

The Literature

BY MELISSA (WEN-JENG) YAO, MD, AND JEFFREY S. SCHULTZ, MD

ADJUSTING INTRAOCULAR PRESSURE FOR CENTRAL CORNEAL THICKNESS DOES NOT IMPROVE PREDICTION MODELS FOR PRIMARY OPEN-ANGLE GLAUCOMA

Brandt JD, Gordon MO, Feng G, *et al*¹

ABSTRACT SUMMARY

According to the Ocular Hypertension Treatment Study (OHTS),² a thin central cornea is one of the strongest independent risk predictors for the development of primary open-angle glaucoma (POAG). In addition, central corneal thickness (CCT) is recognized as a potential confounder in the determination of IOP using Goldmann applanation tonometry (GAT).³ Numerous formulas have therefore been developed to attempt to “correct” the IOP for CCT.⁴⁻⁸

The purpose of Brandt and colleagues’ study was to determine if the accuracy of the baseline prediction model for the development of POAG in patients with ocular hypertension could be improved by correcting IOP for CCT. The researchers reanalyzed the baseline prediction model using five different correction formulas for unadjusted IOP in 1,433 of 1,636 participants randomized to OHTS who had complete baseline data for factors in the prediction model: age, IOP, CCT, vertical cup-to-disc ratio, and pattern standard deviation. The investigators calculated the reanalysis using the same baseline variables (age, IOP, CCT, vertical cup-to-disc ratio, and pattern standard deviation), except that IOP was adjusted for CCT using correction formulas to determine if CCT would still make an independent contribution to the risk of developing POAG. A separate Cox proportional hazards model was run using IOP adjusted for CCT by each of the five formulas published to date. Brandt *et al* ran models that included and excluded CCT.

The correlation between the adjusted IOPs as calculated by the five correction formulas was high (0.89-0.99). Not surprisingly, the multivariate hazard ratio (range, 1.10-1.17) for the risk of developing POAG for adjusted IOP was statistically significant with and without CCT in the model. Furthermore, CCT was found to be a statistically independent predictor for the development of POAG in all prediction models, irrespective of whether the IOP was adjusted or unadjusted.

In models that included adjusted IOP and CCT, the hazard ratio for CCT ranged from 1.38 to 1.69, depending on the correction formula the researchers used. They performed statistical analysis using C statistic and calibration chi-square to compare the predictive accuracy of the prediction models of adjusted and unadjusted IOP. As a reference, the C statistic ranges from 0.5 (chance) to 1.0 (perfect agreement) to indicate the degree of agreement between IOP and the observed probability of POAG development. In this study, C statistics for prediction models that used IOP adjusted for CCT by various formulas ranged from 0.75 to 0.77, which was no better than the original prediction model (0.77) that did not adjust IOP for CCT.

DISCUSSION

Based on the study, should physicians routinely adjust IOP determined by GAT for CCT in the prediction of a patient’s risk of developing POAG?

A 2007 report by the American Academy of Ophthalmology (AAO) states that the determination of CCT is an important component of a complete ocular examination of patients being evaluated for their risk of developing POAG. The Academy recommended that the measurement of CCT should be included in the examination of all patients with ocular hypertension.⁹ Many clinicians still believe that CCT is a part of every glaucoma evaluation mainly so that it can be used to adjust the IOP for error as determined by GAT. They then use the corrected IOP in order to assess a patient’s risk of developing POAG. This well-designed study showed that CCT adjusted for IOP using five different formulas did not eliminate CCT as an independent risk factor for glaucoma. Furthermore, adjusting IOP for CCT did not improve the predictive value for POAG in ocular hypertensive patients when compared with unadjusted IOP. The study also did not find an IOP adjustment formula that was better than the others.

This study is in line with previous reports that suggest that CCT should be included in every individualized, clinical, glaucoma evaluation. The authors clearly demonstrate that the importance of CCT in a glaucoma examination, however, does not solely correlate with the correction for tonometric measurement error. Instead, CCT should continue to be recognized as an

“The advantages of ocular imaging devices are that the tests can be performed quickly, they do not cause discomfort for patients, and they are not reliant on patients’ test performance.”

independent predictive factor for the development of POAG, as suggested by numerous previous studies.¹⁰⁻¹² From this study, there does not appear to be any reason for physicians to engage in the laborious use of corrective formulas to adjust IOP for CCT. In the assessment of glaucoma patients, using IOP as directly measured on GAT proves to be simpler and equally accurate.

TRENDS IN USE OF ANCILLARY GLAUCOMA TESTS FOR PATIENTS WITH OPEN-ANGLE GLAUCOMA FROM 2001 TO 2009

Stein JD, Talwar N, Laverne AM, et al¹³

ABSTRACT SUMMARY

In the past 10 years, new ocular imaging technology such as optical coherence tomography has gained popularity for enabling clinicians to detect structural damage to the optic nerve fiber layer. The advantages of ocular imaging devices are that the tests can be performed quickly, they do not cause discomfort for patients, and they are not reliant on patients’ test performance. The tests have been found to have a sensitivity ranging from 68% to 91% for detecting open-angle glaucoma (OAG).^{14,15}

Stein et al retrospectively analyzed a large managed care network’s claims data to examine the pattern of utilization of visual field (VF) testing, fundus photography (FP), and other ocular imaging (OOI) testing for patients with OAG or suspected glaucoma from 2001 to 2009. Furthermore, the investigators looked for differences in the use of ancillary tests by optometrists versus ophthalmologists in the same time period.

The study included 169,917 individuals with OAG and 395,721 individuals with suspected glaucoma. Both patient populations were predominately white, and all patients were at least 40 years of age. When ancillary testing patterns were compared for patients who were newly diagnosed with OAG in 2003 versus 2007, the results showed statistically significant differences. The

use of VF testing without any OOI testing decreased from 34% in 2003 to 25% in 2007. In the first 12 months of OAG diagnosis, the use of OOI testing increased from 38% to 53%, and the use of FP rose from 17% to 23%.

For patients with OAG, the odds of undergoing VF testing decreased by 36% from 2001 to 2005, by 12% from 2005 to 2009, and by 44% from 2001 to 2009. By comparison, the odds of having OOI testing increased by 100% from 2001 to 2005, by 24% from 2005 to 2009, and by 147% from 2001 to 2009. Probabilities of undergoing FP were relatively low (13%-25%) for both types of providers and remained fairly steady over the decade. For patients cared for exclusively by optometrists, the probability of VF testing decreased from 66% in 2001 to 44% in 2009. Among patients seen exclusively by ophthalmologists, the probability of VF testing decreased from 65% in 2001 to 51% in 2009. The probability of undergoing OOI testing increased from 26% in 2001 to 47% in 2009 for the patients of optometrists and from 30% in 2001 to 46% in 2009 for the patients of ophthalmologists. By 2008, patients with OAG receiving care exclusively from optometrists had a higher probability of undergoing OOI than VF testing.

DISCUSSION

Based on this study, are there notable differences in the utilization of VF testing, FP, and OOI testing in the evaluation of patients over the past decade?

According to the AAO’s Preferred Practice Patterns in 2005, patients with OAG should undergo VF testing and an optic nerve assessment every 1 to 12 months, and glaucoma suspects should undergo VF testing and nerve examinations every 3 to 24 months.^{16,17} Even though the AAO noted that OOI testing can identify structural damage to the optic nerve and retinal nerve fiber layer, the Academy did not recommend that OOI replace VF testing or the examination of the optic nerve. In fact, the AAO did not comment on the frequency with which OOI scans should be used in glaucoma surveillance in the organization’s Preferred Practice Patterns.

Since the advent of OOI application in glaucoma evaluation, there has been little literature about the actual usage rates for the different ancillary glaucoma tests. This study found that, in the past decade in a large managed care network, there has been a dramatic decrease in VF testing and an equally significant increase in the use of OOI testing for OAG patients and glaucoma suspects. Toward 2008, patients had a similar probability of undergoing VF as OOI testing.

“The likelihood of ophthalmologists’ using OOI testing grew from 2001 to 2009, but the increase was much more dramatic for optometrists.”

Interestingly, the probability of undergoing FP stayed relatively low 2001 to 2008.

Are there any differences between testing performed by an optometrist versus an ophthalmologist?

When the study further analyzed the data according to the type of provider that rendered care, more interesting results were found. The likelihood of ophthalmologists’ using OOI testing grew from 2001 to 2009, but the increase was much more dramatic for optometrists. Furthermore, the probability of performing VF testing in 2009 compared to 2001 decreased in both provider groups, but the decline was much more impressive for optometrists.

This study provides strong evidence that the use of OOI testing in glaucoma surveillance is widely accepted and here to stay. Many factors have contributed to the speedy incorporation of OOI in clinical practices: the tests are noninvasive, have a quick acquisition time, do not require the patient’s cooperation, and do not need patients to have good visual acuity. Furthermore, patients with OAG appear to prefer OOI testing to VF testing.¹⁸ Providers may also be quick to adopt the technology in order to stay “cutting edge” in their practices. Financially speaking, once the expensive OOI equipment is purchased, it makes sense that providers would use it often in order to defray the cost.

The greater use of OOI, however, should not preclude or decrease providers’ utilization of VF testing. This study may show an alarming trend among eye care providers of using OOI instead of VF testing. Although the OOI technology has advanced dramatically since its inception, it still has limitations. For example, the normative databases of the devices do not adequately represent all races or age groups. Furthermore, OOI is known not to generate reliable data in patients who have myopia, tilted discs, or discs that are exceptionally large or small.¹⁹

OOI continues to be a hot topic and a major area of glaucoma research. The companies that developed these devices continue to enhance the technology, both

in terms of data acquisition and software development to design ways to correlate the structural changes with glaucomatous functional damage. Until more research shows that OOI can consistently detect glaucomatous changes or progression when compared with VF testing, however, practitioners should continue to consider the latter to be the gold standard test to order for every glaucoma patient. ■

Melissa (Wen-Jeng) Yao, MD, is an assistant professor in the Department of Visual Science at Albert Einstein Medical School and Montefiore Medical Center in Bronx, New York. Dr. Yao may be reached at wyao@montefiore.org.

Jeffrey S. Schultz, MD, is an associate professor in the Department of Ophthalmology and Visual Sciences and director of the Glaucoma Service at Montefiore Medical Center in Bronx, New York. Dr. Schultz may be reached at jss248@aol.com.



1. Brandt J, Gordon MO, Gao F, et al. Adjusting intraocular pressure for central thickness does not improve prediction models for primary open-angle glaucoma. *Ophthalmology*. 2012;119(3):437-442.
2. Gordon MO, Beiser JA, Brandt JD, et al; Ocular Hypertension Treatment Study Group. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. *Arch Ophthalmol*. 2002;120:714-720.
3. Goldmann H, Schmidt T. Applanation tonometry. *Ophthalmologica*. 1957;134:221-242.
4. Ehlers N, Bramsen T, Sperlings S. Applanation tonometry and central corneal thickness. *Acta Ophthalmol*. 1975;53:34-43.
5. Whitacre MM, Stein RA, Hassanein K. The effect of corneal thickness on applanation tonometry. *Am J Ophthalmol*. 1993;115:592-596.
6. Orseng GJ, Pye DC. Determination of the true intraocular pressure and modulus of elasticity of the human cornea in vivo. *Bull Math Biol*. 1999;61:551-572.
7. Doughty MJ, Zaman ML. Human corneal thickness and its impact on intraocular pressure measures: a review and meta-analysis approach. *Surv Ophthalmol*. 2000;44:367-408.
8. Kohlhaas M, Boehm AG, Spoerl E, et al. Effect of central corneal thickness, corneal curvature, and axial length on applanation tonometry. *Arch Ophthalmol*. 2006;124:471-476.
9. Dueker DK, Singh K, Lin SC, et al. Corneal thickness in the management of primary open-angle glaucoma: a report by the Academy of Ophthalmology. *Ophthalmology*. 2007;114(9):1779-1787.
10. Leske MC, Heijl A, Hyman L, et al; EMGT Group. Predictors of long-term progression in the Early Manifest Glaucoma Trial. *Ophthalmology*. 2007;114:1965-1972.
11. Leske MC, Wu SY, Hennis A, et al; BESS Study Group. Risk factors for incident open-angle glaucoma: the Barbados Eye Studies. *Ophthalmology*. 2008;115:85-93.
12. Francis BA, Varma R, Chopra V, et al; Los Angeles Latino Eye Study Group. Intraocular pressure, central corneal thickness, and prevalence of open-angle glaucoma: the Los Angeles Latino Eye Study. *Am J Ophthalmol*. 2008;146:741-746.
13. Stein JD, Talwar N, LaVerne AM, et al. Trends in use of ancillary glaucoma tests for patients with open-angle glaucoma from 2001 to 2009. *Ophthalmology*. 2012;119:748-758.
14. Deleón-Ortega JE, Arthur SN, McGwin G Jr, et al. Discrimination between glaucomatous and nonglaucomatous eyes using quantitative imaging devices and subjective optic nerve head assessment. *Invest Ophthalmol Vis Sci*. 2006;47:3374-3380.
15. Badala F, Nouri-Mahdavi K, Raoof DA, et al. Optic disk and nerve fiber layer imaging to detect glaucoma. *Am J Ophthalmol*. 2007;144:724-732.
16. American Academy of Ophthalmology Glaucoma Panel. *Preferred Practice Pattern. Primary Open-Angle Glaucoma*. San Francisco, CA: American Academy of Ophthalmology; 2010:32.
17. American Academy of Ophthalmology Glaucoma Panel. *Preferred Practice Pattern. Primary Open-Angle Glaucoma*. San Francisco, CA: American Academy of Ophthalmology; 2010:12.
18. Gardiner SK, Demirel S. Assessment of patient opinions of different clinical tests used in the management of glaucoma. *Ophthalmology*. 2008;115:2127-2131.
19. Park CY, Kim YT, Kee C. Evaluation of the influence of tilt of optic disc on the measurement of optic disc variables obtained by optical coherence tomography and confocal scanning laser ophthalmoscopy. *J Glaucoma*. 2005;14:210-214.