

Optic Discs of the Ocular Hypertension Treatment Study

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Do not give up on the Ocular Hypertension Treatment Study (OHTS) just yet. After reading about optic discs and OHTS, take the quiz at the end of the article to test your knowledge of all three OHTS installments.

I want to thank the contributors to our first “Landmark Studies” series. These investigators and scientists covered many aspects of OHTS, which should have a beneficial impact on clinical care. I encourage readers to e-mail comments and suggestions to me, and I will incorporate your feedback into next year’s columns. I certainly have learned a great deal, and I hope you have as well.

—Section Editor Ronald L. Fellman, MD

A subset of OHTS patients were observed with confocal scanning laser ophthalmoscopy (CSLO) as part of the CSLO Ancillary Study. Did this research reveal anything about racial differences in optic disc topography?

The OHTS CSLO Ancillary Study was initiated in 1995 to include annual CSLO imaging using the Heidelberg Retina Tomograph (HRT; Heidelberg Engineering GmbH, Heidelberg, Germany) at seven of the 21 OHTS study centers.¹⁻⁴ All HRT images were sent to the CSLO Reading Center at the University of California, San Diego, for centralized quality review, image processing, and analysis. Over 400 participants enrolled in the CSLO Ancillary Study, and approximately 17% were of African descent. We specifically evaluated racial differences in optic disc topography at the baseline examination and found that, in this cohort of ocular hypertensive subjects, African Americans had significantly larger optic discs, optic cups, neuroretinal rims, and cup-to-disc ratios than did other racial groups.⁴ However, we also reported that the differences in optic disc topography between African Americans and other racial groups are largely explained by the larger disc size of the African American participants. In other words, when we included disc size in models comparing optic disc topography, the

racial differences in cup-to-disc ratio, rim area, and other measures were no longer statistically significant. These results highlight the need to consider both race and optic disc size when evaluating the optic nerve head for diagnosing glaucoma and detecting glaucomatous progression.

Did OHTS demonstrate that certain baseline disc-imaging characteristics predict the development of primary open-angle glaucoma (POAG)? If so, what disc-imaging parameters are the most important to follow while evaluating glaucoma suspects? For example, should clinicians pay more attention to the cup or the rim measurements?

As discussed in the first installment of *Glaucoma Today’s* “Landmark Studies” column,⁵ OHTS developed a predictive model and risk calculator⁶ to assist clinicians in estimating the risk of developing glaucoma in ocular hypertensive patients who resemble the participants in OHTS. It confirmed an earlier risk calculator that had been developed at the University of California, San Diego, using ocular hypertensive patients from the Diagnostic Innovations in Glaucoma Study (DIGS).⁷ Both of these risk calculators included five predictive factors: baseline age, IOP, central corneal thickness, vertical cup-to-disc ratio, and visual field pattern standard deviation.^{6,8} The OHTS calculator was validated in the European Glaucoma Prevention Study (EGPS).⁶ The OHTS CSLO Ancillary Study substituted CSLO imaging parameters for the stereophotograph-based cup-to-disc ratio measurements used in the OHTS predictive model. The CSLO Ancillary Study demonstrated that baseline HRT topographic measurements of the neuroretinal rim and optic cup—alone or in combination with age, IOP, central corneal thickness, and visual field pattern standard deviation—could be used to predict the development of POAG in OHTS participants.^{1,2}

Moreover, the study showed that optic cup and neuroretinal rim parameters were as effective as stereophotograph-

based cup-to-disc ratios in the predictive model for assessing the likelihood of the development of POAG in ocular hypertensive subjects.¹ In a different study population of ocular hypertensive subjects, baseline HRT linear cup-to-disc ratio could be used interchangeably with the stereophotograph-based cup-to-disc ratio to estimate the patient's risk of conversion from ocular hypertension to glaucoma.⁹ It should also be mentioned that, at the baseline visit included in the OHTS CSLO Ancillary Study analysis, the visual fields and optic discs of all of the eyes had a normal appearance, as classified by OHTS Visual Field and Optic Disc Reading Centers.

In addition to cup and rim parameters, we evaluated HRT global and regional indices using the Moorfields Regression Analysis (MRA) and Glaucoma Probability Score (GPS). They compare results to an internal normative database and indicate whether the value is outside normal limits, borderline, or within normal limits. We showed that eyes with a baseline result that was outside normal limits on the GPS or MRA were more likely to develop POAG than eyes without a baseline result that was outside normal limits.¹ It is important to note that, although a parameter is predictive of the development of POAG, it does not suggest that all eyes with a result outside normal limits will develop POAG. Rather, the positive predictive value (ie, the proportion of eyes with a baseline result outside normal limits that developed POAG) is relatively modest—between 20% and 24% for GPS and 32% and 62% for MRA, depending on the region analyzed.

Although the OHTS CSLO Ancillary Study did not find large differences in the predictive ability of rim area and cup area measurements, a growing body of evidence shows that CSLO rim area measurements are among the most promising for monitoring changes over time.^{10,11} In results that have not yet been published, the OHTS CSLO Ancillary Study found that the rate at which rim area was lost was five times faster in eyes that developed POAG than in eyes that did not develop the disease.¹² These findings suggest that measuring the rate of structural change can provide important information for the clinical management of ocular hypertensive patients.

Based on OHTS, is a large disc an important predictor of glaucoma? Is it useful for a clinician to analyze the size of the disc when he or she is evaluating a glaucoma suspect?

To date, the OHTS CSLO Ancillary Study has not found that a large disc predicts the development of glaucoma.^{1,2} However, it is extremely important to evaluate the size of the disc when evaluating a glaucoma suspect so that estimates of the cup and rim can be interpreted appropriately. A relatively large cup area in a small disc is likely to

be more clinically important than the same cup area in a large disc.

Should clinicians throw out their disc photographs and rely solely on disc-imaging technology?

Although the OHTS CSLO Ancillary Study did not directly address this important question, there are several reasons why photographs, particularly high-quality baseline stereophotographs, are useful in glaucoma management. First, clinical examination and follow-up photographs can be compared to the baseline photograph, a simple technology that will never become obsolete. In contrast, many imaging devices have become antiquated, because software and/or hardware improvements often are not backwards compatible with the original baseline image. Fortunately, the HRT I—or “HRT classic”—used in the OHTS CSLO Ancillary Study, is compatible with later versions of the HRT, and we were able to analyze OHTS images using the latest software available for the HRT II or III.

In addition, a few features important for the assessment of glaucoma or its risk, such as disc hemorrhages or peripapillary atrophy, may not be as visible with some imaging technologies (eg, optical coherence tomography or scanning laser polarimetry) as on photographs. With the HRT, one can detect disc hemorrhages and peripapillary atrophy by visually inspecting the image. How the detection of these features on the HRT compares to detection on photographs has not yet been completed with the OHTS CSLO Ancillary Study data. For these and other reasons, the World Glaucoma Association 2011 consensus panel included the following consensus statement: “serial optic disc stereo-photography and RNFL photography are valuable and enduring methods for monitoring structural progression.”¹³

What is the most important point to learn about the optic disc from OHTS?

The first sign of glaucoma can be either a change in the optic disc or a change in the visual field. In fact, approximately 55% of initial POAG endpoints were due to the detection of structural change alone.¹⁴ These results highlight the need to evaluate and monitor ocular hypertensive patients for both structural and functional changes in order to detect the first sign of glaucoma.

In addition, we learned that, for the management of ocular hypertensive patients, it is important to consider the disc's size when evaluating structural features of the optic nerve head. □

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THE OCULAR HYPERTENSION TREATMENT STUDY QUIZ

1. The ancillary confocal scanning laser ophthalmoscopy (CSLO) section of the Ocular Hypertension Treatment Study (OHTS) found that African Americans had significantly larger optic discs, optic cups, neuroretinal rims, and cup-disc ratios than other racial groups. True or False
2. The OHTS CSLO Ancillary Study found that a large disc size helps predict the development of glaucoma. True or False
3. Heidelberg Retina Tomograph (Heidelberg Engineering GmbH, Heidelberg, Germany) optic cup and neuroretinal rim parameters are as effective as stereophotograph-based cup-to-disc ratios in the predictive model for the development of primary open-angle glaucoma (POAG) in ocular hypertensive patients. True or False
4. In about 25% of OHTS patients, a glaucomatous visual field defect appeared before changes to the optic disc. Twenty-five percent of patients had changes in the disc and field at the same time, and 50% had changes in the disc before the field. True or False
5. In OHTS, after one abnormal visual field, the next field was normal 86% of the time, and even after two abnormal visual fields in a row, the next visual field was normal 36% of the time. True or False
6. The earliest visual field defect in a patient with ocular hypertension who converts to POAG is usually a combined form of localized and diffuse loss. True or False
7. The occurrence of an optic disc hemorrhage increases the risk of developing POAG approximately threefold. True or False
8. The most surprising finding from OHTS was that central corneal thickness was a powerful predictor for the development of POAG. True or False
9. Two abnormal visual fields in a row are sufficient to diagnose the onset of glaucomatous visual field loss. True or False
10. Delaying treatment for a mean of 7.5 years had a significant effect across the board for all OHTS patients. True or False

Answers: 1. True; 2. False; 3. True; 4. True; 5. True; 6. True; 7. True; 8. False; 9. True; 10. False

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