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The Relationship between Corneal Biomechanics and Corneal Shape in Normal Myopic Eyes

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Abstract

Objectives: To investigate the possible association between corneal biomechanical parameters and morphological properties in a normal myopic population.

Methods and patients: The study consisted of 480 normal myopic eyes (240 healthy volunteers), with ages ranging from 18 to 44 years (mean, std 23.84 ± 5.08 years), and mean spherical equivalent (MSE) ranging from -14.00 to -1.13 D (mean, std –5.68 ± 2.17 D). Corneal hysteresis (CH) and corneal resistance factor (CRF) were measured using the Ocular Response Analyser (ORA; Reichert Ophthalmic Instruments, Depew, New York, USA) in both eyes. Pentacam (Oculus GmbH, Wetzlar, Germany, and software version 1.17r27) were used to obtain corneal central elevation and corneal asphericity (Q value within 6 mm diameters) of both anterior and posterior surfaces, corneal central thickness (CCT), corneal volume (CV) and corneal spherical aberration values. Corneal volume was calculated within diameters from 1.0 to 6.0 mm with 0.5 mm steps centered on the apex to create the corneal-volume distribution. Pearson correlation coefficient was used for analysis on relationships between CH, CRF and Pentacam parameters (CV, elevation, Q-value, spherical aberrations, et al).

Result: The values of CH and CRF presented normal distribution and the mean CH was (10.38 ± 1.36) mmHg, and the mean CRF was (10.70 ± 1.59) mmHg. There is a good correlation between CH, CRF and CCT (CH: r=0.54, *P*=0.000*, CRF: r=0.61, *P*=0.000*), and a stable correlation with each CV value (r≈0.5, *P*=0.000*) within central 6 mm diameter corneal region. On the other hand, CH and CRF were negatively correlated with anterior central elevation (CH: r=-0.136*, *P*=0.002*; CRF: r=-0.152*, *P* =0.001*), positively correlated with Q value of anterior surface (CH: r=0.136*, *P*=0.002; CRF: r=0.132*, *P*=0.003) and corneal spherical aberration (CH: r=0.184*, *P*=0.000*; CRF: r=0.191*, *P* =0.000*).

Conclusions: There is a homogeneous relationship displayed between corneal biomechanical parameters (CH and CRF) and corneal morphological features. Our results suggest high biomechanical values might be related to central flattening and oblate corneal shape.

Keywords: Corneal biomechanics; Ocular response analyzer; Corneal morphology

Introduction

In a broad review, evidence that the corneal biomechanical properties influence the results and outcomes of various ocular measurements and procedures has existed for some time [1,2]. However, assessing the biomechanical properties of corneal tissue *in vivo* has previously not been possible. With the recent introduction of the Reichert Ocular Response Analyzer (ORA), direct clinical measurements of the corneal biomechanical response are now available and provide novel ways for the preoperative screening of refractive surgery candidates. The ORA uses a high-speed air puff to deform the cornea and records two corneal biomechanical metrics termed corneal hysteresis (CH) and corneal resistance factor (CRF). CH may predominantly reflect the viscous properties [3], whereas CRF is thought to reflect overall viscoelastic resistance of the cornea [4].

The ORA has been widely used to study corneal biomechanical properties [5-7], and it has been suggested that different clinical conditions would affect corneal biomechanical properties, such as the decrease in CH with keratoconus and corneal surgeries [8]. Meanwhile, more recently published studies have set out to discover the exact clinical features and value of CH and CRF as corneal biomechanical metrics [9,10]. Recently, it has been reported that CRF strongly correlates with corneal spherical-like aberrations, especially in severe keratoconus, which implies it should be considered an additional factor in keratoconus grading [11]. Additionally, it is well known that keratoconus is an ectatic disease of the cornea, with progressive thinning and anterior protrusion, eventually leads to an irregular conical alteration of the corneal shape. Using this information, the corneal biomechanical properties showed corresponding relationship with spherical aberrations in keratoconus patients, to a large degree might be related to its corneal shape variation based on the natural property of keratoconus disease. Because of this, in this study, the main purpose was to collect normative ORA data in normal myopic subjects and to evaluate the relationship between corneal morphological features and ORA-generated corneal biomechanical properties, in order to explore the potential clinical correlation of ORA-generated corneal biomechanical metrics.

Methods

Subjects

The study was performed with the approval by the Institutional

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Review Board at Tianjin Medical University School of Medicine and met the tenets of the Declaration of Helsinki. Informed consent was obtained from each subject. 240 healthy volunteers (60 males and 180 females) were recruited at random from refractive surgery candidates of Tianjin eye hospital, Tianjin medical university. Subjects were evaluated sequentially from October 2009 through March 2010.

Each subject underwent a comprehensive ophthalmologic examination, which included a medical history review, best corrected visual acuity, refraction test, slit-lamp and fundoscopic examinations, Pentacam topographic evaluation (Oculus, Wetzlar, Germany), and ORA measurements (Reichert Ophthalmic Instruments). All eyes of the participants were examined by one of the investigators (Lili Xie). Exclusion criteria included unstable refraction, evidence of keratoconus on topography, any history of systemic or ocular disease, previous ocular surgery, systemic or ocular medications, pregnancy, and an immunocompromised state. Soft contact lenses were removed 2 weeks before these measurements and hard contact lenses, at least 3 weeks before.

Ocular response analyzer (ORA) measurement

The ORA (Reichert Ophthalmic Instruments, Depew, New York, USA) is a new device, which measures the corneal response to indentation by a rapid air pulse. The ORA produces two measurements of corneal biomechanical properties, corneal hysteresis (CH) and the corneal resistance factor (CRF). The corneal hysteresis phenomenon is a result of viscoelastic dampening in the cornea, in other words, the tissue's ability to absorb and dissipate energy. Corneal resistance factor, CRF, maximizes the correlation to CCT reflecting the overall biomechanical strength of the cornea is regarded as an optimized corneal biomechanical parameter.

CH and CRF were measured with ORA between 10 AM and 4 PM, for each of these examinations at least four successive measurements were performed on each eye, all of which showed symmetric peak heights and similar widths. The final values of these parameters were calculated as the average of the saved measurements.

Pentacam scheimpflug evaluation

All subjects were imaged with the Pentacam HR (Oculus GmbH, Wetzlar, Germany, software version 1.17r27) in both eyes. The Pentacam is a rotating Scheimpflug camera that measures 138,000 true elevation points to compute corneal topography. Patients were asked to blink twice and then look at the fixation device. Image acquisition was a 2-second scan of 50 rotational Scheimpflug images through the corneal sighting point, the point where the ray of light from the fovea to the fixation device crossed the cornea. All measurements were performed just after a blink to minimize the effect of tear film alteration on the data. Acceptable maps had at least 10.0 mm of corneal coverage with no extrapolated data in the central 9.0 mm zone.

The Pentacam software calculates the corneal volume contained within different diameters centered on the apex. In present study, corneal volume was selected within diameters from 1.0 to 6.0 mm with 0.5 mm steps.

Statistical analysis

Statistical analysis was performed using the software SPSS version 13.0 for Windows (SPSS, Chicago, Illinois, USA). Descriptive statistical results included mean, standard deviation, minimum, and maximum values. Normality of all data samples was checked by means of Kolmogorov-Smirnov Test. Pearson bivariate correlation statistical analysis was used to obtain the linear fit of the relationship between variables. Statistical significance was set at a level of 0.05.

Results

Subjects

The study consisted of 480 normal myopic eyes (240 healthy volunteers), with ages ranging from 18 to 44 years (mean, std 23.84 ± 5.08 years), and mean spherical equivalent (MSE) ranging from -14.00 to -1.13 D (mean, std –5.68 ± 2.17 D) (Table 1).

Mean normative CH and CRF

Table 2 and Figure 1 show the values of CH and CRF presented normal distribution and the mean CH was (10.38 ± 1.36) mmHg, and the mean CRF was (10.70 ± 1.59) mmHg in this studied normal Chinese myopic population.

Correlations of biomechanical parameters with CCT, age and refractive errors

Figure 2 shows the corneal biomechanical parameters (CH, CRF) as a function of corneal central thickness in the study eyes. In present study, the values of corneal central thickness are sub-divided into the four CCT groups, the mean value of CH and CRF in the Table 3. With CH and CRF increasing gradually with CCT, this also has been reflected by the statistical result on the relationship between corneal biomechanical parameters and corneal central thickness (CH: r=0.54*, *P*=0.000*; CRF: r=0.61*, *P*=0.000*). However, no statistical significant correlation was found between CH, CRF and age, spherical equivalent, cylinder equivalent, and mean refractive spherical equivalent.

Correlations of biomechanical parameters with CV

The corneal volume distribution at the different diameters (from 1.0 to 6.0 mm with 0.5 mm steps) is shown in Figure 3. As can be seen in the box plot profile, CV in normal myopic eyes shows a homogeneous increase from center to periphery. In addition, the Pearson correlational analysis on the relationship between CV and CH (Table 4), CRF display a significant and positive correlation along all selected diameters zones, Taken a step further, CV presents a stable and homogeneous correlation with corneal biomechanical properties (r≈0.5, *P*=0.000*) within the central 6.0 mm diameter corneal zone.

Gender (%) **Age (y)** **Mean Spherical Equivalent (D)**	**Male (25%)** **23.84 ± 5.08** **-5.68 ± 2.17**	**Female (75%)** **18-44** **-14.00-1.13**

Table 1: Demographics of the study population.

	Mean ± SD	**Range**
CH (mmHg)	10.38 ± 1.36	6.30-19.23
CRF (mmHg)	10.70 ± 1.59	5.57-19.47

Table 2: The mean value and range of corneal hysteresis (CH) and the corneal resistance factor (CRF) in normal myopic eyes.

Group(Number of eyes)	**CH (mmHg)**	**CRF (mmHg)**
<500 µm (63)	8.90 ± 1.06	8.62 ± 1.16
500-550 µm (202)	10.12 ± 1.13	10.39 ± 1.33
551-600 µm (179)	11.14 ± 1.15	11.68 ± 1.17
>600 µm (36)	12.18 ± 2.11	13.06 ± 1.87

Table 3: Distribution of CH and CRF in different CCT groups.

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Corneal Volume	CH		CRF	
	r	*P*	r	*P*
CV (1.0 mm)	0.513*	0.000*	0.588*	0.000*
CV (1.5 mm)	0.535*	0.000*	0.588*	0.000*
CV (2.0 mm)	0.534*	0.000*	0.585*	0.000*
CV (2.5 mm)	0.560*	0.000*	0.615*	0.000*
CV (3.0 mm)	0.557*	0.000*	0.604*	0.000*
CV (3.5 mm)	0.558*	0.000*	0.603*	0.000*
CV (4.0 mm)	0.565*	0.000*	0.603*	0.000*
CV (4.5 mm)	0.570*	0.000*	0.602*	0.000*
CV (5.0 mm)	0.574*	0.000*	0.598*	0.000*
CV (5.5 mm)	0.575*	0.000*	0.588*	0.000*
CV (6.0 mm)	0.580*	0.000*	0.585*	0.000*

CH: Corneal Hysteresis; CRF: Corneal Resistance Factor
*denotes statistically significant (*P* <0.05) predictor coefficients

Table 4: Pearson Correlation Analysis on the relationship between CV and CH, CRF.

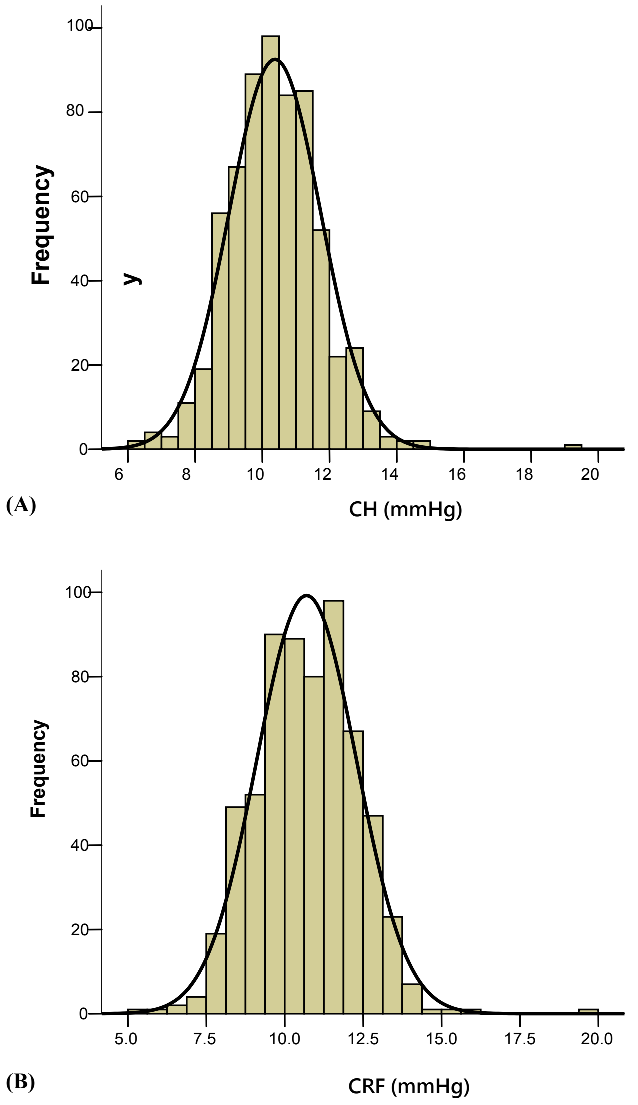


Figure 1: Histogram of CH (A) and CRF (B) distribution in normal myopic eyes.

Correlations of biomechanical parameters with morphological parameters

As can be seen in Table 5, CH and CRF were correlated with central corneal elevation of anterior surface (CH: r=-0.136*, P=0.002*; CRF:

Morphological Index	CH		CRF	
	r	*P*	r	*P*
Central elevation (anterior)	-0.136*	0.002*	-0.152*	0.001*
Central elevation (posterior)	-0.014	0.748	0.082	0.068
Q value (anterior)	0.136*	0.002*	0.132*	0.003*
Q value (posterior)	0.015	0.731	-0.095*	0.034*
Corneal spherical aberration	0.184*	0.000*	0.191*	0.000*

CH: Corneal Hysteresis; CRF: Corneal Resistance Factor
*denotes statistically significant (*P* <0.05) predictor coefficients

Table 5: Pearson Correlation Analysis on the relationship between corneal morphological parameters and CH, CRF.

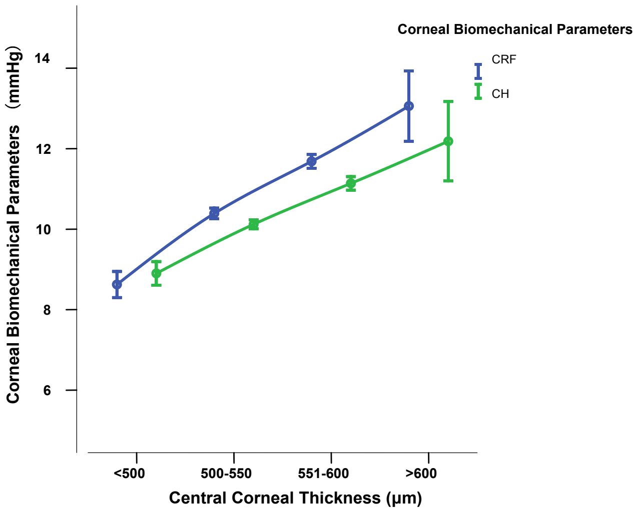


Figure 2: The distribution of CH and CRF in different CCT groups.

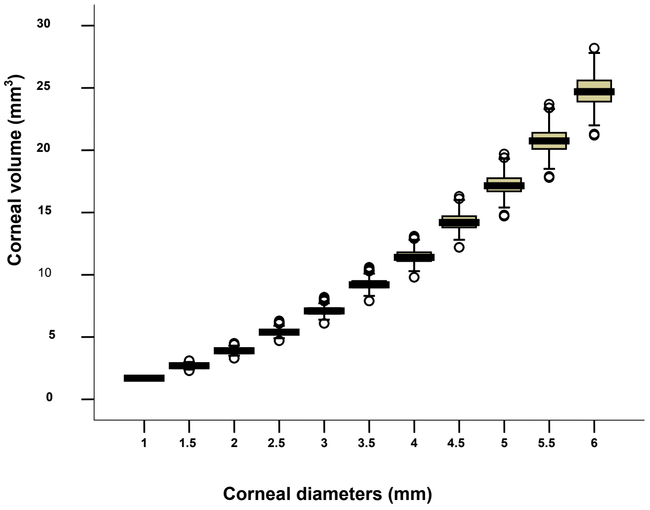
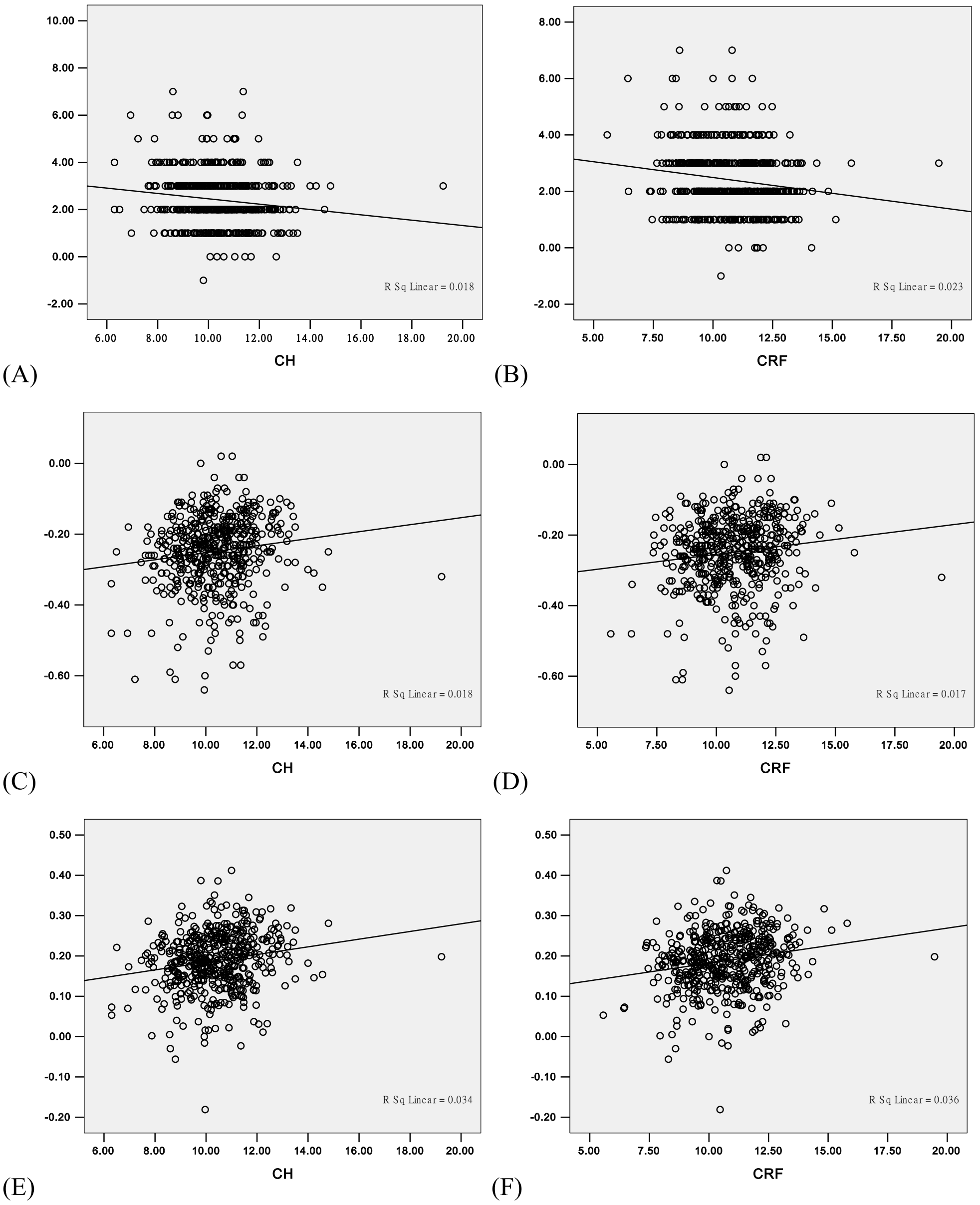


Figure 3: Box plot showing Corneal Volume (CV) distribution within the different diameter discs centered on the apex.

r=-0.152*, *P*=0.001*) and Q value of anterior surface (CH: r=0.136*, P=0.002*; CRF: r=0.132*, *P*=0.003*), positively with corneal spherical aberration (CH: r=0.184*, P=0.000*; CRF: r=0.191*, *P*=0.000*). However, no significant correlations are found between CH, CRF and corneal morphological index on posterior corneal surface. The correlations between corneal biomechanical parameters (CH, CRF) and corneal anterior central elevation value, Q value and spherical aberration are also shown in Figure 4.

Discussion

In present study, we collected normative ORA data from 240 healthy volunteers (480 eyes), and the normative data for CH and CRF were consistent with other reports based on healthy eyes. As can be seen in Table 6, it details the normative ORA data reported during these years. Generally, both mean CH and CRF ranged between 9.0 and 11.0 mm Hg, which is broadly in agreement with the data from our study population.



A) Linear regression relating CH to corneal anterior elevation, (*r* =-0.136, *P*=0.002*)
B) Linear regression relating CRF to corneal anterior elevation, (*r*=-0.152, *P*=0.001*)
C) Linear regression relating CH to corneal Q value (anterior), (*r*=0.136, *P*=0.002*)
D) Linear regression relating CRF to corneal Q value (anterior), (*r*= 0.132, *P*=0.003*)
E) Linear regression relating CH to corneal spherical aberration, (*r*=0.184, *P*=0.000*)
F) Linear regression relating CRF to corneal spherical aberration, (*r*= 0.191, *P*=0.000*)

Figure 4: Scatter plot of relationship between corneal biomechanical parameters (CH, CRF) and corneal anterior central elevation value, Q value and spherical aberration.

Source	**Subjects (eyes)**	**CH (mmHg)**		**CRF (mmHg)**	
		Mean ± SD	Range	Mean ± SD	Range
Luce [12]	339	9.6			
Shah et al. [13]	207	10.7 ± 2.0	6.1 to 17.6	10.3 ± 2.0	5.7 to 17.1
Hager et al. [14]	156	10.6 ± 2.3		10.9 ± 2.4	
Shah et al. [15]	207	10.7 ± 2.0	6.1 to 17.6		
Ortiz et al. [16]	164	10.8 ± 1.5		11.0 ± 1.6	
Kynigopoulos et al. [17]	49	10.68 ± 1.8	6.9 to 16.3	11.26 ± 1.79	7.4 to 16.3
Sullivan-Mee et al. [18]	71	10.2 ± 1.3			
Hurmeric et al. [19]	28	10.1 ± 1.3		10.1 ± 1.8	
Fontes et al. [20]	86	10.13 ± 1.75	5.95 to 14.58	10.06 ± 1.97	5.45 to 15.10
Detry-Morel et al. [21]	24	10.8 ± 1.8	7.5 to 14.5	11 ± 2	8.1 to 15.7
Plakitsi et al. [22]	99	10.4 ± 1.2		10.1 ± 1.5	
Present study	480	10.38 ± 1.36	6.30 to 19.23	10.70 ± 1.59	5.57 to 19.47

Table 6: literature review on normal value and range of corneal biomechanical parameters (CH, CRF).

Previous studies, including present study, indicate a strong positive relation between CRF and CH with CCT [23], however in agreement with earlier studies [24-26] that CH and CRF have been found no significant correlations with either age or the amount of myopia in present data. It has been suggested that even though CH is CCT independent, it was not associated with corneal swelling induced by soft contact lens wear [27], which may be indicative of an inherent biomechanical property.

In order to better understand the correlation between corneal biological feature and biomechanical metrics, we explored the analysis between corneal volume distribution and ORA metrics in this study. Corneal-volume distribution, which originates in 3-dimensional (3-D) reconstruction of the cornea, opens new horizons to evaluate corneal structural and biological features and has been of great utility in clinical practice [28,29]. Using the information from corneal-volume, Ambrósio et al. [29] found significant differences in corneal-volume distribution and percentage increase in volume between keratoconic and normal corneas and suggested it could serve as indices to diagnose keratoconus and screen refractive candidates. Recently, Mannion et al. [30] reported that corneal volume showed decreased in keratoconus, especially in central area, which has confirmed its clinical value. Corneal volume as a new parameter showed stable moderate correlations with ORA-generated biomechanical metrics in this study. The observed similarities of correlations with CV in all the selected corneal zones might be associated with the microscopic structure of stromal lamellar organization [30], and Hurmeric V et al. [19] has confirmed a significant relationship between CRF and keratocyte density in their confocal microscopy (CM) study. Taking all the above-mention correlations into the comprehensive consideration, it supposedly takes into account the biomechanical properties of the cornea and has been adjusted not only for central corneal thickness but also for corneal volume distributions, which enables better understanding on correlations of ORA-generated parameters with corneal structural and biological properties.

It is evident from previous corneal mechanical study that corneal shape may be a passive consequence of several forces involving intraocular pressure (IOP) [31] and cohesive forces between lamellae [32]. Any changes in morphology of cornea often reflect their biomechanical variation and physiological status. Therefore, the shape of the cornea is not random but a function of the corneal structure, material properties, and biomechanical properties of the corneal tissue [33]. In the present study, the corneal biomechanical parameters (CH and CRF) showed a negative correlation with anterior central elevation, a positive correlation with Q value and a positive correlation with corneal spherical aberrations, respectively.

With regards to elevation, it can be expressed in micrometers as the height of the actual surface relative to a chosen reference surface (best-fit-sphere, BFS), which has led to a better understanding of the surface since created from the x, y, and z coordinates of the usual representation of data in a 3-D world [34]. Based on present results, a low CH value could be associated with a high central anterior elevation, which means, the higher or steeper the central corneal surface exhibits, the lower corneal biomechanical properties might be. On the other hand, there is a trend toward positive correlation between CH, CRF and Q value with a weak positive r value (CH: r=0.136*, P=0.002*; CRF: r=0.132*, P=0.003*). As is well known, most of the normal human corneal contour is close to aspheric and prolate shape (flattening of the radius of curvature from the apex toward the periphery), and mostly modeled by Q value [35]. When Q is negative, the surface is prolate; whereas, Q value towards positive, it indicates the surface becomes more oblate, flattening from periphery to center [36]. The aforementioned relationship between CH, CRF and Q value, showed that a more oblate (positive Q value) corneal surface would be more likely to have higher corneal biomechanical values, which, in turn, from the viewpoint of corneal structural stability, oblate corneal shape takes some superiority.

Moreover, the current study was also undertaken to evaluate the correlation of optical properties of the cornea, CH and CRF displayed significant positive correlations with corneal spherical aberration values. This result coincides with that in other previous study [9], which has showed CRF strongly correlates with corneal spherical-like aberrations in keratoconus patients. However, this time the relationship has been found in normal population, and thus corneal biomechanical parameters might be considered as a new indicator for screening candidates for refractive surgery. In summation, all these correlations between corneal morphological parameters and corneal biomechanical metrics strengthen the same interaction, that the more oblate the central anterior corneal surface exhibits, corresponding to the higher spherical aberration values, the higher corneal biomechanical properties have. Actually, it is understandable that higher corneal biomechanical properties [37] would be more effective to avoid ectasia and contribute to a much more stable corneal shape.

In this study, we have investigated the relationship between corneal biomechanical properties and corneal shape in healthy volunteers, and to a certain extent, some distinctive characteristic of corneal shape may possess higher biomechanical properties. Further work, including population and longitudinal studies, are required to determine the clinical role of corneal biomechanics as independent predictors of corneal ectasia or keratoconus susceptibility.

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