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Detection of Nonexudative Choroidal Neovascularization and Progression to Exudative Choroidal Neovascularization Using OCT Angiography

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Purpose: To detect nonexudative choroidal neovascularization (CNV) in age-related macular degeneration (AMD) with OCT angiography (OCTA) and determine the risk of exudative CNV developing compared with eyes without nonexudative CNV.

Design: Prospective, longitudinal, observational study.

Participants: Consecutive patients with drusen and pigmentary changes in the study eye and exudative neovascular AMD in the fellow eye.

Methods: In this prospective observational study, participants underwent spectral-domain OCTA (AngioVue; Optovue, Inc, Fremont, CA), clinical examination, and structural OCT at baseline and 6-month intervals for 2 years. OCT angiography images were exported for custom processing to remove projection artifact and calculate CNV vessel area.

Main Outcome Measures: Rate of developing exudation in eyes with and without nonexudative CNV as detected by OCTA on regular follow-up.

Results: Sixty-three study participants were followed up every 6 months and 48 completed the 2-year study. Mean age was 78 years and 60.3% were female. On the baseline visit, 5 eyes (7.9%) were found to have nonexudative CNV by OCTA, and 3 of them demonstrated exudation. Of 58 eyes with a normal OCTA on baseline visit, 5 eyes developed nonexudative CNV during a follow-up visit. All 5 of these nonexudative CNV went on to develop exudation in subsequent visits. Overall, 8 of the 10 eyes with nonexudative CNV developed exudation with a mean time of 8 months and mean CNV area growth rate of 20% per month ($P = 0.014$, exponential model). Initiation of antiangiogenic treatment halted their growth. In comparison, exudation occurred in only 6 of the 53 eyes (11%) that lacked a precursor nonexudative CNV. Cox proportional hazard analysis showed that having nonexudative CNV detected was associated with an 18.1-fold increase in the rate of exudation subsequently developing ($P < 0.0001$).

Conclusions: Nonexudative CNV frequently is detected by OCTA in the fellow eyes of those with exudative CNV. These lesions carry a high risk of exudation developing within the first year after detection and could benefit from close monitoring. The high risk of progression may justify prophylactic treatment; further studies are needed. *Ophthalmology Retina 2019;3:629-636 © 2019 by the American Academy of Ophthalmology*

Age-related macular degeneration (AMD) is a leading cause of vision loss and blindness.[1] Choroidal neovascularization (CNV), the hallmark feature of neovascular AMD, refers to pathologic angiogenesis from the choroid that can result in exudation, hemorrhage, and fibrosis formation damaging the outer retina, resulting in vision loss.[2] Current treatment of neovascular AMD with anti−vascular endothelial growth factor (VEGF) is effective at preventing vision loss; however, only 30% to 40% of patients show vision improvement.[3–5] Earlier detection of CNV and timely anti-VEGF treatment before vision loss should result in better visual outcomes.

Historically, the gold standard for CNV diagnosis is fluorescein angiography (FA).[6] Choroidal neovascularization endothelium is incompetent, allowing fluorescein molecules to exit the vasculature, resulting in characteristic hyperfluorescence patterns allowing CNV diagnosis. Therefore, by definition, CNV detected with FA is exudative. It would be better to have a test that can identify CNV before the development of exudation. In a prior study using indocyanine green angiography (ICGA) in a cohort of 432 study eyes with drusen and CNV in the fellow eye, 11% were found to have abnormal ICGA results. Eyes with abnormal ICGA results were almost 3 times as likely to show exudative neovascular AMD after a mean follow-up of 21.7 months. Because ICGA is not used widely and clinically and because it is invasive, it is not likely to be used as a

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screening technique. Structural OCT is noninvasive and useful for detecting and monitoring exudation associated with CNV, and there are several characteristic features on structural OCT in addition to fluid that suggest the presence of CNV, such as pigment epithelial detachment or subretinal hyperreflective material. However, structural OCT is not able to distinguish blood vessels clearly from hemorrhage or variable reflective material within pigment epithelial detachments.[6,7] In 2013, Querques et al[8] described treatment-naïve quiescent CNV based on multimodal imaging, including FA, ICGA, and OCT. These subclinical lesions harbored CNV that grew slowly over time and did not demonstrate exudation over a 2-year period.

OCT angiography (OCTA) is a functional extension of OCT that uses intrinsic contrast generated by the motion of blood cells to visualize retinal and choroidal blood vessels. OCT angiography does not rely on dye leaking patterns for CNV detection. Instead, the 3-dimensional nature of OCTA allows CNV to be detected as pathologic blood flow in the outer retinal–retinal pigment epithelium (RPE) slab, between the outer boundary of the outer plexiform layer and Bruch's membrane.[9] Because OCTA does not rely on exudation to detect CNV, it is possible to detect CNV before the development of exudation and vision loss.[10–18] In addition to detection CNV, OCTA-derived CNV quantitative metrics can be used to monitor nonexudative CNV growth over time.[15,17]

In this study, we selected eyes at high risk for CNV developing based on risk factors identified in the Age-Related Eye Disease Study.[19] Fellow eyes of exudative neovascular AMD were followed with semiannual OCTA to determine the rate of nonexudative CNV detection and the risk for exudation developing.

Methods

This prospective study was approved by the institutional review board of Oregon Health and Sciences University and included patients who were recruited from the retina clinics at the Casey Eye Institute, Oregon Health and Sciences University (Portland, OR), from September 22, 2014, through February 8, 2016. All research adhered to the tenets of the Declaration of Helsinki and all study participants provided informed consent prior to participation in the study. The inclusion criteria for study eyes required drusen and pigmentary changes without hemorrhage or exudation on clinical examination and no intraretinal fluid (IRF) or subretinal fluid (SRF) on structural OCT. Fellow eyes were required to have a history of exudative neovascular AMD. Exclusion criteria for the study eyes were vision worse than 20/200 and media opacity that would interfere with OCTA image quality. Study visits occurred every 6 months (±1 month) for a minimum of 2 years. Early Treatment of Diabetic Retinopathy Study visual acuity, dilated fundus examination, structural spectral-domain OCT (Spectralis; Heidelberg Engineering, Heidelberg, Germany), and OCTA scans were obtained at each visit. After being enrolled in the study, if neovascular AMD developed, diagnosis and the need for FA was determined by the treating physician (STB, TH, AL, PL, CF). All cases of neovascular AMD were reviewed in a retrospective manner to confirm appropriate diagnosis by one of the authors (STB).

The Avanti/AngioVue OCT/OCTA system (Optovue, Inc, Fremont, CA) was used for OCTA scanning. Both 3 × 3-mm^2 and 6 × 6-mm^2 scans of the macula were obtained at each visit. Each volumetric scan consisted of 304 × 304 transverse locations. Flow signal was computed with a commercial version of the split-spectrum amplitude-decorrelation algorithm.[20] Two orthogonal raster scans—1 vertical-priority and 1 horizontal-priority raster scan—were registered and merged to form a single volume to reduce motion artifacts.[21]

Two certified graders (AMH and OT) reviewed images on the AngioVue OCTA system, including both en face and cross-sectional OCTA images. If CNV was suspected, scans were exported for custom processing. To suppress projection artifact, the projection-resolved OCTA algorithm was used.[22,23] An automated algorithm[24] was applied to segment the outer retinal slab as between the outer boundary of the outer plexiform layer to Bruch's membrane. A grader inspected the segmentation boundary and applied manual correction if necessary. En face OCTA images of the outer retinal slab were generated by maximum projection. Choroidal neovascularization was detected as flow within this slab. If CNV was detected, cross-sectional projection-resolved OCTA was reviewed to classify flow as type 1, flow detected between Bruch's membrane and RPE; type 2, flow in the outer retina above the RPE; and type 3, flow in the outer retina that was contiguous with flow signal from the deep retinal capillary plexus.[25] Senior graders (STB and YJ) adjudicated instances of uncertainty or grader disagreement. All cross-sectional structural OCT images were reviewed to determine the presence or absence of IRF and SRF and classify the CNV as either exudative or nonexudative. Choroidal neovascularization flow signal was distinguished from the background speckle noise by a saliency-based CNV detection algorithm, and CNV vessel area was determined by the number of pixels containing flow.[26] After detection of nonexudative CNV, treating physicians were notified, and OCTA was attempted to be captured at follow-up intervals at their detection. If signs of exudation such as IRF or SRF were present, the treating physician determined the need for treatment and need for FA.

The follow-up data were plotted as Kaplan-Meier survival curves. If nonexudative CNV was detected, the baseline was set at the time of detection. Otherwise, the baseline was the initial enrollment date. For the survival analyses, data were censored if the participant completed the study or were lost to follow-up.

The growth of CNV vessel area was measured using both linear and exponential models. Simple linear regression was applied to the vessel area in the linear model. In the exponential model, the vessel areas were converted to a logarithmic scale before linear regression. The log-scale slope was then converted to percent change per month. All statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC).

Results

Of 65 study participants, 2 were excluded because of poor image quality. For the remaining 63 study participants, mean age was 78 years and 60.3% were women. Mean Early Treatment Diabetic Retinopathy Study visual acuity was 0.14 logarithm of the minimum angle of resolution units. Fifteen study participants dropped out during the follow-up period because of poor health, death, or preference to be seen at a satellite clinic where OCTA was not available. Forty-eight study participants completed 24 months of follow-up.

At the enrollment visit, nonexudative CNV was detected by OCTA in 5 of 65 eyes (7.9%). Three of these eyes developed exudation an average of 10 months (range, 6–12 months) after detection. During subsequent follow-up, nonexudative CNV was

Table 1. Characteristics of Nonexudative Choroidal Neovascularization

Patient No.	Age (yrs)	Choroidal Neovascularization Type	Early Treatment Diabetic Retinopathy Study Visual Acuity			Time to Exudation (mos)	Vessel Area (mm^2)		Growth Rate	
			Baseline	*At Detection*	*At Exudation*		*At Detection*	*At Conversion*	*Linear (mm^2/mo)*	*Exponential (%/mo)*
1	82	1	20/40	20/32	20/32	2	0.05	—	—	—
2	81	1	20/32	20/32	20/25	1	0.01	—	—	—
3	77	1	20/25	20/50	20/63	11	0.44	0.61	0.02	4
4	82	1	20/32	20/25	20/25	12	0.18	1.9	0.14	22
5	66	1	20/40	20/50	20/50	4	0.09	0.21	0.03	20
6	89	1	20/25	20/25	20/40	12	0.07	0.24	0.014	11
7	79	3	20/20	20/20	20/50	5	0.01	0.06	0.01	43
8	70	1	20/20	20/20	20/40	14	0.03	0.75	0.04	20
9	67	1	20/32	20/32	NC	NC	0.36	NC	0.01	2
10	88	1	20/25	20/25	NC	NC	0.28	NC	—	—

— = follow-up OCTA not obtained; mo = month; NC = never converted to exudative CNV.
Conversion indicates the initial detection of exudation in a previously nonexudative choroidal neovascularization.

detected in 5 additional eyes. All of these eyes developed exudation a mean of 6 months (range, 1−12 months) after detection. Overall, OCTA detected nonexudative CNV in 10 eyes and 8 of these eyes (80%) developed exudation. Seven of these 8 eyes demonstrated exudation in the area of the nonexudative CNV that was being observed. One patient showed exudative CNV that arose from a different location and was not associated with the nonexudative CNV that was being observed. The average time for all nonexudative CNV to convert exudation was 7 months and 23 days after first detection with OCTA.

All cases of nonexudative CNV were asymptomatic at the time of diagnosis. The mean distance from the center of the foveal avascular zone to the nonexudative CNV cases was 1.04 mm with a range of 0.37 to 1.81 mm. Nonexudative CNV was detected throughout the macula, including an inferior location in 3 eyes, inferior nasal location in 1 eye, superior location in 1 eye, temporal location in 2 eyes, superior temporal location in 2 eyes, and nasal location in 1 eye. There was no evidence that a specific distance from the fovea or sector increased the risk of exudation. The fellow eye was receiving anti-VEGF treatment at the time of detection of nonexudative CNV for all patients except patient 9; in this patient, a treatment-naïve exudative CNV was detected at the baseline visit. The detection of nonexudative CNV was not associated with any reduction in visual acuity (Table 1) with the exception of patient 3, in whom visual acuity loss was attributable to geographic atrophy. Interestingly, in this patient, an irregular RPE elevation was suspicious for type 1 CNV between areas of geographic atrophy; however, no flow was detected with OCTA. Six months later, nonexudative CNV was detected within this RPE elevation. Exudation developed 11 months after first detection and the IRF resolved with anti-VEGF treatment (Fig 1). Of the 8 eyes in which exudation developed, visual acuity loss occurred in 3 eyes because of foveal involvement. The vision returned to baseline in 2 eyes after treatment. Five eyes demonstrated exudation without foveal involvement and treatment was provided before vision loss.

Two eyes with nonexudative CNV never developed exudation (Table 1). In 1 patient, follow-up was limited to 5 months because the patient experienced a stroke (patient 10). In the other patient (patient 9), a subfoveal nonexudative CNV remained inactive for 42 months of clinical follow-up and visual acuity remained stable. The study participant underwent 15 months of OCTA follow-up scans before transferring care to a satellite clinic that lacked OCTA. Over 15 months, this nonexudative CNV enlarged slowly; however, exudation never developed (Fig 2). The growth rate in this patient was 2% per month, which was the slowest among the patients with nonexudative CNV.

In 6 patients with nonexudative CNV (patients 3−8), vessel areas were measured at both the time of detection and exudation (Table 1). The nonexudative CNV vessel area increased from 0.14 ±0.16 mm^2 (mean±standard deviation) to 0.63±0.68 mm^2. The mean exponential growth rate of 20% per month was significantly more than 0 ($P = 0.014$). The mean linear growth rate was 0.04 mm^2/month ($P = 0.09$).

In 2 patients, CNV growth rates were measured both before and after exudation (Fig 3). In patient 3, a type 1 nonexudative CNV showed a linear growth rate of 0.017 mm^2/month and exponential growth rate of 4%/month. After the onset of exudation and initiation of PRN anti-VEGF treatment, the CNV shrunk at a linear rate of −0.014 mm^2/month and exponential rate of −3% per month. In patient 7, a type 3 precursor lesion was detected as flow in the outer retina contiguous with the deep retinal capillary plexus. The linear growth rate was 0.01 mm^2/month, and the exponential growth rate was 43% per month. After initiating anti-VEGF treatment, the lesion shrunk at a linear rate of −0.004 mm^2/month and exponential rate of −5% per month.

Of the 14 eyes in which exudation developed, OCTA detected precursor nonexudative CNV in 8 eyes (57%). In the 6 eyes in which OCTA did not detect precursor lesions, the average time between the prior OCTA scans showing negative results and presentation of exudation was 4.2 months (range, 2−7 months). It is unknown if an intermediary precursor nonexudative CNV was present in these eyes before their development of exudation. Kaplan-Meier survival analysis (Fig 4) showed that eyes with OCTA-detected nonexudative CNV demonstrated exudation at a faster rate ($P < 0.0001$, log-rank test) than study eyes without nonexudative CNV. The Cox proportional hazard ratio was 18.1.

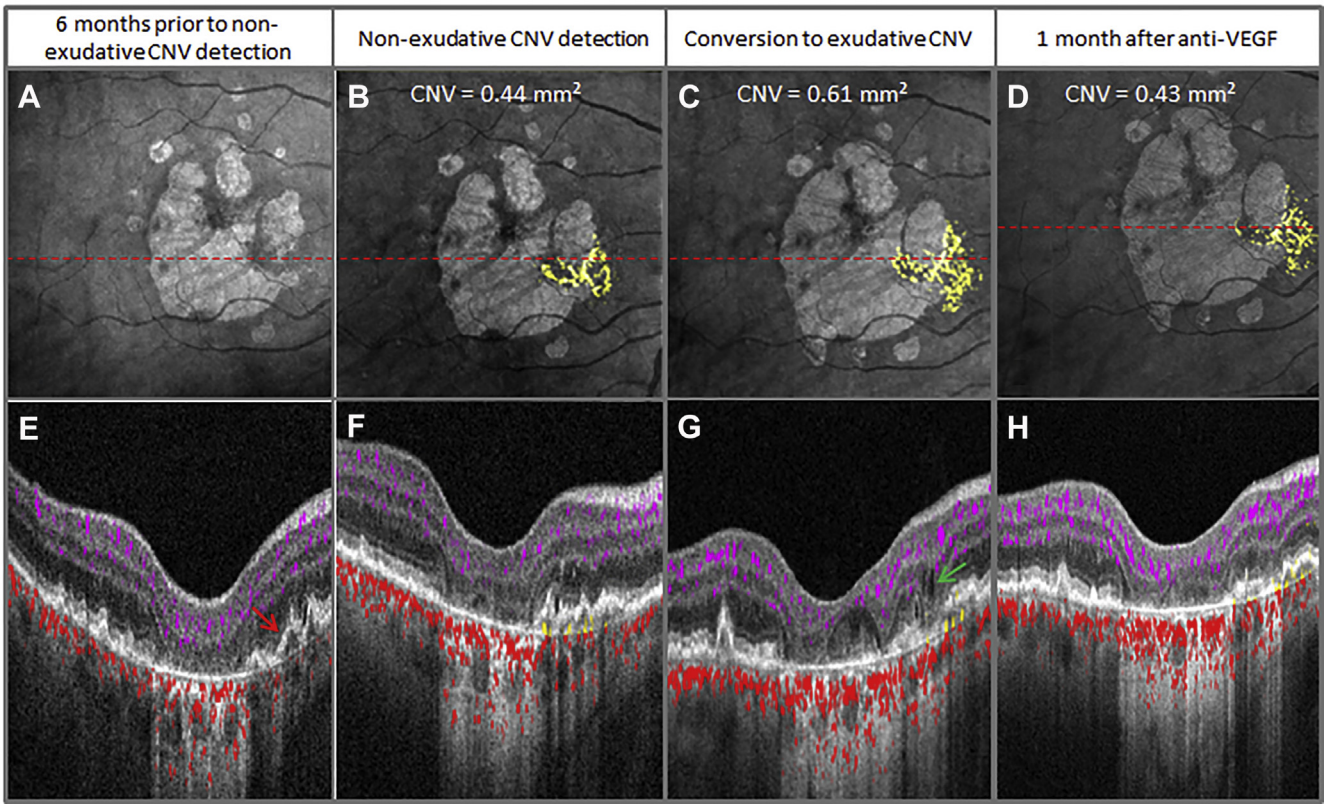

Figure 1. Development of nonexudative choroidal neovascularization (CNV) between areas of geographic atrophy: (**A**–**D**) 6 × 6-mm en face outer retinal OCT angiography (OCTA) displayed over en face structural OCT with (**E**–**H**) red dashed line corresponding to cross-sectional OCTA. **B**–**D**, The CNV vessel area (in square millimeters) presented on respective en face images. Six months before nonexudative CNV detection, (**A**) en face structural OCT revealed geographic atrophy without flow detected with overlying outer retinal en face OCTA and (**E**) no flow present in irregularly elevated retinal pigment epithelium with cross-sectional OCTA (red arrow). **B**, **F**, Nonexudative CNV first detected (CNV flow highlighted with yellow) in between areas of geographic atrophy. **C**, Over 11 months, increased CNV vessel area with growth along the edges of geographic atrophy. **G**, Conversion to exudation with intraretinal fluid (IRF) detected (green arrow). One month after anti–vascular endothelial growth factor (VEGF) treatment, (**D**) reduced CNV flow and (**H**) resolution of prior IRF.

Discussion

It has been well documented that the fellow eyes of those with exudative CNV carry high risk for exudative CNV developing, and in eyes with drusen and pigmentary changes, the rate approaches 50% over a 5-year period.[19] Because OCTA is noninvasive and can be acquired rapidly without disrupting a busy clinical practice, it has potential to become a useful screening tool. Several studies have demonstrated that OCTA can detect asymptomatic CNV before exudation; however, our study design is unique in that OCTA was obtained at regular fixed intervals to detect nonexudative CNV and monitor their growth.

Pooled rates of fellow eyes in which neovascular AMD developed for the Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular Age-Related Macular Degeneration and the Anti-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in Age-Related Macular Degeneration study was 32.1% at 2 years.[27] The 2-year rate in the Comparison of Age-Related Macular Degeneration Treatments Trials was 18.6%.[28] Our rate of 29% of fellow eyes demonstrating neovascular AMD was similar to these larger multisite clinical trials. OCT angiography detected a precursor nonexudative lesion in just more than half of the eyes in which exudation developed over 2 years.

Two previous studies reported prevalence rates of nonexudative CNV detected with OCTA. A study by de Oliveira Dias et al[14] detected subclinical macular neovascularization (their term for nonexudative CNV) with OCTA in 14.4% of 160 fellow eyes of those with exudative AMD. Another study, by Yanagi et al,[17] detected nonexudative CNV in 19% of eyes. This cohort consisted of 60% with polypoidal choroidopathy, and 40% showed typical AMD. Our prevalence rate was calculated from the number of cases of nonexudative CNV detected with OCTA on the first study visit and was 7.9%. This rate is lower than that of the other 2 studies; however, given the relatively small sample sizes and different patient characteristics, some variability is not surprising.

Several smaller case reports using OCTA have suggested nonexudative CNV may be relatively benign.[12,15,16,29] Other recent and larger studies have found that nonexudative CNV

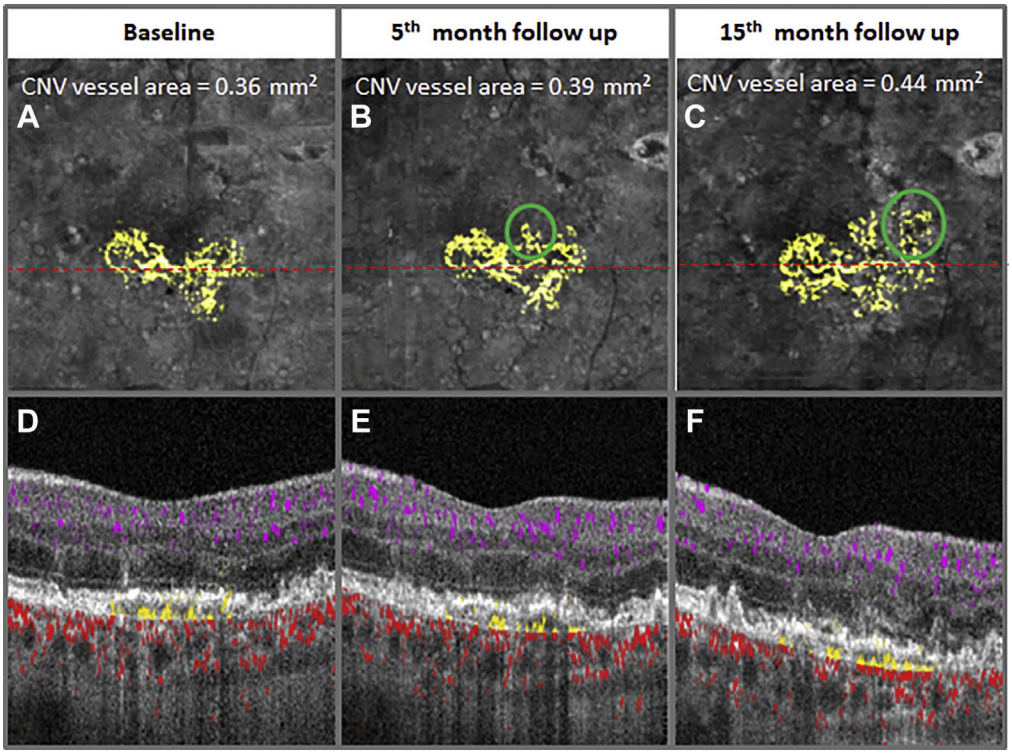

Figure 2. Slow enlargement of nonexudative choroidal neovascularization (CNV) over 15 months. **A**–**C**, Three × 3-mm en face outer retinal OCT angiography (OCTA) displayed over en face structural OCT with CNV flow highlighted with yellow; (**A**) baseline *en face* OCTA with subfoveal CNV. Emerging vascular branches (green circles) at (**B**) 5-month and (**C**) 15-month follow-up visit. **D**–**F**, Cross-sectional OCTA demonstrating flow between Bruch's membrane and retinal pigment epithelium (yellow) without development of exudation.

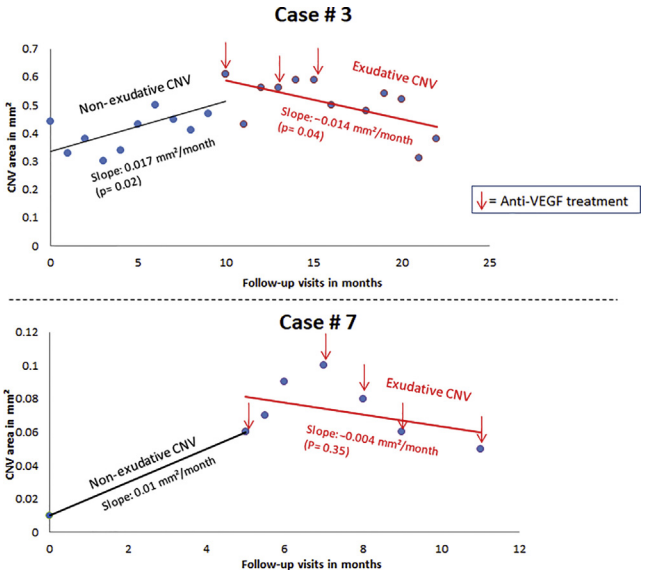

Figure 3. Graphs showing choroidal neovascularization (CNV) vessel area (in square millimeters) plotted over time (months) for patient 3 (top) and patient 7 (bottom). Nonexudative CNV slope (black line) calculated from first detection until exudation. Exudative CNV slope (red line) calculated from the first signs of exudation to the last follow-up while receiving pro re nata anti–vascular endothelial growth factor (VEGF) treatment (red arrows). Statistically significant ($P < 0.05$) linear regression growth rate per month.

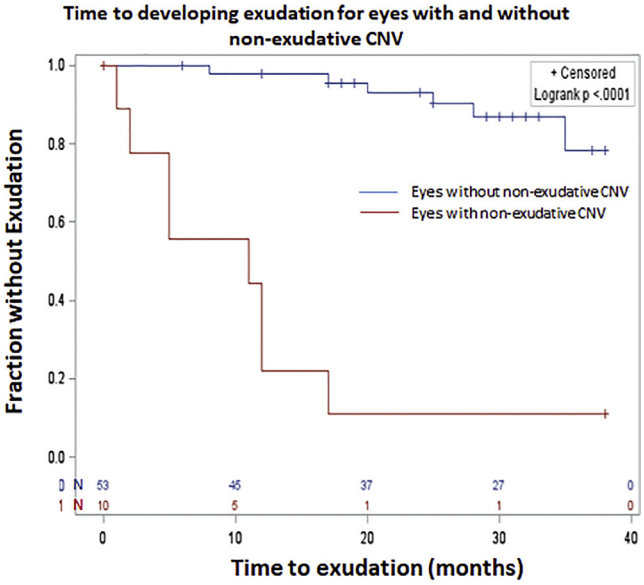

Figure 4. Kaplan-Meier plots showing time to exudation for eyes with (red) and without (blue) OCT angiography-detected nonexudative choroidal neovascularization (CNV). For eyes with nonexudative CNV, baseline visit is defined when nonexudative CNV was first detected. n = number of participants at risk.

carries an increased risk of exudation developing. Yanagi et al[17] reported that 22.2% (4/18) of eyes with nonexudative neovascularization demonstrated exudation after 6 months, and the odds ratio for exudation developing was 10.3 ($P = 0.01$). In an additional study, de Oliveira Dias et al[14] reported the development of exudation in 21.1% of eyes with subclinical macular neovascularization (their term for nonexudative CNV) over 12 months of follow-up. In our study, the presence of nonexudative CNV increased the risk of exudation developing 18-fold ($P < 0.0001$, Cox proportional hazard ratio). There are several explanations for why our study showed a higher rate (80%) of exudation developing. First, our follow-up period was longer, thus allowing a longer period for exudation to develop. Second, our study design was different and all eyes underwent regularly scheduled OCTA every 6 months. Nonexudative CNV was detected in 5 eyes at the first study visit, and 5 eyes demonstrated new nonexudative CNV during a follow-up study visit with a prior normal baseline OCTA. All 5 eyes with nonexudative CNV detected during a follow-up visit developed exudation. Nonexudative CNV lesions that were discovered at the first OCTA imaging may have existed already for a long period without exudation developing, and therefore showed a selection bias for being less active. Collectively, these studies suggest that nonexudative CNV carries significant risk for exudation. However, the absolute incidence varies from study to study.

Several authors have used different terms to describe treatment-naïve CNV in AMD that lacks exudation. The term *nonexudative CNV detected with OCTA* is likely the same entity as or very similar to *subclinical macular neovascularization*. Studies observing these eyes required the fellow eye to show exudative AMD. The term *treatment-naïve quiescent CNV* carried slightly different inclusion criteria than our study and others. First, eyes with these lesions required 6 months of follow-up without development of exudation before enrollment in their longitudinal studies. Second, the fellow eye was not required to show exudative CNV. The 2 differences may explain the reported lower rate of exudation (6.6%) after 1 year of follow-up.[30]

It is unclear if treatment of nonexudative CNV with anti-VEGF injections is necessary. Because nonexudative CNV may recapitulate the choriocapillaris and protect against geographic atrophy, some have suggested that treating nonexudative CNV may hasten geographic atrophy and lead to negative long-term visual effects.[10,14,31–33] However, given the high rate of exudation in our series, early treatment may prevent vision loss associated with SRF, IRF, or hemorrhage. Three patients lost vision because of exudation in our study, and fortunately, vision returned to baseline in 2 of them after treatment with anti-VEGF injections. Because most patients do not gain vision with anti-VEGF treatment, it is reasonable to hypothesize that prophylactic treatment preventing exudation could save vision. Therefore, there is need for a randomized controlled trial to evaluate both the short- and long-term effects of treating nonexudative CNV versus frequent observation.

One difficulty with designing a prophylactic treatment trial is determining appropriate clinical end points that could guide treatment for nonexudative CNV. Current treatment of exudative CNV is based on presence or absence of fluid with structural OCT. Because nonexudative CNV lacks exudation, an alternative metric is needed. OCT angiography-derived vessel density is a noninvasive metric that may help to guide treatment. We observed growth of nonexudative CNV as well as a trend that slower growth was associated inversely with developing exudation. Halting the rapid growth of CNV could be a plausible treatment end point, because we have demonstrated that anti-VEGF injection could reverse the growth of these lesions in our study (Fig 3). The range of growth rates reported in this article could serve as a preliminary reference for what constitutes slow versus rapid growth.

The limitations of this study include the relatively small sample size and a moderate dropout rate. We did not use ICGA to confirm the nonexudative CNV detected by OCTA because such validation was provided by previous studies.[10,11,16] Finally, we had to export the OCTA data for processing by custom software to remove projection artifacts and provide automated quantification of CNV area. Because projection artifacts can result in false-positive identification of CNV, it is important that this artifact is removed to prevent false-positive CNV detection.[34] Our results may not be applicable to routine clinical practice using currently available commercial technology because we used custom software and certified graders. However, the commercial OCTA platforms are advancing rapidly and some systems have adapted projection resolution and semiautomated CNV area measurement software.

In summary, routine screening with OCTA can detect nonexudative CNVs that are asymptomatic and undetectable with clinical examination or structural OCT. Nonexudative CNV is a high-risk precursor for conversion to exudative CNV and frequent follow-up is suggested. Nonexudative CNV of known recent origin (previous negative OCTA results) or higher growth rate may suggest an even higher risk for exudation. A clinical trial to assess the potential benefit of prophylactic anti-VEGF treatment is warranted, and CNV vessel area growth could be a metric for titrating treatment.

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Abbreviations and Acronyms:
AMD = age-related macular degeneration; **CNV** = choroidal neovascularization; **FA** = fluorescein angiography; **ICGA** = indocyanine green angiography; **IRF** = intraretinal fluid; **OCTA** = OCT angiography; **SRF** = subretinal fluid; **VEGF** = vascular endothelial growth factor.

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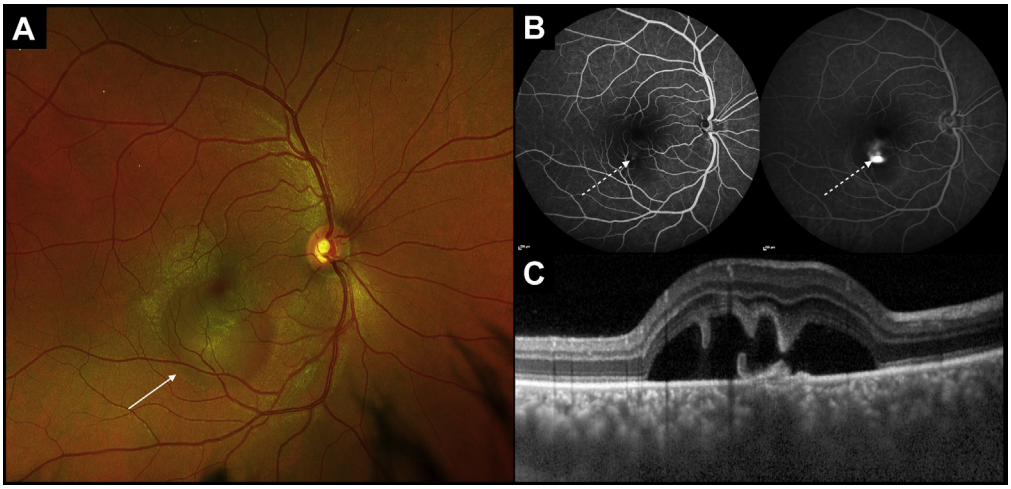
Pictures & Perspectives



Expanding the OCT Spectrum of Acute Central Serous Chorioretinopathy: The Stalagmite–Stalactite Pattern

A 31-year-old man sought treatment for acute unilateral vision loss. Visual acuity was 20/32 in the right eye and 20/20 in the left eye. Fundus photography revealed round serous macular detachment (**A**, white arrow). Early-phase fluorescein angiography disclosed a single leakage point evolving into the inkblot pattern and altered smokestack pattern in the late phase (**B**, white dashed arrows). Spectral-domain OCT demonstrated subretinal fluid with a singular stalagmite and stalactite appearance (**C**). First described in Waldenström maculopathy, the stalagmite–stalactite OCT pattern may occur in acute central serous chorioretinopathy. It corresponds to a variant of the dipping sign, which is characterized by sagging of the posterior layer of the neurosensory retina resulting from tractional fibrinous exudates at the leakage site.

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