

Study of Macular Capillary Network Changes after Branch Retinal Vein Occlusion (BRVO) on Optical Coherence Tomography Angiography (OCT-A)

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ABSTRACT:

Background: Branch retinal vein occlusion (BRVO) is the focal occlusion of a first or second-order branch of a retinal vein, which occurs most frequently at an arteriovenous (AV) crossing. Direct ophthalmoscopy, color fundus photography, and fluorescein angiography facilitate observation of AV crossings parallel to the retinal plane. **Aim and objectives:** To analyze the macular microvasculature changes in eyes with branch retinal vein occlusion (BRVO) using optical coherence tomography angiography (OCT-A). **Subjects and methods:** This case-control cross-sectional study carried out on a total of 40 eyes (mean age 64.2 ± 8.02 range between 52 years and 76 years) 20 of them were recently diagnosed with BRVO (i.e. patient had fundus findings such as intraretinal hemorrhages, cotton wool spots, macular edema, and vascular congestion) and other 20 eyes were healthy and served as control, all of them were evaluated by optical coherence tomography angiography (XR-Avanti; Optovue). The macular angiography scan protocol covered a 6 mm x 6 mm area. The angiography analysis focused on two retinal layers: superficial and deep vascular networks. The following

vascular morphological parameters were assessed at the foveal area in both the superficial and deep networks: foveal avascular zone area diameter, foveal vascular density, capillary non-perfusion occurrence, foveal avascular zone distribution (i.e. loss of the intact perifoveal capillary arcade greater than one quadrant), presence of cystoid spaces and collaterals connecting the occluded vein to an adjacent patent vein **Results:** there was an increase in superficial vascular density in patients than control group respectively ($p < 0.001$) (29.38 ± 9.79 , 16.41 ± 5.61). While no changes were found in deep vascular density between the patient and control group respectively ($p = 0.589$) (35.04 ± 10.82), (33.49 ± 6.69). There was a decrease in foveal avascular zone area diameter ($p < 0.001$) (0.167 ± 0.115 , 0.344 ± 0.079) for the patient and control group, respectively and Non-perfusion areas were Present in the deep vascular layer only in 12 BRVO patients (60 %) and in both layers (superficial and deep) in 8 BRVO patients (40%) and never found in the superficial vascular layer only. FAZ

distribution was present in the deep vascular layer only in 14 BRVO patients (70 %) and in both layers (superficial and deep) in 6 BRVO patients (30%) and was never found in the superficial layer only. Cystoid Macular Edema and Collaterals were found in all patients. **Conclusion:** OCTA can assess macular changes after BRVO and follow-up in a rapid, noninvasive, safe manner. OCTA imaging revealed an increase in superficial vascular density and a decrease in FAZ area diameter in BRVO eyes compared to control eyes with more changes in deep capillary vascular plexus.

Keywords: Macula, angiography, vein, retina.

Introduction

Branch retinal vein occlusion (BRVO) is a common retinal vascular disorder in middle-aged and elderly with a history of hypertension, diabetes mellitus, smoking, or open-angle glaucoma [1]. Branch retinal vein occlusion (BRVO) is an acute cause of visual impairment secondary to thrombotic events, external compression, vessel wall pathology, or combination [2]. Patients with BRVO develop varying degrees of retinal hemorrhage, retinal ischemia, tortuous retinal vessels, and macular edema, which is a predominant cause of vision loss in BRVO [3]

Fluorescein angiography (FA) is the gold standard for evaluating the structural and functional status of retinal vasculature in BRVO. However, it is an invasive procedure and may lead to some side effects, such as allergic reactions and nausea [4]. Optical coherence tomography angiography (OCTA) is a new imaging modality that allows noninvasive visualization of retinal blood flow without exogenous dyes [5]. layer specific imaging capabilities of OCTA have the potential to simultaneously visualize both superficial and deep retinal capillaries by segmentation of each layer [6].

So, Optical Coherence Tomography

angiography technology can be a useful clinical tool for BRVO diagnosis and follow-up, providing stratigraphic vascular details that have not previously been observed by standard fluorescein angiography [2]. The ability of OCTA 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 [7]

This study analyzed the changes in macular microvasculature in eyes with branch retinal vein occlusion (BRVO) using optical coherence tomography angiography (OCT-A).

Patients and methods

This case-control cross-sectional study was conducted in (the Ophthalmology Center – Benha University Hospitals) in Benha, Qalyubia, Egypt (from October 2021 to October 2022.). It was approved by the local Research Ethics Committee (Benha Faculty of Medicine Research Ethics Committee (Ms 24-8-2021), and the principles of the Declaration of Helsinki were observed. Informed consent was taken from all patients before the study.

All Included subjects were classified

into a control group (group A) and a patient group (group B); subjects included in group A had No history of eye diseases or eye surgery and were not diabetic or hypertensive. While subjects included in group B were recently diagnosed with BRVO. (Acute BRVO, i.e., the patients have fundus findings such as intraretinal hemorrhages, cotton wool spots, and macular edema [8] had no media opacity as cataract or vitreous hemorrhage, and no history of therapeutics such as anti-VEGF or retinal laser treatment. Subjects with media opacity or vitreous hemorrhage or had previous anti-VEGF or laser treatment was excluded from the study. After history taking, all included subjects underwent Full ophthalmologic examination as follows: Visual acuity assessment: BCVA by Snellen chart then converted to log mar (Logarithm of the Minimum Angle of Resolution) for statistical purposes. Anterior segment examination, IOP measurement by air puff tonometer, Fundus examination, Clinical diagnosis of acute BRVO was confirmed by FA then all included subjects were imaged by OCT-A.

Statistical analysis and data interpretation:

Data analysis was performed using SPSS software, version 25 (SPSS Inc., PASW Statistics for Windows version 25. Chicago: SPSS Inc.). Qualitative data were described using numbers and percentages. Quantitative data were described using median mean \pm Standard deviation for normally distributed data after testing normality using Shapiro Wilk test. The significance of the obtained results was

judged at the (0.05) level. Chi-Square was used to compare qualitative data between groups as appropriate. Student t-test was used to compare two independent groups for non-normally distributed data. Spearman's rank-order correlation is used to determine the strength and direction of a linear relationship between two non-normally distributed continuous variables.

Results:

This cross-sectional case-control study was carried out on 40 eyes of 40 subjects 20 of them were healthy (control)(group A), and 20 were diagnosed recently with branch retinal vein occlusion (acute BRVO (i.e., the patient had fundus findings such as intraretinal hemorrhages, cotton wool spots, macular edema) (8)

Group B:

The study showed that the mean age for group A was (52.05 \pm 6.95) 80% were female, 20% were males while the mean age for group B was (55.85 \pm 5.89) 55 % of them were males and 45% were females, 70% were hypertensive, 75% of them were right eye BRVO, major BRVO occlusion was 60% (12 patients) and macular BRVO occlusion was 40 % (8 patients) and all of the patients were ischemic BRVO type ALSO.

Groups A and B: has no statistically significant difference regarding demographic characteristics.

Also, the study showed that mean BCVA was (0.079 \pm 0.089), (0.568 \pm 0.241) for groups A and B

respectively with a statistically significant decrease in mean BCVA ($p < 0.001$) in group B than A and showed no statistically significant difference between the studied groups regarding Eye Side and Intraocular pressure (mm/Hg).

In addition to the previous result, the study showed that mean superficial vascular density (SVD) was (16.41 ± 5.61), (29.38 ± 9.79) for groups A and B (**figure 1**) respectively with a statistically significant increase in superficial vascular density ($p < 0.001^*$) in group B than group A (figure 2 and 3) While mean deep vascular density was (33.49 ± 6.69), (35.04 ± 10.82) for groups A and B (**figure 2**) respectively, with no statistically significant difference between groups A and B regarding deep vascular density. [**Table 1**]

Also study showed that mean foveal avascular zone area diameter (FAZ) was (0.344 ± 0.079), (0.167 ± 0.115) for group A and B with a statistically significant decrease in FAZ area diameter ($p < 0.001^*$) in group B than A [**table 1**].

Also, the study showed that Non-perfusion areas (NPAs)(regions without visible perfused capillaries)(3) were Present in the deep vascular layer only in 12 BRVO patients (60 %) and in both layers (superficial and deep) in 8 BRVO patients (40%) and never found in the superficial vascular layer only, and FAZ distribution (loss of the intact perifoveal capillary arcade greater than one quadrant)(3) was Present in the deep vascular layer only in 14 BRVO patients (70 %) and in both layers(superficial and deep) in 6 BRVO patients (30%) and never found in the superficial layer only. Cystoid Macular Edema and Collaterals (between the occluded vein and adjacent patent vein) were found in all patients. [**Table 2**]

Regarding multivariate correlation, in group A there was a statistically significant positive correlation between deep vascular density and visual acuity ($R = 0.457^*$) while in group B there and was a statistically significant positive correlation between superficial vascular density and visual acuity ($R = 0.484^*$). [**Table 3**]

Table (1): comparison of quantitative imaging data (vascular density and foveal avascular zone area foveal thickness) among studied groups:

	Group A (Control) N=20	Group B (BRVO) N=20	test of significance
Superficial vascular density	16.41±5.61	29.38±9.79	t=5.14 p<0.001*
Deep vascular density	33.49±6.69	35.04±10.82	t=0.545 p=0.589
Foveal avascular zone area	0.344±0.079	0.167±0.115	t=5.35 p<0.001*
Central foveal (macular) thickness	236.25±13.83	475.95±195.08	t=5.48 p<0.001*

t: Student t test , *statistically significant

Table (2): qualitative imaging data of BRVO patient (group B) :

	N	%
Non perfusion areas		
Present in both layers	8	40.0
Present in deep layer only	12	60.0
FAZ distribution		
In both layers	6	30.0
In deep layer only	14	70.0
Presence of cystoid macular edema	20	100.0
Presence of collaterals	20	100.0

Table (3): correlation between vascular density, age , and visual acuity among BRVO patient (group B)

		Superficial vascular density	Deep vascular density	Foveal zone diameter	avascular zone diameter
Age/years	R	-.024	.109	.393	
	P	.920	.646	.086	
BCVA	R	.484*	.233	.001	
	P	.030	.324	.996	

r:Spearman correlation coefficient , *statistically significant

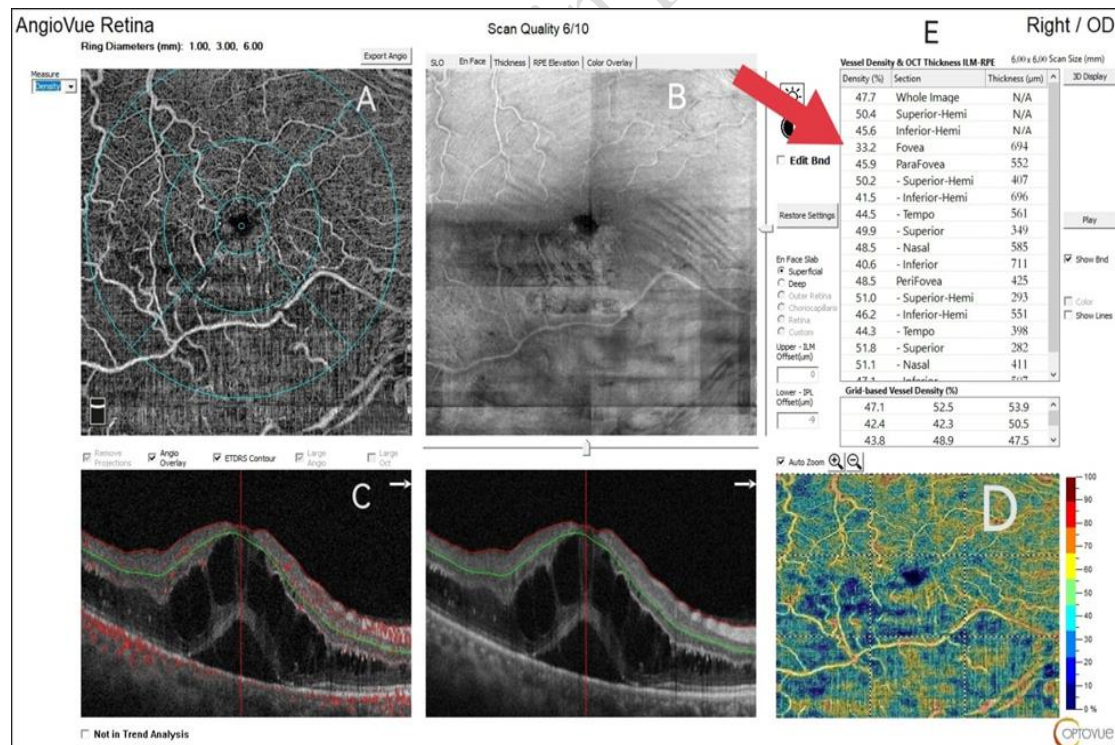


Figure (1): OCTA scan (6 × 6 mm) in a right eye with major inferior BRVO(group B), (A) OCTA at the level of the superficial capillary plexus (SCP) showing vascular tortuosity, dilation, and telangiectasia (collaterals) along with non-perfusion areas inferiorly (B) En face OCT at the level of the SCP showing the presence of cystoid edema corresponding to dark circular areas without vessel signals in OCTA (C) B-scan OCT with perfusion overlay and segmentation lines showing cystoid macular edema (D) Color-coded vascular density map. (E) Numerical report of the vascular density showing foveal superficial vascular density (%) 33.2% (red arrow).

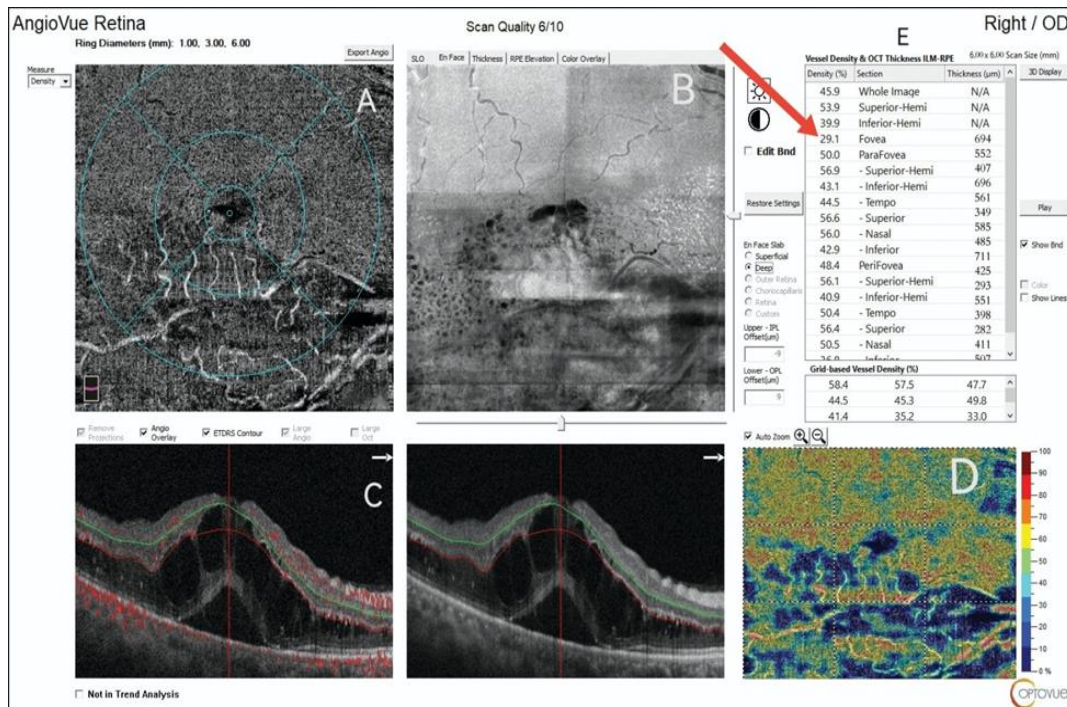


Figure (2): OCTA (6 × 6 mm) in a right eye with major inferior BRVO(group B). (A) OCTA at the level of the deep capillary plexus (DCP) showing vascular tortuosity, dilation, and telangiectasia (collaterals) along with non-perfusion areas. And disturbed FAZ inferiorly (B) En face OCT at the level of the DCP. Note the presence of cystoid edema corresponding to dark circular areas without vessel signals in OCTA. (C) B-scan OCT with perfusion overlay and segmentation lines. (D) Color-coded vascular density map. (E) Numerical report of the vascular density showing foveal deep vascular density (%) 29.1% (red arrow).

Discussion:

Branch retinal vein occlusion (BRVO) is a common retinal vascular problem in patients with lifestyle-related diseases like hypertension and arteriosclerosis. [9].

Fluorescein angiography (FA) is helpful to confirm the diagnosis of BRVO and evaluate complications. However, dense retinal hemorrhages and/or macular edema make interpreting FA images difficult because of blocked or pooled fluorescein. In addition, FA does not visualize the deeper capillary network in the retina well, besides dye complication and risks [19]

Optical coherence tomography angiography (OCT-A), a recent imaging facility, has enabled researchers to visualize microvascular in different retinal layers. It also provides us with qualitative

information about the perfusion status of the macula, microvascular changes such as telangiectasia, retinal capillary nonperfusion, and disruption of the foveal avascular zone also microvascular density changes in different vessel layers of the macula was reported with quantitative analysis [1]

In this study, all BRVO patients' age range was from 50 to 60 years old, and that went with multiple studies which mentioned the same previous BRVO age range [11 & 12]. Also there was no sex difference in BRVO incidence, and hypertension was a vital risk factor, and that was confirmed by others [12]. Patient's visual acuity ranged from 0.8 to 0.3 by LOG MAR, and that was confirmed a study [4], which attributed this decrease in visual acuity to

macular edema and macular vascular changes occurring in BRVO while we found that the IOP range was from 13 to 17 mmHg with no difference between groups A and B as all patients included were acute BRVO with a short time range of one week to 2 months, and that was confirmed by other researchers who mentioned that BRVO rarely causes an increase in IOP and also needs long-term follow-up [15]. Also, the study showed an increase in superficial vascular density in group B than A, while deep vascular density remained unchanged in both groups. Still, previous results were incompatible with the study done in 2020 which reported a decrease in SCV and DCV density in patients compared to control patients [4].

However, it was reported that VD was not significantly different between the involved and uninvolved areas in acute BRVO ($p = 0.551$). However, the difference was significant in chronic BRVO ($p = 0.013$), so vascular impaired patterns in the retinal layer differed between acute and chronic BRVO. These results may suggest that vascular change and remodeling develop differently in acute and chronic phases in BRVO, and since this study was carried out on acute BRVO eyes then, that explains relatively no changes in deep vascular density between patient eyes and control eyes [22]

Changes in vascular density in the presence of macular edema have been reported, but the results of different studies differ. A significant positive correlation between macular thickness and the vascular density in superficial and deep was reported, and this correlation has been ascribed to the high levels of VEGF, which increases both the macular thickness and the vascular diameter, thereby increasing the percentage of reported flow pixels

by the instrument [23].

Meanwhile, decreased SCP vascular density in the presence of macular oedema due to RVO was compared to that in eyes without oedema. In contrast, DCP and vascular densities were not affected. [3]also, In 2019, a study reported that repeatability of VD measurement in patients with RVO using OCTA is greatly affected by the CMT [22]

In addition, this study showed a decrease in FAZ area diameter in patients than the control group, which went with the recent study that reported the mean FAZ area in BRVO eyes was significantly lower compared to fellow eyes [17]. But Shiihara et al. reported in their research on Eyes with BRVO without apparent macular edema that the mean FAZ area was larger in BRVO eyes than in controls, and that contradicts previous data about FAZ [25]

When trying to explain this contradiction, we find that FAZ size may vary considerably in normal individuals and cause a significant overlap among healthy and diseased individuals, making it difficult to recognize the difference between study groups [4]. This overlap already occurred in this study as the control FAZ range was (0.265- 0.423 mm²) and the BRVO FAZ range was (0.052 – 0.282mm²). Also, studies conducted on healthy subjects show that OCTA has excellent repeatability in FAZ measurements. However, few studies have considered macular degeneration, such as macular ischemia or edema evaluated the reliability of FAZ area measurements using OCTA in eyes with RVO [24].

According to the previous data, we could explain the contradiction in FAZ area size by wide variation in FAZ area

size and overlapping between both controls and patients, small sample size, also artifacts like ischemia and edema should be taken into consideration, especially since most of the cases included in this study were had macular edema so FAZ area best to use in follow up of same patient values not in comparing between two different groups

Furthermore, the study showed qualitative changes as NPAs, FAZ disruption, and collaterals affected mainly DCVP with or without SCVP affection; these results confirmed by reports from several authors that ischemic damage in RVO is preferentially main-seated in the DCP and often precedes SCP ischemia [18 & 14]. The explanation is that central arterioles and especially major venules can independently connect to the deep capillary plexus (DCP) without first communicating with the superficial capillary plexus (SCP) and also that the DCP could have a primarily venous role [18]

Also, this study showed a positive significant correlation between BCVA and SVD, and while there was an insignificant correlation between BCVA and DVD, Zhang et al. confirmed the previous relation in their study when they reported that there is a strongly positive correlation between vascular density and visual acuity [20].

Conclusion

OCTA can be used to assess macular changes after BRVO (qualitative and quantitative assessment) and in rapid, noninvasive, and safe follow-up. OCTA imaging revealed an increase in vascular density and a decrease in FAZ area in patient eyes compared to control eyes, with significant changes in the deep capillary vascular plexus.

References

1. Rogers S, McIntosh RL, Cheung N, Lim L, Wang JJ, Mitchell P, et al, International Eye Disease Consortium. The prevalence of retinal vein occlusion: pooled data from population studies from the United States, Europe, Asia, and Australia. *Ophthalmology*. 2010 Feb 1;117(2):313-9.
2. Rispoli M, Savastano MC, Lumbroso B. Capillary network anomalies in branch retinal vein occlusion on optical coherence tomography angiography. *Retina (Philadelphia, Pa.)*. 2015 Nov;35(11):2332.
3. Jaulim, A., Ahmed, B., Khanam, T. & Chatziralli, I. P. BRANCH RETINAL VEIN OCCLUSION. *Retina*, 2013; 33: (5), 901-910.
4. Chen, L., Yuan, M., Sun, L., Wang, Y. & Chen, Y. Evaluation of microvascular network with optical coherence tomography angiography (OCTA) in branch retinal vein occlusion (BRVO). *BMC Ophthalmology*, 2020; 20: (1).
5. Pechauer AD, Jia Y, Liu L, Gao SS, Jiang C, Huang D. et al. Optical Coherence Tomography Angiography of Peripapillary Retinal Blood Flow Response to Hyperoxia. *Investigative ophthalmology & visual science*. 2015 May 1;56(5):3287-91.
6. Spaide, R. F., Klancnik, J. M. & Cooney, M. J. Retinal Vascular Layers Imaged by Fluorescein Angiography and Optical Coherence Tomography Angiography. *JAMA Ophthalmology*, 2015; 133: (1), 45.
7. Freiberg, F. J., Pfau, M., Wons, J., Wirth, M. A., Becker, M. D. & Michels, S. Optical coherence tomography angiography of the foveal avascular zone in diabetic retinopathy. *Graefe's Archive for Clinical and Experimental Ophthalmology*, 2016; 254: 1051-1058.
8. Chung, C. S., Nesper, P. L., Park, J. J. & Fawzi, A. A. Comparison of Zeiss Cirrus and Optovue RTVue OCT Angiography Systems: A Quantitative and Qualitative Approach Examining the Three Capillary Networks in Diabetic Retinopathy. *Ophthalmic Surgery, Lasers and Imaging Retina*, 2018; 49: (11).
9. Noma, H., Yasuda, K. & Shimura, M. Cytokines and the Pathogenesis of Macular Edema in Branch Retinal Vein Occlusion. *Journal of Ophthalmology*, 2019: 1-9.

10. Zhu, D.-d. & Liu, X. Neutrophil/Lymphocyte Ratio and Platelet/Lymphocyte Ratio in Branch Retinal Vein Occlusion. *Journal of Ophthalmology*, 2019; 1-5.
11. Dave, V. P., Pappuru, R. R., Gindra, R., Ananthakrishnan, A., Modi, S., Trivedi, M., et al. OCT angiography fractal analysis-based quantification of macular vascular density in branch retinal vein occlusion eyes. *Canadian Journal of Ophthalmology*, 2019; 54: (3), 297-300.
12. Song P, Xu Y, Zha M, Zhang Y, Rudan I. Global epidemiology of retinal vein occlusion: a systematic review and meta-analysis of prevalence, incidence, and risk factors. *Journal of global health*. 2019 Jun;9(1).
13. Polat, N. & Yoloğlu, S. Optical coherence tomographic comparison of naive macular edema due to ischemic and nonischemic retinal vein occlusion. *International Ophthalmology*, 2020; 40: (8), 2085-2093.
14. Choi YJ, Jee D, Kwon JW. Characteristics of major and macular branch retinal vein occlusion. *Scientific Reports*. 2022 Aug 18;12(1):14103.
15. Vural, G. S. & Karahan, E. Central corneal thickness, axial length, anterior chamber and optic disc structure in patients with central and branch retinal vein occlusion. *European Journal of Ophthalmology*, 2022; 33: (2), 1077-1083.
16. Tsai, G., Banaee, T., Conti, F. F. & Singh, R. P. Optical coherence tomography angiography in eyes with retinal vein occlusion. *Journal of ophthalmic & vision research*, 2018; 13: (3), 315.
17. Jin, XIN. Application of quantitative OCTA in retinal vein occlusion. *International Eye Science*, 2021; 711-714.
18. Moussa M, Leila M, Bessa AS, Lolah M, Abou Shousha M, El Hennawi HM, et al. Grading of macular perfusion in retinal vein occlusion using en-face swept-source optical coherence tomography angiography: a retrospective observational case series. *BMC ophthalmology*. 2019 Dec;19:1-3.
19. Gomaa, S., Abd El Hadi, A. & Mohamed Morsy, S. Optical coherence tomography angiographic normative data for macular perfusion in egyptian. *Alexmed ePosters*, 2021; 3: (4), 77-78.
20. Zhang, M., Wang, J., Pechauer, A. D., Hwang, T. S., Gao, S. S., Liu, L., et al. Advanced image processing for optical coherence tomographic angiography of macular diseases. *Biomedical Optics Express*, 2015; 6: (12), 4661
21. Mendis, K. R., Balaratnasingam, C., Yu, P., Barry, C. J., McAllister, I. L., Cringle, S. J., & Yu, D. Y. (2010). Correlation of histologic and clinical images to determine the diagnostic value of fluorescein angiography for studying retinal capillary detail. *Investigative ophthalmology & visual science*, 51(11), 5864-5869.
22. Oh, Jaeryung, and Jaemoon Ahn. "Comparison of retinal layer thickness and vascular density between acute and chronic branch retinal vein occlusion." *Korean Journal of Ophthalmology* 33.3 (2019): 238-248
23. Mastropasqua R, Toto L, Di Antonio L, Borrelli E, Senatore A, Di Nicola M, et al. Optical coherence tomography angiography microvascular findings in macular edema due to central and branch retinal vein occlusions. *Sci Rep*. 2017;7:40763. [PMC free article] [PubMed] [Google Scholar] [Ref list]..
24. An, Weiting, and Jindong Han. "Research progress of UWFFA and OCTA in retinal vein occlusion: A review." *European Journal of Ophthalmology* 31.6 (2021): 2850-2855.
25. Shiihara, H., Terasaki, H., Sonoda, S., Kakiuchi, N., & Sakamoto, T. (2018). Evaluation of shape of foveal avascular zone by optical coherence tomography angiography in eyes with branch retinal vein occlusion. *Journal of VitreoRetinal Diseases*, 2(3), 138-145.

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