The relationship between central corneal thickness-adjusted intraocular pressure and glaucomatous visual-field loss

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Background: Although measurement of central corneal thickness (CCT) is increasingly becoming an important component of glaucoma risk analysis, significant controversy exists regarding the benefit of calculating a corrected intraocular pressure (IOP) value from measured IOP and CCT data.

Methods Three hundred forty-four male subjects were identified from a VA eye clinic with one of the following clinical diagnoses: ocular hypertension (OHT), primary open-angle glaucoma (POAG), normal tension glaucoma (NTG), and normal tension glaucoma suspect (NTGS). Using one eye per subject, multivariate logistic regression and correlational analyses were performed to determine relationships between glaucomatous visual-field loss and several glaucoma risk factors, including adjusted IOP values.

Results: Multivariate logistic regression analysis did not identify CCT-adjusted IOP values as independent risk factors for development of either NTG or POAG-related glaucomatous visual-field loss. CCT, however, was found to be strongly associated with both NTG and POAG-related visual-field loss. Correlational analysis revealed a weak correlation between Ehlers-adjusted pre-treatment IOP and severity of POAG-related visual-field loss, but no other adjusted IOP values significantly correlated with severity of visual-field loss in either POAG or NTG.

Conclusions: Our results suggest that adjusted IOP, as calculated using current algorithms, is not useful within glaucoma risk analysis, since adjusted IOP was unable to predict either presence or severity of glaucomatous visual-field loss in this study. CCT, conversely, was found to be a robust and independent predictor of glaucomatous visual-field loss. These findings, while supporting routine CCT measurements for all glaucoma suspects, do not support routine clinical computation of adjusted IOP values using current algorithms.

Key Words: Cornea, glaucoma, intraocular pressure, tonometry

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When Goldmann designed his applanation tonometer in 1957,[1] he theorized that variation in central corneal thickness (CCT) could significantly influence applanation tonometry measurements. This potential effect was mostly ignored, however, because the prevailing opinion in his era was that the range of normal CCT was narrow. In the last decade, new research—which was initially driven by the popularity of iatrogenic thinning of the cornea via refractive surgery—has revealed that the normal range of CCT is much broader than originally believed in Goldmann's time.[2] Furthermore, as Goldmann predicted, applanation tonometry measurements have been found to be artificially lower in patients with thin corneas and artificially higher in patients with thick corneas.[3,4] Most importantly, researchers have found convincing evidence that thinner central corneal thickness is strongly associated with the development of glaucoma,[5-9] a finding that has primarily been explained by CCT-induced IOP measurement error.[5]

In an attempt to compensate for CCT-related applanation tonometry measurement error, investigators have used various approaches to derive CCT-based IOP correction factors. Methods that have been utilized include cannulation studies,[10-12] clinical correlation studies,[13-15] meta-analysis studies,[2] and empirical derivation studies.[16] Results from these studies, however, vary widely. The smallest correction factor, reported by Whitacre et al.,[11] is 0.2 mmHg for every 10-μm change in CCT. The largest factor, reported by Ehlers et al.,[10] is 0.7 mmHg for every 10-μm change in CCT. Alternately stated, a 100-μm difference in CCT would correspond to an adjustment of 2 mmHg or 7 mmHg, depending on which algorithm is used. Furthermore, individual variability in the relationship between IOP and CCT is considerable,

as demonstrated by the significant data scatter within the IOP/CCT scatterplots from the respective studies.[11,13] Brandt et al.[17] have speculated that this variability may reflect a complex, nonlinear relationship between CCT and IOP that is oversimplified by linear algorithms. Considering these issues, and because no research has been published that validates one correction method over another, no specific correction algorithm has been universally embraced by practicing clinicians. Some clinicians have even suggested that corrected IOP values are of no consequence in clinical assessment of glaucoma risk.[12,15,18]

The intent of this study is to examine the relationship between glaucomatous visual-field loss and IOP values that are adjusted for central corneal thickness. By investigating how well adjusted IOP values predict presence and severity of glaucomatous visual-field loss, we hope to clarify whether calculation of adjusted IOP is useful for glaucoma risk analysis.

Methods

After Institutional Review Board approval from the Albuquerque VA Medical Center and the University of New Mexico School of Medicine, retrospective identification of all Albuquerque VA Medical Center eye clinic patients diagnosed as primary open-angle glaucoma (POAG), normal tension glaucoma (NTG), ocular hypertension (OHT), and normal tension glaucoma suspect (NTGS), who were seen from September 2002 through May 2003, was completed. Once potential subjects were identified, retrospective chart review was completed to determine definitive eligibility for study inclusion.

For the purposes of this study, diagnosis of primary open-angle glaucoma (POAG) and normal tension glaucoma (NTG) required optic nerve morphology consistent with glaucomatous optic neuropathy[19] (e.g., rim configuration abnormalities, including focal erosion or thinning, vertical elongation of the cup), as well as a corresponding glaucomatous visual-field defect detectable on 24-2 Humphrey threshold visual-field testing (e.g., arcuate scotoma, nasal step defect, paracentral defect). Subjects who demonstrated diffuse visual-field loss only and subjects who demonstrated field defects that did not correspond to the optic neuropathy were excluded. POAG diagnosis also required at least one documented IOP measurement—via pre-dilation Goldmann applanation tonometry—that was statistically elevated (22 mmHg or higher), and NTG diagnosis required that no applanation tonometry readings measured 22 mmHg or higher.

Diagnosis of ocular hypertension (OHT) required at least one documented measurement of statistically elevated intraocular pressure (IOP) via pre-dilation Goldmann applanation tonometry, and no glaucomatous visual-field loss on threshold visual-field testing. OHT subjects were also required to demonstrate no definitive glaucomatous optic nerve morphology. The diagnosis of normal tension glaucoma suspect (NTGS) required that no IOP measurements were 22 mmHg or higher, in conjunction with optic nerve morphology that suggested glaucoma, but without glaucomatous visual-field loss on threshold visual-field testing.

Additional inclusion criteria required that subjects had:

- best-corrected visual acuity of at least 20/50;
- dilated, stereoscopic optic nerve evaluations using a 60-D or 78-D lens;
- open angles by 4-mirror gonioscopy (subjects were excluded from this study if visibility of the scleral spur was obscured in any quadrant);
- reliable ultrasound pachymetry measurements that were not influenced by corneal pathology; and
- reliable, achromatic Humphrey 24-2 SITA-standard threshold visual-field testing results for each eye.

Exclusion criteria included:

- secondary forms of open-angle glaucoma;
- corneal pathology that could influence pachymetry and/or intraocular pressure measurements;
- history of refractive or corneal surgery; and
- visual-field defects due to non-glaucomatous entities such as retinal pathology, non-glaucomatous optic nerve pathology, and visual tract compromise.

Because ethnic differences in CCT have been reported,[17,20-22] we obtained race information for our subjects via self-reported information in the medical record. In subjects in which race was documented as "unknown," we evaluated the surname, and if the surname was clearly of Hispanic or American Indian origin, we categorized the subject in the appropriate category. If the surname did not specifically suggest a particular origin, the