Clinical Application of the 20-Year Results from the Ocular Hypertension Treatment Study

To the Editor Kass et al[1] published an extensive report on individuals who were randomized 20 years ago in the Ocular Hypertension Treatment Study (OHTS). The article provides a myriad of data and analyses to contemplate, a remarkable achievement for the investigators. I would like to call attention to one finding that is easy to overlook and to ask the investigators to elaborate on the clinical implications.

In eTable 4,[1] it looks as if, in the end, no difference was found in the final condition of patients whether they started treatment when ocular hypertension was discovered or later, perhaps when glaucomatous abnormality in the disc or visual field started to emerge. Does this mean that patients with ocular hypertension might just as well be monitored carefully rather than starting treatment immediately? This approach may not reduce the need for office visits because monitoring the optic discs and visual field test results would still be necessary, but it would relieve the expense and bother of treatment to lower intraocular pressure. Moreover, the frequency of monitoring might be adjusted if the patient did not start to show signs of glaucomatous damage.

Do factors associated with risk challenge the wisdom of this approach in some patients? The factors associated with risk determined in the study[1] informed the probability of developing glaucomatous signs (disc and field) or perhaps how quickly such signs may develop. However, does that mean that we should be more inclined to lower intraocular pressure in patients with high risk, or should we suspect that, even if they develop early signs of glaucoma, the ultimate outcome following treatment is the same whether or not treatment is delayed until signs of glaucoma begin? Does the choice between observation and treatment depend on whether the patient has greater concern about potential decline in vision or about adverse effects associated with treatment?

The OHTS was initiated to resolve differences among various opinions about how ocular hypertension is best managed. The questions posed here are aimed at the practical clinical questions that prompted the OHTS in the first place, and a summary conclusion would be welcome.

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1. Kass MA, Heuer DK, Higginbotham EJ, et al; Ocular Hypertension Study Group. Assessment of cumulative incidence and severity of primary open-angle glaucoma among participants in the Ocular Hypertension Treatment Study after 20 years of follow-up. *JAMA Ophthalmol*. 2021;139(5):1-9. doi:10.1001/jamaophthalmol.2021.0341

In Reply We thank Dr Anderson for his interest in our recent publication[1] reporting clinical outcomes of patients with ocular hypertension after 20 years of follow-up or within 2 years of death. He asked key questions about how the findings of the Ocular Hypertension Treatment Study (OHTS)[1] inform the treatment of patients with ocular hypertension (OHT). Dr Anderson proposed that most patients with OHT might be observed without treatment until they manifest early signs of glaucomatous damage. He asked how a prediction model for developing primary open-angle glaucoma (POAG) would modify this overall approach.

Dr Anderson referred to eTable 4 of our article,[1] which showed no overall difference in the visual outcomes between the observation and the medication groups. However, eTable 4[1] pooled data from all ascertained participants by their randomization groups and did not separate data between participants who did or did not develop POAG. In OHTS 1,[1] when participants were randomized to observation or medication, the 5-year cumulative incidence of POAG was higher in the observation group (9.5%) than in the medication group (4.4%).[2] Furthermore, POAG developed a mean of 2.7 years earlier in the observation group and was more likely to be bilateral. The difference in incidence in OHTS 1[1] persisted into OHTS 3,[1] where the cumulative incidences were 49.3% in the observation group and 41.9% in the medication group even though the observation group was taking medication after OHTS 1. While it is clear that the incidence of POAG was reduced by treatment, it is not clear if early treatment reduced the severity of POAG. We are currently analyzing data to determine the long-term prognosis of the participants who developed POAG in the observation group vs the medication group in OHTS 1.

In 2002, we published a baseline prediction model[3] (baseline age, IOP, central corneal thickness, visual field pattern standard deviation, and vertical cup-disc ratio) that categorized participants as being at low, medium, or high risk of developing POAG. This model performed well out to 20 years of follow-up. Clinicians can use this model to assist in decisions about the potential benefit of early preventive treatment and the frequency of office visits.[4] After establishing stable baseline measurements, patients at low risk might be examined once a year, which would reduce costs, patient burden, and unnecessary visits. Patients at high risk could be examined more often to monitor for early signs of POAG.

Patients with OHT and clinicians should discuss the frequency of examinations and the potential benefit of preventive treatment. These discussions should take into consideration the patient's age, health status, estimated life expectancy, and personal preferences. Dr Anderson was correct in stating that such decisions will be influenced by "whether the patient has greater concern about potential decline in vision or about adverse effects associated with treatment." However, we believe the prediction model will provide quantitative information that will be useful to patients and clinicians in making decisions about the management of ocular hypertension.

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