Optical Coherence Tomography Angiography (OCTA) Analysis of Perifoveal Capillary Arcade in Patients with Retinal Vein Occlusion Treated with Anti-VEGF

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ABSTRACT

Objective: To evaluate the changes in perifoveal capillary arcade in patients with retinal vein occlusion treated with intravitreal injections of anti-vascular endothelial growth factor for macular edema resulting from retinal vein occlusion with OCTA.

Study Design: Quasi-experimental study.

Place and Duration of Study: Armed Forces Institute of Ophthalmology, Rawalpindi Pakistan, from Jul 2018 to Jul 2019.

Methodology: Patients diagnosed as case of retinal vein occlusion underwent complete eye examination. Optical coherence tomography angiography (OCTA) was done in all the patients. Patients having macular edema were prescribed intravitreal anti-vascular endothelial growth factor inhibitors on monthly basis. OCTA was repeated at the third month.

Results: In this study, 50 eyes were evaluated. After treatment patients having perifoveal capillary arcade of less than two quadrants increased from 47.7-68.8% (p<0.002) in the superficial capillary plexus and in deep capillary plexus this number increased from 50% to 88.6% (p<0.05). There was also a significant decrease in the number of macular cysts in the superficial and deep capillary plexus post treatment (p<0.05). Mean En face vascular density in superficial capillary plexus decreased in all the quadrants specially the foveal zone.

Conclusion: Optical coherence tomography angiography (OCTA) showed a qualitative improvement in perifoveal arcade disruption and decrease in the number of cystic spaces. Quantitative analysis revealed a significant reduction in vessel density in all quadrants. It enables us to follow up patients with retinal vein occlusion and study the vascular arcade changes with time and treatment.

Keywords: Optical coherence tomography angiography (OCTA), Perifoveal capillary arcade, Retinal vein occlusion, Vascular density.

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INTRODUCTION

Retinal vein occlusion is the second most common cause of retinal vascular disease and vision loss.[1,2] Occlusion of the prominent veins of the retinal circulation results in raised intraluminal pressure, haemorrhage and oedema.[3] Macular oedema is a frequent cause of visual acuity loss from RVO. Other causes include macular ischemia and neovascular complications such as vitreous haemorrhage and neovascular glaucoma.[4-6] Retinal vein occlusion can be classified into central retinal vein occlusion, branch retinal vein occlusion and hemi retinal vein occlusion.[7]

Features of retinal vein occlusion, including perifoveal arcade disruption, macular oedema, peripheral non-perfusion area and neovascularization, can easily be seen and described on fluorescence angiography.[8] Recently, the introduction of OCTA has provided an advanced non-invasive method for imaging the capillary network in the retina. Optical coherence tomography angiography (OCTA) uses the split-spectrum amplitude-decorrelation angiography algori-thm to detect erythrocyte movement.[9,10]

Areas of non-perfusion and capillary arcade disruption after retinal vein occlusion could be precisely delineated at the superficial and deep capillary plexus using OCTA compared to FFA. A recent version of the software released by the AngioVue system allows quantification of vascular density around the macula.[10]

Minimal international data is available on this aspect of RVO, but no local data is available. Therefore, our study aimed to see the effects of antivascular endothelial growth factor (Anti-VEGF) on patients with RVO using OCTA by comparing disruption of the perifoveal capillary arcade in the superficial and deep capillary plexus, macular density in the superficial capillary plexus before and after treatment.

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METHODOLOGY

This quasi-experimental study was conducted in the Armed Forces Institute of Ophthalmology, Rawalpindi Pakistan, from July 2018 to July 2019. The Ethical Review Committee approved the study design (189/ERC/AFIO). All patients gave informed written consent for participation in the study, and patients were selected through consecutive sampling.

The sample size was calculated using the WHO sample size calculator using the population proportion of retinal vein occlusion as 1.6%.[11]

Inclusion Criteria: Patients with macular oedema secondary to central retinal vein occlusion, hemi retinal vein occlusion or branched retinal vein occlusion were included in the study.

Exclusion Criteria: Patients with poor quality image on OCTA, previous retinal surgeries, pathological myopia, ocular trauma and uncontrolled diabetes were excluded from the study.

We evaluated 50 eyes of patients with macular oedema secondary to retinal vein occlusion. Patients reported to the Armed Forces Institute of Ophthalmology with a sudden decrease in vision. All patients underwent complete eye examination, including best-corrected visual acuity, anterior segment examination, intraocular pressure measurement, and an indirect slit-lamp ophthalmoscopy Patients having retinal vein occlusion were referred to a retina specialist where their diagnosis was confirmed. OCTA was done using the split spectrum amplitude-decorrelation angiography algorithm on Angiovue OCTA system version 2015. Macular oedema was confirmed on OCTA, and disruption in the perifoveal arcade in the superficial and deep capillary plexus was noted. Macular vessel density in four quadrants in the perifoveal area was also registered.

After confirmation of OCTA, 1.25 mg intravitreal Bevacizumab was given every month for two months, and OCTA was repeated after four weeks of the second injection.[12] All the parameters noted before the treatment were noted after the treatment.

OCTA images were analyzed, and a qualitative analysis of OCTA was done, which included determining the disruption of the perifoveal arcade at the superficial and deep capillary plexus in the four ETDRS quadrants (superior, inferior, temporal, nasal).[12,13] Two groups of patients were made, one having perifoveal arcade disruption in ≤2 quadrants and the other having a disruption in >2 quadrants. The number in each group was noted before and after treatment. Enface OCT enabled macular oedema cysts to be evaluated in the central, paracentral and diffuse macular fields. Quantitative follow up was done by measuring the vascular density. Vascular density is defined as the percentage of sample area occupied by vessels. A ring with a diameter of 2.5 mm around the fovea was analyzed. The mean vascular density in the perifoveal area was determined in the superior, temporal, inferior, and nasal quadrants.[12-14] All these parameters were compared before and after treatment.

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. The graphs were produced using Microsoft Excel. Quantitative variables were summarized as mean ± SD. The paired t-test was applied to observe the significance of intravitreal Bevacizumab injection with perifoveal vascular arcade disruption and macular vessel densities. The *p*-value of ≤0.05 was considered statistically significant.

RESULTS

Fifty eyes of patients were examined who experienced retinal vein occlusion. There were 17 patients with CRVO, 33 patients with BRVO. There were 30 were males, and 14 were females. OCTA was done in all the patients who presented to us with macular oedema due to retinal vein occlusion. All the patients had developed macular oedema for which intravitreal Bevacizumab was given. The second dose of IVA was given after a month. OCTA was done to see the results in the third month. The initial and final OCTA results were compared, giving due consideration to the perifoveal capillary arcade (Figure-1 to Figure-4).

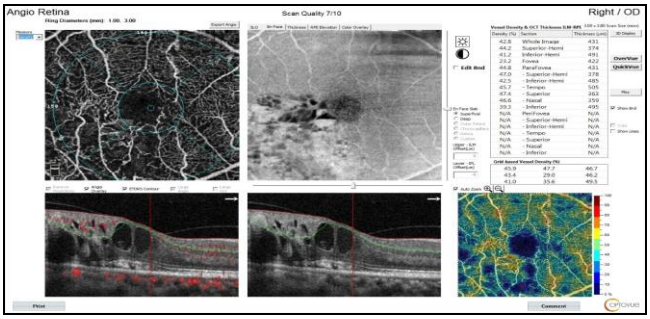

Figure-1: Optical coherence tomography angiography of the superficial capillary plexus at baseline is shown. At the SCP level, 4 quadrants (superior, inferior, temporal, and nasal) and perifoveal capillary ring is shown: focal perifoveal capillary arcade disruption in the temporal and inferior quadrant with venous dilatation and ectasia; En face optical coherence tomography shows dark central cysts and central cystoid edema; macular vessel density map shown in the lower left corner shows predominant lack of vessels in the inferior and temporal quadrant.

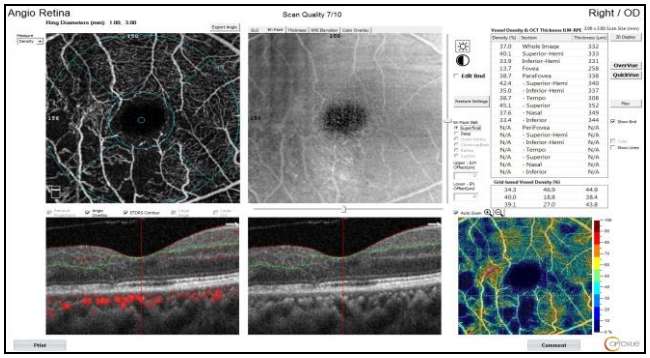

Figure-2: After IVA Optical coherence tomography angiography shows persistence of perifoveal capillary arcade disruption but decrease number of dark central cysts on En face optical coherence tomography; macular vessel density map shows macular vessel density further decreased in inferior and temporal quadrants after this treatment.

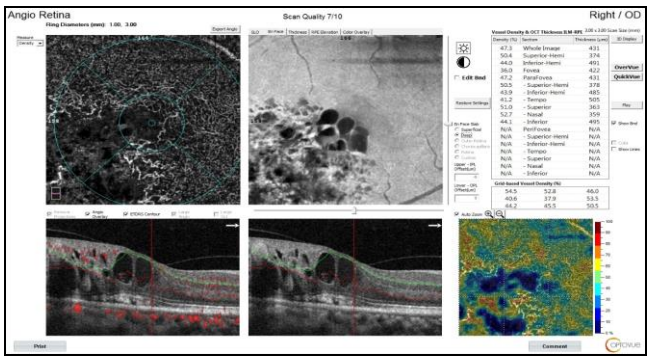

Figure-3: This OCTA of the deep capillary plexus of the same patient shows complete disruption of perifoveal capillary arcade in inferior and temporal quadrant. En face OCT shows numerous dark central cysts. Macular vessel density map shows a decrease in macular vessel density and perfusion area in inferior quadrant.

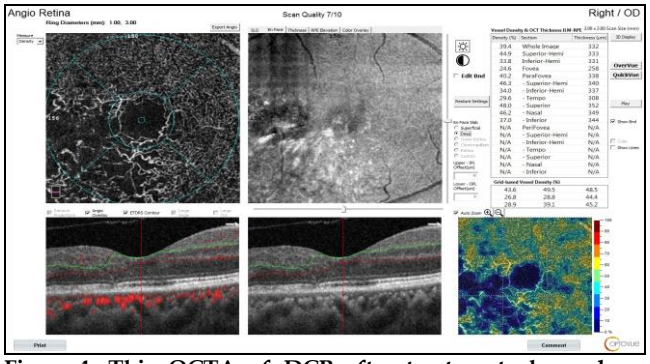

Figure-4: This OCTA of DCP after treatment shows lesser disruption of perifoveal capillary arcade. En face OCTA shows absence of central dark cysts and resolved macular edema. Macular vessel density shows a further decrease in vessel density in the inferotemporal quadrant even after treatment.

On OCTA, the perifoveal capillary arcade involved two or less than two quadrants in 47.7% of eyes and more than two quadrants in 23 (53.3%) of the eyes in the superficial capillary plexus. Similarly, in deep capillary plexus, the perifoveal arcade involvement of two or less than two quadrants was seen in 22 (50%) patients and more than two quadrants in 22 (50%) patients (Table).

Table: Perifoveal capillary arcade on OCTA.

Number of quadrants having disruption in Superficial Capillary Plexus			
	Initial	**Final**	***p*-value**
2 or less than 2	21(47.7%)	30 (68.82%)	0.002
More than 2	23 (52.3%)	14 (31.8%)	0.002
Number of Quadrants Having Disruption in Deep Capillary Plexus			
2 or less than 2	22 (50%)	39 (88.6%)	<0.05
More than 2	22 (50%)	5 (11.4%)	<0.05
Macular vessel density in Superficial capillary plexus			
Macular Vascular Density	Baseline	Four Weeks After 2nd Injection	*p*-value
Foveal Vascular Density	35.52%	28.25%	<0.05
Temporal Vascular Density	43.23%	37.43%	<0.05
Nasal Vascular Density	43.96%	38.83%	<0.05
Superior Vascular Density	41.314%	36.74%	<0.05

After treatment, there was a significant decrease in perifoveal arcade disruption as the number of patients with two or less two-quadrant disruption increased from 47.7-68.82% in the superficial capillary plexus and from 50-88.6% in deep capillary plexus. Furthermore, there was also a significant decrease in macular cysts in the superficial (88-6%) and deep capillary plexus (84.1-18.2%) post-treatment.

The mean En faces vascular density in the superficial capillary plexus decreased in all quadrants, especially in the foveal zone, and this decrease was statistically significant. Six patients in this study were lost to follow up.

DISCUSSION

Anti-VEGF injections are commonly used to treat cystoid macular oedema effectively.[15] Patients with RVO were followed up using OCTA before and after treatment, which showed a significant decrease in perifoveal arcade disruption both in the superficial and deep capillary plexus after three months following two intravitreal Bevacizumab injections. The number of cysts also decreased in both the plexus. On the contrary, there was a significant decrease in macular vascular density in all the layers, especially the foveal

vascular density in the superficial capillary plexus during the follow-up period.

Tsai *et al,* showed qualitative improvement in perifoveal arcade disruption, but the vascular density slightly decreased in DCP (44.37-43.8%) and SCP (43.2-42.76%).[16] Four people in the study also showed an increase in vascular density in the superficial capillary plexus, whereas, in our study, none of the patients showed an increase in either plexus. Another study by Khodabandeh *et al*, showed a decrease in whole vascular density in SCP (p<0.001) and DCP (p<0.001) in eyes affected with retinal vein occlusion when compared with the fellow normal eye.[17] Further evaluation of vascular densities after treatment was not done. At the same time, findings in our study show that densities further decrease with time despite treatment. Chatziralli *et al*, showed that treatment with anti-VEGF does slow the progression of capillary non-perfusion areas but does not completely stop it.[18] It could also be because the retinal non-perfusion areas that were already present could only be viewed after the resolution of cysts.

Another study by Sellam *et al,*[19] revealed an improvement in perifoveal arcade disruption and a decrease in macular vessel density after treatment, but this decrease was not statistically significant.[20,21] Results of our study showed statistically significant improvement in perifoveal arcade disruption and reduction in the number of cystic spaces for retinal vein occlusion treated with anti-VEGF. The reduction in vessel density in both superficial and deep capillary plexus was also significant.

In conclusion, OCTA of patients treated with intravitreal Bevacizumab showed a qualitative improvement in perifoveal arcade disruption and reduced the number of cystic spaces. Quantitative analysis revealed a significant reduction in vessel density in all quadrants, especially in the foveal zone with time and even after treatment. Further studies would be required for more details of retinal vein occlusion with OCTA to compare vascular densities of healthy subjects and those with RVO before and after treatment and by correlating the peripheral perfusion areas on FA with macular vessel densities.

LIMITATION OF STUDY

The limitation of this study was a small sample size. Furthermore, it requires a steady gaze, as blinking hinders the image quality. In addition, there was no comparison in quantitative analysis between the non-perfusion and cystic areas.

CONCLUSION

Optical coherence tomography angiography (OCTA) showed a qualitative improvement in perifoveal arcade disruption and decrease in the number of cystic spaces. Quantitative analysis revealed a significant reduction in vessel density in all quadrants. It enables us to follow up patients with retinal vein occlusion and study the vascular arcade changes with time and treatment.

Conflict of Interest: None.

Authors' Contribution

NW:Designing and writing, WM: Supervising and editing, MAA: Data collection.

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