Hydroxychloroquine screening practice: a survey of doctors requesting mfERG testing

Hydroxychloroquine (HCQ) is a disease-modifying antirheumatic drug. HCQ retinopathy is an adverse effect associated with prolonged treatment and increased dosage.[1,2] Patients with HCQ retinopathy are initially asymptomatic, and the disease progresses slowly with poor visual recovery after therapy is stopped, making early detection difficult but essential.

Early-stage HCQ toxicity involves thinning of the outer retina, affecting the retinal pigment epithelium and photoreceptors. Structural changes can be observed using spectral-domain optical coherence tomography (SD-OCT) and fundus autofluorescence (FAF).[3,4] Functional deficits may precede detectable structural changes, and automated visual fields (AVFs) and multifocal electroretinogram (mfERG) may be more sensitive in detecting early HCQ retinopathy.[5,6]

American Academy of Ophthalmology (AAO) screening guidelines recommend a baseline fundus examination for all patients, supported with AVF and SD-OCT if maculopathy is present. Annual screening with AVF and SD-OCT is recommended after 5 years or treatment for patients with no other major risk factors; mfERG and FAF may be useful additional tests.[7] Royal College of Ophthalmology guidelines recommend annual testing after 5 years of treatment using structural imaging (SD-OCT and FAF) and functional (AVF) testing.[8] mfERG is suggested where structural and functional test results disagree. Toxicity is diagnosed when abnormalities are identified on AVF and any of SD-OCT, FAF, or mfERG.

To determine whether patients referred for mfERG testing for HCQ retinopathy are representative of patients treated with HCQ, this paper examines the practice of Ontario health care providers requesting mfERG testing for patients at risk of developing HCQ retinopathy. This study was approved by the Research Ethics Board of the University of Toronto (Protocol no. 38866).

An online survey was emailed to all providers who referred to our electrophysiology service for mfERG screening for HCQ retinopathy between July 2017 and December 2019. The survey addressed the provider's screening practice for patients at baseline (within 1 year of starting therapy), between years 1 and 5, and after 5 years of therapy. Survey questions, anonymous survey responses, and analysis code are available to download from Mendeley Data (https://data.mendeley.com/datasets/vyjxsprph9/1).

Data analysis was performed using R software (R Foundation, Vienna, Austria).[9] The nonparametric Kruskal–Wallis test by ranks was used to determine group differences; post hoc Mann–Whitney testing was used for pairwise comparisons with Holms correction to control for multiple testing significance.

Responses were received from 23 of 34 providers: 12 ophthalmologists, 10 retinal specialists, and 1 optometrist. Most respondents (13 of 23) always or often start routine screening immediately after the baseline test; after 5 years of treatment, all start annual screening.

At baseline, most respondents always or often obtained SD-OCT (21 of 23), Humphrey visual field (19 of 23), and

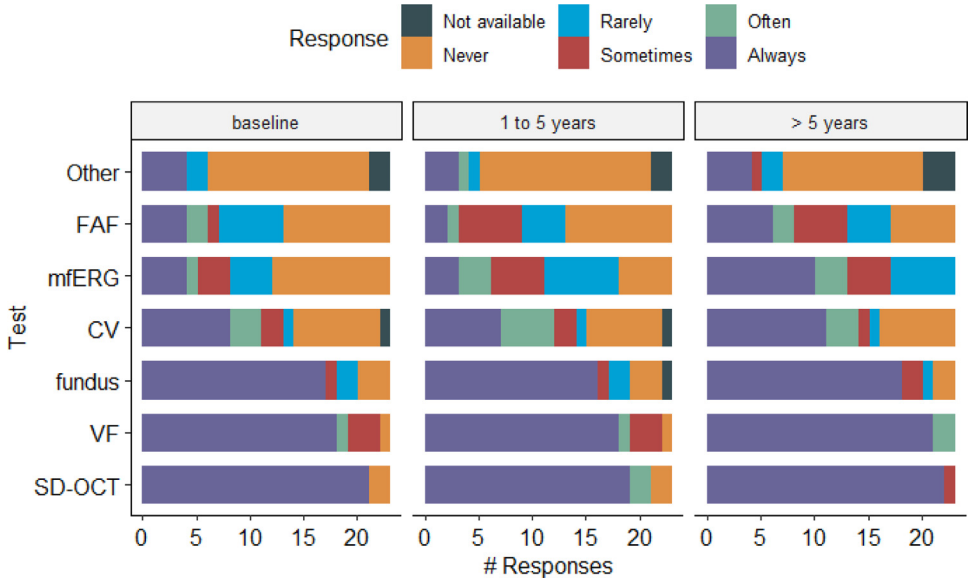

Fig. 1—Requested screening tests with increasing duration of therapy. FAF = fundus autofluorescence; mfERG = multifocal electroretinogram; CV = colour vision; VFs = visual fields; SD-OCT = spectral-domain optical coherence tomography (other tests included Amsler grid, pattern electroretinography, and electro-oculography)

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fundus examination/photography (17 of 23), as shown in Figure 1. Colour vision testing (11 of 23), FAF (6 of 23), mfERG (5 of 23), and other tests (4 of 23) were requested less frequently. mfERG was the only test requested more frequently for patients with a treatment duration >5 years when compared with baseline ($p = 0.003$) or at 1–5 years ($p = 0.019$). mfERG testing was more likely obtained following an abnormal result on another test ($p < 0.001$; Fig. 2A) or in the presence of other risk factors ($p = 0.006$; Fig. 2B). HCQ therapy at a daily dose higher than the recommended level was the most commonly considered risk factor ($p < 0.01$; Fig. 2B).

With prevalence estimates of HCQ retinopathy as high as 7.5%,[2] regular ophthalmic screening is important, but diagnostic testing creates a time and cost burden for the health care system and patient. Although no guidelines recommend routine screening for patients taking HCQ for <5 years, SD-OCT, AVFs, and fundus examination are the most common tests performed during this period.

Most respondents follow the earlier AAO guidelines with SD-OCT and AVFs at all time points. Few routinely obtain FAF, possibly because FAF is not publicly funded. Colour vision and fundus photographic abnormalities have been reported, but both guidelines consider them insufficiently objective or sensitive for use as diagnostic criteria for early HCQ retinopathy. Despite this, 74% of respondents always or often consider fundus photography, and 48% consider colour vision testing.

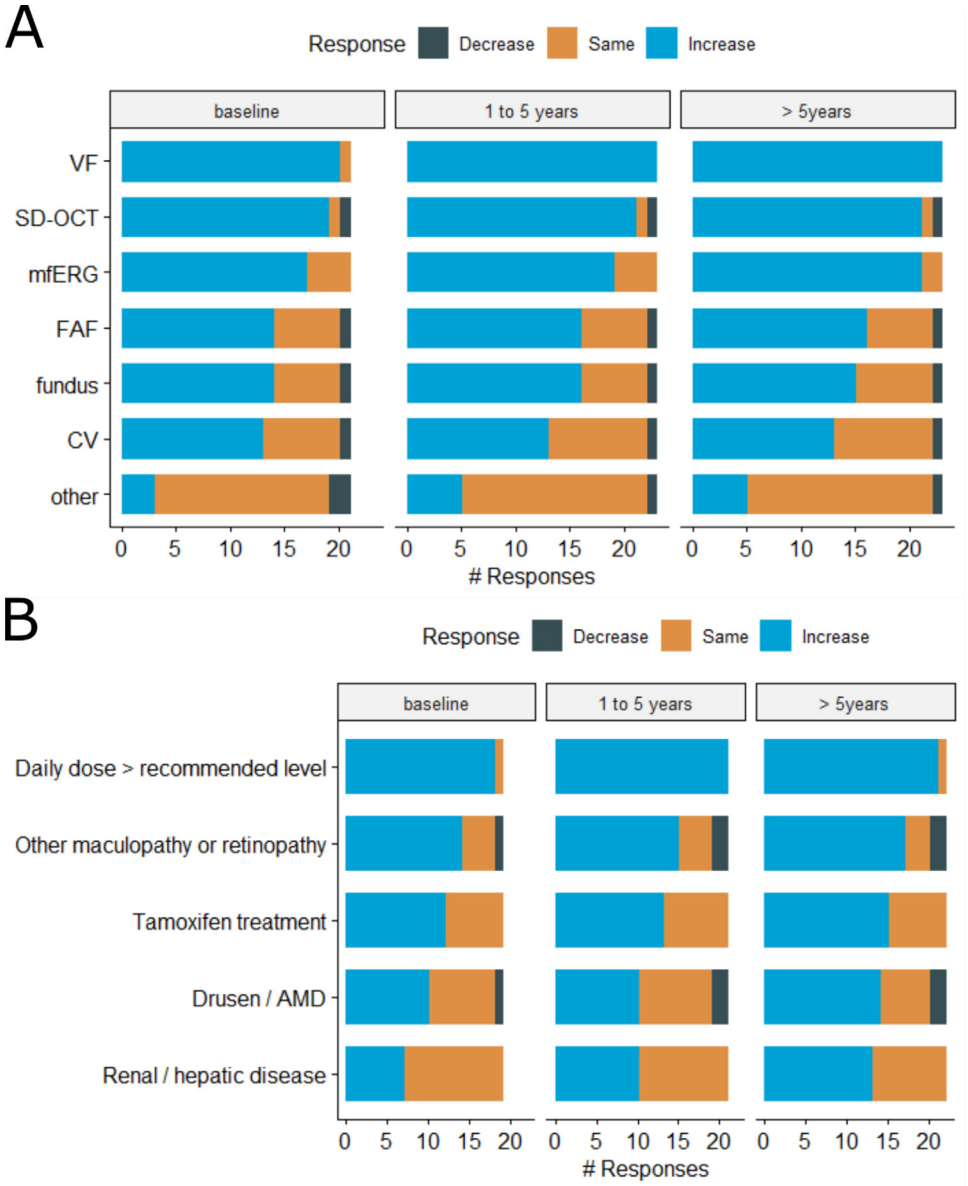

Fig 2—Effect of (A) abnormal test results and (B) associated risk factors and comorbidities on the physician's decision to consider multifocal electroretinogram testing. CV = colour vision; mfERG = multifocal electroretinogram; FAF = fundus autofluorescence; VFs = visual fields; OCT = optical coherence tomography; AMD = age-related macular degeneration

Respondents generally follow screening schedules recommended by the AAO, with the addition of screening visits for patients on therapy for 1 to 5 years. Patients with additional risk factors for toxicity, abnormal test results, or other comorbidities such as macular degeneration are more likely to be referred for mfERG testing, suggesting that the subset of patients receiving mfERG testing has a higher pretest probability of HCQ retinopathy.

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Footnotes and Disclosure

The authors have no conflicts or proprietary interests to disclose.