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Original article

Corneal biomechanics in normal Saudi individuals

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Abstract

Purpose: The aim of this study was to determine and relate corneal biomechanical metrics with demographic, tomographic and refractive data in healthy Saudi people.
Design: Prospective, cross-sectional, observational study.
Participants: The study included 215 normal Saudi adult individuals.
Methods: Corneal hysteresis (CH) and corneal resistance factor (CRF), Goldmann-correlated intraocular pressure (IOPg) and corneal-compensated intraocular pressure (IOPcc) were measured by ocular response analyzer. The central keratometry (CK), central corneal thickness (CCT), and anterior chamber depth (ACD) were measured using Pentacam system. The spherical equivalent of refraction (SER) was obtained by an Auto-refractometer.
Results: The mean CH was 11.16 ± 2.11, CRF was 11.07 ± 2.31 and IOP was 15.12 ± 3.5. Mean CK, ACD, CH and CRF were distinct among gender with the significant *P* values of 0.05, 0.006, 0.020, and 0.047 respectively. CRF was negatively correlated with ACD ($r = -0.146$, $P = 0.032$). A positive correlation was found between CRF and SER ($r = 0.176$, $P = 0.010$), CCT ($r = 0.447$, $p = 0.000$) and CH ($r = 0.878$ and $p = 0.000$). CH was negatively correlated with IOPcc (-0.433, $p = 0.000$). A positive correlation was found between CH and ACD ($r = -0.14$, $p = 0.044$), SER ($r = 0.617$, $p = 0.014$), CCT ($r = 0.412$, $p = 0.000$) and IOPg ($r = 0.183$, $p = 0.007$).
Conclusion: This study demonstrated a distinct difference among gender values of corneal hysteresis and corneal resistance factor being higher in female Saudi subjects. CH and CRF values were higher in Saudi subjects than values in other populations. This may suggest the presence of ethnic differences in ocular parameters and support the importance of establishing population norms for corneal biomechanical parameters.

Keywords: Corneal resistance factor, Corneal hysteresis, Corneal biomechanics, Anterior chamber depth, Central corneal thickness

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Introduction

Studying corneal biomechanics is a growing science that attracted attention of researchers in the last decade. Ophthalmologists have been trying to set parameters to help improve the evaluation of both diagnostic and prognostic measures especially in the field of corneal ectasia prediction, refractive surgery and glaucoma. Successful corneal treatments depend on interactions between biological and biomechanical factors and their impact on surrounding ocular tissues.

The introduction of the Ocular Response Analyzer (ORA; Reichert Ophthalmic Instruments, Depew, NY) by Luce in 2005, who was the first to report in vivo corneal biomechanics evaluation, allowed direct clinical assessment

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of the biomechanical properties of the cornea.[1,2] The availability of ORA led to a progressive gain of attention from the ophthalmic society.

The ORA depends on ability of the cornea to regain its shape after exposure to stress by applying a force via a jet of air and recording the behavior of corneal tissue. Corneal biomechanical parameters measured by ORA include corneal hysteresis (CH) and corneal resistance factor (CRF), and non-contact intraocular pressures such as the Goldmann-correlated intraocular pressure (IOPg) and corneal-compensated intraocular pressure (IOPcc). Hysteresis can be defined as a measure of the energy absorption during the stress–strain cycle of viscoelastic materials.[3] Corneal hysteresis (CH) is calculated as the difference in air pressures between force-in applanation (P1) and force-out applanation (P2), or (P1–P2). Corneal hysteresis corresponds to the ocular resistance due to the combined effect of various parameters such as central corneal thickness (CCT) and viscoelastic properties. These parameters can also be affected by hydration, connective tissue composition, age and regional pachymetry.[4] It has been shown that corneal hysteresis is lower in keratoconus, Fuchs' dystrophy, glaucoma patients, and after refractive surgery.[5–8] Measurement of CH provides a complete characterization of the contribution of corneal resistance to intraocular pressure measurements than central corneal thickness (CCT) alone. CRF is a measurement of corneal resistance that is relatively independent of IOP. Thus, corneal hysteresis reflects the corneal viscous property and corneal resistance factor represents corneal elastic property.

Refractive surgeons and glaucoma specialists are the most to benefit from corneal biomechanical measurements. Moreover, clinical approach toward the patient's diagnosis and management may be customized by corneal biomechanical metrics results. ORA capacity to measure these parameters shows good reproducibility and clinical reliability.[9]

Both corneal hysteresis and corneal resistance factor have been studied in healthy individuals of different ethnic origins; with variable values being reported.[10–12] In healthy Japanese subjects[10] CH was 10.2 ± 1.3 mmHg, Brazilian[11] CH was 10.17 ± 1.82, and CRF was 10.14 ± 1.8 and Chinese subjects[12] had CH of 10.6 and CRF 10.1 mmHg. Leite et al.[13] reported that healthy black subjects in a US population had even lower CH and CRF compared with white subjects, although the differences were not significant. To our knowledge, no study has been published on the measurement of corneal biomechanics in normal eyes of Saudi individuals. Such a study will be a good reference for normal data of the Saudi population.

The aim of this study was to assess, determine and relate corneal biomechanical metrics (CH and CRF including IOP measurements) with demographic, tomographic and refractive data in healthy Saudi people. We have intended to correlate CCT and IOPg to CH in Saudi subjects.

Material and methods

This is an observational, cross-sectional study. It has been approved by Ethical Committee in Dhahran Eye Specialist Hospital (DESH) in August 2010 and the Medical Research Review Board in September 2010. The study adheres to the tenets of the Declaration of Helsinki.

Two hundred and fifteen, healthy Saudi volunteers were sequentially recruited from October 2010 to November 2013. All participants had no ophthalmic diseases other than refractive errors. They were informed about the purpose of the study.

Demographic and clinical data were obtained including age and gender. Each subject underwent a comprehensive ophthalmologic examination including review of medical history, best spectacle-corrected visual acuity, slit-lamp microscopy, Goldmann applanation tonometry measurements (IOPg), fundoscopic examination, Pentacam tomographic evaluation and ORA measurements.

Exclusion criteria were age under 18 years, previous corneal or ocular surgery, eye disease (e.g. glaucoma, uveitis, corneal ectatic disease, Fuchs' dystrophy, and diabetic retinopathy) use of topical drugs, corneal scars and/or opacities, irregular astigmatism, any systemic disease and contact lens wearers.

Participants undertook testing with the ORA and Pentacam by trained optometrists and an ophthalmologist during the same visit. All measurements were taken between 4 p.m. and 9 p.m. Three consecutive ORA measurements were done on both eyes and results were averaged.

Spherical equivalent refraction (SER) was obtained by an Auto-refractometer. Central keratometry (average central K), central corneal thickness (CCT), and anterior chamber depth (ACD) were calculated by Pentacam. The Pentacam (Oculus Inc., Wetzlar, Germany) is connected to a personal computer, with automated program. The system uses two rotating Scheimpflug cameras and a monochromatic slit light source (blue LED at 475 nm) that rotate together. After appropriate alignment of the participant's face, a fixation object is shown that guides the participant's look. A real-time image of the participant's eye is shown to the examiner on the computer screen and the image is focused and centered manually. The rotating camera was set to take 25 slit images of the anterior eye segment in around 2 s with 500 true elevation points integrated in each slit image. The minimal eye movements were caught by a second camera and corrected accordingly. A single point of pachymetry reading of the entire cornea is measured from the calculated front and back corneal surfaces. The CCT, average central K, and ACD are measured in each of the single images of a scan.

The ORA determines corneal biomechanical properties using an applied force–displacement relationship. It records corneal inward and outward locomotion after delivery of a metered collimated air pulse, determining its viscoelastic properties. Hysteresis is a measurement of the energy absorption during the stress–strain cycle of viscoelastic materials. A precisely metered air pulse is delivered to the eye leading the cornea to move inward, past a first applanation, and into a slight concavity. Milliseconds after the first applanation, the air pump is shut down and the pressure applied to the eye decreases in an inverse-time, symmetrical fashion. As the pressure declines, the cornea undergoes a second applanation state while returning from concavity to its normal convex curvature. Energy absorption during fast corneal deformation delays the inward and outward applanation signal peaks, resulting in a difference between the applanation pressures. The difference between the inward and outward pressures is called corneal hysteresis (Fig. 1). CH reflects the capability of corneal tissue to absorb and disperse

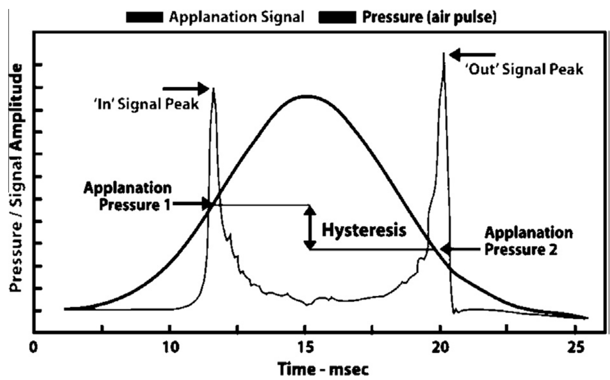

Figure 1. Pressure–applanation plot generated by ocular response analyzer.

energy. Corneal resistance factor was derived to maximize correlation to CCT.

The statistical method used for analysis was the ANOVA test that determines the *P* value of clinical significance ($p < 0.05$). The coefficient correlation was calculated using Spearman's rank correlation.

Results

This is an observational cross-sectional study done on 215 Saudi participants, 82 were females and 133 were males. Mean age of the participants was 33.6 ± 11.75 years. Demographic characteristics of participants are shown in Table 1.

Mean CK, ACD, CH and CRF were distinct among gender with the significant *P* values of 0.05, 0.006, 0.020, and 0.047 respectively, which are presented in Table 2 and Fig. 2 that show plots of CH in relation to gender.

CRF was negatively correlated with ACD ($p = 0.032$). A positive correlation was found between CRF and SER, CCT, and CH with p values of 0.010, 0.000, and 0.000 respectively as shown in Table 3.

CH was negatively correlated with IOPcc ($p = 0.000$). No significant correlation was found between CH and CK ($P = 0.339$). A positive correlation was found between CH and ACD, SER, CCT and IOPg with significant *P* values of 0.044, 0.014, 0.000, and 0.007 respectively as demonstrated in Table 4.

Table 1. Demographic characteristics of 215 Saudi participants.

Characteristics	Mean ± SD
Age (y)	33.6 ± 11.75
CKR (D)	43.2 ± 1.40
CCT (μm)	551.8 ± 32.87
ACD (mm)	2.96 ± 0.34
SER (D)	−0.77 ± 1.97
CH	11.16 ± 2.11
CRF	11.07 ± 2.31
IOP	15.12 ± 3.5

Discussion

The current study aimed to measure corneal biomechanics in Saudi population and to correlate central corneal thickness CCT and Goldmann applanation IOP to CH. We found a distinct difference among gender regarding CH and CRF values, which agrees with the similar, gender-related variation reported by Fontes et al.[11] though they concluded that their findings may be related to the increased female proportion in their sample. Narayanaswamy et al.[12] in a population-based, cross-sectional study found women to have greater CH and CRF than men.

The mean CH and CRF values in our study sample of Saudi subjects were 11.16 and 11.07 mmHg, respectively. A linear relationship between CH and CRF is found as demonstrated in Fig. 3. Lower mean values have been reported in studies involving healthy Japanese subjects[10] as CH was 10.2 ± 1.3 mmHg, in Brazilian subject[11] CH was 10.17 ± 1.82 and CRF was 10.14 ± 1.8 and in Chinese subjects[12] CH was 10.6 and CRF was 10.1 mmHg. Leite et al.[13] reported that healthy black subjects in a US population had even lower CH and CRF compared with white subjects, although the differences were not significant. This difference between previously reported CH and CRF and our sample may suggest the presence of ethnic differences in ocular parameters. This

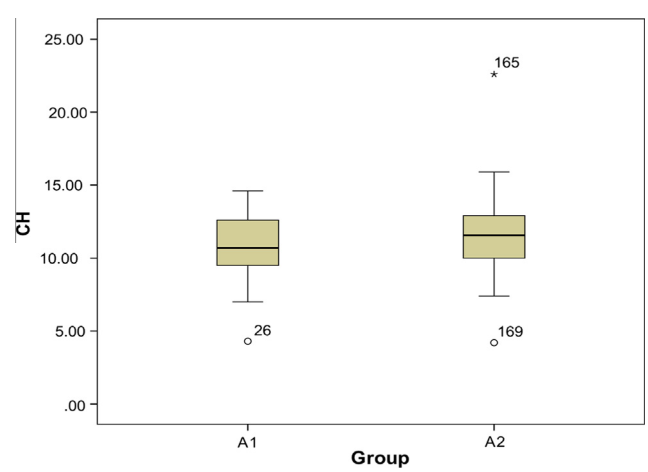

Figure 2. Box-and-whisker plots for corneal hysteresis averages with gender (A1 Males, A2 Females).

Table 2. Comparison of the corneal biomechanical metrics between males and females.

Corneal biomechanical metrics	Males (Mean ± SD)	Female (Mean ± SD)	*P* value	95% CI
CKR (D)	43.03 ± 1.43	43.43 ± 1.52	0.057*	−0.80110 to 0.01194
CCT (μm)	551.15 ± 31.9	552.85 ± 34.48	0.714	−10.81303 to 7.42150
ACD (mm)	3.034 ± 0.34	2.901 ± 0.32	0.006*	0.03843 to 0.22698
SER (D)	−0.831 ± 2.12	−0.710 ± 1.844	0.670	−0.68208 to 0.43928
CH	10.90 ± 1.90	11.59 ± 2.35	0.020*	−1.26583 to −0.10864
CRF	10.83 ± 2.18	11.47 ± 2.48	0.047*	−1.28104 to −0.00738
IOP	15.50 ± 3.87	16.67 ± 12.92	0.328	−3.53712 to 1.18590

* *P* value < 0.05 is taken as statistically significant.

Table 3. Correlation of CRF with various corneal biomechanical metrics.

Corneal biomechanical metrics	*r* value	*P* value	Correlation
ACD (mm)	−0.146	0.032*	Negatively correlated
SER (D)	0.176	0.010*	Positively correlated
CCT (μm)	0.447	0.000*	Positively correlated
CH	0.878	0.000*	Positively correlated

* *P* value < 0.05 is taken as statistically significant.

Table 4. Correlation of CH with various corneal biomechanical Metrics.

Corneal biomechanical metrics	*r* value	*P* value	Correlation
ACD (mm)	−0.140	0.044*	Negatively correlated
SER (D)	0.617	0.014*	Positively correlated
CCT (μm)	0.412	0.000*	Positively correlated
CK	−0.058	0.339	No correlation
IOPcc	−0.433	0.000*	Negatively correlated
IOPg	0.183	0.007*	Positively correlated

* *P* value < 0.05 is taken as statistically significant.

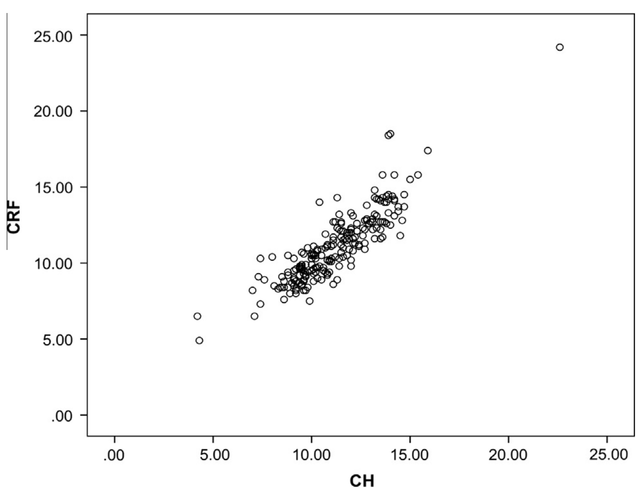

Figure 3. Scatterplot of relationship between CRF and CH (positively correlated).

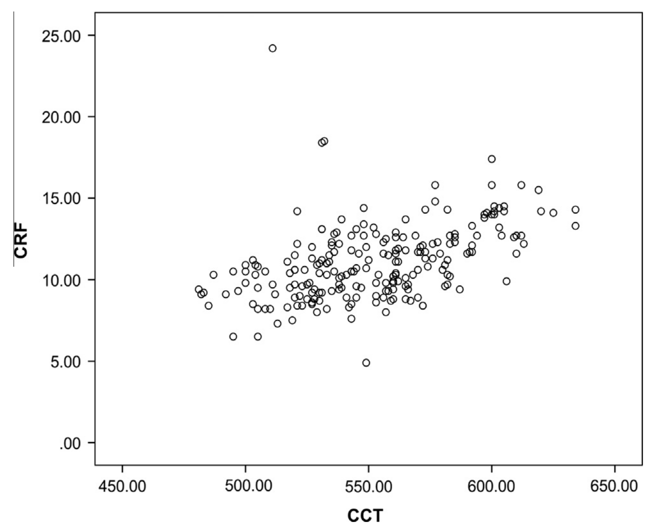

Figure 4. Scatterplot of relationship between CRF and CCT (positively correlated).

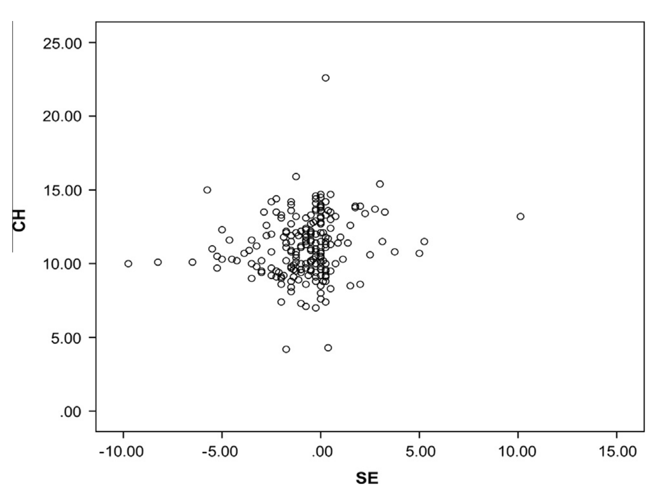

Figure 5. Scatterplot of relationship between CH and SE (positively correlated).

would also support the importance of establishing population norms for corneal biomechanical parameters.

A positive correlation between CH and CCT (Fig. 4) and between CRF, CCT and CH was observed in our study. These findings can be explained by the influence of the CCT on the corneal rigidity. The correlation between CH and CCT has been evaluated previously in normal eyes and a positive correlation has been demonstrated by Lam et al.[14] and Shah et al.[15]. Broman et al.[3] also demonstrated that CH was correlated with CCT in patients at the glaucoma clinic.

The positive correlation between CH/CRF and SER in our study indicates higher CH/CRF with hyperopic shift of refraction and vice versa with myopia. Similar findings by Chang et al.[16] showed lower CH and CRF in eyes with longer axial length. The reduced CH in myopic eyes might represent a primary alteration of the corneal collagen properties that make these eyes more susceptible to the expansive force of the normal IOP. Furthermore, we noted a negative correlation of CH/CRF with the anterior chamber depth (a lower CH/CRF was associated with deeper ACD) (Fig. 5). While the literature provides conflicting evidence of correlation between ACD and CH and/or CRF both studies by Narayanaswamy et al.[12] and Chang et al.[16] found a negative correlation of ACD with CH but no significant correlation with CRF. In a later study Hwang et al.[17] did not establish significant correlations between ACD and CH and CRF. The reduced CH in myopic eyes and the negative correlation of CH/CRF and ACD suggest a possible role for CH/CRF measurement in the prediction of biometric alteration in high myopic eyes.

In conclusion, this study which included 215 normal Saudi adult individuals demonstrated a distinct difference among gender values of CH and CRF that were higher in females. CH and CRF values were higher in Saudi subjects than values in other populations. This would suggest the presence of ethnic differences in ocular parameters and support the importance of establishing population norms for corneal biomechanical parameters. SER, ACD, CCT and IOPg seem to be relevant parameters to define the corneal stiffness and corneal viscoelastic properties and further evaluation of their impact on outcomes of refractive surgery needs to be clarified in the future.

While our study had a few number of volunteers, a larger number of individuals are needed to have a good reference data to corneal biomechanical metrics for our region. Although our data agree with the previous studies published, further studies are recommended.

Conflict of interest

The authors declared that there is no conflict of interest.

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