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Optical coherence Tomography Angiography versus Fundus Fluorescein Angiography in chronic central serous chorioretinopathy

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Abstract

The detection of a clear vascular network by OCTA was superior to that by FFA. 10 eyes showed as a thick, interlocking filamentous neovascular membrane that was well characterised. Statistics showed that the difference was substantial (P 0.001)**.** Additionally, in our study, the distinct dye leakage patterns of the Chronic CSC on FA did not correlate with the CNV shown on OCTA, supporting the idea that OCTA identifies the choroidal neovascular network by depth and is independent of dye leakage detected on FA. To evaluate and study the role of OCT Angiography in eyes with chronic CSCR with CNV and non CNV group in comparison with fundus fluorescein angiography. This a comparative cross–sectional study. It was performed in AL Zahraa hospital (Al -Azhar University) in the period from March 2021 to Jun 2022. Clinical data and images were obtained from 20 eyes. Ink-Blot pattern was the most common FFA findings like other studies which was found in 8 cases out of 10 (80%) of Chronic CSR without CNV and was found in 9 cases out of 10 (90%) of Chronic CSR with active CNV. As a non-invasive, quick, and dependable angiographic imaging method, OCTA has advantages over FA. The ability to view the retinal and choroidal vasculature in various layers is another benefit of OCTA. The narrow field of vision of OCTA, inability to detect leakage, difficulty detecting blood flow below a particular level.

Keywords: Optical; Coherence; Tomography; Fundus; Fluorescein.

1. Introduction

Central serous chorioretinopathy (CSCR) is a disease in which a serous detachment of the neuro- sensory retina occurs over an area of leakage from the choriocapillaris through the retinal pigment epithelium, (RPE). Affected mid aged male more than female [1]. It is a self-limited macular disease marked by distortion, blurry vision and metamorphopsia. Other causes for RPE leaks, such as choroidal neovascularization (CNV), inflammation or tumours, should be ruled out to make the diagnosis [2]. May be related to a wide range of risk factors, including hypertension, helicobacter pylori infection, use of steroids, sleeping disturbances,

autoimmune diseases, pregnancy and others [3].

CSC is characterized by localized subretinal fluid (SRF) at the posterior pole that typically resolves spontaneously within a few months. In chronic cases, however, SRF can persist, damaging the photoreceptors and retinal pigment epithelium (RPE) and resulting in irreversible vision loss [4].

Chronic CSCR is defined as persistent symptoms for at least 6 months from the onset of acute attack or persistent sub retinal fluid associated with retinal pigment epitheliopathy. Some patients can also develop choroidal neovascularization (CNV), which leads to severe loss in visual acuity [5].

Based on the onset of symptoms and the retinal and RPE changes that result, CSC can be subgrouped into several forms: an acute form with self-resolving SRF, a non-resolving form with SRF persisting longer than 4 months, a chronic atrophic form revealing widespread RPE atrophy with or without fluid, and an inactive form without SRF [6].

The typical diagnostic clinical workup of CSC consists of a basic slit-lamp examination, optical coherence tomography (SD-OCT), fundus autofluorescence (FAF), fluorescein angiography (FA) and indocyanine green angiography (ICG). However, none of these methods provide a detailed, high-resolution image of the CSC to enable insight into the currently proposed path mechanism [7]. FFA is the oldest and classic imaging technique for CSC evaluation, which is often used to establish the diagnosis and to rule out other differential conditions. It helps to determine the type of leakage pattern and to localize the leakage point [8]. Optical coherence tomography angiography (OCTA) is a new, non-invasive, non-dye, depth-resolved technique, which may be to investigate patients with CSC. The concept of OCTA is the detection of changes in blood flow in the vessels, in a static eye, without need for dye injection [9]. OCTA images may be studied by isolated segmentation in different vascular layers, thus allowing analyzing the vascular structure in detail with no darkening due to staining or leakage [10].

It is a non-invasive dye-less imaging modality that has been introduced for depth-resolved imaging of the retinal and choroidal vasculature by detection of endoluminal flow [11].

OCTA provides qualitative and quantitative assessment of retinal vascular changes in retinal vasculitis but is also helpful for the diagnosis and monitoring of several inflammatory and ischemic choroidal pathologies [12].

OCTA is an advanced imaging technology that enables imaging, segmentations and quantifications of blood flow in the retina and choroid [13]. This paper aims to evaluate and study the role of OCT Angiography in eyes with chronic CSCR with CNV and non CNV group in comparison with fundus fluorescein angiography.

2. Patients and Methods

This a comparative cross–sectional study. It was performed in AL-Zahraa hospital (Al -Azhar University) in the period from March 2021 to Jun 2022. Clinical data and images were obtained from 20 eyes divided into two groups:

2.1 Sampling Size and Method

Twenty cases will be classified randomly in 2 groups: Group 1 (G1): include 10 Eyes with chronic CSR with CNV Group 2 (G2): include 10 Eyes with chronic CSR without CNV.

2.2 Inclusion Criteria

Age (20-55 y), patients with Presence of SRF involving the fovea on structural OCT and patients with clinical history of CSC and visual impairment.

2.3 Exclusion Criteria

Existence of an ocular disease that could contribute to the decreased visual acuity, presence of significant media opacities (e.g cataract or corneal opacity), sub retinal fibrosis, age-related macular degeneration, macular or retinal vascular disease and vitreoretinal disease or retinal surgery, and hereditary retinal dystrophy) were excluded from the study

2.4 Study Tools and Procedures

2.4.1 Demographic Data

History taking (Age, gender, history of DM, HTN, Past history of any ocular surgery, refractive surgery or ocular trauma).

2.4.2 Full ophthalmological examination including:

2.4.2.1 Assessment of visual acuity:

Visual acuity examinations included measurements of BCDVA, and unaided VA (UCVA) and measurements of visual acuity (UCVA) and best corrected visual acuity (BCVA) using Landolt's broken ring chart. All types of VA were converted to logMAR VA chart for statistical purposes.

2.4.2.2 Device

TOPCON Slit lamp examination of anterior segment and posterior segment using Volk lens +90 diopter.

2.4.2.3 Fundus Appearance:

The fundus appearance of the lesion is almost always diagnostic, elevation of macular area, circular ring reflex on the retina, round or ovoid blister like sensory retinal detachment of various sizes, foveal reflex is absent or distorted, after few weeks of onset of the disease, tiny irregular white or yellow precipitates become deposited on the retina, atrophic RPE changes, in chronic cases, a fine brown and white pigment epithelial scar will develop and Extra macular RPE tracts.

2.4.2.4 Measuring IOP using the aplanation tonometery. 4- **Fluorescein angiography**:

FFA images were captured by ZIESS (The VISUCAM 524 fundus camera from ZEISS). A web-based ophthalmic data management platform, used IMAGEnet6, for processing the image.

Figure (1): FFA ZIESS

Technique:

Inform the patient about why and how (briefly) the procedure is being performed, the side effects and also elicit history that would be a contraindication for the procedure (or would necessitate more caution**.**

Obtain informed consent:

Tell the patient about the essence of time during the angiographic procedure and that a great deal would depend on his co-operation during the actual procedure, dilate pupils with a short acting mydriatic-cycloplegic (tropicamide 1%) one hour before the photography, prepared adrenaline, antihistaminic and oxygen at angiography unit for any possible side effect, prepare injection site by introducing a scalp vein, guide patient to the fundus camera and help him seat comfortably with chin placed on the chin rest and forehead abutting the forehead rest, color and red

free fundus photography were taken and IV injection of 5ml of a 10% fluorescein solution containing 500 mg sodium fluorescein was injected rapidly as bolus dose within approximately 5 seconds.

2.4.2.5 Optical coherence tomography angiography examination:

we used a newly developed SD-OCT device (OptoVue RTVue XR Avanti AngioVue; Optovue, Inc., Fremont, CA).

Figure (2): OCTA Optovue

Technique was explained to the patient, chain hight, imaging instrument and chin rest was adjusted to approximate position, the subject was asked to look at internal fixation target and circular scan 6x6 with circle diameter of 320x320 mm was centered around macula, OCTA is a 3D imaging modality that provides high-quality static images of the retinal and choroidal vasculature without the need for any dye Injections — dye free study of the chorioretinal vasculature, sequential B-scans are taken of the same retinal location and then subjected to analysis to determine if there was any change in the amplitude or phase of the scan, if changes are detected, this signifies movement in the retinal tissue of this location and the obtained signal can then be amplified (SSADA split spectrum amplitude decorrelation angiography) and digitally processed to provide an en face view of the vasculature at different layers of the retina.

2.5 Statistical Analysis:

data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when parametric. Also, qualitative variables were presented as number and percentages. The comparison between groups regarding qualitative data was done by using Chi-square test and/or Fisher exact test when the expected count in any cell found less than 5.

The comparison between two independent groups with quantitative data and parametric distribution was done by using independent t-test.

Receiver operating characteristic curve (ROC) was used to assess the best cut off point with its sensitivity, specificity, positive predictive value, negative predictive value and area under curve (AUC) of the studied marker.

Kappa agreement to assess the variability between two qualitative variables

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P-value > 0.05: Non-significant (NS), P-value < 0.05: Significant (S) and P-value < 0.01: Highly significant (HS).

3. Results

It includes 20 eyes which are divided into 2 groups) chronic CSR with CNV and chronic CSR without CNV groups).

Table 1: Comparison between FFA results and OCTA results. (no significant):

		FFA	OCTA	Test value	P-value	Sig.
		No. (%)	No. (%)			
CNV	No CNV	10 (50.0%)	10 (50.0%)	0.000*	1.000	NS
	Active CNV	10 (50.0%)	10 (50.0%)			
PED	No	16 (80.0%)	16 (80.0%)	0.000*	1.000	NS
	Present	4 (20.0%)	4 (20.0%)			
Foveal area	No	3 (15.0%)	5 (25.0%)	0.625*	0.429	NS
	Yes	17 (85.0%)	15 (75.0%)			
Lower temporal	No	14 (70.0%)	12 (60.0%)	0.440*	0.507	NS
	Yes	6 (30.0%)	8 (40.0%)			
Lower nasal	No	18 (90.0%)	18 (90.0%)	0.000*	1.000	NS
	Yes	2 (10.0%)	2 (10.0%)			
Upper temporal	No	19 (95.0%)	18 (90.0%)	0.360*	0.549	NS
	Yes	1 (5.0%)	2 (10.0%)			
Temporal paracentral area	No	20 (100.0%)	19 (95.0%)	1.026*	0.311	NS
	Yes	0 (0.0%)	1 (5.0%)			

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant, *: Chi-square test

Table 2: Relation between FFA and OCTA to assess CNV. (highly significant)

		FFA		Test value	P-value	Kappa agreement (95% CI)
		No CNV	Active CNV			
		No. (%)	No. (%)			
OCTA	No CNV	10 (100.0%)	0 (0.0%)	20.000*	<0.001	1.000 (1.000 – 1.000)
	Active CNV	0 (0.0%)	10 (100.0%)			

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant, *: Chi-square test

Table 3: Relation between FFA and OCTA to assess PED. (highly significant)

		FFA		Test value	P-value	Kappa agreement (95% CI)
		No PED	Present PED			
		No. (%)	No. (%)			
OCTA	No PED	16 (100.0%)	0 (0.0%)	20.000*	0.000	1.000 (1.000 – 1.000)
	Present PED	0 (0.0%)	4 (100.0%)			

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant, *: Chi-square test

Table 4: Relation between CNV activity and demographic data. (significant).

		No CNV (FFA)	Active CNV (FFA)	Test value	P-value	Sig.
		No. = 10	No. = 10			
Age	Mean ± SD	46.60 ± 3.75	39.40 ± 9.71	2.188•	0.042	S
	Range	42 – 52	25 – 53			
Sex	Female	0 (0.0%)	4 (40.0%)	5.000*	0.025	S
	Male	10 (100.0%)	6 (60.0%)			
Laterality	Unilateral	6 (60.0%)	4 (40.0%)	0.800*	0.371	NS
	Bilateral	4 (40.0%)	6 (60.0%)			

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant, *: Chi-square test; •: Independent t-test

Table 5: Relation between CNV activity and FFA results. (no significant)

FFA		No CNV (FFA) No. = 10	Active CNV (FFA) No. = 10	Test value	P-value	Sig.
Early FFA	Normal arm of retinal circulation	10 (100.0%)	10 (100.0%)	–	–	–
Late FFA	Pooling	1 (10.0%)	3 (30.0%)	1.250*	0.264	NS
	Hyperfluorescent +leakage	9 (90.0%)	7 (70.0%)			
FFA pattern	Ink bolt	9 (90.0%)	8 (80.0%)	0.392*	0.531	NS
	Smock stuk	1 (10.0%)	2 (20.0%)			
No. of leakage	1 point	5 (50.0%)	3 (30.0%)	1.700*	0.637	NS
	2 point	2 (20.0%)	3 (30.0%)			
	3 point	3 (30.0%)	3 (30.0%)			
	4 point	0 (0.0%)	1 (10.0%)			
PED	No	8 (80.0%)	8 (80.0%)	0.000*	1.000	NS
	Present	2 (20.0%)	2 (20.0%)			
Site of Chronic CSR	Foveal area	8 (80.0%)	9 (90.0%)	0.392*	0.531	NS
	Lower temporal	2 (20.0%)	4 (40.0%)	0.952*	0.329	NS
	Lower nasal	2 (20.0%)	0 (0.0%)	2.222*	0.136	NS
	Upper temporal	1 (10.0%)	0 (0.0%)	1.053*	0.305	NS
	Temporal paracentral area	0 (0.0%)	0 (0.0%)	–	–	–
Neurosensory detachment	Present	10 (100.0%)	10 (100.0%)	–	–	–

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant, *: Chi-square test.

Table 6: Relation between CNV activity and OCTA results (Highly significant).

OCTA		No CNV (FFA) No. = 10	Active CNV (FFA) No. = 10	Test value	P-value	Sig.
Superfecial cap.plex	Normal FAZ	10 (100.0%)	10 (100.0%)	–	–	–
Deep capillary plx	Subretinal fluid	10 (100.0%)	10 (100.0%)	–	–	–
Outer retina	No vascular lesion	10 (100.0%)	0 (0.0%)	20.000	0.000	HS
	Hyper reflective vascular lesion	0 (0.0%)	10 (100.0%)			
Choriocapilaris	Dark area	8 (80.0%)	0 (0.0%)	20.000	0.000	HS
	Dark area + Dark spot	2 (20.0%)	0 (0.0%)			
	Dark area + Abnormal blood vessels	0 (0.0%)	8 (80.0%)			
	Dark area + Dark spot + Abnormal bl. vessle	0 (0.0%)	2 (20.0%)			
CNV	No CNV	10 (100.0%)	0 (0.0%)	20.000	0.000	HS
	Active CNV	0 (0.0%)	10 (100.0%)			
PED	No	8 (80.0%)	8 (80.0%)	0.000	1.000	NS
	Present	2 (20.0%)	2 (20.0%)			
Site of Chronic CSR	Foveal area	8 (80.0%)	7 (70.0%)	0.267	0.606	NS
	Lower temporal	3 (30.0%)	5 (50.0%)	0.833	0.361	NS
	Lower nasal	2 (20.0%)	0 (0.0%)	2.222	0.136	NS
	Upper temporal	1 (10.0%)	1 (10.0%)	0.000	1.000	NS
	Temporal paracentral area	0 (0.0%)	1 (10.0%)	1.053	0.305	NS
Neuorosensory detachment	Present	10 (100.0%)	10 (100.0%)	–	–	–

4.CASES

Case1: OCTA and FFA in CCSR

This figure shows OCTA and FFA finding in chronic CSR

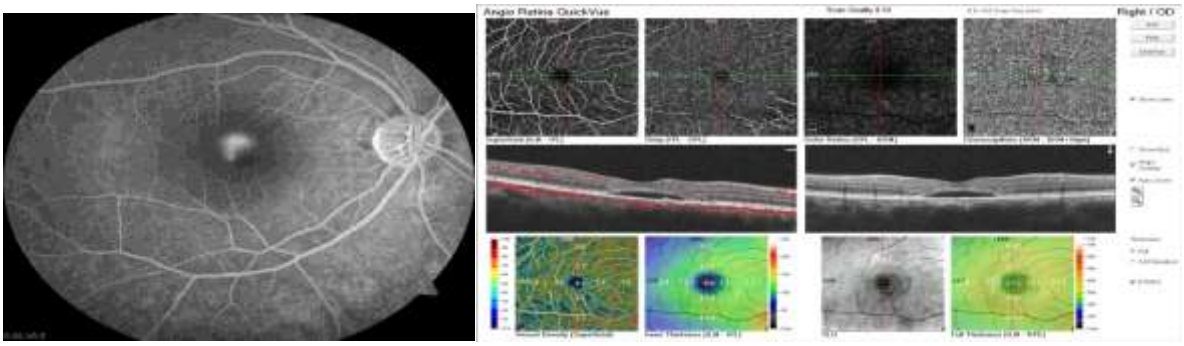

Figure 3): a. suparfecial capillary plexus b. Deep capillary plexus c. Outer retina d. Choriocapillaris e. B-scan of macula f-ffa smock stuk appearance in ccsr.

Case 2: CCSR with CNV compare between FFA and OCTA

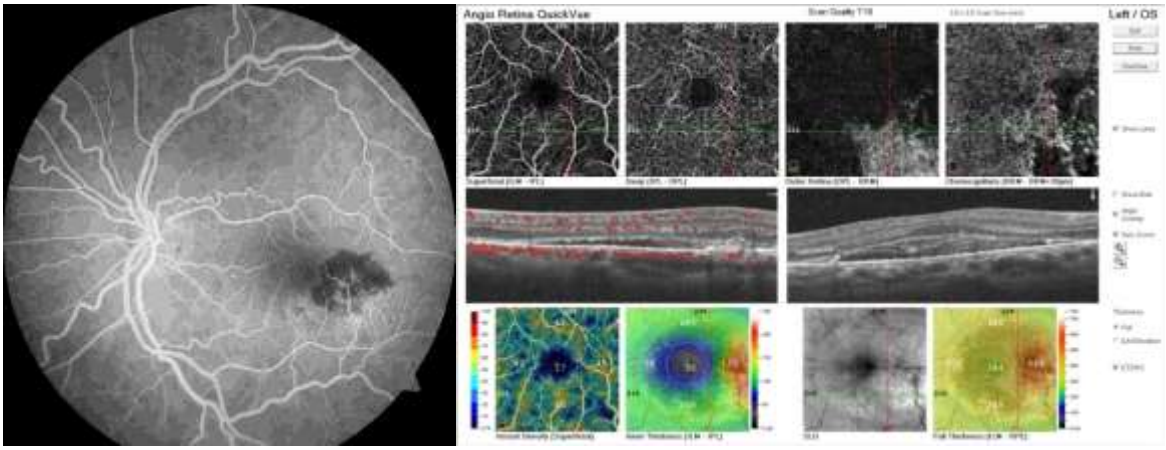

Figure 4: FFA show normal retinal arm,early hyperfluorescence consistant with the RPE atrophy that shows no leackag in late phases. Dot hyper fluorescence could be seen within the lower temporal macular area that shows leackag in late phase

5. Discussion

After reviewing the voluminous literature on the etiology and pathogenesis of CSC, it certainly seems that CSC is a multifactorial disease. It appears to result from a complex interaction of known and unknown environmental and genetic factors. This ultimately leads to a Bilateral disease with systemic associations.

The mean age group of the present study was 44 years, which was similar to previous various studies of CSCR [14]. Various studies proved that male shows a preponderance toward the disease 5–10 times more than female (15). In our study we had a male: female ratio of 4:1. The incidence of B/L CSCR at the initial visit reported in literature is 5%–18% as in (16). The tendency of bilaterality was found to increase with long-term follow-up of 33.3% of our cases presented with Bilateral disease. Various studies have shown that most CSCR patients are hard-driven and tense as in [17].

It is now a well-established fact that CSCR is a stress-related disease, and people with Type A personality are more prone. hypothesized that medical and social factors have a stress-related component could be more prevalent among ICSC patients than controls [15].

The most common associated risk factors of CSCR in our study was found to be sleep deprivation and stress. The acute form is characterized by the presence of SRF, detectable on fundus examination and on OCT, with limited focal or multifocal RPE alterations that may be limited to small PEDs, and leakage through the RPE on FA [16].

In our study, SRF was present in 20 eyes, 4 eyes showed associated PED (20 %).

In our study Ink-Blot pattern was the most common FFA findings like other studies which was found in 8 cases out of 10 (80%) of Chronic CSR without CNV and was found in 9 cases out of 10 (90%) of CCSR with active CNV. Those were the recurrent cases mainly and might suggest chronicity.

In our study, we compared OCT angiography characteristics of patients with chronic CSC to FA findings. We found typical changes in the choriocapillary flow pattern of chronic CSC patients, which Ten cases of Chronic CSR without CNV was detected with both OCTA and FFA with no significant and Ten cases of CCSR with CNV was detected with OCTA early than FFA.

Bansal et al. (18) detected CNVM by OCTA in 9 (20.9%) eyes and by FA in 13 (30.2%) eyes. The higher number in the FA group is due to a high number of false positives, which can be attributed to multiple findings in CCSC causing hyper-fluorescence on FA such as subretinal or intraretinal fluid,

Maftouhi et al. [19] demonstrated CNVM in 7 (58%) of 12 eyes of chronic CSC by OCTA imaging. The affected zones on FA demonstrated alternating hypo and hyperfluorescence in early phase.

The late phase showed hyperfluorescent leaking points or small leaking points with staining of detached neurosensory retina. The ICGA failed to detect any of these membranes, showing only the characteristic choroidal hyperpermeability of chronic CSC. On the other hand, OCT B scans helped to characterize the CNVM in these seven eyes, which corresponded to small undulations within the slightly detached RPE, suggesting its vascularized nature. The remaining five (42%) eyes with no CNVM on OCTA showed a flat RPE profile on OCT and normal choroidal circulation on ICGA. None showed intraretinal cystic degeneration.

Costanzo et al. study [20], compared OCTA and multimodal imaging findings, including FA, ICGA, and SD-OCT. Due to our experience in the field of CSC, we could ascertain the absence of CNV in some cases, based on multimodal imaging. However, we could assume that the irregular choroidal pattern revealed a pathological choroidal vasculature that could correspond either to abnormally dilated choroidal vessels or to CNV. This study disclosed two previously unreported findings in CSC patients: dark areas and dark spots at the choriocapillaris. The choriocapillaris has a fine, densely packed, honeycomb-like microvasculature at the central fovea

In Soomro and Talks [21] OCTA and FFA are not equivalent tests as FFA shows leak and OCTA the neovascular network by detecting flow; so direct comparison may not be appropriate as both add to the assessment of the neovascular lesion. OCTA technology has the potential to be a significant adjunct to traditional multimodal imaging assessment for choroidal neovascularisation.

Bansal et al. [18], the specific dye leakage patterns of Chronic CSC on FA did not correlate with CNVM seen on OCTA, strengthening the fact that OCTA detects choroidal neovascular network by depth (flow in outer retina) and is independent of FA-detected dye leakage. It is also possible that presence of vessels on OCTA but not on FA could represent a subtype of CNVM in long-standing CSC that is beginning to evolve slowly but not actively leaking on FA.

Bansal et al. [18], When compared with OCTA, the FA was unable to characterize CNVM in CCSC (with a very low sensitivity and moderate specificity) as

none of the specific dye leakage patterns on FA correlated with CNVM seen on OCTA, limiting its usefulness and accuracy in CCSC eyes with CNVM.

Chhablani et al. [22], shown that OCTA appears to be superior in choroidal neovascularization detection over dye-based angiographies (FFA) in eyes with CSCR. Thus, it is prudent to replace the dye based angiographies with this recent non-invasive imaging.

Samir et al. [23], OCTA images of the superficial and deep retinal plexus, outer retina, and choriocapillaris did not reveal altered flow patterns directly associated with the leakage point in acute CSCR. However, OCTA was able to visualize altered choroidal flow in some of the included eyes and was the best among all other modalities in detection of CNV in eyes with chronic CSCR.

Amar et al. [24], OCTA allowed for a clearer delineation of the flow patterns in chronic CSCR eyes while defining the polypoidal choroidal vasculopathy. Retinal neovascularization in three dimensions is reconstructed using OCTA for choroidal vasculature imaging, underlining the value of OCTA while verifying CNV lesions where FA has failed, and other techniques.

6. Conclusion

As a non-invasive, quick, and dependable angiographic imaging method, OCTA has advantages over FA. The ability to view the retinal and choroidal vasculature in various layers is another benefit of OCTA. The narrow field of vision of OCTA (which has been somewhat addressed in certain commercially available devices), inability to detect leakage, difficulty to detect blood flow below a particular level, and inconsistent image quality are some of its drawbacks.

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