Comparison of Intraocular Pressure Measurements by the Ocular Response Analyzer and Goldmann Applanation Tonometer after Penetrating Keratoplasty in Keratoconic Patients

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Abstract

***Purpose*:** To compare intraocular pressure (IOP) readings measured by the Ocular Response Analyzer (ORA) with those measured by the Goldmann applanation tonometer (GAT) in keratoconic eyes following penetrating keratoplasty (PKP) and evaluate the influence of anatomical and biomechanical properties of the grafts on the IOP measurements

***Methods*:** In this cross-sectional study conducted on 45 keratoconic eyes of 36 patients (24 men and 12 women) undergoing PKP, IOP using the GAT (IOP GAT) and corneal hysteresis (CH), corneal resistance factor (CRF), Goldmann-related IOP (IOPg), and cornea-compensated IOP (IOPcc) using the ORA and central graft thickness (CGT) were measured. Bland-Altman and mountain plots were used to evaluate agreement between the tonometers. The correlation of graft curvature and astigmatism; CGT; and corneal biomechanical properties with IOP readings was investigated using multivariate regression analysis.

***Results*:** The mean age of patients was 29.8±6.1 years and they were followed up for 91.2±35.4 months postoperatively. Mean CH, CRF, and CGT were 10.2±2.1 mmHg, 10.1±2.2 mmHg, and 567.5±38.8 µm, respectively. Mean IOP GAT, IOPg, and IOPcc were 12.2±2.4, 15.1±3.5, and 15.8±3.3 mmHg, respectively (P<0.001). The 95% limit of agreement between IOP GAT and IOPg ranged from -3.6 to 9.3 mmHg. CH and CRF, but not CGT or keratometric astigmatism were significantly associated with IOP GAT, IOPg, and IOPcc.

***Conclusion*:** Following PKP in keratoconus, graft biomechanics had more influence on IOP values than anatomical features. In comparison to the GAT, the ORA yielded higher IOP values.

***Keywords*:** Goldmann applanation tonometer, Ocular Response Analyzer, Goldmann-related Intraocular Pressure, Cornea-Compensated Intraocular Pressure, Graft Biomechanical Properties

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Introduction

The main aim of corneal transplantation in most cases is to restore optical properties of the eye. However, whether it can restore biomechanical properties in certain indications, such as keratoconus, remains to be elucidated. This may be of particular importance when attempting to correct intraocular pressure (IOP) measurements for increased or decreased ocular rigidity or when refractive surgery of the transplanted cornea is anticipated.

Monitoring IOP after penetrating keratoplasty (PKP) is extremely important, as high IOP can lead to graft failure[1] and is encountered in transplanted eyes with a high incidence, ranging from 10% to 42%.[2-5] Although Goldmann applanation tonometry (GAT) is considered as the gold standard for measuring IOP, the high astigmatism and surface irregularity following PKP can decrease its accuracy.[6,7] Furthermore, decreased rigidity of the ocular wall in some conditions, such as keratoconus, may result in an underestimation of the IOP measured with GAT.

In an attempt to circumvent the problems with GAT in grafted eyes, several tonometers have been tried and compared to find an ideal alternative.[8-10] Recently, Reichert Ophthalmic Instruments (Buffalo, NY, USA) have introduced a new technology for non-contact tonometers which measures IOP, independent of corneal thickness and rigidity, as well as new metrics called corneal hysteresis (CH) and corneal resistance factor (CRF).[11] The Ocular Response Analyzer (ORA) uses a precisely metered air pulse that causes the cornea to deform inwards. Thus, the cornea passes through applanation (inward applanation). Milliseconds after applanation, the air puff shuts off resulting in pressure decrease in a symmetrical fashion; during this phase the corneal shape returns to its normal shape. During this process the cornea again passes through an applanation phase (outward applanation). An electro-optical collimation detector system monitors the corneal curvature change in a 3.0 mm diameter during inward and outward applanation and uses an arbitrary coefficient to translate these deformations into two applanation pressures. Theoretically, these two pressures should be the same but this is not the case. Hysteresis, which is said to be a function of corneal viscosity, is the difference between the inward and outward applanation pressures. Hysteresis is influenced by corneal thickness and rigidity.[11] CRF is another metric measured by the ORA which is believed to be dominated by the elastic properties of the cornea and appears to be an indicator of the overall resistance of the cornea.[12] By taking an average of these two applanation pressures, a Goldmann-related IOP (IOPg) is calculated.[11] Cornea-compensated IOP (IOPcc) determines IOP values independent of corneal properties such as central thickness.[11]

Although there are studies that show a good agreement between the values measured by the ORA and GAT in normal corneas,[12-14] there is no report that evaluates the accuracy of the former tonometer following PKP. In the present study, the agreement between the ORA and GAT in keratoconic patients who underwent PKP was evaluated and the influence of other factors including central graft thickness (CGT), graft astigmatism and steepness, and its biomechanical properties (CH and CRF) on the IOP measurements were investigated.

Methods

In this cross-sectional comparative study, a group of keratoconic patients who underwent PKP were evaluated. The participants had a clear graft and all sutures were removed at least 6 months before entering the study. The presence of any ocular disease other than keratoconus; systemic disorders such as diabetes mellitus; a history of additional ocular surgery, such as a previous corneal graft, cataract extraction, or refractive surgery of any kind; and use of contact lenses or topical ocular medications led to patient exclusion. This study was approved by the Institutional Ethics Committee and written informed consent was signed by all participants after explaining the nature of the study.

An ocular examination including Snellen uncorrected visual acuity (UCVA) and best spectacle-corrected visual acuity (BSCVA) using the Snellen acuity chart, slit-lamp examination, manifest refraction, and keratometry was performed. As measuring IOP by one tonometer may influence the

following measurement, the tonometers were used in random order with a 5-minute interval between readings to minimize the effect of IOP fluctuation. To avoid the effect of sleeping and diurnal variation on corneal properties such as CGT, CH, CRF, and IOP as well, the measurements were obtained in the morning at least 3 hours after awakening, when postawakening decline had already occurred. All measurements were performed by a single qualified ophthalmologist (S F).

In each eye, IOP was measured twice using Goldmann applanation tonometry AT 020 (Carl Zeiss Meditec Inc., Dublin, California, USA) and averaged, after anesthetizing the cornea with a drop of tetracaine 0.5%. In order to reduce the effect of corneal astigmatism on the measurement, the tonometer head was rotated 43 degrees to the least-curved meridian. Additionally, to consider the effect of CGT on IOP readings, for every 10 µm above 520 µm, 0.7 mmHg was reduced from IOP GAT.

The ORA was used to measure CH, CRF, IOPg, and IOPcc. Briefly, the patients were seated and asked to keep their eyes wide open while fixating on a green target light at the center of red lights. After releasing an air puff, the measured parameters were displayed on the monitor. For each patient, 4 readings were obtained immediately and consecutively at the same session and averaged after excluding the outliers (defined as irreproducible values not having good quality or two distinct peaks).

The last examination performed was central graft pachymetry using an ultrasonic contact probe (A/B scan; Sonomed Inc, Lake Success, NY, USA) after instillation of topical tetracaine 0.5%. The probe was held perpendicular to the center of the graft and 5 measurements within a range of ±2 µm were obtained and averaged for statistical analysis.

Statistical analysis

Statistical analysis was performed with SPSS (version 14, SPSS Inc., Chicago, IL, USA) for Windows XP. For general statistical reporting, mean±standard deviation was calculated after the data were examined for normal distribution. Paired t-test was used to compare mean IOP readings by the ORA and GAT. The agreement between the two tonometers was evaluated with Bland-Altman and mountain plots. The correlation of CGT, refractive status (mean keratometry and graft astigmatism), and graft biomechanical properties (CH and CRF) with the IOP readings by both tonometers was investigated using multivariate regression analysis. P<0.05 was considered statistically significant.

Results

A total of 49 keratoconic eyes which had undergone PKP were enrolled. Four eyes were excluded, because the parameters measured with the ORA were either out of scale (n=3) or abnormally high (n=1). Therefore, 45 (21 right) eyes of 36 patients (24 men and 12 women), aged between 17.0 and 44.0 years (mean 29.8±6.1 years), remained for analysis. They were followed up for 91.2±35.4 (21 to 296) months postoperatively. At the time of study all grafts were clear. Mean recipient and donor trephine size were 7.78±0.22 (7.50 to 8.0) mm and 8.09±0.25 (7.75 to 8.50) mm, respectively, with a trephine disparity of 0.25 mm in 30 and 0.50 mm in 15 eyes. Spherical equivalent refractive error, mean keratometry, and keratometric astigmatism were -2.87±2.8 (-11.50 to +2.25) D, 44.87±1.9 (40.0 to 49.75) D, and 4.47±2.9 (0 to 14.50) D, respectively. CGT was 567.5±38.8 (441 to 654) µm, CH was 10.2±2.1 (6.4 to 15.7) mmHg, and CRF was 10.1±2.2 (7.3 to 16.0) mmHg.

IOP GAT (12.2±2.4 mmHg) was significantly lower than IOPg (15.1±3.5 mmHg; P<0.001) and IOPcc (15.8±3.3 mmHg; P<0.001) and the difference between IOPg and IOPcc reached a significant level (P=0.04). The Bland-Altman and mountain plots show the agreement between pressure measurements obtained with ORA and GAT (Figure 1). The mean difference between IOPg and IOP GAT was 2.83±2.0 mmHg (range, -5.30 to 9.00 mmHg; and 95% confidence interval [CI] = 1.84 to 3.81 mmHg) and between IOPcc and IOP GAT was 3.56±3.1 mmHg (range, -2.80 to 10.20 mmHg and 95% CI=2.60 to 4.53 mmHg). As indicated, the mean differences remained relatively stable at two extremes of IOP measurements.

A significant association was found between IOP GAT and IOPg (R^2=0.44, P=0.004) expressed by the equation: IOP GAT=7.8+0.29×IOPg, and between IOP GAT

and IOPcc (R^2=0.42, P=0.005) expressed by the equation: IOP GAT=7.5+0.30×IOPcc.

Multivariate regression analysis showed that CH and CRF, but not CGT or keratometric astigmatism were significantly associated with IOP GAT, IOPg, and IOPcc. A significant association was found between mean keratometry as well as postoperative mean spherical equivalent refractive error and IOP GAT (Table 1). CGT was significantly associated with CRF (R^2=0.43, P=0.003), but not with CH (R^2=0.25, P=0.10).

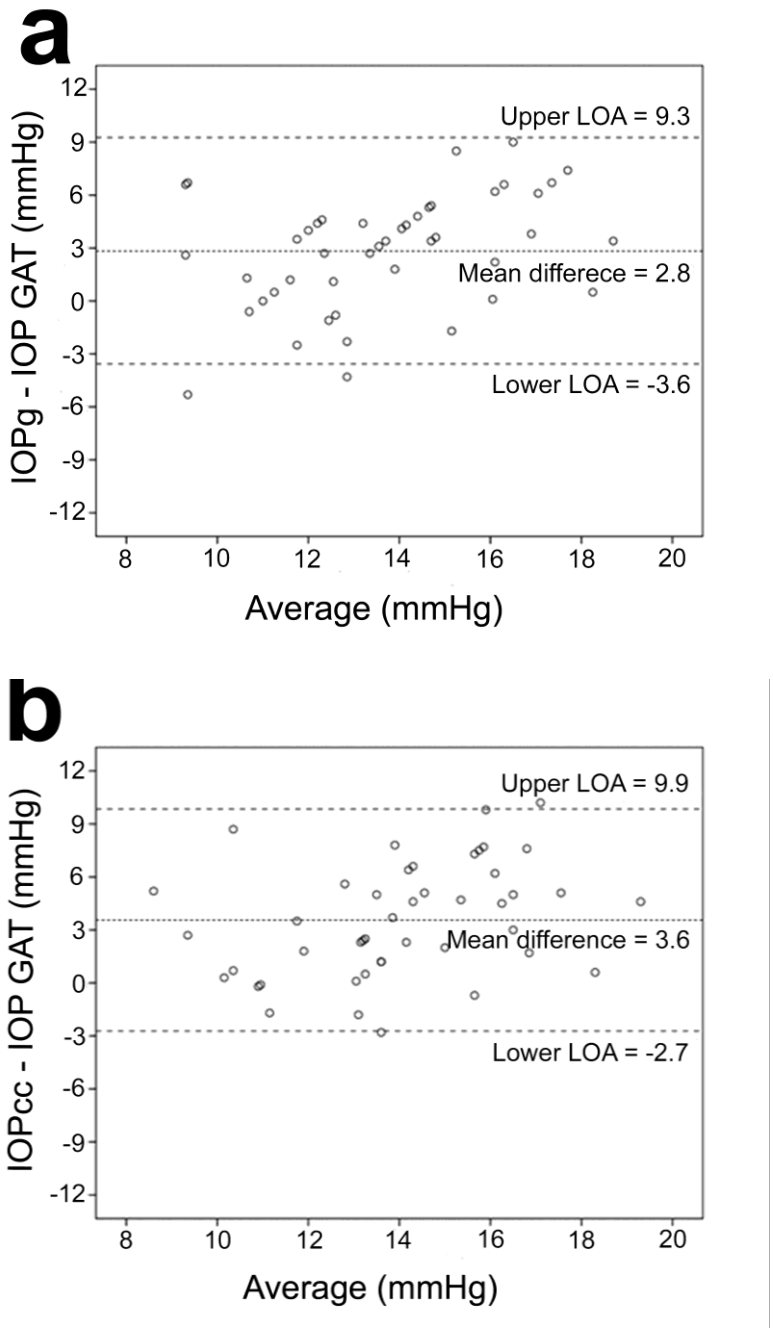

Figure 1. Bland-Altman plots representing the difference between IOP GAT and IOPg versus the mean of both (a) and the difference between IOP GAT and IOPcc versus the mean of both (b) The dotted lines represent the upper and lower borders of the 95% limits of agreement.

LOA: Limits of agreement, IOP GAT: Intraocular pressure by Goldmann applanation tonometer, IOPg: Goldmann-related IOP, IOPcc: Cornea-compensated IOP

Table 1. Correlations of biomechanical and anatomical properties with different techniques for measuring intraocular pressures

Characteristics	Correlation coefficient (β)	Statistical significance
CH vs.		
IOP GAT	1.27	<0.001
IOPg	2.82	<0.001
IOPcc	3.51	<0.001
CRF vs.		
IOP GAT	1.21	<0.001
IOPg	3.31	<0.001
IOPcc	2.85	<0.001
CGT vs.		
IOP GAT	-0.01	0.56
IOPg	0.001	0.26
IOPcc	0.001	0.25
Keratometric astigmatism vs.		
IOP GAT	-0.13	0.20
IOPg	0.011	0.41
IOPcc	0.004	0.77
Mean keratometry vs.		
IOP GAT	0.47	0.01
IOPg	-0.04	0.08
IOPcc	-0.03	0.14
Spherical equivalent vs.		
IOP GAT	-0.31	0.01
IOPg	0.02	0.09
IOPcc	0.03	0.08

CH: Corneal hysteresis, CRF: Corneal resistance factor, CGT: Central graft thickness, IOP GAT: Intraocular pressure by Goldmann applanation tonometer, IOPg: Goldmann-related IOP, IOPcc: Cornea-compensated IOP by ORA

Discussion

As high IOP after PKP is the leading cause of non-immune graft failure,[1] it should be closely monitored to detect and treat ocular hypertension in such eyes, which reportedly have a high incidence of increased IOP, ranging from 10% to 42%.[2-5] GAT is considered the gold standard in clinical measurement of IOP, however, one can question its appropriateness, as its accuracy is severely decreased by corneal edema and irregularity and any alteration in the corneal thickness and rigidity. Furthermore, it has been originally designed for measuring IOP in normal corneas, thus any biomechanical changes within the graft or host-graft complex can negatively impact its accuracy following PKP.

Different studies have examined different tonometers to find a reliable alternative that can circumvent the problems encountered with IOP measurements by GAT after keratoplasty.[8-10] These studied found either no difference[8] or considerable variations between values obtained by GAT and other tonometers.[9,10] Comparing IOP measurements after PKP using four different tonometers including GAT, TonoPen XL, Pascal Dynamic Contour tonometer, and ORA, Chou et al[15] found the least agreement between the ORA and GAT. Fabian et al[16] found that IOP GATcc was significantly lower than IOPcc but, comparable to IOPg after PK.

The present study compares the ORA with the GAT after PKP. All patients had the same

indication for PKP (keratoconus) and the results of this study should be interpreted in this context, because the abnormal recipient corneas remaining after trephination may have an influence on graft metrics and IOP readings.

ORA was safe in our patients, as wound dehiscence did not develop in any of the cases. This observation implies that after complete suture removal, the surgical wound is strong enough to sustain inward deformation of the graft caused by a rapid air puff. In 4 eyes, the machine could not analyze the data, indicating an out-of-scale measurement, or presented abnormally high figures inconsistent with the clinical findings. Abnormal signals, specially as the cornea was returning to its original curvature, have also been previously reported in a transplanted cornea.[11]

In the current study, there was no correlation between corneal astigmatism and IOP readings by the two tonometers. To reduce the effect of corneal astigmatism on readings by GAT, the tonometer tip was rotated 43 degrees to the least-curved meridian. There are other ways to compensate for the under- or overestimation of IOP by GAT resulting from high astigmatism, which include taking an average from values measured at two axes 90 degrees apart or reducing or adding 1 mmHg for every 4 D against-the-rule or with-the-rule astigmatism, respectively.[17] However, a wide range of graft astigmatism could affect the accuracy of measurements by GAT. In contrast to this observation, IOP GAT, but not IOPg or IOPcc had a significant positive association with the mean keratometry and spherical equivalent refractive error. Corneal curvature is another variable that can affect the accuracy of IOP measurement, possibly because of the difference in the volume of the displaced fluid after a given area is flattened. Young previously described the relationship between the corneal deformation under IOP and the corneal curvature as well as thickness.[18] According to him:

$$\Delta R = IOP \times R^2 \times (1-v) / 2E \times t$$

where ΔR is corneal deformation along the radial direction, IOP is the true IOP, R is the radius of the corneal curvature, t is the corneal thickness, E is Young's modulus (defined as the ratio of the stress and the strain), and v is Poisson's ratio (characterizing the deformation perpendicular to the direction of the load) of the cornea. This equation which indicates the corneal radius of curvature has a relationship with IOP readings supports the positive significant association between the graft curvature and IOP GAT observed in the present study. It is possible that steeper corneal grafts cause overestimation of IOP readings by the GAT, an effect which is cancelled by the ORA.

Among different corneal parameters, CH and CRF showed a significant positive correlation with IOP GAT, IOPg, and IOPcc, while graft thickness was not associated. Meanwhile, CGT was significantly correlated with CRF. Judging from these observations, it can be concluded that although CH, CRF, and CGT are related; they represent different physical/biomechanical properties. As demonstrated by Young,[18] central corneal thickness has an effect on IOP readings; it is overestimated in eyes with thick corneas and underestimated in those with thin corneas.[19] However, this study failed to show any association between CGT and IOP readings by either ORA or GAT. This observation is in line with other studies evaluating the correlation between CGT and IOP.[8,10,20] It is possible that corneal transplantation alters the normal relationship between central thickness as well as material properties (Young's modulus and Poisson's ratio) and IOP observed in non-grafted eyes.[18] For example, the scar that develops between recipient and donor corneas can contribute to the biomechanical properties of a host-donor cornea as a whole, dominating other influential factors like CGT. Given this, CH and CRF are likely to measure cumulative effects of corneal stiffness, viscosity, elasticity, and factors contributed by the wound scar in transplanted eyes, and hence, demonstrate better correlation with IOP than CGT.

In the current study, both IOPg and IOPcc were significantly higher than IOP GAT, although the values were all correlated. Additionally, IOPcc was significant higher than IOPg by 0.73±1.6 mmHg. However, the large standard deviation means the difference varied among different individuals (from -5.7 to 5.6 mmHg). Using the information provided

by CH, IOPcc is intended to compensate for corneal thickness and provide a value independent of corneal factors.[11] This is likely the reason for the results in the current study demonstrating IOPcc values higher than IOP GAT and IOPg values.

Considering GAT as the gold standard and comparing other tonometers to it, some studies found a variation of ±3 mmHg in the readings between these tonometers acceptable.[21,22] Using the same criterion for our study, only 39.1% of IOPg readings lie within this range. One explanation for this discrepancy can be a linear calibration coefficient used to convert the average of the 2 applanation pressures by ORA to a IOPg which has been developed by the manufacturer for non-grafted eyes. It is possible that biomechanical properties of non-grafted eyes, for which the coefficient has been developed, change after PKP and hence, another coefficient may be required. In the present study, this coefficient was calculated to be 0.29 for the grafted eyes, based on the equation:

$$\text{IOP GAT} = 7.8 + 0.29 \times \text{IOPg}.$$

Conclusion

To sum up, the ORA is a safe non-contact method to measure IOP after PKP. However, it yielded considerably higher values which can be converted to IOP GAT values using a coefficient. Without performing intracameral manometry, however, it is not possible to decide which device provides true IOP measurements. A study with a larger sample size is advocated to investigate the role of the ORA after PKP. Also, comparing IOP and corneal biomechanical properties before and after PKP for keratoconus will help determine to what extent corneal transplantation can alter these parameters.

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