Original Article

Optical coherence tomography angiography versus fluorescein angiography in diagnosing choroidal neovascularization in chronic central serous chorioretinopathy

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Purpose: Diagnosis of choroidal neovascular membrane (CNVM) is difficult in chronic central serous chorioretinopathy (CCSC) due to overlapping features of both on conventional dye angiography. Optical coherence tomography angiography (OCTA) allows a quick and noninvasive detection of CNVM in these eyes. We compared the fluorescein angiography (FA) features of CNVM with those of OCTA to assess the role of FA in detecting CNVM in CCSC eyes. Methods: Patients with CCSC undergoing FA, spectral domain (SD)-OCT, and OCTA were identified (March 2015–June 2015). Four retina specialists individually reviewed FA images (without OCTA and SD-OCT) to determine whether CNVM was present. In parallel, two other retina specialists reviewed all images (FA/SD-OCT/OCTA) for CCSC features and confirmed whether CNVM was present using OCTA as the gold standard. The inter- and intraobserver variability was measured by Kappa (k) coefficient. The FA features of CNVM were compared and correlated with those on OCTA. Results: Of 43 eyes (26 patients, mean age 45.6 ± 8.5 years, all males), a definite CNVM (detected by OCTA) was present in nine (20.9%) eyes. FA alone detected CNVM in 13 (30.2%) eyes [sensitivity 44.4% (95% confidence interval (CI): 11.9-76.9), specificity 73.5% (95% CI: 58.7-88.3), positive and negative predictive values 30.8% and 83.3%, respectively, and accuracy 67.44% (95% CI: 53.4-81.4)]. Conclusion: 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 detecting CNVM in these eyes.



Key words: Choroidal neovascular membrane, chronic central serous chorioretinopathy, fluorescein angiography, OCT angiography

Visual outcome of the chronic central serous chorioretinopathy (CCSC) is guarded due to a number of factors including persistent subretinal fluid (SRF) and limited response to conventional treatment.^[1] Presence of choroidal neovascular membrane (CNVM), although rare in CCSC, complicates it further.^[2-6] Both fluorescein angiography (FA) and spectral domain optical coherence tomography (SD-OCT) may show overlapping features in CCSC eyes with or without CNVM. Timely diagnosis of CNVM may be critical in improving the visual outcome in these patients.

OCT angiography (OCTA) allows a quick, noninvasive detection of CNVM and is claimed to be as sensitive as FA in detecting CNVM in CCSC eyes.^[7] Several studies have demonstrated the superiority of OCTA over other imaging techniques in detecting CNVM in CCSC eyes.^[8-15] We carried out this study to see whether patients with CNVM diagnosed on OCTA showed any FA characteristics that could be used to diagnose CNVM in the absence of OCTA imaging tool.

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Methods

This retrospective study included patients with CCSC (defined as at least 6 months of visual acuity symptoms with documented clinical features of CCSC, such as SRF and retinal pigment epithelium (RPE) changes in macula on FA and SD-OCT) who were following up in our retina clinic and underwent OCTA during the period from 21st March and 15th June, 2015. Institute Ethics Committee approval was obtained, and the study was conducted in accordance with the Declaration of Helsinki. Patients with history of previous laser treatment or intravitreal injection and/or those with significant media opacity precluding fundus imaging were excluded. As a routine workup in the clinic, all patients underwent a baseline ophthalmic evaluation including best-corrected visual acuity, intraocular pressure measurement, and slit-lamp biomicroscopic examination of

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anterior and posterior segments before and after pupillary dilatation. All patients underwent a dilated digital color fundus photography and fundus autofluorescence (Visupac 450 plus fundus camera, Carl Zeiss Meditec, Inc.), along with SD-OCT using Spectralis HRA + OCT system (Heidelberg Engineering, Heidelberg, Germany) as a standard assessment for CCSC during every visit. All enrolled patients had also undergone a conventional baseline FA (within last 3 months) on the same fundus camera. The indocyanine green angiography (ICGA) is not performed routinely in all patients due to cost limitations and is done only in selected cases in our clinic. All patients underwent OCTA (RTVue XR 100; Optovue Inc., Fremont, CA, USA) scans (3 × 3 mm and 6 × 6 mm) centered at the macula, or at the area of interest when specified.

The multimodal image analysis of all study eyes was done by two retina specialists (AG and RB) with more than 10 years of experience in medical retina, who performed routine reporting of FA, SD-OCT, and OCTA images for CCSC features. The FA features of CCSC that were looked in detail included window defects, inactive granular hyperfluorescence, retinal pigment epithelium detachment (RPED), active pin-point RPE leaks, ink-blot/smoke stack pattern of dye leakage, gravitational tracks, diffuse leakage of dye in late phase without or with underlying focal RPE leaks, and a stippled early hyperfluorescence without progressive leakage. A diagnosis of CNVM was made on FA on the basis of presence of a lacy pattern/network with an early hyperfluorescence that persisted/increased in size and intensity in the late phase. SD-OCT scans were analyzed in detail for cystoid spaces, intraretinal or SRF, and a flat, irregular RPED. These two observers also served as independent readers for OCTA images and performed a qualitative analysis on OCTA depictions of vascular flow representing CNVM and the morphologic appearance of CNVM. Presence of a CNVM on OCTA was defined by the appearance of abnormal choroidal vessels with distinct, high-flow, tangled pattern in the choriocapillaris layer, characterized by a lacy wheel pattern (well circumscribed) or long filamentous pattern (poorly circumscribed).^[7]

In parallel, four other retina specialists (MRD, VG, RS, and DK), also with more than 10 years of experience in medical retina, individually reviewed FA images (without OCTA and SD-OCT) to determine whether CNVM was present. Unlike the first two observers who analyzed the FA images for all the CCSC features, they served as independent readers for performing the qualitative analysis of FA images to look for the presence of CNVM. They were masked to OCTA images and SD-OCT images (to have an unbiased opinion on the presence or absence of CNVM on FA and to avoid a mixed opinion about CNVM due to overlapping features on SD-OCT). All the frames of FA images of each study eye from the database were displayed on the same viewing station connected to the respective camera through a server, and projected individually to each of the four observers at two separate time points on different days, and the responses were recorded as CNVM present/CNVM absent by Observer 1 A (first analysis) and B (second analysis), Observer 2 A and B, and so on.

We used OCTA as the gold standard for identification of CNVM to correlate the findings on FA. While dye-based angiography (FA) is the standard for diagnosing CNVM,^[16] Bonini *et al.* demonstrated sensitivity and specificity of OCTA comparable with FA for detection of CNVM in CCSC and suggested OCTA as a viable alternative and a first step for diagnosing CNVM in CCSC. If the OCTA demonstrated CNVM in an eye, the FA image was considered a true positive if any of the readers identified a CNVM in that eye, or a false negative if the CNVM was not visualized on FA. If a CNVM was not seen on OCTA, the FA image was considered a false positive if a CNVM was visualized on FA, or a true negative if no CNVM was seen on FA.

Statistical analysis

Statistical analysis was done using SPSS Windows 17 (SPSS Inc., Chicago, IL, USA). The association between the responses given by the observers (inter- and intraobserver variability) was measured by Chi-square test and their measure of agreement by Kappa (k) coefficient. The pairwise kappas (k) were calculated between each pair of four observers (for interobserver variability) and between the two analyses by the same observer (for intraobserver variability). The k coefficient is a statistic that corrects the possibility of agreement by chance alone. Kappa equal to 1.0 means "perfect" agreement, and values less than 1 mean less than perfect agreement, which may be interpreted as follows: poor agreement (0.40–0.60), good agreement (0.60–0.80), and very good agreement (0.80–1.00).^[17,18]

Results

There were 26 patients (43 eyes). All were males. Seventeen patients had bilateral and nine had unilateral CCSC. The mean age was 45.6 ± 8.5 years (range 26–58 years). The CNVM was detected by OCTA in 9 (20.9%) eyes (by first two observers) and by FA in 13 (30.2%) eyes by the other four masked observers. Table 1 shows the comparison of OCTA versus FA (analyzed by the four masked Observers 1, 2, 3 and 4) for presence or absence of CNVM in 43 eyes. Observer 1 diagnosed CNVM on FA in 7 eyes (of 43 eyes) at each of the two different time points A and B, of which 3 eyes had CNVM on OCTA also (true positives), whereas 4 eyes did not have CNVM on OCTA (false positives) [Table 1]. Observer 2 diagnosed CNVM on FA in nine eyes at time point A (of which four were true positives and five false positives when compared with OCTA) and in eight eyes at time point B (of which three were true positives and five false negatives). Observer 3 diagnosed CNVM on FA in seven eyes at each of the two time points A and B, of which four eyes had CNVM on OCTA also (true positives), whereas three eyes did not have CNVM on OCTA (false positives). Observer 4 diagnosed CNVM on FA in four eyes at each time points A and B (two were true positives and two false negatives). Table 1 also shows the level of agreement by k statistics when comparing OCTA-based diagnosis of CNVM with FA-based detection of CNVM by the four observers. Observers 1 and 4 had poor agreement (k = 0.168 and k = 0.151, respectively) at both time points, Observer 2 had fair agreement (k = 0.221) at time point A and poor agreement (k = 0.128) at time point B, and Observer 3 had fair agreement (k = 0.306) at both time points.

For each pair of the two analyses (A and B) by each of Observers 1, 3, and 4, there was a perfect agreement between their two attempts of analysis (k = 1 for each pair), indicating no intraobserver variability *within* the observer. Observer 2 also had a good level of agreement (k = 0.779) between the two analyses. When compared *between* the

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observers for interobserver variability, Observer 1 had a good agreement with Observer 2 (k = 0.64), moderate agreement with Observer 3 (k = 0.5), and good agreement with Observer 4 (k = 0.7). Observer 2 had a fair agreement with Observers 3 and 4 (k = 0.34 each) and Observer 3 a moderate agreement with Observer 4 (k = 0.48).

Table 2 shows the FA signs of CCSC reported by the two authors (RB and AG) during baseline image analysis. When FA features were compared between eyes having CNVM on OCTA (9 eyes) with those not having CNVM on OCTA (34 eyes), none was found to be statistically significant. All signs such as window defects (28 eyes), granular inactive hyperfluorescence (43 eyes), active pin-point RPE leaks (17 eyes), diffuse leakage of dye in late phase without (7 eyes) or with (9 eyes) underlying focal RPE leaks, a stippled early hyperfluorescence without progressive leakage (6 eyes), RPED (17 eyes), gravitational tracks (5 eyes), and ink-blot/smoke stack pattern of dye leakage (8 eyes) were comparable between the two groups of eyes. Eyes having CNVM on OCTA were more commonly associated with an early stippled hyperfluorescence without progressive leakage (3 of 9 eyes; 33.3%), when compared with eyes with no CNVM on OCTA (3 of 34 eyes; 8.8%), although the difference was not statistically significant. In contrast, diffuse leakage of dye in late phase with underlying focal RPE leaks (all 9 eyes) and PED (16 of 17 eyes) was almost exclusively found in eyes that had no CNVM on OCTA, although the difference was statistically insignificant.

The four masked readers (MRD, VG, RS, and DK) analyzed the FA features for detecting CNVM. CNVM was detected on FA by the four observers in 7, 9, 7, and 4 eyes, respectively. Overall, FA alone detected CNVM in 13 (30.2%) eyes [sensitivity 44.4% (95% confidence interval (CI): 11.9-76.9), specificity 73.5% (95% CI: 58.7–88.3), positive and negative predictive values 30.8% and 83.3%, respectively, and accuracy 67.44% (95% CI: 53.4–81.4)]. Among these various signs, presence of an early hyperfluorescence that persisted/increased in size and intensity in the late phase was the most common sign looked at by the observers for diagnosing CNVM on FA. Considering the OCTA-based diagnosis of CNVM as the gold standard, Table 3 shows the comparison of nine eyes with a confirmed diagnosis of CNVM with their detection on FA by four observers. While eyes no. 1 and 4 were detected to have CNVM on FA by all four observers (true positives), the FA was unable to detect CNVM in eyes no. 3, 5, 6, 8, and 9 (false negative; Fig. 1). Eyes no. 2 and 7 were true positives for CNVM on FA by two and three observers, respectively [Fig. 2]. FA signs that led to a false diagnosis of

Table 1: Comparison of eyes with diagnosis of CNVM by FA versus CNVM by OCTA by the four masked observers							
CNVM detected on FA by different observers	CNVM seen on OCTA (<i>n</i> =9) (true positives)	No CNVM on OCTA (<i>n</i> =34) (false positives)	<i>P</i> (Fisher's exact test)	Kappa values (<i>k</i>)			
Observer 1							
A (<i>n</i> =7)	3 (33.3%)		0.147 0.168				
В (<i>n</i> =7)	3 (33.3%)	4 (11.8%)					
Observer 2							
A (<i>n</i> =9)	4 (44.4%)	5 (14.7%)	0.073	0.221			
B (<i>n</i> =8)	3 (33.3%)	5 (14.7%)	5 (14.7%) 0.332				
Observer 3							
A (<i>n</i> =7)	4 (44.4%)	3 (8.8%)	0.026	0.306			
В (<i>n</i> =7)	4 (44.4%)	3 (8.8%)					
Observer 4							
A (<i>n</i> =4)	2 (22.2%)	2 (5.9%)	0.188	0.151			
B (<i>n</i> =4)	2 (22.2%)	2 (5.9%)					

CNVM=Choroidal neovascular membrane, FA=Fluorescein angiography, OCTA=Optical coherence tomography. A=First analysis by each observer; B=Second analysis by each observer

Table 2: Findings of fluorescein angiography in eyes with/without CNVM on OCTA					
	No CNVM on OCTA (<i>n</i> =34)	CNVM present on OCTA (<i>n</i> =9)	<i>P</i> (Fisher's exact test)		
Window defects (n=28)	21 (61.8%)	7 (77.8%)	0.458		
Granular inactive hyperfluorescence (n=43)	34 (100%)	9 (100%)	-		
Active pin-point RPE leaks (n=17)	14 (41.2%)	3 (33.3%)	1.000		
Diffuse leakage of dye in late phase without underlying focal RPE leaks (n=7)	4 (11.8%)	3 (33.3%)	0.147		
Diffuse leakage of dye in late phase with underlying focal RPE leaks (n=9)	9 (26.5%)	0	0.166		
A stippled early hyperfluorescence without progressive leakage (n=6)	3 (8.8%)	3 (33.3%)	0.095		
Pigment epithelium detachment (n=17)	16 (47.1%)	1 (11.1%)	0.065		
Gravitational tracks (n=5)	4 (11.8%)	1 (11.1%)	1.000		
Ink-blot/smoke stack pattern of dye leakage (n=8)	7 (20.6%)	1 (11.1%)	1.000		
Flat, irregular PED (OCT) (<i>n</i> =9)	5 (14.7%)	4 (44.4%)	0.073		

CNVM=Choroidal neovascular membrane, OCTA=Optical coherence tomography angiography

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Table 3: Fluorescein angiographic detection of CNVM by four masked observe	ers in nine eyes with confirmed (OCTA)
diagnosis of CNVM	

Eyes with CNVM on OCTA	Fluorescein angiographic diagnosis of CNVM by four observers				Fluorescein angiographic
	Observer 1	Observer 2	Observer 3	Observer 4	diagnosis of CNVM
1	+	+	+	+	True positive by all four observers
2	-	+	+	-	True positive by second observers
3	-	-	-	-	False negative by all four observers
4	+	+	+	+	True positive by all four observers
5	_	-	-	-	False negative by all four observers
6	-	-	-	-	False negative by all four observers
7	+	+	+	-	True positive by three observers
8	-	-	-	-	False negative by all four observers
9	-	-	-	-	False negative by all four observers

CNVM=choroidal neovascular membrane, OCTA=optical coherence tomography angiography. + = CNVM present on fluorescein angiography. - = no CNVM on fluorescein angiography



Figure 1: Fundus fluorescein angiograms of a 52-year-old patient with chronic CSC, with early (a) and late (b) phases showing a stippled hyperfluorescence without any progressive increase, which was diagnosed by all four observers as not having any CNVM on FA (false negative). The early and late phases of ICGA (c and d) showed a hypercyanescent complex under the fovea. SD-OCT scan (e) showed an irregular RPED with a mixed hyper- and hyporeflectivity beneath it (arrows). The *en face* OCTA showed a neovascular complex in the outer retina (f) and choroid (g)

CNVM on FA by either of the observers (nine eyes) included a diffuse leakage of dye in late phase *without* underlying focal RPE leaks (three of seven; P = 0.147), diffuse leakage of dye in late phase *with* underlying focal RPE leaks (four of nine; P = 0.073), and a stippled early hyperfluorescence without progressive leakage (two of six; P = 0.589). These signs also coincided with a missed diagnosis of CNVM (total seven eyes) on FA, which included one of seven eyes with a diffuse leakage of dye in late phase *without* underlying focal RPE leaks (P = 1.000), and a stippled early hyperfluorescence without progressive leakage (three of six; P = 0.045). The latter was significantly associated with a missed diagnosis of CNVM on FA.

Among the OCT findings [SRF (26 eyes), intraretinal fluid (6 eyes), serous RPED (14 eyes), and flat, irregular RPED (10 eyes)] that were looked for their association, a flat, irregular RPED was significantly associated with OCTA-based CNVM diagnosis. Five of nine eyes with CNVM (55.6%) had flat, irregular RPED, whereas only 5 of 34 eyes without CNVM (14.7%) had flat, irregular RPED (P = 0.020). Of 34 eyes with no CNVM on OCTA, 20 (58.8%) had SRF on SD-OCT, whereas 6 of 9 eyes (66.7%) with CNVM on OCTA had SRF (P = 1.000). Of six eyes with intraretinal fluid, three (8.8%) were associated with no CNVM on OCTA and three (33.3%) with CNVM on OCTA (P = 0.095). Of 14 eyes with serous (dome-shaped) RPED, almost all (13 eyes) had no CNVM on OCTA [13/34 (38.2%) vs. 1 (11.1%); P = 1.000].

Discussion

The first use of OCTA in detecting CNVM was reported by Jia *et al.* in five cases using a prototype swept-source OCT.^[19] This

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Figure 2: Fundus fluorescein angiograms of a 48-year-old patient with chronic CSC, with early (a) and late (b) phases showing a stippled hyperfluorescence without any progressive increase, which was diagnosed as CNVM by two of four observers on FA (true positive). SD-OCT scan (c) showed an irregular RPED with subretinal fluid. The *en face* OCTA showed a neovascular complex, subtle in the outer retina (d) and prominent in the choroid (e). The automated segmentation allowed visualization of a more prominent and denser CNVM (f)

was followed by de Carlo *et al.* reporting the utility of AngioVue OCTA system using a commercially available SD OCT engine in detecting CNVM.^[8] Their series reported CNVM in 48 eyes with neovascular age-related macular degeneration (31 eyes), CSC (7 eyes), and other causes (10 eyes). The authors found a high specificity of OCTA (but a low sensitivity of about 50%) in detecting CNVM compared with FA and characterized the CNVM morphology based on its size and appearance. Of 8 eyes (of 27 eyes) diagnosed to have CNVM based on FA imaging analysis, Bonini *et al.* reported 100% sensitivity and 100% specificity of OCTA (SD-OCT system) in detecting and excluding CNVM in CCSC.^[7] The authors recommended OCTA (being a completely noninvasive tool) as a first step in identifying CNVM in CSC.

While a majority of studies of OCTA in CCSC have reported its utility in detecting CNVM,^[7-14] Teussink *et al.* compared FA and ICGA findings with OCTA characteristics in patients with chronic CSC to elucidate the pathogenesis of chronic CSC but did not study the existence of CNVM in these eyes.^[13] They found late-phase ICGA and FA abnormalities collocating with those on OCTA. Fujita *et al.* reported additional use of OCTA in CCSC for evaluating choriocapillaris after half-dose verteporfin photodynamic therapy (hd-PDT).^[14] The irregular choriocapillaris flow seen on OCTA before hd-PDT tended to recover at 1 month following hd-PDT, making it a useful tool for evaluating the therapeutic effects of hd-PDT in CCSC.

In CSR, CNVM can occur *de novo*, post focal laser, or in the setting of pachychoroid neovasculopathy. The latter is a phenotype of the pachychoroid spectrum, occurring at a younger age than AMD, characterized by the presence of type 1 neovascularization and thicker choroids in the absence of age-related degenerative changes.^[20] It develops slowly and may occur in eyes with pachychoroid pigment epitheliopathy (PPE), another phenotype of pachychoroid spectrum, with CSC-like pigmentary RPE changes without any evidence of current or previous SRF.^[20] Our study eyes differed from PPE in having documented CSC features. In our study, OCTA demonstrated CNVM in 20.9% of eyes with CCSC. However, FA showed variable findings by different observers for CNVM detection. As we attempted to characterize the FA features that could suggest the presence of CNVM, we did not find any feature of FA findings that could be diagnostic or predictive of an underlying CNVM in these eyes.

Maftouhi *et al.* demonstrated CNVM in 7 (58%) of 12 eyes of chronic CSC by OCTA imaging.^[9] 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.

Cakir *et al.* reported utility of OCTA in demonstrating areas of focal hypo- and hyperperfusion in the choriocapillaris and reliably detecting CNVM (even in the absence of exudative activity) in eyes with CCSC. In their study, OCTA revealed CNVM in two of three cases detected by FA/ICGA. Additionally, OCTA revealed CNVM in one eye which was not detectable by FA or ICGA.^[11] FA findings in CCSC are difficult to assess and often interpreted as equivocal.

Morara *et al.* studied 10 elderly patients with CSC, all of which along with serous retinal detachment had thin PED. OCTA detected CNVM in 4 of these 10 eyes, as seen by a distinct choroidal neovascular pattern in the choriocapillaris, previously undiagnosed by conventional imaging modalities.^[12]

The role of OCTA in detecting CNVM in CCSC more frequently than the other imaging (FA and/or ICGA) modalities in eyes with flat irregular PEDs was reported by Bousquet et al.[15] While the OCTA detected CNVM in 36.5% of eyes with flat irregular PEDs, the combination of other imaging modalities (SD-OCTA, FA and ICGA) detected CNVM in only 25% of these eyes. All eyes that were avascular on OCTA had hyporeflective flat irregular PEDs, whereas those associated with CNVM on OCTA had at least partially hyperreflective flat irregular PEDs. Conversely, we 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 hyperfluorescence on FA such as subretinal or intraretinal fluid, widespread transmission defects, scattered RPE leak points, and RPEDs. Costanzo et al. also were unable to correlate OCTA findings of CNVM with other multimodal imaging.^[21] They detected abnormal vessels in 12 of 33 CCSC eyes by OCTA, which were frequently (but not systematically) confirmed as CNVM by multimodal imaging.

In our study also, the specific dye leakage patterns of CCSC 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. Moreover, pattern recognition of early or subtle signs of mild to moderate hyperfluorescence on FA might generate a new classification of CNVM in CCSC in larger prospective studies. The limitations of our study include a small number of eyes (and patients) with CNVM and lack of ICGA in a majority of patients. Also, no longitudinal study and follow-up are available for the eyes with CNVM that received antivascular endothelial growth factor therapy. Furthermore, while motion artefacts or projection artefacts may be misinterpreted as candidate CNV leading to its overdiagnosis, we attempted to eliminate this possibility while analyzing the OCTA images by manually adjusting the segmentation between RPE and 30 µm beneath it, in addition to the conventional automatically segmented outer retina and choriocapillaris layers.

Conclusion

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.

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Conflicts of interest

There are no conflicts of interest.

References

- 1. Loo RH, Scott IU, Flynn HW Jr, Gass JD, Murray TG, Lewis ML, *et al*. Factors associated with reduced visual acuity during long-term follow-up of patients with idiopathic central serous chorioretinopathy. Retina 2002;22:19-24.
- Gomolin JE. Choroidal neovascularization and central serous chorioretinopathy. Can J Ophthalmol 1989;24:20-3.
- Spaide RF, Campeas L, Haas A, Yannuzzi LA, Fisher YL, Guyer DR, et al. Central serous chorioretinopathy in younger and older adults. Ophthalmology 1996;103:2070-9.
- 4. Spaide RF, Hall L, Haas A, Campeas L, Yannuzzi LA, Fisher YL, *et al.* Indocyanine green videoangiography of older patients with central serous chorioretinopathy. Retina 1996;16:203-13.
- Yannuzzi LA, Shakin JL, Fisher YL, Altomonte MA. Peripheral retinal detachments and retinal pigment epithelial atrophic tracts secondary to central serous pigment epitheliopathy. Ophthalmology 1984;91:1554-72.
- Fung AT, Yannuzzi LA, Freund KB. Type 1 (sub-retinal pigment epithelial) neovascularization in central serous chorioretinopathy masquerading as neovascular age-related macular degeneration.

Retina 2012;32:1829-37.

- Bonini Filho MA, de Carlo DE, Ferrara D, Adhi M, Baumal CR, Witkin AJ, et al. Association of choroidal neovascularization and central serous chorioretinopathy with optical coherence tomography angiography. JAMA Ophthalmol 2015;133:899-906.
- de Carlo TE, Bonini Filho MA, Chin AT, Adhi M, Ferrara D, Baumal CR, *et al*. Spectral domain optical coherence tomography angiography of choroidal neovascularization. Ophthalmology 2015;122:1228-38.
- Maftouhi MQ, Maftouhi AE, Eandi CM. Chronic central serous chorioretinopathy imaged by optical coherence tomographic angiography. Am J Ophthalmol 2015;160:581-7.
- Hage R, Mrejen S, Krivosic V, Quentel G, Tadayoni R, Gaudric A. Flat irregular retinal pigment epithelium detachments in chronic central serous chorioretinopathy and choroidal neovascularization. Am J Ophthalmol 2015;159:890-903.
- 11. Cakir B, Reich M, Lang SJ, Buhler A, Stahl A, Bohringer D, *et al.* Possibilities and limitations of OCT-Angiography in patients with central serous chorioretinopathy. Klin Monbl Augenheilkd 2017;234:1161-8.
- Morara M, Veronese C, Melucci M, Tassi F, Balducci N, Ciardella A. Optical coherence tomography angiography of chronic central serous chorioretinopathy in elderly patients. Invest Ophthalmol Vis Sci 2015;56:3349.
- Teussink MM, Breukink MB, van Grinsven MJ, Hoyng CB, Klevering BJ, Boon CJ, et al. OCT angiography compared to fluorescein and indocyanine green angiography in chronic central serous chorioretinopathy. Invest Ophthalmol Vis Sci 2015;56:5229-37.
- Fujita K, Yuzawa M, Kawamura A. Choriocapillaris changes imaged by OCT angiography after half-dose photodynamic therapy for chronic central serous chorioretinopathy. Ophthalmic Surg Lasers Imaging Retina 2017;48:302-10.
- Bousquet E, Bonnin S, Mrejen S, Krivosic V, Tadayoni R, Gaudric A. Optical coherence tomography angiography of flat irregular pigment epithelium detachment in chronic central serous chorioretinopathy. Retina 2018;38:629-38.
- Do DV. Detection of new-onset choroidal neovascularization. Curr Opin Ophthalmol 2013;24:244-7.
- Landis JR, Koch CG. The measurement of inter observer agreement for categorical data. Biometrics 1977;33:159-74.
- Fleis JL. Statistical Methods for Rates and Proportions. 2nd ed. New York: Wiley; 1981. p. 218.
- Jia Y, Bailey ST, Wilson DJ, Tan O, Klein ML, Flaxel CJ, et al. Quantitative optical coherence tomography angiography of choroidal neovascularization in age-related macular degeneration. Ophthalmology 2014;121:1435-44.
- 20. Pang CE, Freund KB. Pachychoroid neovasculopathy. Retina 2015;35:1-9.
- Costanzo E, Cohen SY, Miere A, Querques G, Capuano V, Semoun O, *et al*. Optical coherence tomography angiography in central serous chorioretinopathy. J Ophthalmol 2015;2015:134783.