

# Changes in Peripapillary Microvasculature and Retinal Thickness in the Fellow Eyes of Patients with Unilateral Retinal Vein Occlusion: An OCTA Study

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## Abstract:

**Background:** Retinal vein occlusion (RVO) is the second most common retinal vascular disease following diabetic retinopathy and is a frequent cause of significant visual loss and associated morbidity. **Aim and objectives:** To assess peripapillary vessel density (VD), retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) in the fellow eyes of patients with unilateral retinal vein occlusion (RVO) (either CRVO or BRVO) using optical coherence tomography angiography (OCTA) and compare it with controls. **Subjects and methods:** This is an observational study that will be conducted on (25) patients with unilateral RVO (either CRVO or BRVO) and (25) normal controls chosen from outpatient clinic. **Results:** The average RNFL thickness in the fellow eyes of RVO patients was significantly thinner than in normal controls (P-value = 0.003), [P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS)]. There was no significant difference between fellow eyes and healthy controls as regard to VD of peripapillary plexus and ganglion cell complex thickness. **Conclusion:** OCTA revealed that RNFL thickness in the fellow eyes of patients with unilateral RVO was significantly decreased. Peripapillary VD and GCC thickness showed no significant difference when compared to healthy controls.

**Keywords:** retinal nerve fiber layer; ganglion cell-inner plexiform layer; retinal vein occlusion; peripapillary OCTA; vessel density.

## Introduction

Retinal vein occlusion (RVO) is the second most common retinal vascular disease following diabetic retinopathy and is a frequent cause of significant visual loss and associated morbidity, which increases with age, and reported a prevalence of approximately 0.7%–1.6%.<sup>(1)</sup>

Various systemic diseases, such as hypertension (HTN), diabetes,

arteriosclerosis, and hyperlipidemia are considered to be risk factors for the development of RVO<sup>(2)</sup>.

Many studies have found an association between RVO and glaucoma and increased intraocular pressure (IOP)<sup>(3)</sup>.

In 1913, Verhoeff first postulated that elevated IOP collapses and compresses the wall of the retinal vein, causing intimal proliferation in the vein. An ocular HTN

study reported that a larger horizontal cup-to-disc ratio was associated with the In recent reports, a decrease in peripapillary microvascular perfusion using OCTA was associated with glaucoma<sup>(5)</sup>.

Kim et al.<sup>(6)</sup> reported that retinal nerve fiber layer (RNFL) thickness decreased in the fellow eyes of unilateral RVO patients, and that RVO and glaucoma may share systemic risk factors, reflecting a common pathogenic mechanism, such as systemic HTN, diabetes mellitus, and arteriosclerosis.

Aim of the work was to assess peripapillary vessel density (VD), retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) in the fellow eyes of patients with unilateral retinal vein occlusion (RVO) (either CRVO or BRVO) using optical coherence tomography angiography (OCTA) and compare it with controls.

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## Subjects and Methods

This is an observational case-control study that was conducted on (25) patients with unilateral retinal vein occlusion (RVO) either central retinal vein occlusion (CRVO) or branch retinal vein occlusion (BRVO) and (25) normal controls chosen from outpatient clinic in ophthalmology department in Benha University in the period between January 2023 and March 2023.

**The exclusion criteria:** in the fellow eyes and controls were as follows: a history of retinal or optic nerve diseases or glaucoma; a best-corrected visual acuity (BCVA) < 6/12; high myopia (spherical equivalent) >6 diopters, axial length > 26mm and significant media opacity.

**Methods:** All patients were undergoing:

A. Ophthalmological examination as following: BCVA using a Snellen chart, IOP and slit-lamp bio-microscopy, dilated fundus examination.

B. OCTA scans acquired: vessel density (VD) of radial Peripapillary plexus

development of RVO<sup>(4)</sup>.

calculated via 4.5×4.5 mm optic disc scans centered on the optic disc. RNFL calculated via 3.45 mm circle scans centered on the optic disc, Ganglion cell complex (RNFL+GC+IPL) calculated.

**Statistical analysis:** The collected data presented in tables and suitable graphs and analyzed by IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value < 0.01: highly significant (HS).

**Ethical considerations:** Ethical approval from Ethics Committee of Benha University obtained in addition to informed consent from patients invited to participate in the research (Ms code :45-11-2022).

All methods were carried out in accordance with relevant guidelines and regulations.

All authors have agreed to submit the work.

This study does not include any data, information or images which could lead to direct identification of persons participated in this research.

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## Results

The current study included 25 patients who had RVO; 44% had right sided RVO and 56% had left RVO. Regarding other comorbidities, 14% had DM and 26% had hypertension.

There is no statistically significant difference between fellow eye and healthy controls as regard the age. There is no statistically significant difference in UCVA, BCVA and IOP between fellow eye and healthy controls.

There is no statistically significant difference between fellow eye and healthy controls as regard the peripapillary, RPCP superior and RPCP inferior, Table (1).

There is statistically insignificant difference in RPCP in the four quadrants in between fellow eye and healthy controls, Table (2).

**Table (1):** Comparison of the Radial peripapillary capillary plexus (RPCP) density of the studied groups.

	Fellow eye No.= 25		Healthy control No.=25		t	P-value	Sig.
	Mean	SD	Mean	SD			
<b>peripapillary</b>	50.82	3.42	51.85	1.52	-1.366	0.178	NS
<b>RPCP superior</b>	51.01	3.27	52.29	1.34	-1.810	0.077	NS
<b>RPCP inferior</b>	50.61	4.03	51.57	2.26	-1.043	0.302	NS

P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

**Table (2):** Comparison of the Radial peripapillary capillary plexus (RPCP) density in the four quadrants of the studied groups

	Fellow eye No.= 25		Healthy controls No.=25		t	P-value	Sig.
	Mean	SD	Mean	SD			
<b>RPCP nasal</b>	48.96	13.73	52.24	1.90	1.183	0.242	NS
<b>RPCP superior</b>	50.64	4.20	51.16	2.64	-0.524	0.603	NS
<b>RPCP temporal</b>	54.20	3.91	55.24	2.17	-1.165	0.250	NS
<b>RPCP inferior</b>	52.08	3.51	52.60	2.50	-0.603	0.549	NS

P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

There is statistically significant lower RNFL in fellow eye than healthy controls as regard the average RNFL, superior half RNFL and inferior half RNFL, Table (3). There is statistically significant lower RNFL in the four quadrants in fellow eye

than healthy controls. There is no statistically significant difference between fellow eye and healthy controls as regard the ganglion cell complex average thickness, Table (4).

**Table (3):** Comparison of the Retinal nerve Fiber layer (RNFL) thickness of the studied groups.

	Fellow eye No.= 25		Healthy controls No.=25		t	P-value	Sig.
	Mean	SD	Mean	SD			
<b>Average RNFL</b>	96.96	8.11	106.48	12.73	-3.154	0.003	HS
<b>SuperiorRNFL</b>	99.92	8.78	111.56	15.92	-3.201	0.002	HS
<b>Inferior RNFL</b>	93.16	10.96	101.32	10.52	-2.685	0.010	HS

P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

**Table (4):** Comparison of the Retinal nerve Fiber layer (RNFL) thickness in the four quadrants and Ganglion cell complex thickness of the studied groups.

	Fellow eye No.= 25		Healthy controls No.=25		t	P-value	Sig.
	Mean	SD	Mean	SD			
<b>RNFL nasal</b>	81.00	16.23	91.32	11.14	-2.621	0.012	S
<b>RNFL superior</b>	121.88	15.23	137.36	23.18	-2.791	0.008	HS
<b>RNFL temporal</b>	75.88	8.28	96.08	22.96	-4.138	0.000	HS
<b>RNFL inferior</b>	116.60	22.77	131.36	10.16	-2.960	0.005	HS
<b>Ganglion cell complex average thickness</b>	95.84	5.02	97.44	5.95	-1.027	0.309	NS

P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

## Discussion

Retinal vein occlusion (RVO) is the second-most common sight-threatening retinal vascular disease after diabetic retinopathy<sup>(7)</sup>.

The relationship between RVO and glaucoma has long been recognized<sup>(8)</sup>. It has been suggested that rather than a cause-and-effect relationship, the relationship between the two is a reflection of underlying systemic vascular diseases such as atherosclerosis, hypertension, and diabetes mellitus<sup>(9)</sup>. Previous study emphasized that vascular dysregulation and autoregulatory dysfunction as extended consequences of insulin resistance may play a pivotal role in the pathogenesis of both RVO and glaucoma<sup>(10)</sup>. The fact that RVO and glaucoma have common systemic risk factors has focused the attention of researchers on the unaffected fellow eyes of patients with RVO, with the consideration that there may be early glaucomatous changes in the fellow eye.

Optical coherence tomography angiography (OCTA) has become a valuable imaging tool for the evaluation of retinal pathologies such as diabetic retinopathy, age-related macular degeneration, and retinal artery & retinal vein occlusions (RVOs). Its ability to delineate the fine microvascular detail of the retinal vasculature in the superficial and deep retinal plexus without dyes is advantageous for diagnosing retinal diseases, which will most likely lead to its widespread use in the future<sup>(11-13)</sup>.

To investigate the association between RVO and glaucoma, it would be ideal to search for glaucomatous damage in RVO eyes. However, this is not practical, for several reasons. First, in the early stage of RVO, retinal edema may occur, leading to increases in RNFL thicknesses in the involved sectors. This may interfere with accurate measurement of RNFL thickness. Second, RNFL thickness may be

decreased in sectors with RVO, which would confound any measurement of glaucomatous thinning of the RNFL. With these limitations in mind, we conducted measurements on the fellow eyes of patients with RVO.

The main aim of this study was to assess peripapillary vessel density (VD), retinal nerve fiber layer (RNFL) and Ganglion cell complex (GCC) in the fellow eyes of patients with unilateral retinal vein occlusion (RVO)- either CRVO or BRVO- using optical coherence tomography angiography (OCTA) and compare it with controls.

This is an observational case-control study that was conducted on (25) patients with unilateral RVO (either CRVO n=7 or BRVO n=18); 44% had right sided RVO and 56% had left RVO and (25) normal controls chosen from outpatient clinic. The duration of the study ranged from 6-12 months. Regarding other comorbidities, 14% had DM and 26% had hypertension. There is no statistically significant difference between fellow eye and healthy controls as regard the age.

The current study showed that there is statistically insignificant difference in UCVA, BCVA and IOP in fellow eye than healthy controls.

These results were reported in other study<sup>(14)</sup> After excluding poor quality of the OCTA images (fellow eyes of RVO: eight patients, controls: five subjects), a total of 83 unilateral RVO patients (50 patients with branch RVO and 33 with central RVO) were enrolled. The mean age of the participants was  $63.3 \pm 10.8$  years (38 males and 45 females). The normal control group included 33 males and 50 females, with a mean age of  $60.6 \pm 9.2$  years. Hypertension was more prevalent in the RVO patients (41 patients, 49.4%) compared with normal controls (24 patients, 28.9%) ( $P = 0.005$ ). There were no significant differences in mean age, sex, diabetes, laterality, UCVA, BCVA, SE, IOP, and AL between the two groups.

In our study, we found that there is statistically significant lower RNFL in fellow eye than healthy controls as regard the average RNFL, superior half RNFL and inferior half RNFL. [ P-value = 0.003, 0.002 & 0.010 respectively]

There is also statistically significant lower RNFL in the nasal, superior, temporal and inferior quadrants [P-value =0.012, 0.008, 0.000 & 0.005 respectively]- especially in the inferior and temporal quadrants- in fellow eye than healthy controls as shown in Table (3) and Table (4).

These results suggest that RVO and glaucoma may share systemic risk factors, reflecting a common pathogenic mechanism, in at least some patients.

Our results were the same as the previous study<sup>(15)</sup> as they reported that the fellow eyes of RVO subjects had a thinner RNFL than did control eyes. Retinal nerve fiber layer thinning was most obvious in the 7-, 10-, and 11 o'clock sectors. Because these sectors represent the area where glaucomatous structural changes are most frequently seen, it may be proposed that thinning of the RNFL in the fellow eyes of patients with RVO may be glaucomatous in nature, or that the mechanism of RNFL thinning is similar, at least in part, to that of glaucoma development.

Similarly, in other study<sup>(14)</sup> they reported RNFL layer thinning in the fellow eyes of RVO was significant in the average, inferior, and temporal quadrants. This finding is consistent with those of a previous study<sup>(15)</sup> that suggested that RVO may have a common mechanism with glaucoma because it is similar to the frequent site of RNFL thinning in glaucoma. Systemic risk factors affecting the vascular pathophysiology, such as HTN, diabetes, and atherosclerosis, have been suggested as possible mechanisms of damage in both glaucoma and RVO. The decreased ocular blood flow and increased retinal venous pressure in the fellow eyes of RVO patients compared with normal controls may be related to the pathogenesis of RVO and glaucoma. However,

glaucoma and RVO are multifactorial diseases, and it is difficult to completely understand the vascular dysregulation related to the pathogenesis. Moreover, another study<sup>(16)</sup> reported that glaucoma in the fellow eyes of patients with unilateral BRVO progressed more rapidly compared with glaucoma patients without RVO suggesting the presence of a similar vascular abnormality in both diseases<sup>(17,18)</sup>.

We further evaluated the RPC network in RVO patients' fellow eyes using OCTA and analyzed whether it was associated with RNFL thinning.

We found that there is no statistically significant difference between fellow and healthy controls as regard peripapillary RPCP superior and inferior as well as all quadrants as shown in Table (1) and Table (2).

These results were opposite to previous study<sup>(14)</sup> as they reported that peripapillary microvascular density in the fellow eyes of unilateral RVO was decreased compared with control eyes. they found that the fellow eyes had lower peripapillary VD and PD compared with those of controls. The average of the inner and outer ring and full areas were significantly decreased. When analyzed by quadrant, the inner inferior quadrant, outer inferior quadrant, and outer temporal quadrant- were significantly decreased in a manner similar to the reduction in the RNFL. The large retinal vessel becomes narrower from the inner to the outer ring. Because small vessels are vulnerable to ischemia, the average of the outer ring may be affected more than that of the inner ring. In the outer ring, the nasal area may be less affected than the temporal area due to the large vessels.

However, other study<sup>(19)</sup> supported our results as they reported that the mean RPC perfusion showed no significant difference between fellow eyes of RVO patients and control eyes in the four quadrants ( $P > 0.05$ , all).

We also evaluated the GCC thickness in RVO patients' fellow eyes using OCTA and compared it with controls.

We found that there is no statistically significant difference between fellow eye and healthy controls as regard the ganglion cell complex average thickness. Results were opposite to previous study<sup>(14)</sup> as they reported. The average RNFL and GC-IPL thicknesses in the fellow eyes of RVO patients- were significantly thinner than in normal controls (93.5 vs. 96.6  $\mu\text{m}$ ,  $P = 0.013$  and 81.3 vs. 84.1  $\mu\text{m}$ ,  $P = 0.003$ , respectively) but keep in mind that they used Carl Zeiss Cirrus system not Optovue RTVue like our study. Zeiss system measures only ganglion cell body and inner plexiform layer thickness. Optovue measures ganglion cell complex including ganglion cell body, inner plexiform layer and also nerve fiber layer.

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### Conclusion:

The RNFL thickness in the fellow eyes of RVO patients was significantly thinner than in normal controls. There was no significant difference between fellow eyes and healthy controls as regard to VD of peripapillary plexus and ganglion cell complex thickness.

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### References

1. Cugati S, Wang JJ, Rochtchina E and Mitchell P. Ten-year incidence of retinal vein occlusion in an older population: the Blue Mountains Eye Study. *Arch Ophthalmol*. 2006; 124: 726–732.
2. Stewart RM and Clearkin LG. Insulin resistance and autoregulatory dysfunction in glaucoma and retinal vein occlusion. *Am J Ophthalmol*. 2008; 145: 394–396.
3. David R, Zangwill L, Badarna M and Yassur Y. Epidemiology of retinal vein occlusion and its association with glaucoma and increased intraocular pressure. *Ophthalmologica*. 1988; 197: 69–74.
4. Barnett EM, Fantin A, Wilson BS, Kass MA and Gordon MO; for the Ocular Hypertension Treatment Study Group. The incidence of retinal vein occlusion in the Ocular Hypertension Treatment Study. *Ophthalmology*. 2010; 117: 484–488.
5. Liu L, Jia Y and Takusagawa HL. Optical coherence tomography angiography of the peripapillary retina in glaucoma. *JAMA Ophthalmol*. 2015; 133: 1045–1052.
6. Kim MJ, Woo SJ, Park KH and Kim TW. Retinal nerve fiber layer thickness is decreased in the fellow eyes of patients with unilateral retinal vein occlusion. *Ophthalmology*. 2011; 118: 706–710.
7. Klein R, Klein BE and Moss SE. The epidemiology of retinal vein occlusion: the Beaver Dam Eye Study. *Trans Am Ophthalmol Soc* 2000; 98: 133–141.
8. Verhoeff FH. The effect of chronic glaucoma on the central retinal vessels. *Arch Ophthalmol* 1913; 42: 145–152.
9. Lockwood A and Clearkin LG. Insulin resistance in retinal vein occlusion and glaucoma. *Lancet* 1992; 340: 1100–1101.
10. Stewart RM and Clearkin LG. Insulin resistance and autoregulatory dysfunction in glaucoma and retinal vein occlusion. *Am J Ophthalmol* 2008; 145: 394–396.
11. Bonini Filho MA, Adhi M, de Carlo TE, Ferrara D, Bauman CR, Witkin AJ, et al. Optical coherence tomography angiography in retinal artery occlusion. *Retina*. 2015; 35:2339–2346.
12. Freiberg FJ, Pfau M, Wons J, Wirth MA, Becker MD and Michels S. Optical coherence tomography angiography of the foveal avascular zone in diabetic retinopathy. *Graefes Arch Clin Exp Ophthalmol*. 2016; 254:1051–1058.
13. Sarraf D, Rahimy E, Fawzi AA, Sohn E, Barbazetto I, Zacks DN, et al. Paracentral acute middle maculopathy: A new variant of acute macular neuroretinopathy associated with retinal capillary ischemia. *JAMA Ophthalmol*. 2013; 131:1275–1287.
14. Shin Y-I, Nam KY and Lee SE. Changes in peripapillary microvasculature and retinal thickness in the fellow eyes of patients with unilateral retinal vein occlusion. *Invest Ophthalmol Vis Sci*. 2019; 60:823–829.
15. Kim MJ, Woo SJ, Park KH and Kim T-W. Retinal nerve fiber layer thickness is decreased in the fellow eyes of patients with unilateral retinal vein occlusion. *Ophthalmology*. 2011;118(4):706–10.
16. Park H-YL, Jeon S, Lee MY and Park CK. Glaucoma progression in the unaffected fellow eye of glaucoma patients who developed unilateral branch retinal vein occlusion. *Am J Ophthalmol*. 2017; 175:194–200.
17. Choi J, Kim KH, Jeong J, Cho H-S, Lee CH and Kook MS. Circadian fluctuation of mean ocular perfusion pressure is a consistent risk factor for normal-tension glaucoma. *Invest Ophthalmol Vis Sci*. 2007;48(1):104.

18. Bonomi L, Marchini G, Marrafa M, Bernardi P, Morbio R and Varotto A. Vascular risk factors for primary open angle glaucoma: the Egna-Neumarkt study. *Ophthalmology*. 2000;107(7):1287–93.
19. Ozcaliskan S and Ozcan Y. Quantitative assessment of macular microvasculature and radial peripapillary capillary plexus in the fellow eyes of patients with retinal vein occlusion using OCT angiography. *J Fr Ophthalmol* 2020; 43: 842–850.

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