Factors Associated With Corneal Deformation Responses Measured With a Dynamic Scheimpflug Analyzer

Atsuya Miki, Naoyuki Maeda, Yasushi Ikuno, Tomoko Asai, Chikako Hara, and Kohji Nishida

Department of Ophthalmology, Osaka University Graduate School of Medicine, Osaka, Japan

Correspondence: Atsuya Miki, Department of Ophthalmology, Osaka University Graduate School of Medicine, 2-2 Yamada-Oka, Suita, Osaka 565-0871, Japan; amiki@ophthalm.med.osaka-u.ac.jp.

Submitted: November 2, 2016
Accepted: December 21, 2016
Citation: Miki A, Maeda N, Ikuno Y, Asai T, Hara C, Nishida K. Factors associated with corneal deformation responses measured with a dynamic Scheimpflug analyzer. Invest Ophthalmol Vis Sci. 2017;58:538–544. DOI:10.1167/iovs.16-21045

PURPOSE. The purpose of this study was to clarify correlations between corneal deformation parameters measured with a dynamic Scheimpflug analyzer and baseline factors such as axial length, intraocular pressure (IOP), age, central corneal thickness (CCT), and corneal curvature.

METHODS. Ninety-six eyes of 96 healthy subjects (mean 55.2 ± 16.1 years of age) were examined using a dynamic Scheimpflug analyzer. Eighteen of 35 deformation parameters were selected for analyses based on measurement reliability and clinical relevance. The associations between corneal deformation parameters and axial length, IOP, age, CCT, and average corneal power were evaluated using multivariate regression analyses.

RESULTS. Deformation parameters were correlated significantly with axial length (n = 13), IOP (n = 13), age (n = 8), and CCT (n = 7) in the multivariate models. Longer axial length corresponded with greater corneal deformability, less viscous damping, and less movement of the entire eye. Higher IOP was associated with greater corneal resistance and less movement of the entire eye. Older age was associated with less corneal deformability and greater movement of the entire eye. Corneal curvature was correlated significantly with only three deformation parameters.

CONCLUSIONS. This study clarified the substantial impact of axial length, age, and IOP on the biomechanical responses of the cornea and the entire eye. In contrast, corneal curvature did not affect most of the deformation parameters. The current results confirmed the importance of corneal biomechanics, especially in eyes with longer axial length and in older subjects.

Keywords: age, axial length, corneal thickness, Corvis

Corneal biomechanics exert considerable influence on ocular clinical practice such as intraocular pressure (IOP) measurements, risk of refractive surgeries, and effectiveness of treatments for corneal diseases.1–3 In other words, corneal biomechanics must be considered when measuring the IOP, performing refractive surgeries, and treating corneal diseases. Consequently, the demand is increasing for an efficient and accurate method for measuring the corneal biomechanical properties in a clinical setting.

The first clinically available device to estimate the biomechanical properties of the cornea was the Ocular Response Analyzer (ORA; Reichert Technologies, Depew, NY, USA).4 The ORA provides the corneal hysteresis (CH) and the corneal resistance factor, which are considered to reflect the corneal biomechanical properties.5 Studies have shown significant differences between the CH and corneal resistance factor values in normal eyes and those in eyes with glaucoma, keratoconus, high myopia, and acquired pit of the optic nerve head and eyes that have undergone refractive surgery.11–13 Although these studies have suggested the relevance of corneal biomechanics in clinical practice, studies also have reported the limitations of CH and corneal resistance factor as diagnostic tools.12

Another device to analyze the corneal dynamic response in vivo, the Corvis ST (Oculus, Wetzlar, Germany), has been introduced into clinical practice. The instrument is a dynamic Scheimpflug analyzer, which obtains images of the anterior segment at a rate of 4330 fps during noncontact tonometry. This device measures a variety of parameters such as length, area, radius, arc length, and velocity of the corneal deformation at several defined time points. Previous studies have reported significant differences between the values of the corneal deformation parameters measured with the Corvis ST in normal eyes and those in eyes with glaucoma and keratoconus and after refractive and keratoplasty surgeries, suggesting the potential clinical relevance of the dynamic Scheimpflug analyzer to those conditions.

In addition to ocular pathologies, the corneal biomechanical parameters are associated with a range of ocular and systemic factors. The ORA parameters are affected by various baseline factors such as refraction, axial length, age, IOP, corneal curvature, and central corneal thickness (CCT). Parameters measured with the Corvis ST are associated with the axial length, age, diabetes, IOP, corneal curvature, and CCT. To clarify the association between ocular disorders and corneal biomechanics, it is essential to adjust for the possible confounding effects of factors that potentially affect corneal biomechanical parameters. Knowledge of the association between corneal deformation parameters and baseline factors also might help improve our understanding of corneal biomechanics.

Since the publication of previous studies, the software of the Corvis ST has been updated to improve measurement reliability and provide more parameters. Therefore, re-evaluation of the
associations between the baseline factors and Corvis parameters, including new parameters, is required. The current study investigated the effect of axial length, age, IOP, CCT, and corneal curvature (average corneal power) on deformation parameters, based on several previous studies that reported the influence of these factors on corneal biomechanics.21-24

METHODS

Participants and Design
The medical records of consecutive subjects who had been examined using the Corvis ST from September 2012 to July 2013 were studied retrospectively. Eyes were included in this study based on the following criteria: an IOP of 21 mm Hg or lower, normal appearance of the optic nerve head on fundus examination, and phakia. The exclusion criteria included the presence of any intraocular disease except for cataract, age under 20 years, and low quality score of the Corvis ST measurement. The Corvis software automatically provides the quality score based on edge detection, alignment, and pressure property. Twenty-three eyes were excluded because of a low quality score. Only the right eye of each subject was included if both eyes were eligible. All participants provided informed consent before enrollment. The institutional review board of Osaka University Hospital approved all study protocols, which followed the tenets of the Declaration of Helsinki.

Examinations
Baseline demographic data such as age and sex and ocular data such as refractive error, corneal curvature, axial length, and lens status were collected from the medical charts. All these ocular examinations were performed within 3 months of the Corvis measurement. The refractive error and corneal curvature were measured using an auto refraction/keratometer (ARK-530, Nidek, Gamagori, Japan). The axial length was measured by laser interferometry (IOLMaster; Carl Zeiss Meditec, Jena, Germany).

All participants underwent corneal deformation response measurements using the Corvis ST. The high-speed Scheimpflug camera obtains 140 images in the horizontal sector of the cornea and anterior chamber up to 8.5 mm in diameter with a resolution of 640 × 480 pixels and a speed of 4530 fps. This imaging system allows visualization of the corneal reaction to an air impulse.

The new analysis software (version 1.3b1361) of the dynamic Scheimpflug analyzer provides 35 parameters, including IOP, CCT, keratometric parameters (zonal K7 [average radius of curvature in the initial state with the 7 mm zone] and sim K3 [radius of curvature in the initial state at 3mm]), and 31 parameters that show the deformation responses. The corneal deformation parameters were calculated in three defined states during deformation: inward applanation or applanation 1 (A1), outward applanation or applanation 2 (A2), and highest concavity (HC). The applanation phase was defined as the transition from a convex to a concave shape (A1) or from a concave to a convex shape. The HC is the time at which the cornea is maximally deformed, also referred to as the corneal deformation amplitude30 or maximal deformation31 in some previous reports. Time, applanation length, velocity, deformation amplitude (DA), deflection length (DL), deflection amplitude (DLA), deflection area (DLA), and delta arc length (ΔArcl) are calculated at each of the three time points (A1, A2, and HC). In addition, the peak distance (PD), radius of curvature (radius), and whole eye movement (WEM) are calculated at the HC. The details of the parameters provided by the Corvis software are listed in Supplementary Table S1.

We originally performed regression analyses among all 31 corneal deformation parameters and baseline factors. However, some of the corneal deformation parameters are of less clinical relevance because of their lower measurement reliability, weaker association with baseline factors, or similarity to other parameters. Therefore, we excluded the following parameters as less important: 6 parameters (A1L, A1dArcL, A2L, HCT, DLAMT, and WEMT) because of poor-to-fair measurement reliability based on our research data (unpublished data); 3 dArcL parameters (A2dArcL, dArcLM, and HCDArcL) because they are correlated strongly with corneal curvature but not with any other baseline factors; deflection amplitude max(imum) (DLAM) because of its similarity to deflection amplitude at the highest concavity; and deformation amplitude parameters (AIDA, A2DA, and HCDDA). Although both DA and DLA describe the vertical movement of the corneal apex, we consider DLA to be more relevant because WEM is compensated for in the DLA but not in the DA.

Exclusion of those parameters limited the discussion to the other 18 clinically relevant parameters (Table 1).

Statistical Analysis
Descriptive statistics such as mean, standard deviation (SD), and range were computed for the baseline clinical factors and Corvis parameters to describe the study population.

To identify factors associated with corneal deformation responses, the correlations between the baseline clinical factors and all Corvis parameters were analyzed statistically. The baseline factors included age, IOP, CCT, axial length, and average corneal power. First, univariate (Pearson) correlation analyses between the baseline clinical factors and Corvis parameters and mutual correlation analyses among the baseline factors were performed (data not shown). The multivariate models with each Corvis parameter as an outcome and all baseline factors as covariates then were established for all Corvis parameters. All statistical analyses were performed using the statistical programming language R (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Descriptive Statistics
Ninety-six eyes of 96 subjects were included (78 women, 81.3%). The mean ± SD age at baseline was 55.2 ± 16.1 years. The descriptive statistics, including the mean, SD, and range of the baseline clinical characteristics of the participants, are summarized in Table 2. Reliable keratometric measurements were obtained in 79 subjects. The descriptive statistics of all the parameters measured with Corvis ST are shown in Supplementary Table S1.

Correlation Analyses
Results of the multivariate correlation analyses between 18 Corvis parameters and baseline factors are listed in Table 3 (all correlation coefficients and P values are detailed in Supplementary Table S2). The axial length was correlated significantly with 13 of 18 parameters. We found a significant, positive correlation between the axial length and five parameters at the highest concavity (HCDDLA, HCDLAd, HCDLL, PD, and radius), which suggested that corneal deformation at the highest concavity is greater horizontally (HCDDLL and PD), vertically (HCDDLA), and in area (HCDLAd) in eyes with a longer axial length. However, the axial length was correlated negatively...
with two parameters at A1 (A1DLAr and A1SIL), which indicates less corneal deformation on applanation horizontally (A1SIL) and in area (A1DLAr). The axial length also was correlated negatively with three deformation parameters at A2 (A2DLAr, A2DLL, and A2SIL), which indicated less corneal deformation on outward applanation. A longer axial length corresponded with a shorter A2T and faster A2V, which indicated faster outward applanation in myopic eyes. Another interesting finding was the negative correlation between the axial length and WEM amplitude (WEMA), which means less WEM in more myopic eyes. Together, our results suggested that myopic eyes tend to have greater corneal deformation, are easily applanated, have less viscous damping properties, and have less WEM than nonmyopic eyes.

The IOP was correlated negatively with the vertical amplitude (HCDLAr), horizontal length (HCDLL and PD), and area (HCDLAr) of corneal deformation parameters and positively with the radius at the highest concavity, which indicated less corneal deformability in eyes with higher IOP. The IOP was correlated negatively with the WEMA, indicating lower magnitude WEM in eyes with a higher IOP. This indicated greater resistance to movement of the entire globe in eyes with a higher IOP. The IOP was correlated positively with the AIT and negatively with the AIV, indicating that a longer time is needed to applanated eyes with high IOP. The IOP also was significantly positively correlated with inward application (A1DLAr and A1SIL) and horizontal outward application (A2DLL).

The patient age was correlated positively with corneal deformation during applanation horizontally (A1DLAr, A1SIL, and A2DLL) and in area (A1DLAr and A2DLAr). Age was correlated negatively with the A1V and A2T. These results indicated greater resistance to deformation in older subjects. Age also was significantly positively correlated with the WEMA, indicating more WEM in older subjects. Taken together, aged eyes exhibit greater resistance to corneal applanation and less resistance to WEM.

The CCT was significantly positively correlated with parameters during applanation (A1DLAr, A1DLL, A2DLAr, A2DLLAr). This means greater deformation is necessary for applanation in eyes with thick corneas. The CCT also was positively significantly correlated with the radius and negatively with HCDLA, suggesting stronger resistance to deformation. The average corneal power was significantly correlated with only three relevant corneal deformation parameters (A1SIL, A1V, and HCDLA).

**DISCUSSION**

Several previous studies using either the ORA or a dynamic Scheimpflug analyzer have reported significant associations between corneal biomechanical properties and various ocular diseases.5–7,10,14–20,29,32,33 Other studies have found that other baseline factors such as axial length,21,25 age,22 and CCT25 also are significantly associated with corneal biomechanical parameters. To accurately understand the relationship between corneal biomechanics and ocular diseases, the effect of baseline factors on corneal deformation parameters must be clarified. In the current study, we examined the correlations between corneal deformation parameters measured with a dynamic Scheimpflug analyzer and baseline clinical factors. We used multivariate models to account for possible confounding effects of other factors. As expected, many parameters showed significant correlations with IOP (n = 13), axial length (n = 13), age (n = 8), and CCT (n = 6) in the multivariate models. In
contrast, corneal curvature was correlated significantly with only three relevant corneal deformation parameters.

Possible Interpretations of Dynamic Scheimpflug Analyzer Parameters

We excluded 4 nonbiomechanical parameters (IOP, CCT, and two keratometric parameters) and 13 less relevant parameters from further discussion. Of the remaining 18 parameters, 17 parameters describe the corneal deformation, and 1 parameter describes the deformation of the entire eye. Of the 17 corneal deformation parameters, 6 parameters were measured at A1, 6 parameters at A2, and 5 parameters at HC. Corneal deformation parameters also can be divided into three categories: time (n = 2), velocity (n = 2), and magnitude of deformation (n = 13). The 13 parameters of deformation magnitude can be divided into 4 categories based on the direction of the measurement: vertical (n = 3), horizontal (n = 6), area (n = 3), and curvature (n = 1).

During applanation, the air pressure increases in proportion to time. Therefore, a higher A1T suggests that higher pressure is required for corneal flattening, which indicates greater resistance to deformation. Similarly, greater deformation at A1 also corresponds to greater resistance to deformation. In contrast, greater deformation at the highest concavity simply reflects greater corneal deformability. Together, both greater deformation during applanation and less deformation at the highest concavity correspond to greater corneal resistance to pressure. Further study is needed to clarify whether there are any differences among greater deformation during applanation and less deformation at the highest concavity and if there are any differences among vertical amplitude, horizontal length, and area of deformation.

Outward applanation (A2) shows corneal recovery from a concave to flat shape. Although A2 can be related to corneal resistance as A1, A2 also can be affected by the corneal viscous damping property. Simply, if both A1 and A2 are fast, that could mean strong corneal resistance, but if there is a difference between A1 and A2, that might reflect the tissue’s viscous damping property or hysteresis (i.e., a difference in the deformation during loading and unloading). Therefore, A2 should be interpreted by corneal resistance and hysteresis, depending on its relationship with A1.

Axial Length

The current study confirmed the great impact axial length has on various corneal biomechanical parameters. In other words, more myopic patients have significantly different parameters than nonmyopic patients. Both greater corneal deformation at the highest concavity and less corneal deformation during applanation in eyes with longer axial length suggested less resistance to corneal deformation in those eyes. The current finding of a negative correlation between axial length and A2T and A2V can be interpreted as a lower viscous damping property, as there was no significant correlation between axial length and A1T and A1V. Another interesting finding was lower WEMA in eyes with a longer axial length. Together, our results suggested that longer axial length corresponds to less corneal resistance.
deformation, less corneal viscous damping properties, and less movement of the whole globe.

Findings from the current study agree with those from the study by Wang et al. in that both reported that axial length was associated negatively with radius. The current study also confirmed the significant negative associations among axial length and A2T, A2V, and radius, reported by Asaoka et al. Lee et al. reported significantly larger A2V and PD values in myopic subjects, which agrees with those from the current study. Together, the current study confirmed more comprehensively the results of the previous investigations that myopic eyes have less corneal deformation. Our new findings included identification of less viscous damping and less whole eye movement of myopic eyes. Several previous studies using the ORA have reported lower CH values in myopic eyes, which agrees with the current study in which less viscous damping capacity was seen in eyes with a longer axial length.

IOP

As expected, the IOP was significantly negatively correlated with vertical, horizontal, and area corneal deformation parameters and positively correlated with the radius at the highest concavity, indicating stronger corneal resistance. A significant positive association between corneal deformation parameters during applanation and IOP also suggested stronger corneal resistance to deformation. These results basically agreed with the results of previous studies. In the current study, the IOP was significantly negatively correlated with the WEMA, meaning that, with higher IOP values, there was less WEM. This could be because the supporting tissues such as the sclera become stiffer with increasing IOP, as reported in an experimental study. The IOP was significantly positively associated with the A1T and negatively associated with the A1V, which indicated slower applanation in eyes with higher IOP and confirmed the results of previous reports. The IOP was significantly negatively correlated with the A2V and A2T, indicating faster recovery to applanation status from maximal concavity in eyes with higher IOP. Together, higher IOP is associated with greater resistance to movement of the cornea and the entire eye.

Age

We found greater deformation during applanation in older subjects. We also found greater WEMA in older subjects, which may indicate less resistance of the sclera or extraocular muscles in older subjects. Taken together, aged eyes exhibited greater corneal resistance and less resistance of the entire eye. Deformation at the highest concavity, another indicator of corneal resistance, was not significantly correlated with axial length in this study. Further study is necessary to elucidate this gap between applanation parameters and HC parameters. Significant positive associations among age and HCDA, HCDLA, and HCT reported in previous studies did not agree with the results of the current study. The significant association between age and A2T reported in another previous study was confirmed by the current study, but the current study did not confirm the associations of age with other parameters (A1T, A2V, radius, and HCDA) reported in the same paper. The inconsistencies among studies might be due to differences in statistical analyses and study populations. The current study was advantageous in that the age distribution was wider and greater even than that in previous studies, and new software to provide more reliable measurements was used in this study. However, the correlation between age and corneal deformation parameters requires clarification in future studies.

Clinical Application

The current study confirmed that corneal biomechanical properties such as deformability and viscous damping property are altered in myopic and aged eyes. These results could be used to establish accurate IOP measurement methods and a risk calculation system for refractive surgeries in those eyes. The current results suggested the potential role of corneal biomechanics in increased susceptibility to ocular diseases in eyes with longer axial length and in aged eyes. In addition, there may be an association between the biomechanical properties of the cornea and those of other ocular tissues such as the sclera and lamina cribrosa. Further study is warranted to elucidate the association between corneal tissue properties and tissue properties of other ocular tissues.

Study Limitations

The current study had several limitations. This study was retrospective with relatively few (96 eyes and subjects) Japanese participants without ocular pathologies. Therefore, we cannot directly extrapolate the study results to other races and eyes with ocular pathologies such as glaucoma. We excluded eyes with ocular pathologies based on self-reporting and medical records, leaving the possibility of including subjects with early stage pathologies without obvious signs or symptoms. Reliable measurements of the corneal curvature were not obtained in 17.7% of participants. Despite these limitations, this is the first study to comprehensively investigate the associations between baseline factors and all 31 corneal deformation parameters, including newly developed parameters, with multivariate regression analyses controlling for possible confounding effects of other factors in normal eyes.
CONCLUSIONS

In conclusion, we evaluated the association between corneal deformation parameters measured with a dynamic Scheimpflug analyzer and baseline clinical factors, using multivariate regression models. We found that longer axial length corresponds to greater deformability and less viscous damping property of the cornea and less movement of the entire eye. We also found that older age is related to greater corneal resistance and greater movement of the entire eye and that the IOP affects the measured values of many corneal deformation parameters. However, corneal curvature was not correlated significantly with corneal deformation parameters. The current results confirmed that the biomechanical properties of the cornea and the entire eye are largely affected by ocular elongation, IOP, and aging.

Acknowledgments

Supported by Japan Society for the Promotion of Science (JSPS) KAKENHI Grant 10892.

Disclosure: A. Miki, Sensimed (F), Santen Pharmaceuticals (R), R-Tech Ueno (R), Pfizer Japan (R), Otsuka Pharmaceuticals (R), Novartis Pharma (R), Topcon (R), Kowa Pharmaceuticals (R); N. Maeda, Alcon Laboratories, Inc. (C, R), JSPS Kakenhi (F), Santen Pharmaceuticals (R), Otsuka Pharmaceuticals (R), Topcon (R), Abbott Medical Optics (R), Johnson & Johnson (R), Tomey Corp. (R); Y. Ikuno, Bayer Yakuhin (C), Norvartis Pharma (C), Tomey (F), Topcon (F); T. Asai, None; C. Harra, None; K. Nishida, Topcon (F), Menicon (F), Wakamoto (F), Rohto Pharmaceutical (F), MSD Japan (F), Senju Pharmaceutical (F, R), Pfizer Japan (F, R), Santen Pharmaceuticals (F, R), Otsuka Pharmaceutical (F, R), Novartis Pharma (F, R), Alcon Japan (F, R), HOYA (F, R), Kowa Pharmaceuticals (F, R), AMO Japan (F), Boehringer Ingelheim Japan (R), Bayer Yakuhin (R), SEED (R), Chuo Sangio (R), Johnson & Johnson Japan (R)

References


