Effect of Central Corneal Thickness on Dynamic Contour Tonometry and Goldmann Applanation Tonometry in Primary Open-angle Glaucoma

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Objective: To compare the dependence of dynamic contour tonometry (DCT) and Goldmann applanation tonometry (GAT) on central corneal thickness (CCT) in primary open-angle glaucoma.

Methods: In a prospective study, the interocular (right vs left eye) difference in intraocular pressure measured by DCT and GAT was compared with the interocular CCT difference in 125 patients with primary open-angle glaucoma.

Results: Dynamic contour tonometry measurements (mean±SD, 19.4±4.1 mm Hg) were significantly (P=.004) higher than GAT measurements (mean±SD, 15.5±3.4 mm Hg), correlating significantly with each other (r²=0.82, P<.001). The interocular difference in intraocular pressure correlated significantly with the interocular CCT difference for GAT (r=0.30, P=.001) and DCT (r=0.23, P=.02) readings. Dynamic contour tonometry and GAT intraocular pressure differences significantly increased with older age (slope, 0.033 [95% confidence interval, 0.002-0.064] mm Hg/yr; P=.03) but not with thicker CCT (slope, 0.006 [95% confidence interval, −0.003 to 0.017] mm Hg/µm; P=.22).

Conclusions: In this series, GAT and DCT measurements were dependent on CCT in patients with primary open-angle glaucoma. Because intraocular pressure differences between DCT and GAT were independent of CCT, DCT and GAT are susceptible to similar measurement biases depending on CCT.

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ELEVATED INTRAOCULAR PRESSURE (IOP) is generally regarded as one of the major risk factors for glaucoma, and its reduction is the most frequently used surrogate of successful management of risk factors. For that reason, accurate IOP is a fundamental variable in clinical practice.

Goldmann applanation tonometry (GAT) is the gold standard for measurement of IOP. However, its accuracy depends on many factors, including corneal thickness and other biomechanical properties.1,2 Goldmann and Schmidt3 calibrated the tonometer for a mean central corneal thickness (CCT) of 520 µm, knowing that the tonometer may be inaccurate in corneas differing from that value. Several studies4-7 have reported that most patients with ocular hypertension have a high CCT, which may lead to a spuriously high IOP measured using an applanation device rather than truly elevated IOP. Other studies8,9,10 found that patients with normal-tension glaucoma have thinner corneas than those of the general population. Therefore, patients with normal-tension glaucoma may have a higher IOP than measured. Furthermore, a thin cornea may be an independent risk factor for the conversion to primary open-angle glaucoma (POAG) in patients with ocular hypertension,11 although such an effect has been called into question. For this reason, it is controversial whether CCT is an independent risk factor for progression of established glaucoma.12-14 The effect of CCT and other corneal abnormalities on the accuracy of GAT continues to be one of the most important drawbacks of tonometry15 and may influence management decisions in clinical practice. For accurate GAT assessment of IOP, measurement of CCT using an ultrasound pachymeter and nomograms for adjustment of GAT readings has been suggested.4 Unfortunately, none of the correction tables seem to be reliable or satisfactory.10,17

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To reduce the corneal effect on IOP measurement and to improve IOP assessment, dynamic contour tonometry (DCT) with a new digital and nonapplanation contact tonometer was developed (Swiss Microtechnology AG, Port, Switzerland). According to the manufacturer18 and recent studies9,20 on cadaver eyes, DCT measurements are minimally dependent on structural properties of the cornea, particularly CCT. The concave surface of the tonometer tip matches the contour of the cornea; this contour matching creates equilibrium between capillary force, rigidity force, appositional force, and force exerted on the cornea by IOP. A piezoelectric sensor integrated into the contoured surface of the tip measures IOP without systematic errors caused by these forces or by changes in the corneal biomechanical properties.21

Recently, the effect of CCT on DCT and GAT measurements has been investigated in healthy eyes. In some studies,22,23 GAT was significantly more affected than DCT by CCT, while in another study24 there was no significant difference between GAT and DCT. The objective of the present study was to assess the relationship between IOP measurement and CCT. In contrast to previous studies22-24 comparing DCT and GAT, we assessed patients with POAG. In addition, to avoid the influence of interindividual factors on IOP, we used a novel approach considering the interocular effect of CCT on IOP measurements.

METHODS

DESIGN

In a prospective single-center study, 125 consecutive patients with POAG were recruited from the glaucoma unit of the Department of Ophthalmology, University Hospital Basel, Basel, Switzerland, during a 6-month period between November 1, 2004, and April 30, 2005. Excluded were patients with pseudoxfoliation, a history of trauma, pigmentary dispersion, nar- row or closed iridocorneal angle, evidence of any secondary glaucoma, any type of preceding refractive surgery and corneal disease, and chronic or recurrent inflammatory eye disease (eg, scleritis or uveitis). In addition, patients with poor cooperation, poor quality of DCT readings, and unreliable measurements due to astigmatism greater than 2 diopters were also excluded. All patients underwent 5 tonometric measurements (2 GAT readings, followed by 3 DCT readings).25,26 After each GAT measurement, a rest period of 3 minutes was allowed to minimize the tonographic effects of applanation tonometry. The mean IOP reading for each measurement method was recorded. Because DCT provides a digital readout of IOP on a liquid crystal display (LCD), prior knowledge of GAT values would not affect the result and make it mandatory to perform GAT measurements first for masking reasons. The right eye was always measured first. After application of topical anesthesia to the cornea, a paper stripe impregnated with fluorescein was used to stain the precorneal tear film immediately before IOP measurement. The patient was asked to blink before measurement to ensure equal distribution. Goldmann applanation tonometry was performed using a slitlamp (Haag-Streit, Koeniz, Switzerland) with a tonometer calibrated according to the manufacturer’s guidelines.20 If IOP fluctuated during the cardiac pulse cycle, GAT measurements were taken in the middle of the pulsation amplitude. Intraocular pressure readings by DCT were computed and displayed by the instrument, thereby reducing possible observer bias. Dynamic contour tonometry provides 5 different quality levels, with 1 being the best and 5 being the poorest. As recommended by the manufacturer, only measurements of quality 3 or less were evaluated and included in the study.26 In addition, CCT was measured immediately after IOP measurements using an ultrasonic pachymeter (SP-3000; Tomey Corporation, Cambridge, Mass). The mean of 5 readings within a range of ±3 µm was used for each eye for analysis.

STATISTICAL ANALYSIS

Correlation analysis between the mean DCT and GAT measurements and CCT was performed using Pearson product moment correlation coefficient (SPSS Inc, Chicago, Ill). The 2 IOP measurement methods studied (DCT and GAT) were further compared for bias and for agreement. Because neither of the 2 methods can at the outset be assumed to be superior to the other, the difference between GAT and DCT was plotted against the mean of the 2 methods for analysis of individual pairs according to the method by Bland and Altman.27 Intraocular pressure differences between the right and left eyes (interocular difference) for GAT and DCT readings were analyzed for correlation with the interocular CCT difference in a linear least squares regression analysis.

A linear mixed-effects model considering the 2 eyes of each patient (including CCT and IOP of both eyes) was computed. Mixed-effects models incorporated fixed and random effects. The patient was the random factor, and the eye side (right vs left) was the fixed factor varying within the patient. Central corneal thickness and mean age were covariates; CCT varied within the patient, but age did not. P<.05 was considered statistically significant.

RESULTS

Five patients (4.0%) were excluded because of previous corneal surgery or disease, and 9 patients (7.2%) were excluded because of poor cooperation or inability to obtain good-quality DCT measurements. The mean±SD age of 111 patients with POAG was 63.8±13.3 years (age range, 29-87 years). The mean±SD CCT was 540.9±42.4 µm (range, 420-650 µm [median, 539.5 µm]). The mean±SD interocular CCT difference was 3.6±12.9 µm. All patients were treated with monotherapy or combined topical therapy. The mean±SD IOP of the 2 GAT readings was 15.5±3.4 mm Hg, and the mean±SD IOP of the 3 DCT readings was 19.4±4.1 mm Hg. Dynamic contour tonometry readings were a mean±SD of 3.9±2.3 mm Hg higher than GAT readings (P=.004); after excluding 3 extreme outliers, they were a mean±SD of 3.9±1.54 mm Hg higher (P<.001) (Figure 1). The measurements of both devices were significantly correlated with each other (r=0.82, P<.001). In the Bland-Altman plot, the difference between DCT and GAT varied with the mean (P=.003); however, after excluding the 4 smallest and largest outliers, the difference did not vary with the mean (slope, −0.011; P=.81). Per 10 mm Hg of IOP increase, the increase in the difference between DCT and GAT is −0.11 mm Hg (95% confidence interval, −0.16 to 0.75 mm Hg). This indicates parallelism between the 2 methods.

The interocular IOP difference between GAT and DCT readings showed significant correlation with the interocular CCT difference in linear least squares regression analy-
sis ($r = 0.301$; $P = .001$) for GAT and $r = 0.228$; $P = .02$) for DCT (Figure 2). The mean IOP difference between DCT and GAT readings was not dependent on CCT ($P = .23$), indicating a comparable dependence of GAT and DCT. In a linear mixed-effects model, the IOP difference between DCT and GAT readings significantly increased with older age (slope, 0.033 [95% confidence interval, 0.002-0.064] mm Hg/y; $P = .03$) but not with thicker CCT (slope, 0.006 [95% confidence interval, -0.003 to 0.017] mm Hg/μm; $P = .22$).

**COMMENT**

Previously published data among nonglaucomatous patients undergoing laser in situ keratomileusis suggested that the new nonapplanation DCT device depended less on CCT than GAT. In another study among healthy subjects, DCT measurements were independent of CCT. The present study investigated whether DCT measurements are less dependent on CCT compared with GAT in patients with POAG when a novel approach considering the interocular effect of CCT on IOP measurements was applied.

There was significant correlation between IOP and CCT using either device. In addition, the interocular difference between DCT and GAT readings was not dependent on CCT, suggesting (to our knowledge) a hitherto undescribed parallelism of the relationship between IOP and CCT using either device. In contrast to healthy subjects, patients with POAG have increased IOP, which is independent of CCT. This may have in part contributed to the present results. Furthermore, the corneal rigidity in patients with glaucoma may be altered primarily or secondarily to topical drugs, possibly affecting IOP measurements, as some antiglaucomatous drugs may modulate the extracellular matrix. Therefore, the potential advantage of DCT relative to CCT independence may not hold true for patients with POAG.

Intraocular pressure measured using DCT was consistently higher compared with GAT measurements in human cadaver eyes, in eyes undergoing refractive surgery, and in healthy eyes. Intraocular pressure differences between DCT and GAT measurements may be attributed to calibration of DCT, which is based on a manometrically controlled pressure and not on applanation. Intraocular pressure obtained by GAT has been found to be lower than true IOP as measured intracamerally. Furthermore, to our knowledge, no significant difference between DCT readings and manometric IOP readings has been found in human cadaver eyes.

The mean IOP difference between DCT and GAT readings in this study is the highest reported in the literature (3.9 mm Hg). At present, it is unclear why the difference in this study population is so large. Recent studies have shown that IOP differences between DCT and GAT are small (0.7-1.0 mm Hg) in nonglaucomatous subjects and are larger (1.7-2 mm Hg) in studies that include patients with glaucoma. However, a study differentiating between patients who had glaucoma and those who did not have glaucoma did not find different results between the 2 groups. In the present study, all patients with POAG had been receiving 1 or 2 topical antiglaucoma eyedrops for months or years. Therefore, we cannot exclude that the use of eyedrops may have had an effect on corneal biomechanics and accordingly on IOP measurement. However, we did not subgroup patients with POAG according to different medication use because of the heterogeneity of the drugs used and the statistical weakness of such stratification. In previous studies, no significant relationship between CCT and the use of some topical IOP-lowering drugs has been reported. Nevertheless, it remains to be elucidated whether various topical glaucoma medications might confound the relationship between CCT and IOP. Likewise, whether there is an effect of topical drugs on biomechanical prop-
erties of the cornea other than CCT needs further validation, as there is evidence that some IOP-lowering drugs may alter tissue by stimulating the degradation of extracellular matrix (e.g., modulation of matrix metalloproteinases in conjunctival and subconjunctival tissue). In addition, CCT is only a surrogate for corneal rigidity. A thicker cornea does not necessarily mean higher rigidity of the cornea in all patients, and corneal factors other than CCT may play a role in the corneal biomechanics affecting IOP readings, such as hydration state, curvature, and age of the patient.

In this analysis, we used an interocular study design that has not been described previously, to our knowledge. The advantage of an interocular or intraindividual comparison is minimal interference from other nonocular factors in different individuals. Corneal structure or biomechanics varies among patients even when CCT is the same. Therefore, consideration of CCT from different patients does not necessarily allow conclusions on the effect of CCT on IOP. From a statistical point of view, the interocular design increases efficiency, with greater degrees of freedom than an interindividual comparison.

Seven percent of patients were excluded from the analysis because of the inability to obtain good-quality DCT. Some patients were unable to sit completely still, breathe quietly, and avoid slight movements of the eye or head. The fact that DCT requires a longer time of measurement than GAT (i.e., approximately 5 cardiac cycles) could be regarded as a disadvantage of DCT, particularly in the older patient. However, the promising advantages of DCT are the short learning curve, the ease of use of DCT in most patients in our experience, and the promising advantage of Ophthalmology, University Hospital Basel, Submitted for Publication:

In conclusion, DCT measurements of IOP depended at least as much on CCT as GAT measurements but were significantly higher than GAT measurements in patients with POAG. Because IOP differences between DCT and GAT were independent of CCT, the measurement devices are susceptible to similar measurement biases depending on CCT, at least in patients with POAG.

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REFERENCES


Ophthalmological Numismatics

Johannes E. Purkinje (1787-1869) was a Czech professor of physiology at Breslau from 1823 to 1850 and then at Prague until his death. He was famous for his work in visual physiology. Shown is a medal engraved by V. Seidan in 1867 honoring his 80th birthday. The obverse depicts his bust facing right. The reverse depicts a seated winged woman, her right hand holding a wreath on a rectangular pillar inscribed 80 LET. Her left hand holds a mirror. On the pillar is a serpent, and beneath her seat are an owl, book, globe, and scroll.

The Republic of Czechoslovakia minted a 25 korun coin in 1969 commemorating the centennial of Purkinje’s death. It was engraved by J. Dostal and J. Harcuba. The obverse depicts Purkinje’s bust facing right, beneath it a small staff of Aesculapius. The reverse depicts a standing lion facing left, a Bohemian or Czech symbol.

Courtesy of: Jay M. Galst, MD, 30 E 60th St, New York, NY 100222.