layers. In retinal vascular disorders, there is a decline in the density of the radial peripapillary capillary (RPC) layer, which is a complex network of capillaries radiating from the optic nerve head (ONH)<sup>(4)</sup>.

Clinicians may have an objective way to track the severity of retinal vein occlusion disease, its progression, and the efficacy of treatments if they can routinely and quantitatively assess the retinal microvasculature <sup>(5)</sup>.Analyzing the pros and cons of OCTA as an imaging technique for the retina for the detection and diagnosis of a range of vascular and optical nerve illnesses <sup>(6)</sup>.

This study aimed to better understand the pathophysiology of vein occlusion and provide a management guide by revealing the effect of CRVO on the vascular density of the optic nerve head utilizing (OCTA).

# PATIENTS AND METHODS

This study was carried out as an observational, case control study at Suez Canal University Hospital, Ismailia, Egypt, and many of the cases had health insurance, which afforded the possibility of investigation in private center after approval of REC, Research Ethics Committee of Medicine, Suez Canal University Hospital. 33 patients who were attending Ophthalmic Outpatient Clinic of Suez Canal University Hospitals and matching our inclusion criteria were enrolled in this study.

### **Inclusion criteria:**

- 2- Age: 40-80 years old.
- 3- Cases with CRVO ischemic, non-ischemic group.

<sup>1-</sup> Both sexes.

4- Group of normal cases (not suffering from any lesions either local or systemic) as a control group.

### **Exclusion criteria:**

1- Eyes with media opacity.

2- Previous intraocular surgery or inflammation or trauma.

- 3- Un-cooperative patients for OCTA examination.
- 4- Absence of retinal pathology other than CRVO.
- 5- Patients with glaucoma or ocular hypertension.

All subjects who fulfilled the inclusion criteria were enrolled in the study and were divided into three equal groups as follows:

- Group 1: CRVO eyes (ischemic group).
- Group 2: CRVO eyes (non-ischemic group).
- Group 3: Normal eyes.

All groups were age and sex matched.

### **First group:**

The patients with central retinal vein occlusion (ischemic) with extensive retinal hemorrhage, marked decrease of visual acuity, and afferent pupillary conduction defects, and also ischemia identified in disc diameters by fundus fluorescein angiography.

### Second group:

The patients with central retinal vein occlusion (nonischemic) with clinical picture (dilatation and tortuosity) of all branches of central retinal vein, with flame shaped and dot hemorrhages, cotton-wool spots, and also with mild optic disc edema.

### Third group:

For normal eyes of healthy individuals with normal fundus picture and normal IOP.

# **METHODS**

Clinical data were collected from the three groups and all eyes included in this study underwent careful history taking and complete eye examination as follows:

# 1. History taking:

*Personal data:* The patient's name, age, sex, residency, address, occupation, and phone number.

*Family history:* family history of blood diseases in a first-degree relative.

• *Ocular history:* History of any previous ocular trauma before examination: (a) History of previous ocular surgery before examination. (b) History of ocular medications before examination.

• Data related to exclusion criteria: (High myope) • Systemic history: (a) History of any systemic diseases or chronic illnesses (e.g., Diabetes, Hypertension). (b) History of drug intake (e.g., steroids).

# 2. Ophthalmic Examination:

# A complete eye examination:

Assessment of unaided visual acuity using Landolt C and decimal notation chart were done. External eye examination: Examination of ocular motility. Measurement of refraction with the ARK-1 autorefractometer (NIDEK Co., Aichi, Japan, 2013). Refraction evaluation using the Landolt C chart and decimal notation for optimal corrected visual acuity. In order to check for anterior segment opacity and detect any, a slit-lamp examination was performed (SL-D7 slit-lamp Topcon Co, Tokyo, Japan). Measurement of intraocular pressure using the Haag Streit Benoxinate hydrochloride 0.4% solution (Benox, a property of EIPICO 2005 in Egypt), which was used as a topical anesthetic for the eyes before implantation. The patient underwent a fundus examination with a binocular indirect ophthalmoscope (Model AAIO-7 Appasamy associates 2014, India) and a Volk double aspheric +20.00D lens (Volk optical, Ohio 1988, USA) following two 30-minute intervals following instillation of cyclopentolate 1.0%.

# 3. Fundus fluorescein angiography (FFA):

Fluorescein angiography for all the cases of the study was done. Obtaining high-quality photos required adequate pharmaceutical mydriasis. Formal consent was obtained after the operation was described. We did not forget to mention the potential negative impacts. Color, red-free, and autofluorescence photos were captured while the patient was comfortably seated in front of the fundus camera. Photos were captured at 1-2 second intervals following fluorescein injection to capture the early transit phases. The frequency of the photos was tapered off after the first 5-10 seconds of injection.

### Angiographic phases:

Each phase of an angiography was built on the one before it: choroidal, arterial, arteriovenous, capillary, venous, and late (recirculation). After photographing the early transit phase in the index eye, it was recommended to obtain control photographs of the opposite eye when dealing with monocular disease.

# 4. Optical Coherence Tomography Angiography (OCTA)

The images were captured using the RTVue XR Avanti with AngioVue, a product of Optovue Inc. in Fremont, CA, USA, for optical coherence tomography (OCT) angiography. The gadget has a light source centered at 840 nm, a bandwidth of 45 nm, and an A-scan-rate of 70,000 scans/second, according to its specifications. Three scans of optic disc cubes sized  $4.5 \times 4.5$  mm were analyzed, with the highest quality image (with a signal strength of 70 or greater) selected. Afterwards, the disc scans were reviewed for collaterals, nonvascular disc degeneration (NVD), and evidence of ischemia (in the quadrants around the peripapillary retina).

# Technique for OCTA procedure:

Pupil was dilated 20 minutes (in some cases) before retinal imaging (e.g., uncooperative patients, patients with narrow pupil) using Mydriacyl<sup>®</sup> eye drops (Alcon, Texas, USA). 1-2 drop was repeated after five minutes. Patient was asked to fixate at the device target and maintained his head and chin resting upon the device head frame thus minimizing any ocular or head movement. Patient was alerted that scan taking about 20-30 seconds was started to attain gaze fixation.

Measurements were taken by OCTA device to estimate percentage of: RPC vessel density by centering OCTA scans on the optic disc. Vascular density in the RPC layer was obtained and expressed as a quantitative percentage of large vessels and RPC vascular density was measured in whole image and in the peripapillary regions (superior, nasal, inferior, and temporal quadrants). Trained operators performed all OCTA imaging. Levels of OCTA imaging for the optic nervevitreous/retina (above optic nerve layer OPL). RPC (ILM/NFL). Choroid (Below RPE).

# **Ethical approval:**

This study was approved by the Suez Canal Faculty of Medicine's Suez Canal Medical Ethics Committee. Following receipt of all information, signed consent was provided by each participant. The Helsinki Declaration was adhered to at every stage of the investigation.

### Statistical methods

Spectral domain system RTVue-XR Avanti (Optovue Inc., Fremont, CA, USA) was used for autoanalysis of the resulting scans and images. The data were entered into a computer statistical application called SPSS after being coded. The numerical and percentage forms of qualitative data were used, whereas the mean  $\pm$  standard deviation was used for quantitative data. Receiver Operating Characteristic (ROC) curve analysis: The diagnostic performance of a test, or the accuracy of a test to discriminate diseased cases from non-diseased cases is evaluated using Receiver Operating Characteristic (ROC) curve analysis. A significant p-value was considered when it is equal or less than 0.05.

# RESULTS

When it came to the side of the eye that was measured, there was no discernible difference between the research groups. With respect to BCVA, there was a notable disparity among the three groups that were examined. Despite the lack of a statistically significant difference in IOP across the groups that were tested (Table 1).

| Table               | Table (1): Comparing the studied groups as regards demographic data, side of examined eye, IOP and BCVA |      |                     |                            |                            |                  |          |  |  |
|---------------------|---|------|---------------------|----------------------------|----------------------------|------------------|----------|--|--|
|                     |   |      |                     | Ischemic CRVO<br>patients  | Non-ischemic CRVO patients | Normal           | P value  |  |  |
| S                   | ex  | Fema | ale                 | 5 (45.5%)                  | 5 (45.5%)                  | 5 (45.5%)        | 1        |  |  |
| Cour                | Count (%) Male  |      | le                  | 6 (54.5%)                  | 6 (54.5%)                  | 6 (54.5%)        | 1        |  |  |
| Age (years) Mean±SD |   | ⊧SD  | 60.45±3.50          | 59.09±6.33                 | 56.27±4.73                 | 0.152            |          |  |  |
| I                   |   | Isc  | hemic CRVO patients | Non ischemic CRVO patients | Normal                     | D voluo          |          |  |  |
|                     |   |      |                     | Count (%)                  | Count (%)                  | Count (%)        | P value  |  |  |
| Side                | Let   | ft   |                     | 5 (45.5%)                  | 7 (63.6%)                  | 6 (54.5%)        | 0.602    |  |  |
| Side                | Rig   | ht   |                     | 6 (54.5%)                  | 4 (36.4%)                  | 5 (45.5%)        | 0.095    |  |  |
|                     |   |      | Isc                 | hemic CRVO patients        | Non-ischemic CRVO patients | Normal           | Dualua   |  |  |
|                     |   |      |                     | Mean ±SD                   | Mean ±SD                   | P value          |          |  |  |
| IOP                 | Mean  | -SD  | 20.18±5.04          |                            | 17.73±1.68                 | $16.64 \pm 2.11$ | 0.051    |  |  |
| BCV                 | A Mear  | h±SD | 0.03±0.01           |                            | 0.14±0.04                  | $0.98 \pm 0.04$  | < 0.001* |  |  |

CRVO: Central Retinal Vein Occlusion, IOP: intraocular pressure, BCVA: best corrected visual acuity.

Best corrected visual acuity was significantly lower among ischemic CRVO patients than the non-ischemic CRVO patients. Both ischemic and non-ischemic CRVO patients had significantly lower BCVA when compared to normal individuals (Table 2).

| Table (2): Post-hoc | pairwise com | parison analy | ysis of BCVA, | macular thickness |
|---------------------|--------------|---------------|---------------|-------------------|
|---------------------|--------------|---------------|---------------|-------------------|

|                   | Ischemic CRVO vs<br>Non-ischemic CRVO patients | Ischemic CRVO<br>Vs Normal    | Non-ischen<br>Vs No | nic CRVO<br>rmal |  |
|-------------------|--|-------------------------------|---------------------|------------------|--|
| BCVA (decimal)    | < 0.001*                                       | < 0.001*                      | < 0.0               | 01*              |  |
|                   | Ischemic CRVO patients                         | Non-ischemic CRVO<br>patients | Normal              | P value          |  |
|                   | Mean ±SD                                       | Mean ±SD                      | Mean ±SD            |                  |  |
| Macular thickness | 732.27±265.30                                  | 574.55±75.13                  | 263.82±6.18         | < 0.001*         |  |

In both of ischemic and non-ischemic CRVO patients, the macular thickness was considerably higher than in normal persons. However, there was no discernible difference in macular thickness between ischemic CRVO and non-ischemic CRVO patients (Table 3).

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### Table (3): Post-hoc pairwise comparison of macular thickness

|                   | Ischemic CRVO vs  | Ischemic CRVO | Non-ischemic CRVO |
|-------------------|-------------------|---------------|-------------------|
|                   | Non-ischemic CRVO | vs            | patients          |
|                   | patients          | Normal        | Vs Normal         |
| Macular thickness | 0.081             | < 0.001*      | < 0.001*          |

Regarding RPC vessel density in the superior, nasal, inferior, and temporal quadrants, there were notable disparities across the three groups that were examined (Table 4).

| Table ( | (4): | Comp | baring | the studied | groups | as regards | RPC | vessel | density |
|---------|------|------|--------|-------------|--------|------------|-----|--------|---------|
|---------|------|------|--------|-------------|--------|------------|-----|--------|---------|

|             | Ischemic CRVO patients | Non-ischemic CRVO patients | Normal     | Dyalua   |
|-------------|------------------------|----------------------------|------------|----------|
|             | Mean ±SD               | Mean ±SD                   | Mean ±SD   | P value  |
| VD superior | 34.27±2.69             | 44.55±3.88                 | 55.55±3.91 | < 0.001* |
| VD inferior | 39.00±3.41             | 51.00±1.18                 | 57.00±3.13 | < 0.001* |
| VD nasal    | 34.55±2.66             | 42.82±3.60                 | 56.36±3.04 | < 0.001* |
| VD temporal | 38.45±9.91             | 44.18±2.27                 | 57.09±3.96 | < 0.001* |

VD: vessel density.

Ischemic CRVO patients had significantly lower RPC vessel density in superior quadrant when compared to nonischemic CRVO patients. Both ischemic and non-ischemic CRVO patients had significantly lower RPC vessel density in superior quadrant when compared to normal individuals. Ischemic CRVO patients had significantly lower RPC vessel density in inferior quadrant when compared to non-ischemic CRVO patients. Both ischemic and non-ischemic CRVO patients had significantly lower RPC vessel density in inferior quadrant when compared to normal individuals. Ischemic CRVO patients had significantly lower RPC vessel density in nasal quadrant when compared to non-ischemic CRVO patients. Both ischemic and non-ischemic CRVO patients had significantly lower RPC vessel density in nasal quadrant when compared to normal individuals. Both ischemic and non-ischemic CRVO patients had significantly lower RPC vessel density in nasal quadrant when compared to normal individuals. Both ischemic and non-ischemic CRVO patients had significantly lower RPC vessel density in nasal quadrant when compared to normal individuals. Both ischemic and non-ischemic CRVO patients had significantly lower RPC vessel density in nasal quadrant when compared to normal individuals. Both ischemic and non-ischemic CRVO patients had significantly lower RPC vessel density in nasal quadrant when compared to normal individuals. Both ischemic and non-ischemic CRVO patients had significantly lower RPC vessel density in temporal quadrant when compared to normal individuals.

### Table (5): Post-hoc pairwise comparison of RPC vessel density

|             | Ischemic CRVO vs<br>Non-ischemic CRVO patients | Ischemic CRVO<br>Vs Normal | Non-ischemic CRVO<br>Vs Normal |  |
|-------------|--|----------------------------|--------------------------------|--|
| D superior  | < 0.001*                                       | < 0.001*                   | < 0.001*                       |  |
| VD inferior | < 0.001*                                       | < 0.001*                   | < 0.001*                       |  |
| VD nasal    | < 0.001*                                       | < 0.001*                   | < 0.001*                       |  |
| VD temporal | 0.124  | < 0.001*                   | < 0.001*                       |  |

A ROC curve was able to distinguish between ischemic and non-ischemic forms of CRVO using a cutoff value of 39.5 for RPC vessel density in the upper quadrant, we found that it has a 1.000 area under the curve, 100% specificity, and 100% sensitivity. By using the cutoff value 47 of RPC vessel density in the inferior quadrant, the ability to differentiate between ischemic and non-ischemic types of CRVO was much improved. The results showed a perfect area under the curve of 1.000, 100% sensitivity, and 100% specificity. With a threshold value of 37 of RPC vascular density in the nasal quadrant, the ability to differentiate between ischemic and non-ischemic types of CRVO was much improved. The results showed an area under the curve of 0.979, 90.9% sensitivity, and 100% specificity. Nevertheless, when comparing ischemic and non-ischemic CRVO according to RPC vessel density in the temporal quadrant, no statistically significant difference was found (Table 6).

| Table ( | (6): | ROC | curve for | differentiation | ng ischem | nic and no | on-ischemic | types | of CRV | VO |
|---------|------|-----|-----------|-----------------|-----------|------------|-------------|-------|--------|----|
|         |      |     |           |                 | 0         |            |             | ~     |        |    |

|             | Area           |          | 95% Confidence Interval |                |        | Songitivity | Specificity |  |
|-------------|----------------|----------|-------------------------|----------------|--------|-------------|-------------|--|
|             | Under<br>Curve | P value  | Lower Bound             | Upper<br>Bound | Cutoff | (%)         | (%)         |  |
| VD superior | 1.000          | < 0.001* | 1.000                   | 1.000          | 39.5   | 100         | 100         |  |
| VD inferior | 1.000          | < 0.001* | 1.000                   | 1.000          | 47     | 100         | 100         |  |
| VD nasal    | 0.979          | < 0.001* | 0.930                   | 1.029          | 37     | 90.9        | 100         |  |
| VD temporal | 0.640          | 0.298    | 0.376                   | 0.905          |        |             |             |  |

ROC curve revealed that macular thickness had no significant discriminative ability for differentiation of the ischemic and non-ischemic types of CRVO (Table 7).

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Table (7): ROC curve for differentiating ischemic and non-ischemic types of CRVO using macular thickness

|                   | Area Under | D voluo | 95% Confidence Interval |                    |  |
|-------------------|------------|---------|-------------------------|--------------------|--|
|                   | Curve      | r value | Lower Bound             | <b>Upper Bound</b> |  |
| Macular thickness | 0.702      | 0.085   | 0.472                   | 0.933              |  |

# ILLUSTRATIVE CASES

Case 1: OCTA (RPC VD) of normal 57 years old man (Right eye). BCVA: 1.0 (Figure 1).



Figure (1): OCT-Angiography of ONH angiograms of normal subject

Case 2: OCTA (RPC VD) of non-ischemic CRVO 62 years old woman (Right eye). BCVA: 0.16 (Figure 2).
Angio Disc QuickVue
Scan Quarky 510
45x45 Scan Stare (sem)
Right / OD



Figure (2): OCT-Angiography of ONH angiograms of non-ischemic CRVO subject.



Case 3: OCTA (RPC VD) of ischemic CRVO 66 years old man (Right eye). BCVA: CF 2 m (Figure 3).

Figure (3): OCT-Angiography of ONH angiograms of ischemic CRVO subject.

#### DISCUSSION

To better understand the pathophysiology of vein occlusion and to provide a direction for care, this study aimed to use OCTA to highlight the effect of CRVO on the optic nerve head vascular density. In the current study, 33 subjects who underwent OCTA at Suez Canal University Hospital and private center, Ismailia, Egypt, were included and divided according to OCTA findings into 3 groups; ischemic CRVO patients group consisted of 11 patients, non-ischemic CRVO patients group consisted of 11 patients and normal group consisted of 11 patients.

When comparing the three groups according to factors like gender, age, examined-eye side, intraocular pressure (IOP), and RPC vessel density in the superior, nasal, inferior, and temporal quadrants of the eye, no statistically significant differences were observed.

With respect to BCVA, there was a notable disparity among the three research groups (P < 0.001). In terms of macular thickness, there was a statistically significant difference among the three groups as: Group 1 had a mean ±SD of 732.27±265.30. 574.55±75.13 was the group 2 average. In group 3, the mean was 263.82±6.18. This indicates that the P value is less than 0.001.

In all three groups, there were notable disparities in RPC vascular density in the superior, nasal, inferior, and temporal quadrants (P<0.001). For the analysis, the highest quality image (with a signal strength of 70 or higher) was chosen from three scans of  $4.5 \times 4.5$  mm optic disc cubes.

In the same line with our findings, **Thapa** et al.<sup>(7)</sup> found also that there was significant difference between the 3 study groups regarding BCVA, macular thickness and RPC vessel density. The BCVA was much lower in CRVO patients compared to healthy controls. CRVO was 0.21% (95% CI: 0.06-0.55), and CRVO was 2.95% (95% CI: 2.23-3.83).

Furthermore, Gadde et al. (8) revealed a notable disparity in the subjects' BCVA, macular thickness, and RPC vessel density in the superior, nasal, inferior, and temporal quadrants (P < 0.0001). Conversely, they found no evidence of a change in the extent of the foveal avascular zone (FAZ) in either the superficial or deep capillary plexus (SCP and DCP) with respect to age.

According to Caliskan et al.<sup>(9)</sup> there was a significant difference among their patients regarding BCVA(P<0.001), macular thickness and RPC vessel density. There was no gender-related significant differences in retinal and OD VDs. Retinal nerve fiber layer thickness (RNFLT) was likewise not observed to vary significantly by gender.

The study showed that the best corrected visual acuity (BCVA) was significantly lower in ischemic CRVO patients when compared to non-ischemic CRVO patients. Ischemic CRVO patients had significantly lower BCVA when compared to normal individuals. Non-ischemic CRVO patients had significantly lower BCVA when compared to normal individuals.

According to Khodabandeh et al. (10) on average. patients had a visual acuity of  $0.47 \pm 0.54$ . The ischemic and non-ischemic types of CRVO were classified according to the patients. Results from comparing their BCVA were consistent with those in the current investigation.

The current study demonstrated that macular thickness was significantly increased in ischemic CRVO patients when compared to normal individuals. Macular thickness was significantly increased in nonischemic CRVO patients when compared to normal individuals.

**Romano** *et al.* <sup>(11)</sup>, in agreement with the present study, found that macular thickness was significantly higher in ischemic CRVO patients when compared to controls. The RNFL damage in CRVO has been studied extensively.

**Shin** *et al.* <sup>(12)</sup> additionally, found that the mean RNFLT in the contralateral eye was considerably lower in patients with unilateral CRVO when compared to healthy controls (P<0.001). Peripapillary RNFLT did not differ significantly between healthy controls and CRVO patients, contradicting earlier findings. The study's inclusion of patients with both acute and chronic CRVO, as well as the fact that the two groups' rates of systemic vascular diseases were distinct, could account for this.

In the present study ischemic CRVO patients had significantly lower RPC vessel density in nasal, superior, and inferior quadrants when compared to nonischemic CRVO patients. Ischemic CRVO patients had significantly lower RPC vessel density in temporal, nasal, superior, and inferior quadrants when compared to normal individuals (P<0.001) in all quadrants

**Shin** *et al.* <sup>(12)</sup> stated that CRVO patients' noticeably thinner skin compared to healthy subjects was shown by the superior quadrant RNFLT analysis; however, the lack of specificity regarding the occluded regions in CRVO patients prevented the establishment of a causal relationship. Additionally, the study found that compared to healthy people, CRVO patients' contralateral eyes had lower RNFLTs in the inferior and temporal quadrants.

Curiously, the aforementioned study <sup>(12)</sup> also indicated that compared to healthy people, CRVO patients had higher RNFLT in all quadrants, with the most noticeable increases in the temporal and nasal quadrants. This can mean that the edema in the optic disc (OD) and the surrounding retina has not yet gone down, or that the edema in the OD has the potential to alter the microstructure of the OD in the long run.

Extreme retinal edema puts mechanical strain on the choriocapillaris flow, which may be exacerbated by inflammatory mediators that affect both the retinal arteries and the choriocapillaris. **Mastropasqua** *et al.* <sup>(13)</sup> found that ischemic CRVO patients had significantly decreased RPC vessel density in the nasal, superior, and ophthalmic regions, and our findings indicate the same.

The current study stated that non-ischemic CRVO patients had significantly lower RPC vessel density in temporal, nasal, superior, and inferior quadrants when compared to normal individuals while no significant difference was reported between ischemic CRVO and non-ischemic CRVO patients regarding RPC vessel density in temporal quadrant.

In the same line with the present study, **Moussa** *et al.* <sup>(14)</sup> found that the RPC vessel density was noticeably lower in non-ischemic CRVO patients compared to controls. In addition, 111 eyes had significantly reduced SCP VD in at least one quadrant, whereas 33 had normal SCP VD. Similarly, 142 eyes had significantly reduced DCP VD in at least one quadrant, while 2 had normal DCP VD.

**Deng** *et al.* <sup>(15)</sup> also discovered that CRVO patients had decreased levels of entire and parafoveal SCP and DCP VDs compared to healthy persons. Additionally, they did not see any variation in foveal SCP and DCP VDs between healthy individuals and CRVO patients.

**Glacet** *et al.* <sup>(16)</sup> in another study using OCTA, reported that non-ischemic CRVO patients had significantly lower RPC vessel density than controls in temporal, nasal, superior, and inferior quadrants

Khodabandeh *et al.* <sup>(10)</sup> assessed the comparison between healthy individuals and patients with CRVO using OCTA to quantify vascular density and flow. Patients with retinal degeneration showed a marked reduction in blood flow across the retina, the choriocapillaris, and the superficial and deep capillary plexuses of the retina.

The study's ROC curve analysis demonstrated that RPC vessel density in the upper and lower quadrants could distinguish between ischemic and non-ischemic CRVO types with a specificity and sensitivity of 100% and an area under the curve of 1.000. With an area under the curve of 0.979, a sensitivity of 90.9%, and a specificity of 100%, the nasal quadrant's cutoff value of 37 for RPC vessel density was able to distinguish between ischemic and non-ischemic CRVO.

In contrast, the research showed that RPC vascular density in the temporal quadrant could not distinguish between CRVOs that were ischemic and those that were not. The ROC curve also showed that macular thickness could not distinguish between ischemic and non-ischemic CRVO types with a significant (P<0.05) degree of discrimination.

In the same line with current study, **Khodabandeh** *et al.* <sup>(10)</sup> reported that RPC vascular density significantly differentiates between non-ischemic and probable ischemic CRVO, with an area under the curve (AUC) of 0.84, 100% sensitivity, and 69% specificity. Consistent with our findings, **Cabral** *et al.* <sup>(17)</sup> also found that CRVO could not be classified as either ischemic or non-ischemic based on macular thickness.

Adhi *et al.* <sup>(18)</sup> found reduced vascular perfusion in approximately 53% of CRVO eyes, including those of individuals without the disease and those with the condition. The researchers also discovered that the patients' foveal avascular zones were considerably bigger than the control group.

### CONCLUSION

The study concluded that early accurate diagnosis of central retinal vein occlusion (CRVO) must be the major goal of the ophthalmologist while facing these cases to avoid the probable dangerous sequences. It also concluded that OCTA could detect ischemia and changes between normal and vein occlusion eyes. OCTA in this study revealed a decrease in RPC vessel density in ischemic CRVO than non-ischemic CRVO and OCTA also can detect ischemic and non-ischemic CRVO.

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### REFERENCES

- 1. Glanville J, Patterson J, McCool R *et al.* (2014): Efficacy and safety of widely used treatments for macular oedema secondary to retinal vein occlusion: a systematic review. BMC Ophthalmology, 14(1): 1-15.
- 2. Seknazi D, Coscas F, Sellam A *et al.* (2018): Optical coherence tomography angiography in retinal vein occlusion: correlations between macular vascular density, visual acuity, and peripheral nonperfusion area on fluorescein angiography. Retina, 38(8): 1562-70.
- **3. Suzuki N, Hirano Y, Yoshida M** *et al.* (2016): Microvascular abnormalities on optical coherence tomography angiography in macular edema associated with branch retinal vein occlusion. American Journal of Ophthalmology, 161: 126-132.
- **4. Baumal C (2016):** Optical coherence tomography angiography of retinal artery occlusion. Dev Ophthalmol., 56: 122-131.
- 5. Kim A, Rodger D, Shahidzadeh A *et al.* (2016): Quantifying retinal microvascular changes in uveitis using spectral-domain optical coherence tomography angiography. American Journal of Ophthalmology, 171: 101-112.
- 6. Taher F, Kandil H, Mahmoud H *et al.* (2021): A comprehensive review of retinal vascular and optical nerve diseases based on optical coherence tomography angiography. Applied Sciences, 11(9): 4158. Doi: ; https://doi.org/10.3390/app11094158
- 7. Thapa R, Bajimaya S, Paudyal G *et al.* (2017): Prevalence, pattern and risk factors of retinal vein occlusion in an elderly population in Nepal: the Bhaktapur retina study. BMC Ophthalmology, 17(1): 1-8.
- 8. Gadde S, Anegondi N, Bhanushali D *et al.* (2016): Quantification of vessel density in retinal optical coherence tomography angiography images using local

fractal dimension. Investigative Ophthalmology & Visual Science, 57(1): 246-252.

- **9.** Caliskan N, Doğan M, Çalışkan A *et al.* (2023): Optical coherence tomography angiography evaluation of retinal and optic disc microvascular morphological characteristics in retinal vein occlusion. Photodiagnosis and Photodynamic Therapy, 41: 103244. doi: 10.1016/j.pdpdt.2022.103244.
- 10. Khodabandeh A, Shahraki K, Roohipoor R *et al.* (2018): Quantitative measurement of vascular density and flow using optical coherence tomography angiography (OCTA) in patients with central retinal vein occlusion: Can OCTA help in distinguishing ischemic from non-ischemic type. International Journal of Retina and Vitreous, 4(1): 1-11.
- **11.** Romano F, Lamanna F, Gabrielle P *et al.* (2023): Update on retinal vein occlusion. The Asia-Pacific Journal of Ophthalmology, 12(2): 196-210.
- 12. Shin Y, Nam K, Lee S *et al.* (2019): Changes in peripapillary microvasculature and retinal thickness in the fellow eyes of patients with unilateral retinal vein occlusion: an OCTA study. Investigative Ophthalmology & Visual Science, 60(2): 823-829.
- **13. Mastropasqua R, Toto L, Di Antonio L** *et al.* (2017): Optical coherence tomography angiography microvascular findings in macular edema due to central and branch retinal vein occlusions. Scientific reports, 7(1): 40763. doi: 10.1038/srep40763.
- Moussa M, Leila M, Bessa A et al. (2019): Grading of macular perfusion in retinal vein occlusion using enface swept-source optical coherence tomography angiography: a retrospective observational case series. BMC Ophthalmology, 19(1): 1-13.
- **15. Deng Y, Zhong Q, Zhang A** *et al.* (2019): Microvascular changes after conbercept therapy in central retinal vein occlusion analyzed by optical coherence tomography angiography. International Journal of Ophthalmology, 12(5): 802-8.
- **16. Glacet A, Sellam A, Coscas F** *et al.* **(2016):** Optical coherence tomography angiography in retinal vein occlusion treated with dexamethasone implant: a new test for follow-up evaluation. European Journal of Ophthalmology, 26(5): 460-468.
- **17.** Cabral D, Coscas F, Glacet-Bernard A *et al.* (2019): Biomarkers of peripheral nonperfusion in retinal venous occlusions using optical coherence tomography angiography. Translational Vision Science & Technology, 8(3): 7. doi: 10.1167/tvst.8.3.7
- **18.** Adhi M, Bonini Filho M, Louzada R *et al.* (2016): Retinal capillary network and foveal avascular zone in eyes with vein occlusion and fellow eyes analyzed with optical coherence tomography angiography. Investigative Ophthalmology & Visual Science, 57(9): 486-494.