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Re: Patel et al: Are Dilated Fundus Examinations Needed for OCT-Guided Retreatment of Exudative Age-Related Macular Degeneration?

Surbhi Agrawal, MD
Rohan Chawla, MD

Dr. Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India

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Correspondence:
Surbhi Agrawal, MD, Dr. Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi 110029, India.
E-mail: dr.agrawalsurbhi@gmail.com.

TO THE EDITOR: We read the study by Patel et al[1] and have a few points of concern about the article.

First, the study does not differentiate between resolving or pre-existing hemorrhage and fresh hemorrhage. This could have been identified by comparing 2 successive dilated fundus examinations or photographs and checking for the presence of fresh blood on fundus photographs. Fresh blood is a marker of active disease that may not always be picked up on OCT.[2] The authors' results may be impacted if only new-onset hemorrhage (versus any hemorrhage) was included in the post hoc analysis.

Second, because the study did not use the presence of hemorrhage or any other fundus-based finding as a re-treatment criterion, this analysis is not likely to show any benefit of fundus screening. If the authors are trying to prove that presence of hemorrhage on fundus examination is a redundant finding in terms of management, a comparison between patients who showed hemorrhage but did not receive an injection at 3 months and patients who showed hemorrhage and received an injection at 3 months would have been more appropriate. It would have provided support to the authors' argument that OCT-based criteria are sufficient to guide treatment.

The authors' argument that vision was stable at 4 months and delaying injection for 1 month does not have any adverse effect takes a very short-term view of the question at hand. Some of these patients require years of therapy; thus, an analysis of 3 months of data is not enough to draw generalized conclusions. Long-term data would lend credibility to the argument.

Third, we disagree with the authors' statement that dilated fundus examination does not add any additional value in the management of patients. The value proposition of fundus examination is not limited to dictating the need of anti−vascular endothelial growth factor injections. Development of additional fundus findings such as hard exudates and polyps may dictate additional investigations such as indocyanine green angiography. Additionally, intravitreal injections are associated with a myriad of adverse effects such as endophthalmitis, uveitis, retinal detachment, and retinal or vitreous hemorrhage that require a dilated fundus examination for early detection and management.[3] Pre-existing retinal pigment epithelium detachments in patients with neovascular age-related macular degeneration have been found to predispose patients to retinal tear formation.[4] The safety evaluation protocol described in the methodology of the original trial report mandates fundus examination in the management of these patients.[5]

For these reasons, we believe that dilated fundus examination is necessary in the management of exudative age-related macular degeneration.

References

1. Patel Y, Miller DM, Fung AE, et al. Are dilated fundus examinations needed for OCT-guided retreatment of exudative age-related macular degeneration? *Ophthalmol Retina*. 2020;4:141−147.
2. Miotto S, Zemella N, Gusson E, et al. Morphologic criteria of lesion activity in neovascular age-related macular degeneration: a consensus article. *J Ocul Pharmacol Ther*. 2018;34:298−308.
3. Solomon SD, Lindsley K, Vedula SS, et al. Anti-vascular endothelial growth factor for neovascular age-related macular degeneration. *Cochrane Database Syst Rev*. 2019;3. CD005139.
4. Tolentino M. Systemic and ocular safety of intravitreal anti-VEGF therapies for ocular neovascular disease. *Surv Ophthalmol*. 2011;56:95−113.
5. Busbee BG, Ho AC, Brown DM, et al. Twelve-month efficacy and safety of 0.5 mg or 2.0 mg ranibizumab in patients with subfoveal neovascular age-related macular degeneration. *Ophthalmology*. 2013;120:1046−1056.

REPLY: We appreciate the letter from Drs. Surbhi Agrawal and Rohan Chawla, and we understand how disturbing it must be for an established retina specialist to consider the possibility that the dilated fundus examination is unnecessary and that OCT imaging may be all that is needed for the management of established exudative age-related macular degeneration (AMD) patients. One of the major points of our study was that we do not differentiate between the various stages of retinal hemorrhages. All we considered was whether a corresponding change on OCT imaging was present that indicated the need for retreatment. Some may consider this a limitation of the current study, which we stated in the article, but we actually believe that this is an important advantage of this study. In summary, we believe it simply does not seem to matter if the hemorrhages are coming or going. Given that our study was a post hoc analysis of the HARBOR study (ClinicalTrials.gov identifier, NCT00891735), the only fundus photographs available were per the protocol, so we did not have as many photographs as we would have liked. Photographs were available only from the initial examination and at 1 week and 1, 2, 3, 4, 6, 9, 12, 18, and 24 months.

Moreover, the photographs were not aimed to monitor changes in the presence of hemorrhage, although hemorrhages were noted in 89% of eyes at baseline. So, we had no way to determine whether the hemorrhage was new or pre-existing, and our point is that it does not matter.

Remember, the HARBOR study was not designed to prove that fundus-based findings were not beneficial at any time point in the management of exudative macular degeneration, but our conclusions are still quite compelling and merit further investigation. Our findings do suggest that the presence of a hemorrhage despite absence of OCT findings may be clinically irrelevant. The comparison made in our current study between patients with hemorrhage who were not treated and patients who showed OCT evidence of active exudative disease is the best we could do under the circumstances of the study. The assumption is not that these patients would not require future treatment, because almost all did, but that the time to treatment could vary widely and it was not deleterious in their clinical course to miss an injection, because if an injection was needed, then the OCT findings at the next visit would indicate the need for the injection. A possibility exists that the subgroup of monthly injection patients with hemorrhage may have benefited more than the monthly cohort as a whole; however, we will never know the answer until a properly designed prospective study is carried out. Given the current coronavirus 2019 pandemic, our results have become even more important given the fact that OCT may be all that is needed, and we may be able to expedite patient care and minimize patient contact by performing only OCT imaging without the need for a dilated fundus examination or photographs.

We also disagree with the argument that the study took a short-term view of vision changes resulting from hemorrhage. We strongly believe that the management of exudative AMD is a life-long exercise for the patient and that long-term OCT monitoring is required, but dilated fundus examinations are not necessary for routine follow-up. We found that if a macular hemorrhage was present on fundus images but OCT assessment did not warrant an injection, then there seemed to be no negative impact on visual acuity in the short term or in the 24 months of follow-up. This suggests that small hemorrhages noted on a dilated examination may not require treatment if OCT findings, such as an increase in subretinal or intraretinal fluid, were not present at the same time.

Our statement that a dilated fundus examination does not add any additional value in the management of patients was in reference to the follow-up examination of patients who are actively undergoing treatment for exudative AMD. It was not meant to imply that dilated examination are not useful at the initial examination. Also, it does not infer that the examination has no place in follow-up care. Of course, possible adverse effects from injections exist, and symptoms should necessitate the need for dilated fundus examination, but retinal detachments and tears are exceedingly rare. Finally, retinal pigment epithelium detachments found on examination also would be detected on OCT imaging, and the appearance or enlargement of a retinal pigment epithelium detachment on OCT imaging is far more sensitive than that seen in a dilated fundus examination or on color fundus imaging. The greatest limitation of our strategy for the retinal specialist is the lost revenue from not performing the dilated fundus examination, but we believe the expedited care far outweighs the monetary loss to the retina specialist. We believe that this analysis provides a solid basis for future studies designed to explore OCT-only guided anti−vascular endothelial growth factor therapy for the treatment of exudative AMD.

Yogin Patel, MD[1]
Daniel Miller, MD, PhD[1]
Anne Fung, MD[2]
Philip J. Rosenfeld, MD, PhD[3]

[1]*Department of Ophthalmology, Cincinnati Eye Institute and University of Cincinnati School of Medicine, Cincinnati, Ohio;* [2]*Genentech, Inc, San Francisco, California;* [3]*Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida*

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