Optical Coherence Tomography Angiography: A Useful Tool for Diagnosis of Treatment-Naïve Quiescent Choroidal Neovascularization

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• PURPOSE: To describe the optical coherence tomography angiography (OCT-A) features of treatment-naïve quiescent choroidal neovascularization (CNV) secondary to age-related macular degeneration, and to estimate the detection rate for neovascularization by means of OCT-A.

• DESIGN: Diagnostic tool validity assessment.

• METHODS: Treatment-naïve quiescent CNV were identified from a pool of patients at 2 retina referral centers. Patients underwent a complete ophthalmologic examination including fluorescein angiography, indocyanine green angiography, spectral-domain optical coherence tomography, and OCT-A. Detection rates of CNV by means of OCT-A were estimated with a second cohort of patients without CNV (negative controls).

• RESULTS: Twenty-two eyes of 20 consecutive patients with quiescent CNV were included. In 4 out of 22 eyes it was not possible to classify the CNV "shape," "core," "margin," and "location," either because the vascular network was not clearly shown (3 cases) or because it was not visible at all (1 case). CNV shape on OCT-A was rated as circular in 8 eyes and irregular in 10 eyes. CNV core was visible in 2 eyes. CNV margin was considered as well defined in 15 eyes and poorly defined in 3 eyes. CNV margin showed small loops in 9 eyes and large loops in the other 6 eyes. CNV location was foveal-sparing in 12 eyes. Sensitivity and specificity of quiescent CNV detection by OCT-A turned out to be 81.8% and 100%, respectively.

• CONCLUSIONS: OCT-A allows the clinician to noninvasively identify treatment-naïve quiescent CNV and may be considered as a useful tool to guide the frequency of return visits and, possibly, make treatment decisions. (Am J Ophthalmol 2016;169:189–198. © 2016 Elsevier Inc. All rights reserved.)

TREATMENT-NAÏVE QUIESCENT CHOROIDAL NEOVAScularization (CNV) is a recently described entity in the setting of age-related macular degeneration (AMD). In quiescent CNV, newly diagnosed sub–retinal pigment epithelium CNV (type 1 neovascularization) detected on fluorescein angiography (FA) and indocyanine green angiography (ICGA) shows absence of intraretinal/ subretinal exudation on repeated spectral-domain optical coherence tomography (SD OCT) for at least 6 months.[1]

FA and ICGA are the current gold standard to diagnose CNV.[2–5] On FA, quiescent CNV appears as a late-phase ill-defined hyperfluorescent lesion, without late-phase leakage or pooling of dye, which defines typical type 1 neovascularization. Similarly to active CNV, ICGA allows the visualization of the hypercyanescent neovascular network of quiescent CNV in early to mid phases and the delineation of the fibrovascular plaque in the late phase.[1] SD OCT reveals, at the site of quiescent CNV, an irregular elevation of the retinal pigment epithelium (RPE) with major axis in the horizontal plane, with moderately reflective material in the sub-RPE space, no intraretinal/subretinal hyporeflective fluid, and clear visualization of hyperreflective Bruch membrane.[1]

OCT angiography (OCT-A) is a novel and noninvasive diagnostic technique used to visualize ocular blood flow in retinal and choroidal vasculature. It is a dyeless, fast, 3-dimensional method, unlike traditional angiography imaging.[6] Utility of OCT-A in CNV detection in different ocular conditions has been extensively described in the literature.[7,8] In this study, we investigated the features of treatment-naïve quiescent CNV in AMD and estimated the detection rate for neovascularization by means of OCT-A.

METHODS

IN THIS OBSERVATIONAL CASE SERIES, TREATMENT-NAÏVE quiescent CNV were identified from a pool of AMD

TABLE 1. AngioPlex and AngioVue Technical Specifications

Device	Algorithm	OCT SS	OCT AID	3 × 3 AIV (B-scan)	AIS Retina
AngoPlex	SSADA	68 000 scans/s	2 mm	245 A-scans	3 × 3, 6 × 6
AngioVue	OMAG	70 000 scans/s	2–3 mm	304 × 304 A-scans	2 × 2, 3 × 3, 6 × 6

AIV = angio imaging volume; AIS = angio imaging size; OCT AID = optical coherence tomography angiography axial imaging depth; OCT SS = optical coherence tomography scanning speed; OMAG = optical microangiography; SSADA = split-spectrum amplitude-decorrelation angiography.

patients consecutively presenting between September 2015 and December 2015 at 2 high-volume referral centers (the Medical Retina & Imaging Unit of the Department of Ophthalmology, University Vita-Salute San Raffaele in Milan, Italy; and the Department of Ophthalmology of University Paris Est, in Creteil, France). The study was conducted in agreement with the Declaration of Helsinki for research involving human subjects and was approved by the local institutional review board at both sites. Included patients signed a written general consent to participate in observational studies. Inclusion criteria for the study group were diagnosis of treatment-naïve "quiescent" CNV,[1] defined as an irregular elevation of the RPE with moderately reflective material in the sub-RPE space, no intraretinal/subretinal hyporeflective fluid on SD OCT, late-phase ill-defined hyperfluorescent lesion, without late-phase leakage or pooling of dye on FA, and hypercyanescent neovascular network in early to mid phases with the delineation of the fibrovascular plaque in the late phase of ICGA; sufficiently clear ocular media; and adequate pupillary dilation and fixation to permit high-quality OCT imaging. Ocular exclusion criteria consisted of any disease other than AMD (including retinal vascular diseases, vitreoretinal diseases, history of central serous retinopathy, or macular dystrophies) and any previous intervention for CNV, such as anti–vascular endothelial growth factor (VEGF) intravitreal injections, photodynamic therapy, laser photocoagulation, or vitrectomy, in the study eye.

Each enrolled patient underwent a comprehensive ophthalmologic examination, including measurement of best-corrected visual acuity (BCVA), dilated slit-lamp anterior segment and fundus biomicroscopy, FA, ICGA, SD OCT (Spectralis + HRA; Heidelberg Engineering, Heidelberg, Germany), and OCT-A. OCT-A was performed through AngioPlex CIRRUS HD-OCT model 5000 (Carl Zeiss Meditec, Inc, Dublin, California, USA) or using AngioVue RTVue XR Avanti (Optovue, Fremont, California, USA). OCT-A was performed in all patients with a scanning area of 3 × 3 mm, centered on the foveal area.

AngioPlex uses optical microangiography (OMAG), a recently developed imaging technique that produces 3D images of dynamic blood perfusion within microcirculatory tissue beds at an imaging depth up to 2.0 mm.[6,9,10] AngioPlex CIRRUS HD-OCT model 5000 contains an A-scan rate of 68 000 scans per second, using a superluminescent diode (SLD) centered on 840 nm. The resultant 3 × 3 angio cube contains 245 B-scan slices repeated up to 4 times at each B-scan position. Each B-scan is made up of 245 A-scans; each A-scan is 1024 pixels deep.

AngioVue relies on a split-spectrum amplitude-decorrelation angiography (SSADA) algorithm. This instrument has an A-scan rate of 70 000 scans per second, using a light source centered on 840 nm and a bandwidth of 50 nm. Each OCT-A volume contains 304 × 304 A-scans with 2 consecutive B-scans captured at each fixed position before proceeding to the next sampling location. Each A-scan is 2–3 mm deep. SSADA was used to extract the OCT angiography information. Each OCT-A volume is acquired in about 3 seconds and 2 orthogonal OCT-A volumes were acquired in order to perform motion correction to minimize motion artifacts arising from microsaccades and fixation changes.

Technical specifications of different devices are listed in Table 1.

The automatic segmentation provided by the OCT-A software was manually adjusted by 2 expert retina specialists (G.Q. and F.C.) for correct visualization of the capillary plexus, outer retinal layers, and choriocapillaris, in order to better identify the CNV plane. The OCT-A images and corresponding OCT B-scans were assessed for CNV shape, CNV core, CNV margin and margin-loops, and CNV location. CNV shape was classified as "circular" or "irregular." CNV core has been defined as a vessel of greater caliber or "trunk vessel" from which other, smaller vessels branch off. CNV core was classified as "visible" or "not visible"; if the core was visible, CNV was classified as "central core" or "eccentric core." CNV margin on OCT-A was classified as "well defined" or "poorly defined" on the basis of its appearance and its borders; moreover, CNV margin was classified as "large loops" or "small loops" when the margin was "well defined." CNV location was classified as "foveal involving" if the lesion involved the foveal center or "foveal sparing" if CNV lesion spared the foveal center.

To estimate sensitivity and specificity of OCT-A for neovascular detection (ie, diagnostic tool validity assessment), an additional cohort of 22 eyes of 22 patients
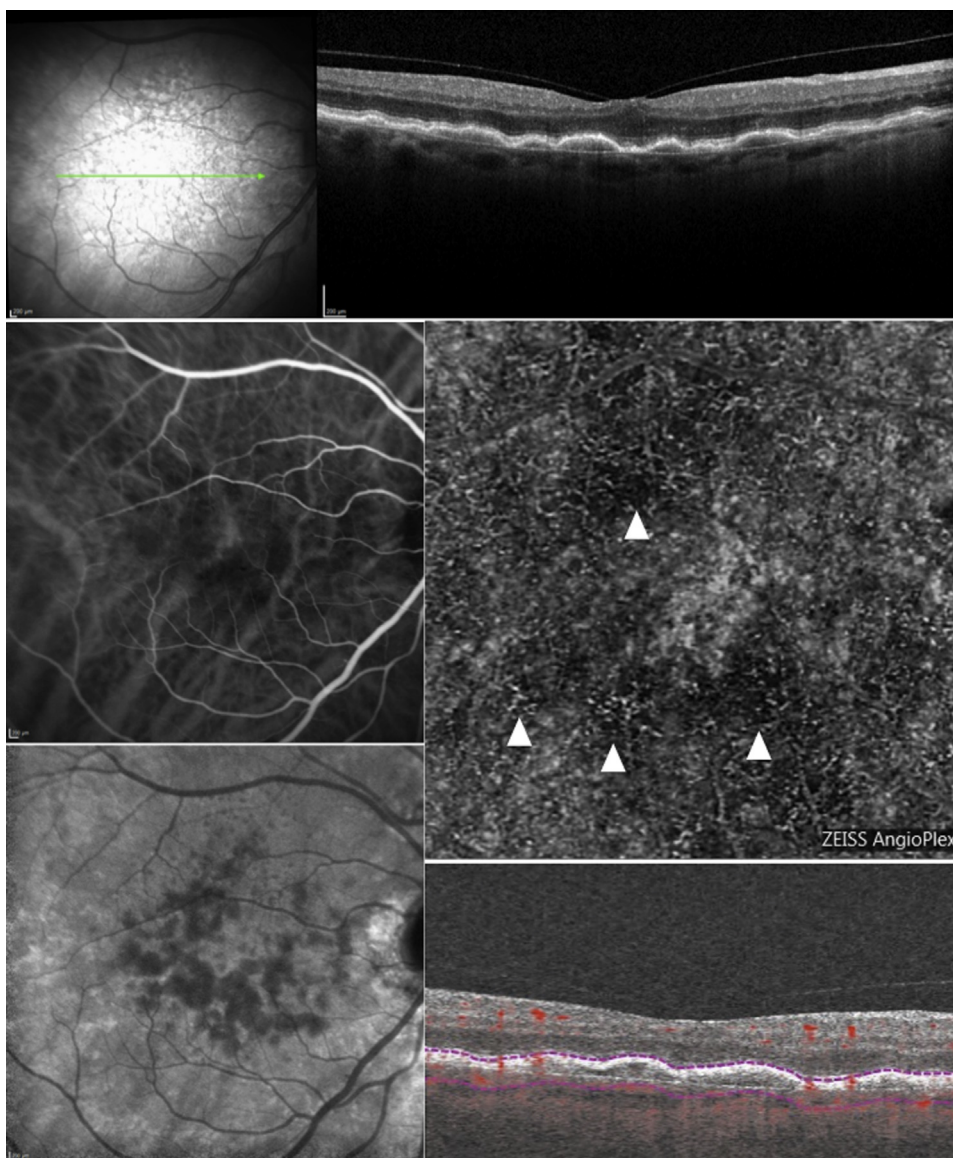
FIGURE 1. Infrared (IR), spectral-domain optical coherence tomography (SD OCT) indocyanine green angiography (ICGA), and optical coherence tomography angiography (OCT-A) of a negative control group eye. (First row) IR and corresponding SD OCT showing several large drusen; (Second and Third row, left panel) Early and late phases of ICGA showing absence of plaque; (Second and Third row, right panel) 3 × 3-mm OCT angiogram of choriocapillary plexus and corresponding OCT B-scan, showing black round areas without neovessels. Note the projection artifacts (arrowheads).

with drusenoid pigment epithelium detachments (PED) derived from adjacent confluent soft drusen, as visualized by structural SD OCT with no evidence of any vascular network at ICGA, were used as negative controls. All these patients had been diagnosed with early non-neovascular AMD (Figure 1). For these patients also, the study was conducted in agreement with the Declaration of Helsinki for research involving human subjects and was approved by the local institutional review board at both sites. Included patients signed a written general consent to participate in observational studies. Ocular exclusion criteria included any disease other than AMD (including retinal vascular diseases, vitreoretinal diseases, history of central serous retinopathy, or macular dystrophies), and anti-VEGF intra-vitreal injections, photodynamic therapy, laser photocoag-ulation, or vitrectomy in the study eye. OCT-A of the 2 cohorts were randomly presented to and independently evaluated by 2 expert readers (A.C. and M.V.C.) to confirm the presence/absence of CNV. If an eye was deter-mined to have a CNV on ICGA, an OCT-A showing an abnormal neovascular network was considered to be a true positive; if a CNV was not visualized on OCT-A, the examination was considered to be a false negative. If the ICGA did not demonstrate a CNV (negative control

Patient No.	Age, y	Sex	Eye	Shape	Core	Margin	Margin Loops	Location	Device
1	80	M	OD	IRR	NV	WD	LL	FS	AngioVue
2	72	F	OS	CIR	NV	WD	SL	FI	AngioVue
3	79	F	OS	CIR	NV	WD	SL	FI	AngioVue
4	77	F	OS	IRR	NV	WD	LL	FS	AngioVue
5	81	F	OD	IRR	NV	WD	LL	FS	AngioVue
6	86	F	OD	IRR	NV	PD	N.C.	FS	AngioVue
7	77	M	OD	IRR	NV	PD	N.C.	FS	AngioVue
8	88	M	OD	CIR	NV	WD	SL	FI	AngioVue
9	72	F	OD	IRR	NV	PD	N.C.	FI	AngioVue
10	83	F	OD	CIR	NV	WD	LL	FS	AngioPlex
11	86	M	OD	CIR	NV	WD	SL	FS	AngioPlex
12	75	M	OD	IRR	NV	WD	SL	FS	AngioPlex
13	73	F	OD	IRR	NV	WD	SL	FS	AngioPlex
13			OS	IRR	V	WD	LL	FI	AngioPlex
14	75	M	OD	CIR	V	WD	SL	FI	AngioPlex
15	73	F	OD	CIR	NV	WD	SL	FS	AngioPlex
15			OS	CIR	NV	WD	SL	FS	AngioPlex
16	58	F	OS	N.C.	N.C.	N.C.	N.C.	N.C.	AngioPlex
17	75	M	OS	IRR	NV	WD	LL	FS	AngioPlex
18	73	F	OD	N.C.	N.C	N.C	N.C	N.C.	AngioPlex
19	80	M	OS	N.C.	N.C.	N.C.	N.C.	N.C.	Both
20	67	M	OS	N.C.	N.C.	N.C.	N.C.	N.C.	AngioPlex

CIR = circular; FI = foveal involving; FS = foveal sparing; IRR = irregular; LL = large loops; N.C. = not classified; NV = not visualized; PD = poorly defined; SL = small loops; V = visualized; WD = well defined.

group), an OCT-A with no evidence of a CNV was considered to be a true negative; if a CNV was detected, the examination was considered to be a false positive.

Statistical analysis was performed using SPSS software 21 (SPSS, Inc, Chicago, Illinois, USA). All data were expressed as mean ± standard deviation; continuous variables were assessed with a Student t test, while categorical variables were analyzed using χ^2 test. P values < .05 were considered to be statistically significant.

RESULTS

• STUDY POPULATION AND CHOROIDAL NEOVASCULARIZATION FEATURES: Twenty-two eyes of 20 consecutive patients (11 female/9 male; mean age 76.5 ± 6.9 years, range 58–88 years) with quiescent CNV secondary to AMD were enrolled (study group). Twelve eyes were enrolled at University Vita-Salute San Raffaele, Milan, Italy, and 9 eyes were enrolled at University Paris Est, Creteil, France. In all eyes, treatment-naïve quiescent CNV were defined as an irregular elevation of the RPE with moderately reflective material in the sub-RPE space; no intraretinal/subretinal hyporeflective fluid on SD OCT; late-phase ill-defined hyperfluorescent lesion,

without late-phase leakage or pooling of dye on FA; and hypercyanescent neovascular network in early to mid phases with the delineation of the fibrovascular plaque in the late phase of ICGA.[1] Of the 20 patients, 2 patients presented with bilateral quiescent CNV, 12 had received anti-VEGF injections (ranibizumab) for actively leaking CNV in the fellow eye, and 6 presented with nonexudative AMD (with no evidence of plaques at ICGA) in fellow eyes. Demographic data and angiographic features of the study group are listed in Table 2.

In 12 eyes OCT-A examinations were acquired with AngioPlex, in 9 eyes with AngioVue, and in 1 eye with both devices. In 4 out of 22 eyes it was not possible to classify the CNV "shape," "core," "margin," and "location," either because the vascular networks were not clearly shown (3 cases) or because they were not visible at all (1 case; Figure 2); therefore, these eyes were excluded from the analysis. Thus, it was possible to analyze the OCT-A features in 18 out of 22 eyes.

In 21 of 22 study patients, OCT-A detected flow (red dots) beneath the small irregular elevation of the RPE, with the major axis in the horizontal plane, and moderately reflective material in the sub-RPE space (typical of quiescent CNV).[1]

Twenty eyes of 22 patients (13 female/9 male; mean age 73.8 ± 6.8 years, range 62–88 years) were enrolled as a negative control group with no significant demographic
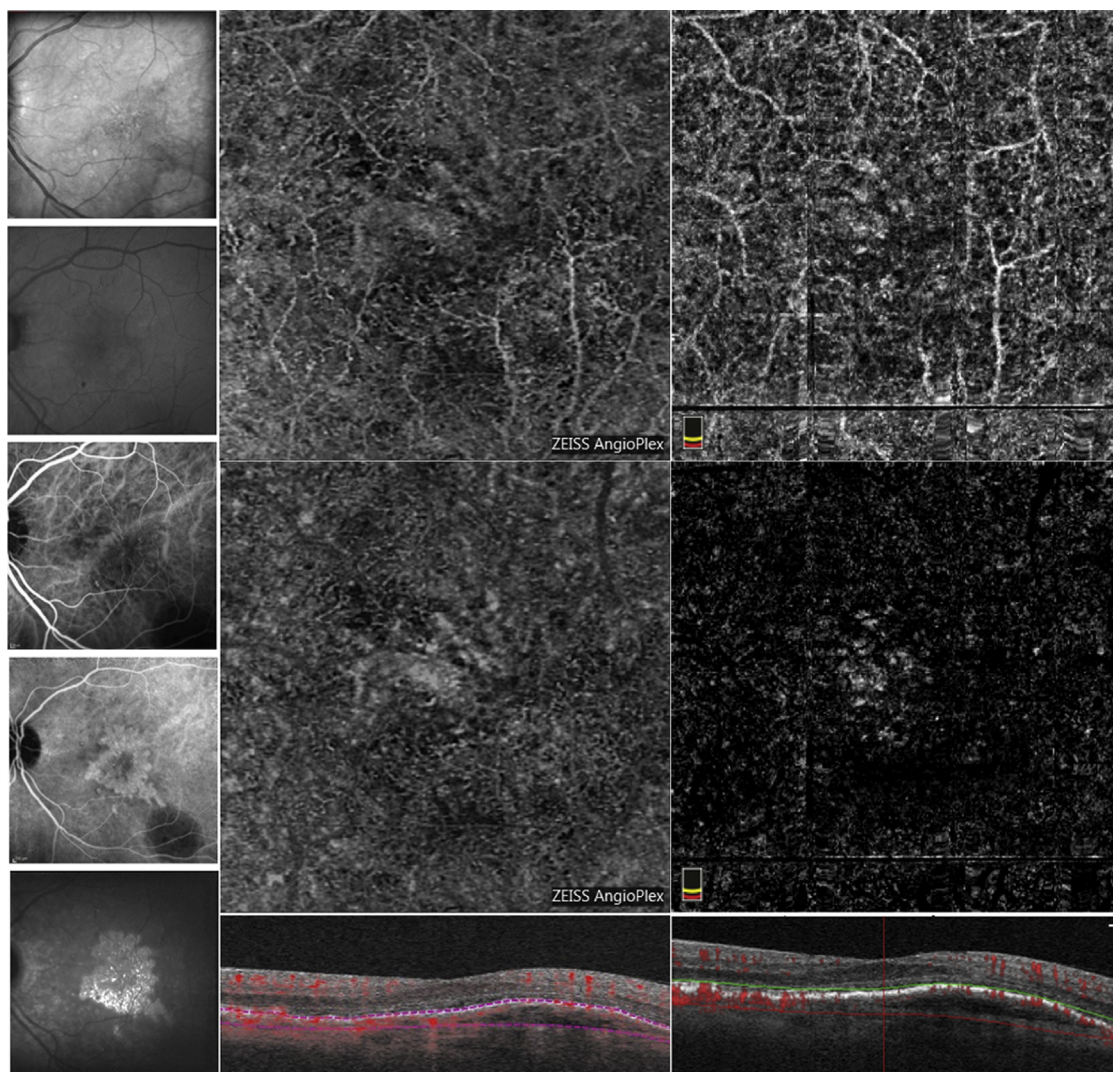
FIGURE 2. Infrared reflectance (IR), fundus autofluorescence (FAF), indocyanine green angiography (ICGA), optical coherence tomography (OCT) B-scan, and OCT angiography (OCT-A) of a quiescent choroidal neovascularization (CNV) not visible in both AngioPlex and AngioVue devices. (First and Second row, left panel) IR and FAF showing, respectively, inhomogeneous reflectance and autofluoresecence in the macula. (Third, Fourth, and Fifth row, left panel) Early, intermediate, and late phases of ICGA showing a large late plaque in the macula that corresponds to the quiescent CNV; (First, Second, and Third row, middle panel) 3 × 3-mm OCT angiogram of choriocapillary plexus with (First row) and without (Second row) automatic removal artifacts in Angio-Plex device and corresponding OCT B-scan. Neovascular network was not visible in both images; (First, Second, and Third row, right panel) 3 × 3-mm OCT angiogram of choriocapillary plexus with (First row) and without (Second row) automatic removal artifacts in AngioVue device and corresponding OCT B-scan. Neovascular network was not visible in both images. On OCT-A B-scans no flow (no red dots) was detected beneath the small irregular elevation of the retinal pigment epithelium (RPE), with major axis in the horizontal plane, despite presence of moderately reflective material in the sub-RPE space.

differences compared with the CNV group (age, $P = .11$; sex, $P = .5$). All OCT-A examinations were acquired with AngioPlex.

In the 18 study group eyes, CNV shape on OCT-A was rated as circular in 8 eyes and irregular in 10 eyes. CNV core was visible in 2 of 18 eyes and was not visible in 16; in the 2 eyes with a visible core, the core position was considered as central in 1 case and as eccentric in the other case. CNV margin was considered as well defined in 15 of 18 eyes and poorly defined in 3 eyes. CNV margin loops were rated as small in 9 eyes and large in 6 eyes; in 3 eyes the margin loops could not be classified because the margins were poorly defined. CNV location was foveal sparing in 12 eyes and foveal involving in 6 eyes. Examples of shape, core, margin, and location are represented in Figures 3 and 4.
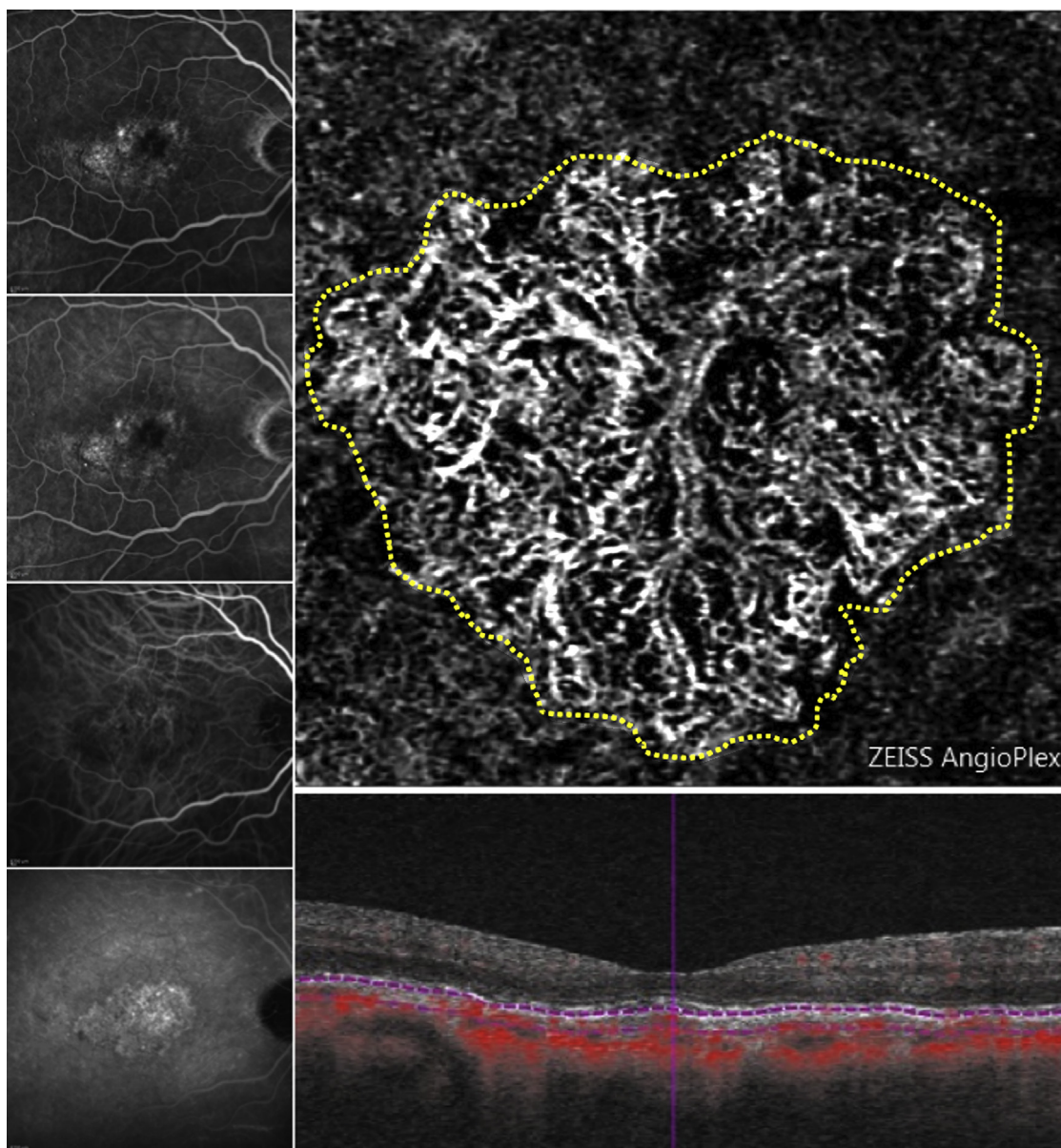
FIGURE 3. Fluorescein angiography (FA), indocyanine green angiography (ICGA), optical coherence tomography (OCT) B-scan, and OCT angiography (OCT-A) of a medium quiescent choroidal neovascularization (CNV). (First and Second row, left panel) Early and late phases of FA showing inhomogeneous small hyperfluorescence without leakage; (Third and Fourth row, left panel) Early and late phases of ICGA showing late plaque that corresponds to the quiescent CNV; (First and Second row, right panel) 3 × 3-mm OCT angiogram of choriocapillary plexus and corresponding OCT B-scan. OCTA shows a circular, well-defined, foveal-involving quiescent CNV with small loops. The central core is visible. Note on OCT-A B-scans presence of flow (red dots) beneath the small irregular elevation of the retinal pigment epithelium (RPE), with major axis in the horizontal plane, and moderately reflective material in the sub-RPE space.

The most frequently observed features (irregular, nonvisible core, well-defined margin, foveal-sparing) were each seen in 6 of 18 eyes.

• ASSESSMENT OF CHOROIDAL NEOVASCULARIZATION DETECTION ON OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY: Both readers correctly identified on OCT-A quiescent CNVs in 18 out of 22 eyes, and correctly excluded all 22 eyes with AMD without CNV. In the same 4 cases in which both readers did not detect quiescent CNV on OCT-A, ICGA clearly showed a late-phase hypercyanescent-staining neovascular plaque (Figure 2). The diagnostic tool validity assessment of OCT-A for quiescent CNV detection showed a sensitivity and specificity of 81.8% and 100%, respectively.
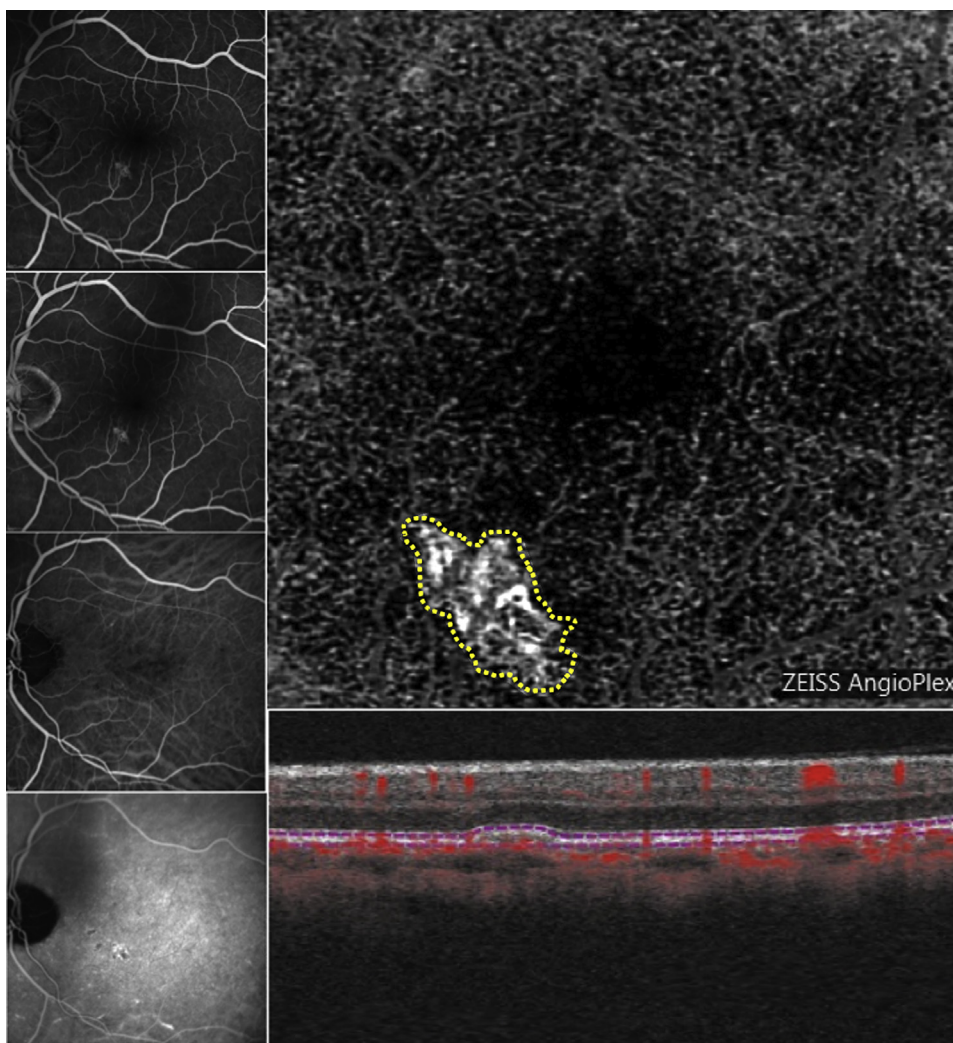
FIGURE 4. Fluorescein angiography (FA), indocyanine green angiography, optical coherence tomography (OCT) B-scan, and OCT angiography (OCT-A) of a small quiescent choroidal neovascularization. (First and Second row, left panel) Early and late phases of FA showing inhomogeneous hyperfluorescence without leakage; (Third and Fourth row, left panel) Early and late phases of ICGA showing late small hyperfluorescent area that corresponds to the quiescent CNV; (First and Second row, right panel) 3 × 3-mm OCT angiogram of choriocapillary plexus and corresponding OCT B-scan. OCT-A shows an irregular, well-defined with large-loop foveal-sparing quiescent CNV. The core is not visible. Note on OCT-A B-scans presence of flow (red dots) beneath the small irregular elevation of the retinal pigment epithelium (RPE), with major axis in the horizontal plane, and moderately reflective material in the sub-RPE space.

DISCUSSION

IN THIS STUDY WE INVESTIGATED THE FEATURES OF TREAT-ment-naïve quiescent CNV[1] in 22 AMD eyes and estimated the detection rate for neovascularization by means of OCT-A. The most frequently observed features (irregular, nonvisible core, well-defined margin, foveal-sparing) were each detected in 6 out of 18 eyes (33%). Additionally, sensitivity and specificity of quiescent CNV detection by OCT-A (diagnostic tool validity assessment) turned out to be 81.8% and 100%, respectively.

Despite the most recent developments in anti-VEGF drugs, neovascular AMD is still the main cause of visual loss in individuals aged 65 years and older in high-income countries.[11] With advances in diagnostic imaging, the segment of the population at highest risk of developing neovascular AMD may be efficiently and effectively screened for CNV with OCT-A.[12]

Currently, dye angiography and SD OCT remain the gold standard for CNV diagnosis and follow-up, and these techniques have been driving the treatment approach to neovascular AMD for years. In fact, for clinical approaches

based on "reactive" therapeutic regimens, intraretinal/subretinal fluid accumulation on OCT, dye leakage on FA, and functional worsening (ie, reduced BCVA) are considered the main criteria for retreatment.[13] However, FA is invasive, is time consuming, provides only 2-dimensional images, and has a low but significant risk profile that includes nausea, allergy, and, rarely, anaphylaxis.[14] Moreover, FA has low sensitivity for type 1 CNV detection, as this type of lesion lacks a discernible, well-demarcated area of leakage in both early and late angiographic frames.[15] On the other hand, SD OCT has limited ability to discriminate the CNV itself; instead it recognizes indirect signs of the pathologic CNV, such as serous exudation, RPE elevation, and retinal thickening. In addition, SD OCT has limited specificity, since it does not always differentiate between active CNV, normal choroidal vasculature, fibrotic scar, and lipid or fibrinous sub-RPE material accumulation.[16] Finally, distinguishing between quiescent CNV and drusenoid PED derived from adjacent confluent soft drusen can be difficult, as both appear as collections of moderately reflective material in the sub-RPE space on SD OCT.[17,18]

Recent studies have shown that OCT-A is able to precisely identify microvascular structures and that it can be used to assess the morphology of type 1, type 2, and type 3 CNV.[7,19–21] OCT-A is noninvasive and it rapidly acquires retinal images. Using OCT-A, neovascular membranes can be visualized in great morphologic detail, allowing the qualitative and quantitative evaluation of their microvascular features; CNV can be characterized by its size, morphology, blood vessel caliber, and presence of retinal fluid.[7] In addition, CNV appearance is not dependent on its activity rate and vascular leakage, so both nonexudative and exudative CNV are detectable by OCT-A.

Quiescent CNV appeared to enlarge over time on ICGA, as described by Querques and associates, without any detectable retinal thickening on OCT.[1] Precise location of the lesion on OCT-A and precise measurement of the CNV area could be a useful tool to monitor nonexudative CNV and it may contribute to treatment decisions. In fact, repeated scans on the neovascular membrane allow early detection of its growth with a faster and safer technique than angiography.

Recently, the ability of OCT-A to detect subclinical type 1 neovascularization has been shown.[22] Nehemy and associates[23] described the OCTA characteristics of a quiescent CNV secondary to AMD, and Roisman and associates[24] reported a comparison of FA, ICGA, and OCT-A in cases that had undergone ICGA for neovascular AMD in which ICGA revealed the presence of macular plaques in their asymptomatic fellow eyes. In our study 2 of 20 patients presented with bilateral quiescent CNV, 12 of 18 patients had received anti-VEGF injections (ranibizumab) for actively leaking CNV in the fellow eye, and 6 of 18 presented with nonexudative AMD (without

evidence of plaques at ICGA) in the fellow eyes. Our findings suggest that quiescent CNV may be heterogeneous in clinical presentation and ocular history, and their presence must be suspected also in eyes with low and intermediate risk of developing advanced AMD (and not only in fellow eyes of patients with neovascular AMD as reported by Roisman and associates[24]). Moreover, in our study 6 out of 18 quiescent CNV were visualized on OCT-A as irregular, well-defined, foveal-sparing networks, and in 16 of 18 eyes the core was not visualized. Probably the absence of a detectable core vessel may represent a protective factor against increased activity from quiescent CNV.

This manuscript is the first to report a high sensitivity and specificity of OCT-A for quiescent CNV detection. These results were achieved with commercially available devices and not with prototypes, which limited the clinical applications of previous studies.[23] However, it is noteworthy that, despite the obvious advantage of OCT-A (a rapid, 3-dimensional visualization method without the use of dye), in 4 out of 22 eyes it was not possible to classify the shape, margin, and location because the neovascular network was not clearly visualized in 3 cases, and because OCT-A was unable to identify the quiescent CNV in 1 case with 2 different devices (Figure 2), despite its evidence on ICGA. OCT-A visualizes the retinal vasculature by detecting intravascular blood flow, and perhaps in this case the flow rate was too low to be recognized by both devices. We do not yet have data regarding the sensitivities of the current devices to detect low flow rates.

It is generally accepted in clinical practice that asymptomatic CNVs do not have associated intraretinal/subretinal exudation on OCT and do not meet the criteria for anti-VEGF therapy.[13] However, CNV enlargement could represent a sign of progression toward more aggressive forms of maculopathy and may require preventive treatment. We did not follow over time quiescent CNV by means of OCT-A, as it was beyond the scope of this study. Further studies will assess the capability of OCT-A to evaluate CNV enlargement.

Imaging neovascular membranes with OCT-A has several limitations. First, poor fixation could severely limit the quality of the images, resulting in noisy images with potentially significant motion artifacts. Low-quality image acquisition decreases the likelihood of detecting small or poorly perfused CNVs. In 1 case in our series, the CNV was missed by OCT-A, as many motion artifacts disturbed the scan acquisition. Projection artifact may also limit accurate evaluation: the light beam that encounters the superficial retinal plexus may pass through the moving blood cells (approximately 45% of photons are estimated to pass across the vessel), and the projection of the scanned vessel may appear on the reconstruction of the deeper retinal plexus.[25]

The high sensibility and specificity for neovascularization in our series may be attributable to absence of intraretinal/subretinal fluid and preserved retinal morphology in

quiescent CNV, which limits the potential artifacts and thus represents an obvious advantage for OCT-A interpretation. Future studies will investigate whether OCTA might possibly be considered as a tool in guiding the frequency of follow-up visits and treatment decisions; moreover, these patients should be followed more frequently and observed without treatment. A limitation of this study is the relatively small cohort of patients, as quiescent CNV are not as common as active neovascularization. Moreover, the fact that 12 out of 20 patients had been treated with an anti-VEGF drug for actively leaking CNV in the fellow eye may have influenced the natural history of the CNV in the study eye. Longitudinal assessment of quiescent CNV and

its features on OCT-A have not been investigated, as the purpose of this study was to characterize quiescent CNV by means of OCT-A and to quantify the ability of this new imaging technique to detect CNV, compared to our standard methods.

In conclusion, we have described the OCT-A features of treatment-naïve quiescent CNV secondary to AMD, and demonstrated that it reliably detects CNV. Using OCT-A allows the clinician to identify noninvasively treatment-naive quiescent CNV and may possibly be considered as a useful tool in guiding the frequency of follow-up examinations and treatment decisions.

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