Corneal biomechanical properties in myopic eyes evaluated via Scheimpflug imaging

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Abstract

Background To investigate the biomechanical properties of the cornea in myopic eyes using corneal visualization scheimpflug technology (Corvis ST). The relationships between the biomechanical properties of the cornea and the degree of myopia were also investigated.

Methods 265 eyes of 265 subjects were included. According to spherical equivalent (SE) in diopters (D), participants were divided into four groups: low myopia/control group (SE: -0.50 to -3.00D), moderate myopia group (SE: -3.00 to -6.00D), high myopia group (SE: -6.00 to -10.00D) and severe myopia group (SE greater than -10.00D). Axial length (AL), anterior segment parameters, and corneal biomechanical properties were obtained with the Lenstar LS900, Pentacam HR and Corvis ST, respectively.

Results Mean (±SD) SE was -7.29±4.31D (range: -0.63 to -25.75D). Mean AL was 26.31±1.82mm (range: 21.87 to 31.94mm). Significant differences were detected within the four groups in terms of six corneal biomechanical parameters: deformation amplitude (DA), time from start until second applanation (A2-time), length of flattened cornea at the second applanation (A2-length), corneal velocity during the first and second applanation (A2-velocity), time from start to highest concavity (HC-time), and central curvature at highest concavity (HC radius). DA was positively correlated with AL (r =0.16, P =0.009) and negatively correlated with SE (r =-0.20, P =0.001). A2-time, A2-velocity, A2-length and HC-time were positively correlated with SE and negatively correlated with AL.

Conclusions The alterations in corneal biomechanics may be associated with the degree of myopia. DA and A2-velocity may be useful corneal biomechanical indicators in patients with myopia.

Introduction

Myopia is the most common ocular disease, affecting 70-80% of the population in many East Asian countries.[1–3] High myopia in Taiwan increased from 26% in 1988 to 40% in 2005.[4] Brien et al.[5] estimated that myopia and high myopia will influence nearly 5 billion people and 1 billion people, respectively, by 2050. More importantly, a series of complications such as glaucoma, cataract, myopic retinal degeneration and retinal detachment are associated with high myopia, some of which may eventually lead to blindness.[6, 7] High myopia is characterized by scleral thinning and a sclera that is
Whether or not similar biomechanical property alterations occur in the cornea of myopic eyes is still under debate. Assessment of the corneal biomechanical properties may be a way to understand the possible etiology of high myopia development, which is of great importance its prevention of development and progression.

Various studies have analyzed the influence of myopia on corneal biomechanics in vivo using the Ocular Response Analyzer (ORA), but their conclusions were not consistent. In addition, the ORA does not directly describe the mechanical behavior of cornea. McMonnies et al. also reported that the corneal hysteresis values from the ORA might not represent an unequivocal corneal property.

The development of the Corneal Visualization Scheimpflug Technology (Corvis ST, Oculus, Wetzlar, Germany), a relatively new noncontact tonometer combined with an ultra-high-speed Scheimpflug camera, makes it possible for us to intuitively assess the corneal deformation response during an air impulse indentation in vivo. Hon and Nemeth have investigated the repeatability and reproducibility of parameters provided by the Corvis ST. There were several studies focusing on the potential differences in corneal biomechanical parameters between myopia and emmetropia. Lee et al. indicated that there were significant differences in outward applanation velocity, peak distance and deformation amplitude in high myopia, low myopia and emmetropia. However, they did not take axial length (AL) into consideration. While Wang et al. suggested that there were significant differences between emmetropia, moderate myopia and high myopia in terms of deformation amplitude, first- and second-applanation time, and radius at highest concavity. However, Matalia et al. showed that cornea deformation parameters were unaffected by myopia. These studies did not investigate the correlation between the degree of myopia and the corneal biomechanical properties in severe myopia, which have an increasing risk of myopic complications and deserve more attention.

The purpose of our study was to investigate the relationship between corneal biomechanical properties and the degree of myopia using the Corvis ST in a large sample taking into consideration AL and anterior segment parameters.

Methods
Research was carried out in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Eye Hospital of Wenzhou Medical University. Informed consent was obtained from each subject before the examination. The study consisted of 265 eyes of 265 participants who presented to The Eye Hospital of Wenzhou Medical University preparing for refractive surgery or comprehensive optometry between January 2015 and December 2015. Subjects were excluded if they had a history of ocular surgery, any other ocular disease (e.g., corneal scaring, glaucoma and keratoconus) other than a refractive error. The exclusion criteria also included the presence of corticosteroid use, or systemic disease which could interfere with the eye such as diabetes mellitus and connective tissue diseases. Subjects who were pregnant or with astigmatism more than 3.0D were also excluded. Participants were required to stop wearing soft contact lens at least 2 weeks and rigid lens at least 1 month before measurements were acquired. Clinician excluded glaucoma according IOP (intraocular pressure), optic nerve head on fundus examination, mild keratoconus according to corneal topography, SE and age. Based on their spherical equivalent (SE), subjects were divided into four groups: low myopia group or control group (SE from −0.50 to -3.00D), moderate myopia group (SE from −3.00 to -6.00D), high myopia group (SE from −6.00 to -10.00D) and severe myopia group (SE greater than −10.00D). In this study, all subjects were axial myopia.

All participants who met the inclusion criteria were selected randomly and then received complete ophthalmic examinations including best visual acuity, subjective refraction, slit lamp microscope examination, fundus examination and measurements with the Pentacam HR (Oculus, Wetzlar, Germany), Lenstar LS900 (Haag-Streit AG, Koeniz, Switzerland), and Corvis ST (Oculus, Wetzlar, Germany). Only the right eye was measured to avoid the influence from high correlation between eyes. In cases were the right eye did not meet the inclusion criteria mentioned above, the left eye was included. All examinations were performed by an experienced ophthalmologist between 9:00AM and 5:00PM. The Corvis ST was the last device that was used, so as to eliminate the bias in corneal biomechanical variables caused by the air puff. All the instrument measurements were completed before pupil dilation. Three measurements with good quality were taken and the average value was used for statistical analysis.
The Pentacam is an comprehensive anterior segment tomographer [23, 24] and the Lenstar LS900 is an optical biometer [25, 26]. Corneal deformation parameters were obtained with the Corvis ST. The Corvis ST is a noncontact tonometer with an ultra-high-speed (4330 frames/s) Scheimpflug camera incorporated. It can dynamically record the deformation process of the cornea to an air impulse covering 8.0 mm. It automatically generates ten parameters: DA (maximum deformation amplitude at the highest concavity), A1-time and A2-time (time from start to the first and second applanation), A1-length and A2-length (length of flattened cornea at the first and second applanation), A1-velocity and A2-velocity (corneal velocity during the first and second applanation), HC-time (time from start to the highest concavity arrives), PD (distance between the two peaks of the cornea at highest concavity), HC radius (radius of curvature at highest concavity). Anterior segment parameters were measured with the Pentacam HR, including steepest keratometry (Ks), flattest keratometry (Kf), central corneal thickness (CCT), corneal volume (CV) and anterior chamber depth (ACD). AL was assessed with Lenstar LS900.

Statistical Analysis
Data were analyzed using SPSS software version 17.0. Normal distribution was assessed with the Kolmogorov–Smirnov test. The Pearson correlation coefficient was calculated to assess the correlations among ocular characteristics and corneal deformation parameters [27]. A one-way analysis of variance (ANOVA) and Fisher’s least significant difference t-test was used to analyze the differences in corneal biomechanical properties among the four groups. A P-value of < 0.05 was considered statistically significant.

Results
Participant demographics are displayed in Table 1. This study included 265 eyes of 265 Chinese participants (129 women and 136 men). Mean age was 27.02 ± 7.32 years (range: 18 to 52 years). Mean SE was −7.29 ± 4.31D (range: -0.63 to -25.75D). Mean AL was 26.31 ± 1.82 mm (range: 21.87 to 31.94 mm). There were significant differences among groups in terms of refractive error and AL (P < 0.001). No significant differences were found between groups for CCT, IOP and CV (P > 0.05). Though there was a significant difference in age among four groups (P < 0.05), the difference was
small. The one-sample Kolmogorov–Smirnov test showed that all data were normally distributed.

Table 1
Participant demographics

| Parameters         | Low myopia (n = 49) | Moderate myopia (n = 61) | High myopia (n = 91) | Severe myopia (n = 64) | P-value |
|--------------------|---------------------|-------------------------|----------------------|------------------------|---------|
| Age (years)        | 29.2 ± 8.85         | 24.58 ± 4.97            | 25.85 ± 5.98         | 29.34 ± 8.56           | < 0.05  |
| SE (D)             | -1.92 ± 0.72        | -4.64 ± 0.85            | -7.84 ± 1.04         | -13.14 ± 3.27          | < 0.001 |
| Kf (D)             | 42.87 ± 1.83        | 42.49 ± 1.16            | 42.87 ± 1.31         | 43.34 ± 1.41           | 0.007   |
| Ks (D)             | 43.85 ± 1.70        | 43.46 ± 1.23            | 44.02 ± 1.44         | 44.56 ± 1.41           | < 0.001 |
| CCT (μm)           | 537.22 ± 30.06      | 536.72 ± 32.95          | 538.92 ± 32.47       | 531.89 ± 31.72         | 0.599   |
| CV (mm^3)          | 60.12 ± 3.07        | 59.89 ± 3.49            | 60.57 ± 3.36         | 59.55 ± 3.42           | 0.291   |
| ACD (mm)           | 3.12 ± 0.38         | 3.37 ± 0.31             | 3.25 ± 0.30          | 3.19 ± 0.31            | < 0.001 |
| AL (mm)            | 24.61 ± 1.28        | 25.42 ± 1.09            | 26.36 ± 1.13         | 28.39 ± 1.52           | < 0.001 |
| IOP (mmHg)         | 12.91 ± 2.21        | 13.07 ± 1.86            | 13.40 ± 2.39         | 13.67 ± 2.43           | 0.262   |

SE: spherical equivalent; AL: axial length; Ks: steepest keratometry; Kf: flattest keratometry; CCT: central corneal thickness; CV: corneal volume; ACD: anterior chamber depth; AL: Axial length; IOP: intraocular pressure.

Six of ten parameters (DA, A2-time, A2-velocity, A2-length, HC-time and HC-radius), were significantly different among the four groups (Table 2). DA in the low, moderate, high and severe myopia groups were 1.14 ± 0.11, 1.12 ± 0.09, 1.13 ± 0.10 and 1.18 ± 0.12 mm, respectively. DA in the severe myopia group was significantly longer than in the low, moderate and high myopia group (P = 0.04, P = 0.001, P = 0.006, respectively). A2-time in the low myopia group was significantly longer than the severe and high myopia group (P = 0.001, P = 0.023, respectively). A2-velocity in severe myopia group was significantly greater than in the low, moderate and high myopia group (P < 0.001, P < 0.001, P = 0.008, respectively). A2-length in the high and severe myopia groups were significantly smaller than in the other two groups. HC-time in the low myopia group was significantly greater than in the moderate, high and severe myopia groups (P = 0.02, P = 0.005, P < 0.001, respectively). HC-radius in the severe myopia group was significantly smaller than in the high myopia group.
The correlation analysis is summarized in Table 3. It showed that DA was positively correlated with AL ($r = 0.16, P = 0.009$, Fig. 1) and age ($r = 0.33, P < 0.001$), and negatively correlated with SE ($r = -0.20, P = 0.001$, Fig. 2), CCT ($r = -0.40, P < 0.001$), CV ($r = -0.32, P < 0.001$) and IOP ($r = -0.78, P < 0.001$). A2-time was positively correlated with SE ($r = 0.20, P = 0.001$) and negatively correlated with AL ($r = -0.20, P = 0.001$), CCT ($r = -0.21, P = 0.001$) and IOP ($r = -0.75, P < 0.001$). A2-velocity was positively correlated with SE ($r = 0.33, P < 0.001$, Fig. 3), CCT ($r = 0.37, P < 0.001$), CV ($r = 0.32, P < 0.001$) and IOP ($r = 0.56, P < 0.001$) and negatively correlated with AL ($r = -0.20, P = 0.001$, Fig. 4). A2-length was positively correlated with SE ($r = 0.25, P < 0.001$), CCT ($r = 0.38, P < 0.001$), CV ($r = 0.32, P < 0.001$) and IOP ($r = 0.28, P = 0.001$) and negatively correlated with AL ($r = -0.19, P = 0.002$) and Ks ($r = -0.20, P = 0.001$). HC-time was positively correlated with SE ($r = 0.24, P < 0.001$) and negatively correlated with AL ($r = -0.22, P < 0.001$) and ACD ($r = -0.23, P < 0.001$). HC-radius was positively correlated with CCT ($r = 0.37, P < 0.001$), CV ($r = 0.28, P < 0.001$) and IOP ($r = 0.45, P < 0.001$).
Table 3

| Parameters     | DA      | A2-time | A2-length | A2-velocity | HC-time | HC radius |
|----------------|---------|---------|-----------|-------------|---------|-----------|
| Age (years)    | 0.33(P < 0.001) | 0.17(P = 0.006) | -0.13(P = 0.041) | -0.06(P = 0.355) | 0.12(P = 0.056) | -0.10(P = 0.090) |
| SE (D)         | -0.20(P = 0.001) | 0.20(P = 0.001) | 0.25(P < 0.001) | 0.33(P < 0.001) | 0.24(P < 0.001) | -0.00(P = 0.967) |
| Kf (D)         | 0.17(P = 0.007) | 0.06(P = 0.360) | 0.18(P = 0.003) | 0.13(P = 0.039) | 0.13(P = 0.037) | -0.12(P = 0.06)  |
| Ks (D)         | 0.16(P = 0.009) | 0.02(P = 0.806) | 0.20(P = 0.001) | -0.16(P = 0.007) | 0.06(P = 0.346) | -0.14(P = 0.021) |
| CCT (mm)       | -0.40(P < 0.001) | -0.21(P = 0.001) | 0.38(P < 0.001) | 0.37(P < 0.001) | 0.09(P = 0.152) | 0.37(P < 0.001)  |
| CV (mm³)       | -0.32(P < 0.001) | 0.14(P = 0.27) | 0.32(P < 0.001) | 0.32(P < 0.001) | 0.11(P = 0.07) | 0.28(P < 0.001)  |
| ACD (mm)       | -0.10(P = 0.091) | -0.06(P = 0.344) | -0.06(P = 0.343) | -0.08(P = 0.171) | -0.23(P < 0.001) | -0.05(P = 0.425) |
| AL (mm)        | 0.16(P = 0.009) | -0.20(P = 0.001) | -0.19(P = 0.002) | -0.20(P = 0.001) | -0.22(P < 0.001) | 0.06(P = 0.316)  |
| IOP (mmHg)     | -0.78(P < 0.001) | -0.75(P < 0.001) | 0.28(P < 0.001) | 0.56(P < 0.001) | -0.04(P = 0.536) | 0.45(P < 0.001)  |

SE: spherical equivalent; AL: axial length; Ks: steepest keratometry; Kf: flattest keratometry; CCT: central corneal thickness; CV: corneal volume; ACD: anterior chamber depth; AL: Axial length; IOP: intraocular pressure.

Discussion

The present study aimed to assess the corneal biomechanics in eyes with different degrees of myopia, especially the severe myopic eyes, using the Corvis ST with a large sample size. In the current prospective study, we found that the severe myopia group had a significantly longer DA than the low, moderate and high myopia group. Moreover, DA was significantly negatively correlated with SE (r=-0.20, P = 0.001) and positively correlated with AL (r = 0.16, P = 0.009). DA is the deformation amplitude at highest concavity and is regarded as a surrogate for corneal stiffness.[18, 21, 28] A higher DA value would represent a softer cornea due to a lower resistance to deformation.[28, 29]

Our findings showed that the higher the degree of myopia or the longer the axial length, the softer of the cornea is, which is consistent with previous studies.[20, 21, 30–33] But Miki et al.[33] did not divide subjects into different groups according to SE or AL with relatively few participants. On the other hand, our research focus on corneal biomechanical properties in severe myopia in a large number of samples with rigorous screening criteria. Xiang et al.[34] suggested that eye elongates particularly fast before the onset of myopia. It’s conceivable that changes of corneal and scleral biomechanics precede the occurrence of myopia. But our data does not prove whether the corneal biomechanical properties changed already before the eye becomes myopic. In clinical practice, if a larger DA indicates a greater risk of axial elongation, preventive methods can be considered. Further,
assessment of corneal biomechanics may also be crucial for surgical planning (and preoperative screening) to reduce the risk of corneal ectasia after refractive surgery.

A2-velocity in the severe myopia group was significantly greater than in the other three groups. A2-time in the high and moderate group was significantly shorter than in the low myopia group. The severe and high myopia groups had a smaller A2-length than other groups. These findings are not in line with those from Wang et al.[21], their study did not show the difference of A2-velocity between groups. Another study, consistent with our results, showed high myopia had greater A2-velocity compared to either low to moderate myopia or emmetropia using the Corvis ST.[20] A2-time, A2-length and A2-velocity were significantly positively correlated with SE and negatively correlated with AL, this agreed with the ANOVA in the present study. A previous study found that A2-time may be an indicator of the total viscoelasticity of the cornea.[35] The higher the degree or the longer the AL of the myopic eye, the less time is needed to go back to the origin after applanation as its viscoelasticity increased. In a recent research,[36] myopia had greater A2-velocity indicating that cornea tends to be more deformable and softer than the emmetropia and hyperopia in children. Therefore, A2-velocity may be another indicator of corneal elasticity, as Lee et al.[20] and Miki et al.[33] suggested, which indicated that less viscous damping capacity was seen in eyes with a longer axial length. Further research about the use of A2-velocity is warranted.

In accordance with a previous study by Wang et al.[21], we found that the HC radius was significantly smaller in eyes with severe myopia than high myopia. Frings et al.[37] demonstrated that in eye following corneal refractive surgery, there was a tendency to have a smaller radius at highest concavity. In other words, the softer the cornea, the easier it is to deform, resulting in a smaller HC-radius. In addition, our findings showed that the other factors, which were age, IOP, CCT and CV, may be potential factors influencing corneal deformation. We found that the cornea becomes softer with longer DA values with increasing age, in agreement with previous studies.[21, 38] However, others supported a view that the cornea becomes stiffer in elderly individuals because of more glycation-induced cross-linking.[39, 40] The relatively narrow range of age in this study may be a reason for the conflicting results. Further study is required to determine the influence of age on corneal
biomechanics. The central corneal thickness might be associated with corneal deformation with thinner corneas representing higher corneal deformation,[18, 41] which is consistent with the findings in the present study. Our correlation analysis showed a lower IOP was associated with less stiffness of the cornea with a larger DA (r=-0.78, P < 0.001). This phenomenon was in accordance with previous studies.[33] Alonso et al. indicated that the variation in corneal deformation may depend on the IOP rather than simply affected by the corneal structure.[42] Tian et al. also found that DA was negatively correlated with IOP in both primary open-angle glaucoma (POAG) and normal eyes.[43] In other words, we should take the corneal biomechanical into consideration when it comes to the accurate measurement of IOP.

It has been suggested that myopic eyes have a lower ocular rigidity than emmetropic eyes,[8, 9] and the diameter of collagen fiber bundles of sclera in highly myopic eyes is less and the sclera is significantly thinner.[44, 45] Less of proteoglycan and glycosaminoglycan synthesis[46–48] and a reduction in the extracellular matrix[49] may explain the remodeling of the sclera during the development of myopia. In this way, the scleral mechanical properties weaken[45] whilst the deformability increases.[50] Since the corneal stroma is the continuation of the sclera,[45] the expansion of the sclera may result in the reduction of corneal stiffness. Recently, translating the unique scleral features into measurable corneal biomechanical properties in myopic eyes has received great attention. If a change in corneal biomechanical properties potentially indicate a risk for myopia development, such measurements may become clinically useful in the management of myopia. On the other hand, various studies have demonstrated that corneal refractive surgery may change corneal biomechanics,[31, 37, 51–53] which can lead to iatrogenic keratectasia.[54] Therefore, a better understanding of the biomechanical characteristics of the cornea is of great importance in the field of corneal refractive surgery.[55]

The main limitations of our study are as follows: first, we did not assess corneal deformation in emmetropia. Second, a longitudinal study is required to clarify whether the parameters of corneal biomechanical properties, such as DA and A2-velocity, can be indicators of myopia progression and axial elongation. Whether changes in corneal biomechanics is the consequence or the cause of
myopia development requires further longitudinal study to investigate.

In conclusion, the myopic eyes with a greater degree and longer AL exhibited longer DA and A2-velocity under stress, suggesting that the cornea in higher myopia tends to be more elastic and deformable. Further research is warranted in this field as this may have clinical significance the management of high myopia and also in the refractive surgery field.

Abbreviations
Corvis ST
Corneal visualization scheimpflug technology
SE
Spherical equivalent
AL
Axial length
DA
Deformation amplitude
A2-time
Time from start until second applanation
A2-length
Length of flattened cornea at the second applanation
A2-velocity
Corneal velocity during the first and second applanation
HC-time
Time from start to highest concavity
HC radius
Central curvature at highest concavity ().
ORA
Ocular Response Analyzer ()
Ks
Steepest keratometry
Kf
Flattest keratometry
CCT
Central corneal thickness
CV
Corneal volume
ACD
Anterior chamber depth
IOP
Intraocular pressure

Declarations
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Figures

Figure 1

The Pearson correlation between deformation amplitude (DA) and axial length (AL).
Figure 2

The Pearson correlation between deformation amplitude (DA) and spherical equivalent (SE).
Figure 3

The Pearson correlation between corneal velocity during the second applanation moment (Vout) and spherical equivalent (SE).
Figure 4

The Pearson correlation between corneal velocity during the second applanation moment (Vout) and axial length (AL).