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Research Article

Imaging of Retinal Vein Occlusion by Optical Coherence Tomography-Angiography (OCTA)

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Abstract

Purpose: To highlight the important findings in OCTA imaging of retinal vein occlusion in comparison to fundus fluorescein angiography, its limitations and added information.

Setting: Cases were referred from Retina Clinic at Kasr Al-Ainy Medical School, Cairo University. Imaging was performed at Bostan Diagnostic Eye Center, Cairo.

Design: Cross sectional, non-randomized observational study.

Subjects and methods: 34 eyes of 32 patients suffering from Retinal Venous Occlusion (RVO) (both central and branch vein occlusion) and diagnosed by Fundus Fluorescein Angiography (FFA) underwent OCT Angiography (OCTA), with 6x6 field imaging. The perifoveal capillary arcades, the detection of retinal capillary non-perfusion qualitatively and quantitatively, telangiectasia, macular edema and photocoagulation scars were highlighted.

Results: Perifoveal Capillary Arcades (PFCA) disruption and Central Non-Perfusion Areas (CNPA) were detected more frequently on OCTA than FFA (100% in OCTA versus 70.59% in FFA) with a highly significant difference (P<0.01).Also Superficial Capillary Telangiectasia (SCT) were detected more clearly in OCTA than FFA (32.35% in OCTA versus 20.59% in FFA) with a highly significant difference (P<0.01). Intraretinal hemorrhages and macular edema; were detected equally by both FFA & OCTA. Microaneurysms (MA) were detected also on OCTA. Peripheral Non-Perfusion Areas (PNPA) as well as disc edema were only detected by FFA.

Deep Capillary Telangiectasias (DCT) were only detected by OCTA in all eyes. Perifoveal capillary disruption and non-perfusion areas were detected in both Superficial Capillary Plexus (SCP) and Deep Capillary Plexus (DCP) in all eyes of the study, while Capillary telangiectasia (32.35% in SCP versus 100% in DCP), Intraretinal cysts (edema) (41.18% in SCP versus 73.53% in DCP), Hemorrhages (5.88% in SCP versus 82.35% in DCP) and Microaneurysms (70.59% in SCP versus 100% in DCP) were detected more in DCP than in SCP with a high statistically significant difference (P<0.01).

Conclusion

OCT angiography adds an advantage in detecting retinal capillary non-perfusion in vascular occlusion quantitatively, with no need of invasive dye injection. However, the limitations of OCTA to scan peripheral retinal vascular changes, the presence of motion artifacts, the need of high-quality images and good patient's fixation, still can't eliminate the role of FFA in the diagnosis of retinal vascular diseases.

Keywords

Fundus Fluorescein Angiography; RVO; OCTA

Introduction

Retinal Vein Occlusion (RVO) is the second most common cause of retinal vascular diseases worldwide after diabetic retinopathy [1].

Many etiologies can be attributed to development of RVO, however, the most commonly accepted are thrombosis and embolism [2], resulting, in longstanding cases, in retinal ischemic changes [3].

Fundus Fluorescein Angiography (FFA) has been the gold standard for the diagnosis of various vascular diseases including retinal vein occlusion. It is particularly useful in highlighting the retinal vascular perfusion especially that of the macular area as well as the peripheral retinal ischemic changes [4]. However, the fact that FFA is an invasive procedure that involves dye injection, puts limitation to its repeatability [5]. Also, FFA does not segment the retina, making the imaging of the different capillary layers especially the deep layers not possible [6]. Furthermore, the poor transmission of fluorescence through the RPE layer makes the evaluation of the choroidal circulation not possible [7].

OCT Angiography (OCTA) is a novel method that measures depth resolved blood flow in the retina using the variance in the intensity and phase of the reflected OCT beam. It has shown many advantages compared to FFA. It is a noninvasive and non-contact technique which may replace FFA in patients for whom dye injection is contraindicated such as patients showing advanced renal disease or allergic reactions [8]. Lesions can be quantified regarding volume, thickness and extent. It visualizes histological vascular structure of the retina *in vivo* [9]. It provides direct blood flow information using blood flow as the intrinsic contrast. It gives 3D vasculature mapping at the microcirculation level [8]. It is of great benefit in studying foveal capillary network in multiple planes in the different layers of the retina.

Boundaries and areas of capillary dropout and neovascularization can be precisely measured [10]. Software is rapidly modifying to allow quantification of capillary non-perfusion and enlarge the scan area of OCTA to be able to elicit the peripheral retinal vascular changes which are of importance in the diagnosis of retinal vascular diseases. Moreover, some artifacts during scanning as well as masking of deeper structures by the superficial ones make the interpretation of the scans operator-dependent and in some cases not conclusive.

To highlight the important findings in OCTA imaging of retinal vein occlusion in comparison to fundus fluorescein angiography, its limitations and added information

Patients and Methods

This is a cross-sectional, non-randomized observational study, carried out on a cohort of 34 eyes of 32 Egyptian patients with a known clinical diagnosis of RVO, whether Central Retinal Vein Occlusion (CRVO) or Branch Retinal Vein Occlusion (BRVO). The study was performed during the time period between January, 2016 and January, 2017. Patients were recruited from the Retina Clinic at Kasr Al-Ainy Cairo University Hospitals. Kasr Al-Ainy Hospitals represent a tertiary referral center for most of the governorates in Egypt. The study was approved by the Research Ethics Committee of the Faculty of Medicine, Cairo University. Data collection conformed to all local laws and was compliant with the principles of the Declaration of Helsinki.

OCTA was performed at Bostan Diagnostic Eye Center in Cairo, by one operator (ZS), images were analyzed and interpreted in comparison to the FFA photos.

All patients received a thorough explanation of the study design, and provided their written consents.

Patients included in this study; were patients with a known clinical diagnosis of RVO (any stage, any type) whether, it is associated or not with systemic hypertension, diabetes mellitus and /or glaucoma and whether, it is previously treated or not. The diagnosis of RVO was done by fundus examination and was confirmed by FFA. Patients excluded from the study; were patients with significant retinal comorbidities (including advanced macular pathologies, severe non-proliferative and proliferative diabetic retinopathy) as well as patients with poor image quality due to media opacity.

Methodology in Details

All patients underwent standard clinical examination and testing as appropriate for their clinical disease, including history taking, measurement of the Best Corrected Visual Acuity (BCVA), pupillary light reflex, Intraocular Pressure (IOP) measurement (using Goldmann applanation tonometer), slit lamp examination of the anterior segment, gonioscopy (using Goldmann three-mirror lens), dilated fundus examination (using slit lamp biomicroscopy and indirect ophthalmoscopy), and multimodal imaging procedures, including; color fundus photography, Fundus Fluorescein Angiography (FFA) and Optical Coherence Tomography Angiography (OCTA).

The mean measurement time of OCTA and FFA was 4.44 months ± 5.25 (ranging from 1-24 months) after the clinical diagnosis of RVO.

Fundus Photography and FFA

FFA was done after pupillary dilatation and intravenous injection of 5 ml of 10% fluorescein sodium, without the occurrence of adverse reactions in any of the patients of the study group. Fundus photography and FFA were done for all patients using the TOPCON TRC-50DX retinal fundus camera. The FFA images were evaluated for the visibility of Perifoveal Capillary Arcade (PFCA) of the superficial capillary plexus and its disruption, the presence of central or peripheral non-perfused areas in early-phases, telangiectatic vessels, areas of intraretinal hemorrhages, areas of diffuse or cystoid macular edema, Microaneurysms (MA), disc leakage in late-phases, photocoagulation scars, Neovascularization Elsewhere (NVE), and Disc Neovascularization (NVD). These findings are the gold standard findings to evaluate a case of RVO and therefore are used for comparison with the novel technique of OCTA.

Optical Coherence Tomography Angiography (OCTA)

OCTA images were obtained using the RTVue XR Avanti (AngioVue; Optovue Inc, Fremont, California, USA) machine and the incorporated AngioVue OCTA system. Algorithm used is Split-Spectrum Amplitude Decorrelation Angiography (SSADA).

A-scan rate of the instrument is 70000 scans/second to compose OCTA volumes consisting of 304 X 304 A-scans. AngioVue system is provided by an orthogonal registration algorithm called Motion Correlation Technology (MCT) which minimizes motion artifacts produced by involuntary saccades and changes in fixation during data acquisition. The scans included in the study were of high signal strength more than 0.7 and they were carefully inspected for motion artifacts. Automatic segmentation of intraretinal layers was done using the automated software of the machine (version 2015.1.0; Optovue Inc) revealing: Superficial Capillary Plexus (SCP), 3 μm below ILM to 15 μm below IPL; Deep Capillary Plexus (DCP) 15 to 70 μm below IPL; Outer retina 70 μm below IPL to 30 μm below Retinal Pigment Epithelium (RPE) reference and finally Choroidal Capillary plexus, 30 μm to 60 μm below RPE reference. Angio-retina scan sizes obtained in this study were 6 X 6 mm for all eyes. Angio Disc scans were obtained for eyes showing disc edema on FFA (4.5 X 4.5 mm). Angiographic analyses were done, focusing on the two vascular layers of the retina; SCP and DCP. The findings evaluated included Perifoveal Capillary Arcade Visibility (PFCAV), Perifoveal Capillary Arcade Disruption (PFCAD), Central Non-Perfusion Areas (CNPA), telangiectasia, Microaneurysms (MA) and macular edema with further evaluation on the co-registered OCT en-face intensity images and OCT B-scan images.

Quantitative flow analysis of the SCP has been performed for selected 29 images of 29 eyes (15 with Central Retinal Vein Occlusion (CRVO) and 14 with Branch Retinal Vein Occlusion (BRVO)). The selected OCTA images were 6 X 6 mm, of high quality for accurate estimation of the vessel density. Quantitative flow analysis, included:

Vessel density measurements were performed on the selected images; Early Treatment Diabetic Retinopathy Study (ETDRS) grid overlay is centered on the FAZ of the SCP and then the software automatically measured the vessel density of the SCP in percentage and displayed it; quantitatively in tables and qualitatively in color coded vessel density maps, where the areas of vascular deficiency are color coded as dark blue. At the time of the study, the vessel density measurement at the DCP wasn't available.

Statistical analysis: The statistical methods that were used in this study, included; range, mean (x), Standard Deviation (SD), percentage (%), Chi-square test ($\chi 2$) for comparison of percentages, t-student test for comparison of means and probability level (*P*) for statistical significance. All P values less than 0.05 were considered statistically significant. All statistical calculations were done using computer program's Microsoft Excel 2016 (Microsoft Corporation, NY) and SPSS (Statistical Package for the Social Science; SPSS Inc, Chicago, IL) version 18 for the Microsoft Windows.

Adobe photoshop CS6 (version 13.0.0) was used to improve resolution of some images and to mark the OCTA and FFA images.

Results

Demographic (Table 1) and Clinical Data (Table 2)

The total number of eyes included in the study is 34 eyes of 32 patients as two cases showed bilateral affection and representing 6.25% of the total number of patients, while unilateral RVO was reported in 30 patients representing 93.75 % of the total number of patients.

	Females	Males
No of patients	16	16
% of sex distribution	50%	50%
$\bar{x}$ (mean of age in years)	52.44	52.75
± SD	± 10.40	± 12.15
t *p*	0.017 >0.50	

Table 1: Demographic data (X: mean; ± SD: Standard Deviation; t: t-student test value; *p*).

	CRVO		BRVO		Total RVO		
	Classic	HRVO	Major	Macular			
N° of eyes	15	4	12	3	34		
%	44.12%	11.76%	35.30%	8.82%	100%		
Total N° of eyes	19		15		34		
%	55.88%		44.12%		100%		
Associations						Comparison between CRVO & BRVO χ^2	*P*
RAPD N° %	3 15.79%		2 13.33%		5 14.71%	0.45	> 0.50
POAG N° %	3 15.79 %		3 20 %		6 17.65 %	1.12	> 0.25
Hypertension N° %	7 38.89 %		6 42.86 %		13 40.63 %	0.41	> 0.50
Diabetes N° %	6 33.33 %		4 28.57 %		10 31.25 %	0.79	> 0.25
Hypertension & Diabetes N° %	3 16.67 %		4 28.57 %		7 21.88 %	8.49	<0.01
BCVA							
Decimal (Range)	0.50-0.01		1-0.01		1-0.01		
LogMAR Range (mean ± SD)	0.30-2.00 (0.82 ± 0.38)		0.00-2.00 (0.67 ± 0.42)		0.00-2.00, (0.75 ± 0.41)	1.07	>0.50

Table 2: Clinical data, systemic associations and BCVA.

RVO: Retinal Vein Occlusion; N°: Number of eyes; CRVO: Central Retinal Vein Occlusion; BRVO: Branch Retinal Occlusion; X: mean; ± SD: Standard Deviation; t: t-student test value; P: Probability level; χ^2: Chi-square test Value; BCVA: Best Corrected Visual Acuity; RAPD: Relative Affect Pupillary Defect; POAG: Primary Open-Angle Glaucoma

Comparison between FA and OCTA regarding retinal Pathological findings (Table 3)

PFCA, PFCA Disruption, Central Non-Perfusion Areas (CNPA) and Superficial Capillary Telangiectasia (SCT) were detected more frequently on OCTA than FFA with a highly significant difference (P<0.01) between the two eyes. Disc Edema was only detected by FFA which could detect disc leakage in 7 eyes with CRVO. OCTA could not detect disc leakage in the 7 eyes with disc edema, but there were some findings on OCTA rather than disc leakage, that were compared to the disc edema detected by FFA, and they are mentioned in discussion.

		FA			OCTA			χ^2	*P*
		CRVO	**BRVO**	**Total**	**CRVO**	**BRVO**	**Total**		
PFCA visibility	N°	11	3	14	18	15	33	23.46	< 0.01
	%	57.89%	20%	41.18%	94.74%	100%	97.06%		
PFCA disruption	N°	14	10	24	19	15	34	12.25	< 0.01
	%	73.68%	66.67%	66.67%	100%	100%	100%		
Central NPA	N°	14	10	24	19	15	34	12.25	< 0.01
	%	73.68%	66.67%	66.67%	100%	100%	100%		
Peripheral NPA	N°	11	1	12					
	%	57.89%	6.67%	35.29%					
SCT	N°	3	4	7	5	6	11	6.72	< 0.01
	%	15.79%	26.67%	20.59%	26.32%	40%	32.35%		
DCT	N°				19	15	34		
	%				100%	100%	100%		
MA	N°	16	12	28	19	15	34	3.78	< 0.05
	%	84.21%	80.00%	82.35%	100%	100%	100%		
Macular edema	N°	14	11	25	15	10	25	No difference	
	%	73.68%	73.33%	73.53%	78.95%	66.67%	73.53%		
Intraretinal hemorrhages	N°	15	13	28	15	13	28	No difference	
	%	78.95%	86.67%	82.35%	78.95%	80.67%	82.35%		
***Disc edema**	N°	7		7					
	%	36.84%		20.59%					

Table 3: Comparison between FA and OCTA regarding the incidence of detected retinal pathological findings of RVO.

FA: Fluorescein Angiography; OCTA: Optical Coherence Tomography Angiography; RVO: Retinal Vein Occlusion; CRVO: Central Retinal Vein Occlusion; BRVO: Branch Retinal Vein Occlusion; χ2: Chi-square test value; N°: Number; P: Probability level; PFCA: Perifoveal Capillary Arcade; NPA: Non-Perfusion Area(s); SCT: Superficial Capillary Telangiectasia; DCT: Deep Capillary Telangiectasia; MA: Microaneurysms

*There were some findings rather than disc leakage that were suspicious for disc edema on OCTA.

modalities. Intraretinal hemorrhages and Macular edema; were detected equally by both FFA & OCTA (with the help of the co-registered en-face OCT) modalities in 28 and 25 eyes respectively. However, co-registered OCT B-Scan could detect macular edema in 29 eyes representing 85.29% of the total number of eyes. Microaneurysms (MA) were detected more frequently on OCTA than FFA, however no significant difference (P>0.05) was found. Peripheral Non-Perfusion Areas (PNPA) were only detected by FFA. Deep Capillary Telangiectasias (DCT) were only detected by OCTA in all

Comparison between incidence of pathological retinal changes of SCP and those of DCP in RVO as revealed by OCTA (Table 4)

Perifoveal capillary disruption and Non-perfusion areas were detected in both SCP and DCP of all eyes of the study, while Capillary telangiectasia, Intraretinal cysts (edema), Hemorrhages and Microaneurysms were detected more frequently in DCP than in SCP with a high statistically significant difference (P<0.01) of the incidence of their detection between the two plexuses.

		SCP			DCP			χ^2	*P*
		CRVO	**BRVO**	**Total**	**CRVO**	**BRVO**	**Total**		
PFCA disruption	N°	19	15	34	19	15	34		
	%	100%	100%	100%	100%	100%	100%		
NPA	N°	19	15	34	19	15	34		
	%	100%	100%	100%	100%	100%	100%		
Capillary telangiectasia	N°	5	6	11	19	15	34	141	< 0.01
	%	26.32%	40%	32.35%	100%	100%	100%		
Cysts	N°	7	7	14	15	10	25	25.41	< 0.01
(Edema)	%	36.84%	46.67%	41.81%	78.95%	66.67%	73.53%		
Intraretinal hemorrhages	N°	0	2	2	15	13	28	994.5	< 0.01
	%	0%	13.33%	5.88%	78.95%	86.67%	82.35%		
MA	N°	14	10	24	19	15	34	12.25	< 0.01
	%	73.68%	66.67%	70.59%	100%	100%	100%		

Table 4: Comparison between Superficial capillary plexus and Deep capillary plexus regarding the incidence of detected retinal pathological findings of RVO.

SCP: Super Capillary Plexus; DCP: Deep Capillary Plexus; RVO: Retinal Vein Occlusion; CRVO: Central Retinal Vein Occlusion; BRVO: Branch Retinal Vein Occlusion; χ^2: Chi-square test value; N°: Number; *P*: Probability level; PFCA: Perifoveal Capillary Arcade; NPA: Non-Perfusion Area(s); MA: Microaneurysms

Quantitative flow analysis is shown in (Table 5)

On 6 X 6 mm scans, the mean vessel density percentage of the superficial vascular plexus in the whole macular area, central and para-central subfields, is shown in table 4, in selected 29 images of 29 eyes (15 with CRVO and 14 with BRVO). There was a statistically significant decrease ($P<0.05$) between the mean value of the superficial macular vessel density of the eyes with RVO in our study and that of the normal eyes in a study conducted by You et al. [21].

	CRVO			BRVO			Total		
	N° (Eyes)	Mean vessel density %	± SD	N° (Eyes)	Mean vessel density %	± SD	N° (Eyes)	Mean vessel density %	± SD
Whole Macular area	15	46.12	3.31	14	44.8	3.19	29	4.48	3.32
Fovea	15	37.28	8.94	14	33.94	5.87	29	35.67	7.8
Parafovea	15	45.87	3.72	14	45.35	3.68	29	45.62	3.71
Parafovea - superior Hemi	15	45.24	4.12	14	47.8	13.33	29	46.48	9.81
Parafovea - inferior Hemi	15	46.47	4	14	46.14	5.13	29	46.31	4.59
Parafovea - Temporal	15	46.84	4.23	14	44.72	4.26	29	45.82	4.39
Parafovea -superior	15	43.2	9.19	14	43.69	4.48	29	44.33	4.82
Parafovea - Nasa	15	45.33	4.65	14	46.88	5.07	29	46.08	4.92
Parafovea - inferior	15	46.28	5.08	14	46.11	6.03	29	46.2	5.56

Table 5: Macular vessel density percentage of the Superficial Vascular Plexus in RVO.

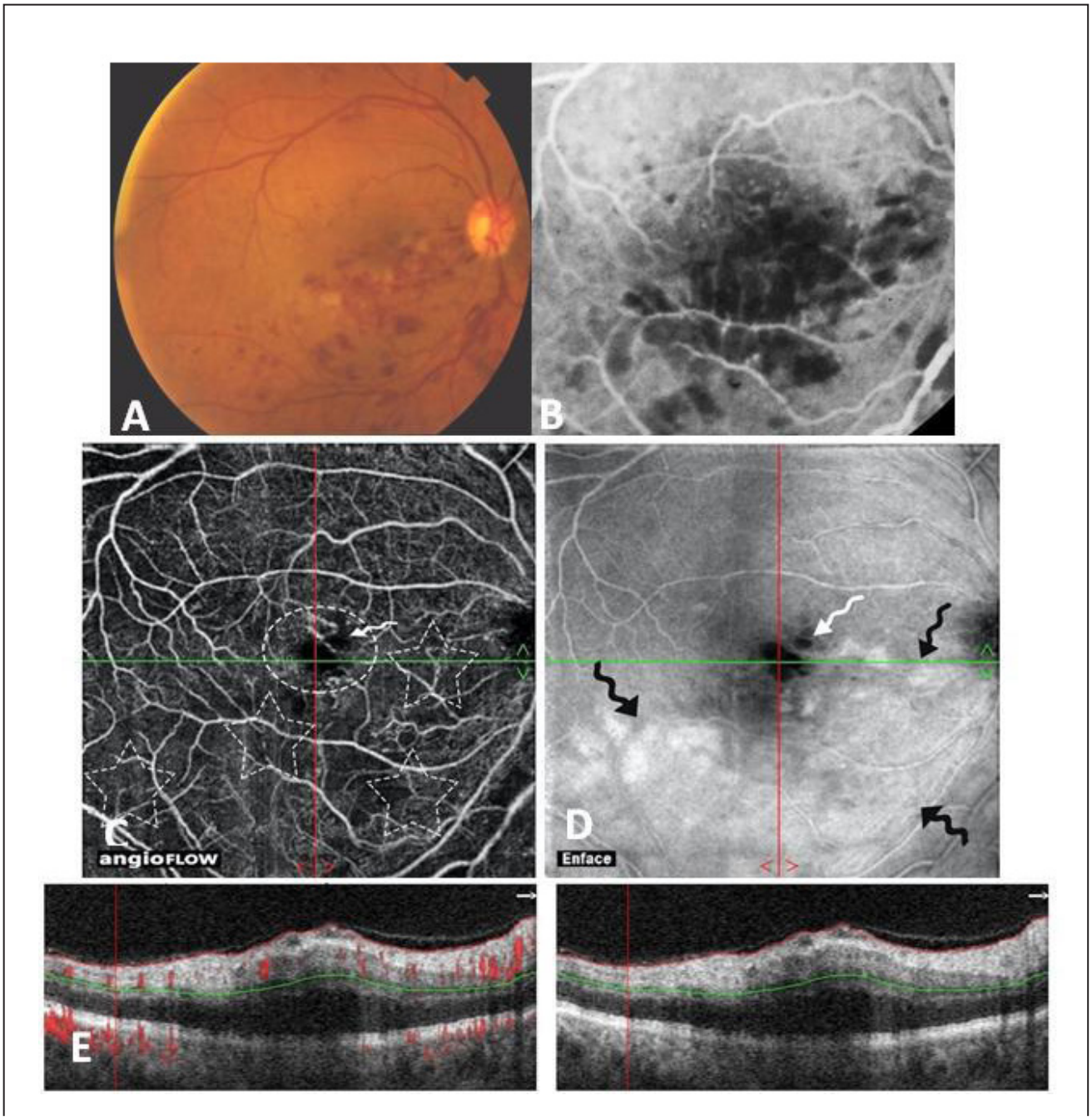
RVO: Retinal Vein Occlusion; N°: Number of eyes; CRVO: Central Retinal Vein Occlusion; BRVO: Branch Retinal Vein Occlusion; ± SD: Standard Deviation of the mean value of vessel density percentage

Discussion

OCTA is a recent modality which provides qualitative and quantitative information about the retinal vascular perfusion. It is a non-invasive modality, not involving dye injection, thus can provide an advantage that may be useful for patients who suffer from advanced renal disease or reported allergic reactions. However, the reproducibility of OCTA is still under investigation.

In this study, the role of OCTA in the assessment of RVO

is being investigated and compared to FFA. OCTA took the upper hand over FFA in the visibility of the Perifoveal Capillary Arcade (PFCA) and Central Non-Perfusion Areas (CNPA) (Table 3). These observations were also pointed out by Suzuki et al., [3] and Coscas et al., [11]. This could be explained by the fact that, PFCA and CNPA were masked in FFA images by either macular hemorrhages or macular edema or both as pointed out by Laatikainen et al., [12] (Figure 1).



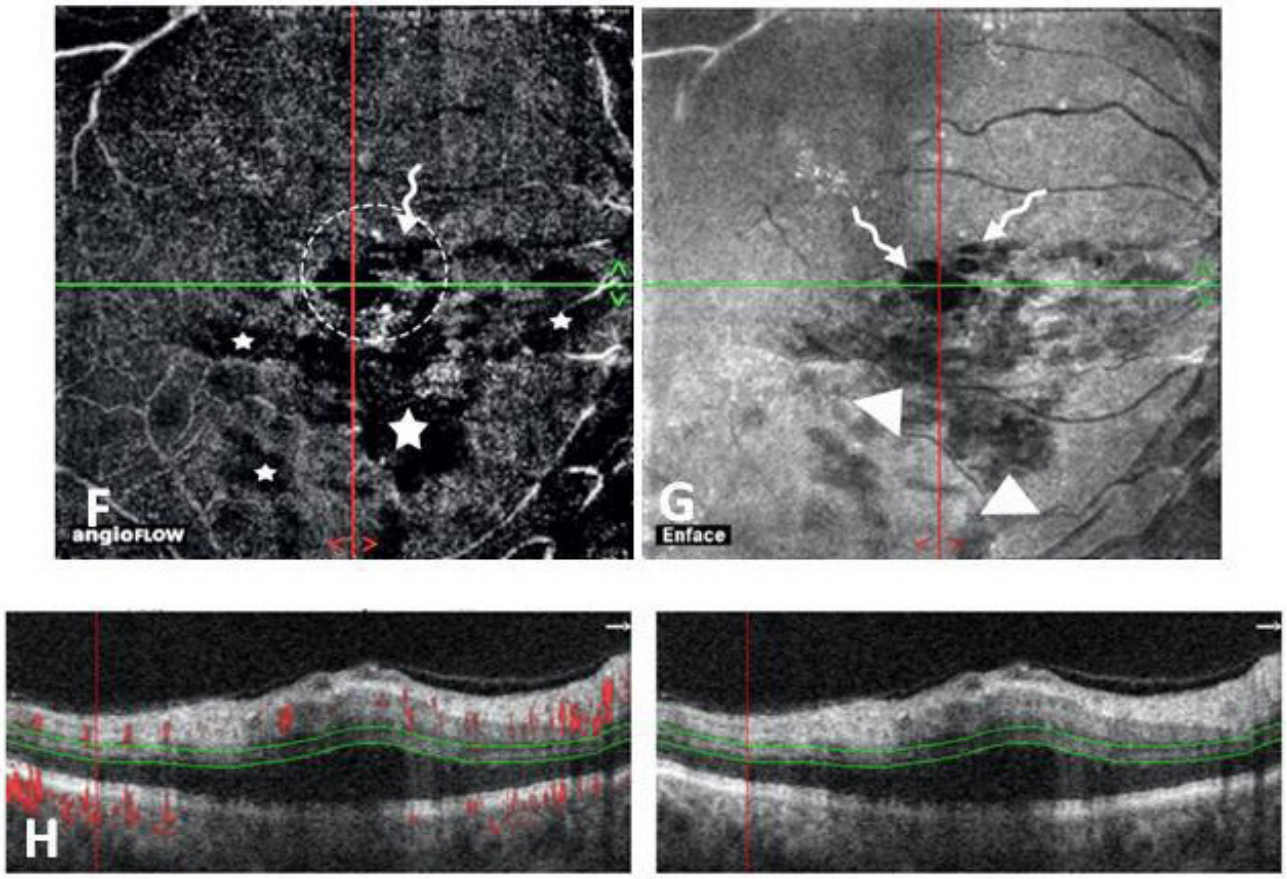


Figure 1: Right BRVO (~1 month' duration) involving inferior temporal and nasal quadrants of the macula (Inferotemporal BRVO).

A: Color fundus photograph shows intraretinal hemorrhage involving infero-nasal quadrant of the macula.
B: Zoom on the fovea in early-phase FFA shows hypo fluorescence due to retinal hemorrhage, which masks the NPA and PFCA in the infero-nasal quadrant of the macula.
C: OCTA image of the superficial capillary plexus showing hypointense dark areas; NPA (white dashed stars), corresponding to whitish infarction which takes the shape of the nerve fiber layer, on the en-face OCT image (black arrows); black cysts with no decorrelation flow signal (white dashed arrow and circle), corresponding to intraretinal cystoid spaces on the en-face OCT image (white arrow).
D: En-face OCT image at the same level of the SCP.
E: OCT B-scan showing the section level used for stratigraphic analysis.
F: OCTA of the deep capillary plexus, showing areas of capillary network disruption due to the presence of hemorrhage (white stars), corresponding to the low reflectivity patches (white triangles) seen on the en-face OCT image of the DCP (G).
H: OCT B-scan showing the section level used for stratigraphic analysis.

Disruption of PFCA of SCP was observed much more frequently (P<0.01) in the images of OCTA than in those of FFA (Table 3). Coscas et al., [11] results supported our observation, who reported the visibility of perifoveal capillary arcade in 52 of 54 eyes (96%) on OCTA and in 45 eyes (83%) on FFA. This arcade was disrupted in 48 eyes (92%) and 39 eyes (72%) on OCTA and FFA, respectively (P=.002) in their study.

PFCAD was revealed in both SCP and DCP of all eyes of our study on OCTA. Coscas et al., [11], reported retinal capillary network abnormalities in both SCP and DCP with more frequent non perfusion areas in the DCP (P<.001).

The observation of PFCAD in all OCTA images might be attributed to the presence of non-perfusion areas, areas masked by intra-retinal hemorrhages, macular edema or hard exudates. The above-mentioned findings appeared as hypo-intense, dark grayish areas on OCTA which were further analyzed concerning the capillary density, capillary network appearance and flow analysis to reach the exact diagnosis. The diagnosis is further confirmed by the co-registered enface OCT images.

In our study, OCTA was superior to FFA in delineating CNPA and differentiating them from the FAZ and also from the surrounding perfused retina. Suzuki et al., [3] and Kashani

et al., [2] reported the same observation.

This observation could be explained by the fact that OCTA machine can provide higher resolution images than those obtained by FFA machines [3]. In addition, FFA is more affected than OCTA by media opacity as OCTA machines use a beam of 840 nm wavelength as a light source which is less affected by media opacities than the emission light of 520 nm of FFA machines [3].

CNPA were revealed in both SCP and DCP of all eyes of our study. Our study was in agreement with the study of Cardoso et al., [13]. However, Coscas et al., [11] reported more Non- Perfusion Areas (NPA) in DCP than in SCP but with no statistically significant difference and Rispoli et al., [14] observed capillary non-perfusion occurrence mainly in SCP.

Whereas OCTA was superior to FFA in the detection of CNPA, Peripheral Non-Perfusion Areas (PNPA) were only detected by FFA. Coscas et al., [11] stated that it was impossible to assess peripheral retina by OCTA. However, they found a positive correlation between peripheral ischemia (capillary dropout on FFA) and PFCAD in SCP (P=0.025), capillary network disruption in DCP (P=0.015) and presence of NPA in DCP (P=0.016). They concluded that when there was no PFCAD in SCP (on OCTA), FFA never showed peripheral ischemia. Therefore, OCTA can help in identifying patient who won't require FFA. In our study, we couldn't do this correlation due to the limited patient number. All eyes in our study were found to have PFCAD in SCP. Cardoso et al., [13] stated that acquiring scans of the retinal periphery by OCTA is difficult and time consuming; however, they demonstrated that in most cases, an 8 X 8 mm OCTA scan centered on the macula could provide enough information about the ischemic or non-ischemic nature of RVO.

In our study, Superficial Capillary Telangiectasia (SCT)could be detected in both studied modalities, however, the number of eyes in which SCT was detected by OCTA is statistically higher than those detected on FFA images (P<0.01) (Table 3). Besides, OCTA could visualize SCT clearer than FFA in addition to the visualization of the detailed capillary network in the SCP. Suzuki et al., [3] registered same observations.

The superiority of OCTA modality in detecting telangiectasia is due to its ability to reproduce scans of higher resolution than FFA modality, and also due to the fact that OCTA is less affected by media opacities [2,3]. The more rapid blood flow in superficial capillary telangiectasia could also enhance their detection by the OCTA [14].

In our study, Deep Capillary Telangiectasia (DCT) could only be detected by OCTA as FFA is a two-dimensional imaging modality. The same observation was reported by Suzuki et al., [3].

Comparing DCP with SCP regarding the presence of telangiectasia, there was a highly significant difference between the two plexuses (P<0.01) in favour for the DCP (Table 4). This observation was in agreement with previous studies as Suzuki et al., [3], Coscas et al., [11], Cardoso et al., [13] and Rispoli et al., [14].

Moreover, our study revealed Superficial Capillary Telangiectasia (SCT) at the edges of NPA in the affected area of RVO and in DCP, telangiectasia was found associated with microaneurysms surrounding cystoid spaces in all eyes except in two eyes, in which it was found surrounding NPA. This observation could be explained by the vascular congestion resulting from the venous obstruction. Rispoli et al., [14] demonstrated that in early BRVO, capillary telangiectasia (vascular congestion) was mainly localized at the edges of healthy tissue, in the deep capillary plexus.

Despite the fact that both modalities showed no statistically significant difference regarding the detection of microaneurysms (P>0.05), yet the study conducted by Suzuki et al., [3] and our study, demonstrated that OCTA, unlike FFA, could facilitate differential layer analysis of microaneurysms in all eyes of the study group. Thereby, OCTA images demonstrated that microaneurysms were present more frequently in DCP than in SCP with high statistically significant difference (P<0.01) of their incidence between the two plexuses (Table 4).

The explanation of how deep capillary plexus is more affected than superficial capillary plexus in retinal vein occlusion regarding telangiectasia and microaneurysms has an anatomical background. The DCP, unlike SCP, is organized into capillary vortexes which show radial convergence of capillaries toward an epicenter; thus, they are drained directly into the superficial venules [15,16]. Therefore, when venous pressure is increased in the major veins in superficial vascular layer due to RVO, this, in turn leads to rapid and higher elevation of venous pressure in the DCP than in the SCP [15,16]. Moreover, capillary densities are much greater in DCP than in SCP contributing again to the marked involvement of DCP in RVO [17]. Also, microaneurysms seem to be a microvascular response to Vascular Endothelial Growth Factor (VEGF) generated from hypoxic retinal tissue and since SCP as stated by Martinet et al., [15] has higher perfusion pressure and oxygen supply in RVO, thus it is better preserved than DCP [18].

There was no statistically significant difference between both modalities, concerning the detection of collateral vessels,

intra-retinal edema and hemorrhages. However, OCTA was superior to FFA in locating the level of the collateral circulation as well as that of the cystoid spaces of macular edema and the hemorrhages which were detected much more frequently in DCP than in SCP (P<0.01) (Table 4). This may be due to the fact that the primary interstitial space within the retina is the Outer Plexiform Layer (OPL) where the fluid in the edematous retina usually accumulates and that the intra-retinal hemorrhages were primarily detected in the deep retinal layers.

In comparison to FFA, our study demonstrated that, on OCTA, the retinal perfusion can only be assessed in the retinal layers superficial to those involved with intraretinal hemorrhages, as the hemorrhages block OCTA signal to some extent and cause disruption of the capillary network with no flow signal. Same observation was reported by Kashani et al. [2].

In our study, disc edema without NVD could only be detected by FFA not by OCTA. However, studying the radial peri-papillary capillary plexus by OCTA revealed their distortion up to their interruption with increase in the caliber of the large vessels which, in addition to the structure of the disc, might give an indication of disc edema by OCTA, yet a satisfying conclusion is not reached [19].

Our study introduced an additional advantage of the OCTA over the conventional FFA imaging modality in RVO, which is the ability of OCTA to perform quantitative flow analysis of the retinal vasculature in RVO. Previous studies used OCTA to quantify the flow in either healthy eyes as the study conducted by Shahlaee et al., [20] or compared healthy eyes with eyes showing retinal pathologies as the study conducted by You et al. [21].

In this study, we reported the retinal microvasculature density at the level of the SCP in both central and branch retinal vein occlusions (Table 5). We found that there is a significant difference between the mean value of the superficial macular vessel density of the eyes with RVO in our study and that of the normal eyes in the study of You et al., [21] (Table 5), which proved that RVO is injurious to the retinal vasculature of the SCP.

The main defect in our study is that the quantitative flow analysis that we have performed, involved only the superficial capillary plexus leaving out the deep capillary plexus, as the software (version 2015.1.0) used for DCP flow density was not available at the time of the study. Also, it lacked the presence of a control group of healthy eyes. In addition, our study did not take into consideration the duration of retinal vein occlusion, whether it is previously treated or not, the type of treatment as well as the age of the selected patient. Therefore, a future study is recommended where quantitative flow analysis is done on both superficial and deep capillary plexuses and where the age of the study population, the duration of retinal vein occlusion disease, previously treated or not and the type of treatment are taken into consideration.

In conclusion, OCTA provides a non-invasive objective tool for quantitative evaluation of the retinal perfusion status which might facilitate the management and follow up of different retinal vascular disorders. However, the variability in the interpretation of the scans due to the presence of artifacts and segmentation defects gives FFA the upper hand till now in the diagnosis of retinal vascular diseases. OCTA may add an accurate prognostic modality for follow-up regarding the ischemic changes and conversion from non-ischemic condition to ischemic.

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