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Fluorescein Angiography Does Not Alter the Initial Clinical Management of Choroidal Neovascularization in Age-Related Macular Degeneration

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Purpose: Fundus fluorescein angiography (FFA) is the standard modality to diagnose and manage choroidal neovascularization (CNV). However, FFA is costly and has considerable morbidity from allergic reactions and a mortality of 1 per 220 000. Since the advent of anti-vascular endothelial growth factor (VEGF) therapy for CNV, OCT has been used extensively to manage CNV, but FFA is still widely used. One recent study found the sensitivity and specificity of OCT compared with FFA in diagnosis of CNV were 100% and 80.8%, respectively. We hypothesize that FFA does not affect the management of patients initially suspected of having CNV to a clinically significant degree.

Design: Evaluation of diagnostic test using vignettes.

Participants: A total of 99 patients (99 eyes) who had an initial presentation of later confirmed CNV.

Methods: We retrospectively extracted in de-identified form the FFA, OCT, and clinical histories of the subjects. Vignettes were created with a standard narrative clinical history, posterior-pole color fundus image, central B-scan OCT of the initial visit, and early, mid, and late FFA of the affected eye. Four masked retinal specialists reviewed, in randomized order, these vignettes without FFA images (FFA- arm) and answered a forced choice management question: observation, 3 consecutive anti-VEGF injections, or other. After re-randomization, experts again reviewed the vignettes with the addition of the FFA images (FFA+ arm).

Main Outcome Measures: Intraobserver and interobserver concordance and reliability statistics within and between specialists.

Results: Among our retina specialists, intraobserver concordances were 89.7%, 88.7%, 88.7%, and 95.9% (average 90.7%, 95% confidence interval [CI], 83.7−97.6). The average interobserver concordance for the FFA− arm was 84.0% (95% CI, 72.6−95.4), and for the FFA+ arm, 81.8% (95% CI, 68.5−95.2); paired *t* testing demonstrated no significant difference between the FFA− and FFA+ arms: t = 0.6, $P = 0.55$.

Conclusions: Our data suggest a high degree of agreement in clinical decision making whether FFA was used or not. There was a similar level of agreement among specialists in the FFA− and FFA+ groups, albeit at higher, not statistically significant, variability. We believe these findings further support deferring the use of FFA in the initial management of CNV in AMD, except in treatment failures and nonstandard cases. *Ophthalmology Retina 2018;2:659-666 Published by Elsevier Inc. on behalf of the American Academy of Ophthalmology*

In developed countries, choroidal neovascularization (CNV) in the context of age-related macular degeneration (AMD) is the leading cause of vision loss among those aged 55 years or older.[1] Fundus fluorescein angiography (FFA) has long been the gold standard for the diagnosis of CNV, as specifically stated in the American Academy of Ophthalmology Preferred Practice Patterns.[2] Intravenous FFA is indicated when the patient experiences new metamorphopsia or has unexplained blurred vision, or when clinical examination reveals elevation of the RPE or retina, macular edema, subretinal blood, hard exudates, or subretinal fibrosis, or the OCT shows evidence of fluid. All recent major AMD clinical trials also include FFA as part of their inclusion criteria.[3−5] However, FFA typically requires placement of an intravenous catheter, dedicated equipment, highly trained operators, and additional time, and carries a spectrum of risk, ranging from mild (i.e., nausea in 1:20), moderate (i.e., urticaria, dyspnea in 1:60), to severe (i.e., anaphylaxis in 1:2000, death in 1:220 000).[6] Historically, FFA was not only clinically useful for diagnosis but also requisite for the management of CNV with focal laser or photodynamic therapy.[7,8] Laser-based modalities have since been largely replaced by intravitreal antivascular endothelial growth factor (VEGF) agents.[9] Various studies have demonstrated a reduction in the progression of vision loss, especially over a 2-year period

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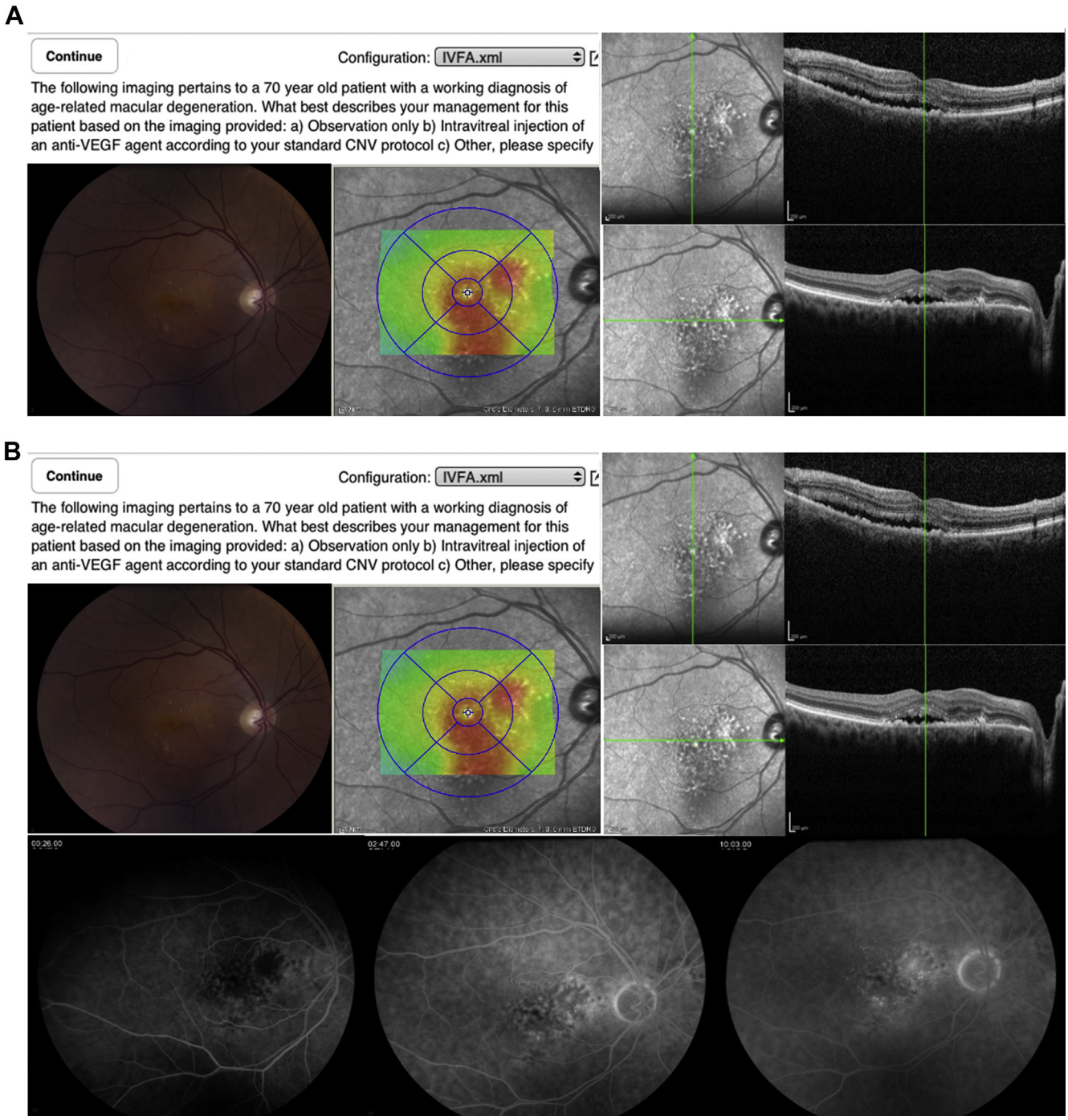

Figure 1. A sample fundus fluorescein angiography (FFA−) (**A**) and FFA+ vignette (**B**) for the same subject.

after starting anti-VEGF treatment.[3,9,10] Both OCT and anti-VEGF therapies have altered practice patterns considerably with decreased FFA use along with increased OCT and anti-VEGF use.[11–13]

Several studies have shown that OCT has generally high sensitivity and moderate-to-high specificity to detect CNV compared with FFA. Sandhu and Talks[14] found that stereo color photographs paired with OCT were 94% sensitive and 89.4% specific in identifying CNV when compared with an FFA reference standard by one expert. Khurana et al[15] analyzed cases with retinal tomographic abnormalities (i.e., intraretinal fluid, cystoid findings, subretinal fluid) in the context of CNV whether or not leakage was seen on FFA and found that spectral-domain (SD) OCT was 90% sensitive to leakage found on FFA but only 47% specific, that is, abnormalities were found on OCT in the absence of leakage, which suggests management decisions based on OCT alone might lead to overtreatment. Wilde et al[16] retrospectively