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Correlation of Serial Scleral and Corneal Pneumatonometry

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Purpose: To evaluate the usefulness of scleral pneumatonometry as an alternative for corneal measurements of intraocular pressure (IOP) over a broad range of IOPs.

Design: Prospective, observational cohort study.

Participants: The study was conducted in the University of California, San Francisco, Retina Clinic between August and November 2013 in 33 adult patients (age range, 34−94 years; mean ± standard deviation, 74.1±13.4 years) receiving anti−vascular endothelial growth factor intravitreal injections, which transiently increase IOP.

Methods: Corneal pachymetry and serial corneal and temporal scleral pneumatonometry (baseline, immediately after, and 10, 20, and 30 minutes after injection) were collected. One-time baseline corneal and scleral pneumatonometry readings were obtained in the noninjected eye.

Main Outcome Measures: Correlation analysis and a Bland-Altman plot were used to evaluate reliability and agreement between scleral and corneal measurements of IOP. A linear mixed model was used to determine the relationship between measurements and to perform covariate analyses.

Results: Scleral and corneal pneumatonometry showed nearly 1:1 linear correlation, although scleral pneumatonometry was biased toward higher values ($r = 0.94$; $P < 0.001$). Scleral pneumatonometry averaged 9.0 mmHg higher than corneal pneumatonometry (95% limits of agreement, −1.5 to 19.5 mmHg). A linear mixed model resulted in the following equation: corneal IOP = 1.04 × scleral IOP − 10.37. Age, central corneal thickness, laterality, and glaucoma and lens status did not impact this relationship. The difference between corneal and scleral pneumotonometry was correlated between the two eyes of individual patients ($r = 0.75$; $P < 0.001$).

Conclusions: Differences between serial scleral measurements reflect differences between serial corneal measurements. Scleral pneumatonometry should be considered as an alternative to corneal pneumatonometry for following patients in whom corneal measurements are unreliable or unobtainable. *Ophthalmology 2015;■:1−6 © 2015 by the American Academy of Ophthalmology.*

Intraocular pressure (IOP) normally is measured over the cornea. However, for patients with significant corneal pathology, such as scarring, thinning, and edema, or for those who have keratoprosthesis implants, corneal tonometry can be inaccurate or impossible to obtain. However, these corneal diseases are associated commonly with either primary or secondary glaucoma. For example, in the case of keratoprosthesis, difficulty with IOP measurement is a significant problem. Glaucoma has been reported to be a preoperative comorbidity in more than two-thirds of patients and to be newly diagnosed in an additional 13% to 25% of patients after keratoprosthesis implantation.[1−3] Furthermore, keratoprostheses are associated with postoperative elevation in IOP and progression of glaucoma, which can become vision limiting.[1−3]

Scleral pneumatonometry has been proposed as an alternative method for IOP measurement in patients for whom corneal measurements are not possible. In a study performed in cadaveric eyes, we previously showed that serial measurements of scleral pneumotonometry correlate strongly and linearly to IOP when IOP was set from 20 to 50 mmHg by infusion cannula.[4] Importantly, this relationship was unchanged after the eyes underwent keratoprosthesis implantation. In patients, a cross-sectional study by Kapamajian et al[5] found a positive correlation between one-time corneal and scleral pneumatonometry in healthy adult patients. However, the IOP range was limited by the physiologic pressures of this population (10.5−27 mmHg), and the relationship between changes in corneal and scleral pneumatonometry in patients was not studied. Furthermore, scleral pneumatonometry generally resulted in higher measurements than corneal pneumatonometry, but this difference was highly variable across individuals (mean ± standard deviation, 8.4±5.7 mmHg).[5]

For scleral pneumotonometry to be a useful clinical tool, scleral measurements should correlate to corneal measurements over a wide range of both physiologic and pathological pressures and have a predictable relationship over multiple measurements when used to follow patients clinically. Therefore, in the current study, we measured serial scleral and corneal pneumatonometry in patients receiving intravitreal injections, which transiently increase IOP, to evaluate the relationship between these 2 measurements over a broad range of IOPs. Since the baseline difference between scleral and corneal pneumatonometry in an eye with corneal disease may be unknown, in the case of

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unilateral or asymmetric disease, we hypothesized that one could use the contralateral eye as a surrogate for the baseline difference in the eye of interest. Thus, we also evaluated whether the difference between corneal and scleral measurements was correlated between the 2 eyes of individual patients.

Methods

Study Design

The Institutional Review Board/Ethics Committee at University of California, San Francisco, approved this prospective observational study. This study complied with Health Insurance Portability and Accountability Act regulations and adhered to the tenets of the Declaration of Helsinki.

Adult patients receiving anti−vascular endothelial growth factor intravitreal injections in the Retina Clinic of the University of California, San Francisco, were recruited between August and November 2013. We had a minimum target enrollment of 28 patients, which was predicted to have a 90% power to detect a correlation coefficient of 0.57 (based on the results from Kapamajian et al[5]) with an α of 0.05 in an a priori sample size calculation. Patients with previous incisional glaucoma surgery, scleral buckle, strabismus surgery, refractive cornea surgery, scleral pathology such as thinning or scarring, or significant corneal pathology such as scarring or edema that would prevent accurate measurement of IOP over the cornea were excluded. The risks and benefits of participation were discussed with each participant and informed consent was obtained. We collected patient information on demographics, diagnosis of glaucoma, and lens status (phakia or pseudophakia) by chart review.

Measurements

A single observer (D.S.K.) obtained all measurements. Eyes were anesthetized with 1% proparacaine. At each time point, IOP measurements were obtained from the central cornea and temporal sclera with the edge of the pneumatonometer probe (Model 30 Classic; Reichert Ophthalmic Instruments, Depew, NY) placed directly temporal 1 mm from the limbus with the patient in primary gaze, which centered the probe approximately 3.5 mm posterior to the limbus. Corneal and temporal scleral pneumotonometry measurements (abbreviated as corneal IOP and scleral IOP, respectively) were obtained at baseline in both eyes before injection, and then serial measurement were obtained in the treated eye immediately after injection and 10, 20, and 30 minutes after injection. All measurements were obtained with patients sitting up. For each pair of measurements, we checked the corneal IOP before the scleral IOP. All corneal measurements had a standard deviation of less than 0.5 mmHg and all scleral measurements had a standard deviation of less than 1 mmHg for IOPs between 0 and 40 mmHg and a standard deviation of less than 1.5 mmHg for IOPs of more than 40 mmHg. The waveform was examined for good quality in all measurements with IOPs of less than 40 mmHg, where it was within the limits of the paper printout. We measured central corneal thickness by pachymetry (DGH-550 Pachette 2; DGH Technology, Inc, Exton, PA), averaging 5 measurements, at the time of the baseline measurements.

Statistical Analysis

The Pearson correlation coefficient is reported herein. For paired data with more than 1 time point for each study subject, an ordinary correlation coefficient is not appropriate because it does not take into account the lack of independence between repeated measurements for the same subject.[6] Instead, we calculated a within-subjects correlation coefficient, which removes the variation between subjects to examine whether an increase in a variable within the same subject is associated with an increase in another variable.[6] Similarly, agreement between scleral and corneal IOP was analyzed using a Bland-Altman plot with correction for multiple measurements per subject using MedCalc Statistical Software (MedCalc Software, Ostend, Belgium).[7] The data were fit with a linear mixed model with random slope and intercept using R (R Foundation for Statistical Computing, Vienna, Austria). Confidence intervals were derived from bootstrap analysis, an iterative resampling of the data. Covariate analysis was performed using the linear mixed model and likelihood ratio test with $P < 0.05$ considered statistically significant.

Results

Thirty-three patients ranging in age from 34 to 94 years were included in the study. Baseline characteristics are shown in Table 1. Pseudophakia was present in 52% of patients and glaucoma was present in 15% of patients. A total of 164 serial paired measurements of corneal and scleral IOP were obtained in the treated eye (1 subject missed 1 time point). Corneal IOPs ranged from 9 to 61.5 mmHg and scleral IOPs ranged from 13.5 to 74 mmHg. Thirty-two patients had baseline measurements of scleral and corneal pneumatonometry in the contralateral untreated eye. At baseline, the difference between scleral and corneal pneumatonometry measurements in the 2 eyes of individual patients was correlated significantly ($r = 0.75$; $P < 0.001$; Fig 1).

We used correlation to analyze the linear association between serial scleral and corneal IOP by pneumatonometry and found that they were significantly correlated ($r = 0.94$; $P < 0.001$) for the injected eyes (Fig 2). The data were fit using a linear mixed model, which takes into account longitudinal measurements over time. This analysis resulted in the following equation: scleral IOP = 0.97 × corneal IOP + 10.0. The standard deviation of the residuals, an error measurement for the entire model, was 2.78 mmHg. The slope (mean ± standard deviation, 0.97±0.21 mmHg) was statistically significant ($P < 0.001$) and showed a nearly 1:1 relationship between changes in scleral and corneal IOP on average with some variability between individual patients (Fig 3A). Similarly, the intercept (mean ± standard deviation, 10.0±5.83 mmHg) was statistically significant ($P < 0.001$), but demonstrated greater variability among patients (Fig 3B).

A Bland-Altman plot was created to examine the agreement of scleral IOP and corneal IOP over a range of IOP using data from

Table 1. Baseline Characteristics

No. of patients enrolled	33
Mean age ± SD (yrs)	74.1±13.4
Eye (no.)	
Right	20
Left	13
Mean CCT ± SD (μm)	552.4±37.0
Lens status (no.)	
Phakic	16
Pseudophakic	17
Glaucoma (no.)	5 (2 POAG, 1 steroid-induced, 2 NOS)

CCT = central corneal thickness; NOS = not otherwise specified; POAG = primary open angle glaucoma; SD = standard deviation.