Best Clinical Practice for Age-Related Macular Degeneration Imaging

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Abstract

Purpose: To identify best clinical practices for macular degeneration imaging. Methods: We reviewed best clinical practices for imaging patients with age-related macular degeneration. These recommendations are based on different levels of evidence (I-III). Results: The type of imaging needed depends to some degree on the clinical scenario: first visit vs follow-up visit vs poorly responsive patient. Conclusions: Imaging technologies that may be useful include optical coherence tomography, fundus photography, fundus autofluorescence imaging, fluorescein angiography, indocyanine green angiography, and optical coherence tomography angiography.

Keywords

age-related macular degeneration, fluorescein angiography, fundus autofluorescence, fundus photography, imaging, indocyanine green angiography, optical coherence tomography, optical coherence tomography angiography

Introduction

Ideally, validation of clinical practice is based on results of randomized clinical trials, ie, level I evidence.1 However, level I evidence does not exist for all aspects of clinical practice, and even when available, certain real-world obstacles make its application challenging.2 While treatment for neovascular age-related macular degeneration (nAMD) has evolved, it has the range of retinal imaging modalities used to establish a diagnosis, assess neovascular lesion characteristics, and guide treatment decisions.

In some cases, the use of imaging in this setting has been validated in randomized trials. For example, fluorescein angiography (FA) provided critical information in the randomized clinical trials evaluating laser photocoagulation3 and verteporfin photodynamic therapy.4 By contrast, although patients underwent optical coherence tomography (OCT) during the initial randomized trials assessing intravitreal anti-VEGF therapy for nAMD,5,6 its value in guiding treatment decisions was established later in a relatively small case series (ie, level II evidence).7 This was followed by OCT-based determination of presence of fluid for treatment decisions in the first large randomized clinical trial of comparative efficacy of intravitreal anti-VEGF therapies.8-10

There are a number of other imaging modalities that, in the proper setting, provide important information enabling clinicians to optimize therapy for patients with nAMD. Although the level of evidence supporting their usefulness ranges from level I to level III (ie, opinion of respected authorities), that variability is a boundary condition that is typical of clinical practice and does not per se invalidate the value of recommendations so derived. With these caveats in mind, our goal is to provide guidelines for best clinical practice regarding the use of imaging studies in the management of patients with nAMD. Image analysis of non-neovascular AMD has been reviewed elsewhere.11-15

Clinical Scenarios

First Visit

When a patient with suspected nAMD first presents for evaluation, some or all of the following imaging tests may be useful for establishing a correct diagnosis, making decisions regarding management, and for educating the patient regarding the treatment plan.

OCT. Because current OCT devices are more sensitive than clinical ophthalmoscopy using a contact lens in detecting certain subtle alterations in retinal structure, ophthalmologists often perform OCT in patients reporting changes in central vision, even when no exudative findings are detected on...
clinical examination. OCT may also detect retinal fluid in patients lacking symptoms. Some clinicians use OCT to help direct their clinical examination, and since OCT does not require dilation, patients can be imaged while their pupils are dilating. OCT allows one to identify and document the extent of subretinal fluid, intraretinal fluid, subretinal hyperreflective material (SRHM), and/or pigment epithelial detachment (PED), which will be used to assess the response to therapy as well as to identify areas of retinal pigment epithelium (RPE) and photoreceptor loss.

Certain characteristic OCT findings may suggest specific neovascular lesion types that may warrant additional imaging. For example, identifying intraretinal fluid surrounding a hyperreflective focus in the outer retina anterior to a PED can help detect cases of type 3 (intraretinal) macular neovascularization (MNV). \(^7,16-22\) The presence of "peaked" PEDs found in association with an adjacent shallow, irregular splitting of the RPE/Bruch membrane complex (double-layer sign) is suggestive of polypoidal choroidal vasculopathy (PCV) also known as neovascular type 1 (sub-RPE) MNV. \(^23\)

It is important to recognize that SHRM may represent different types of exudative material, including hemorrhage, so clinical examination and/or additional imaging is often required to completely evaluate its presence. Not infrequently, patients with no fluid and normal vision may harbor nonexudative MNV that can be seen with OCT. These patients warrant close follow-up so treatment can be initiated if fluid develops.

**Fundus photographs.** Color (including multicolor) photographs may be useful to document the extent of geographic atrophy (GA) and/or fibrosis, extent of subretinal hemorrhage (eg, for comparison at the next visit), as well as for patient education. \(^^{11,21}\)

**Fundus autofluorescence imaging.** Fundus autofluorescence (FAF) may be useful to document the extent of associated GA, which may progress and may contribute to changes in visual acuity not attributable to CNV activation. \(^{21,24,25}\) FAF imaging also can help clinicians distinguish GA from other similar entities such as acquired vitelliform lesions. \(^{26}\)

**FA (rate of anaphylaxis: ~1/222 000\(^{27}\)).** An FA, unless contraindicated, may be useful to assist in distinguishing masquerade conditions such as choroiditis or central serous chorioretinopathy (CSC) from MNV. \(^{21}\)

**Indocyanine green angiography (rate of anaphylaxis: ~1/200 000\(^{28,29}\)).** An indocyanine green angiogram (ICGA) may be useful for detecting MNV beneath areas of macular hemorrhage and for identifying PCV (ie, neovascular type 1 [sub-RPE] MNV\(^{23}\) ). If OCT/FA are not diagnostic, ICGA may also help distinguish MNV related to AMD vs CSC or other non-AMD entities. \(^{21,30}\)

**OCT angiography.** An OCT angiogram (OCTA) may substitute for an FA, provided one recognizes its limitations such as limited ability to image flow beneath PEDs. Also, with OCTA, there is a need for reasonably clear media and steady fixation. \(^{31-34}\) OCTA also can identify occult, nonexudative type 1 MNV in cases of intermediate AMD. This finding may have a predictive value in patients at higher risk for progressing to clinically active MNV. \(^{35,36}\)

**Follow-Up Visit**

Routine follow-up visits usually require less-extensive imaging than the first visit. If a patient has unexplained visual loss or appears refractory to therapy, more-extensive imaging may be indicated.

**OCT.** OCT imaging is important for most follow-up visits, as reactivation or persistent activity of MNV may not be evident on clinical examination alone, even with contact lens biomicroscopy. Clinicians should not rely solely on thickness maps and should check for segmentation errors by reviewing structural B-scans. \(^37\) Changes in OCT thickness >10% of the previous value (eg, increased retinal thickness from 300 \(\mu\)m to 335 \(\mu\)m) that do not arise from imaging artifacts are probably clinically significant. \(^{18}\)

Additional imaging is appropriate to document changes from baseline or to evaluate unexplained clinically significant changes in visual acuity or uncertain anatomic findings on OCT. Depending on the circumstances, these additional studies may include FA, ICGA, FAF, and color photographs.

OCTA may provide information not available with FA or OCT and may be useful if there is an unexplained change in visual acuity or if OCT findings are not clear. \(^{38-40}\)

**Poorly Responsive Patient**

If a patient responds poorly to intravitreal anti-VEGF therapy, it may be prudent to consider alternative diagnoses including CSC, large drusenoid PED, or an acquired vitelliform lesion for which additional imaging may be needed to correctly identify the condition. If the patient previously responded to anti-VEGF therapy and no longer seems responsive, then more extensive imaging is undertaken both to ascertain possible changes in disease anatomy (eg, development of foveal atrophy causing visual loss in the absence of CNV activity) as well as to confirm the correct diagnosis. Repeat imaging at times earlier than 1 month following the previous anti-VEGF injection can help identify patients who respond to therapy but require more-intensive treatment than monthly injections. \(^{41}\)

**OCT.** Consider enhanced-depth imaging OCT or swept-source OCT to identify choroidal thickening typical of CSC. \(^{42,43}\)

**ICGA.** Consider ICGA to identify PCV or choroidal hyperpermeability consistent with CSC. \(^{30}\)

**FA.** Repeat FA may be useful.

**OCTA or FAF.** OCTA or FAF may be useful in identifying masquerade entities.
Conclusions

Given the variable presentations of nAMD and the variable clinical response to therapy, it is not appropriate to provide rigid guidelines regarding the use of retinal imaging in evaluating a patient with AMD. Fortunately, a wide array of imaging technologies is now available to assist physicians in diagnosing and guiding treatment decisions for these patients. These technologies should be deployed on an as-needed basis. With the evolution of machine learning,\textsuperscript{44-46} it is likely that physicians will become increasingly reliant on image analysis to make treatment decisions for patients with exudative manifestations of nAMD.

Ethical Approval

Not applicable.

Statement of Informed Consent

Not applicable.

Declaration of Conflicting Interests

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