Diabetes Mellitus: Evaluation of Cornea Biomechanics with Corvis-ST

Amir masood Rafie manzelat (am_rafiemanzelat@yahoo.com)
Isfahan University of Medical Sciences https://orcid.org/0000-0002-4263-2474
Farzaneh Dehghanian Nasrabadi
Iran University of Medical Sciences: Tehran University of Medical Sciences
Ebrahim jafarzadehpour
Iran University of Medical Sciences: Tehran University of Medical Sciences
Alireza Peyman
Isfahan University of Medical Sciences

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Abstract

Objective: We conducted the present work to evaluate cornea biomechanics, using Corvis-ST device parameters amongst patients with diabetes mellitus.

Methods: In this cross-sectional study, 62 type II diabetic patients and 28 non-diabetic individuals were recruited. Following slit-lamp examination, the participants were further assessed and compared with Corvis-ST device (OCULUS Germany) in order to evaluate the cornea biomechanical response.

Result: The Applanation 2 Velocity variable was significantly different between the diabetic and non-diabetic patients (-0.3±0.04, respectively) (P value=0.02).

Conclusion: This study revealed an increased corneal biomechanical strength amongst diabetic patients.

Introduction :

Diabetes mellitus (DM) is a well-known cause of vision alteration, affecting nearly 240 million people worldwide.[1] Studies have revealed that DM might be able to change ocular tissues, including cornea, lens, optic nerve, and other features.[2] The effect of diabetes mellitus on ocular surface can reduce endothelial cell density and percentage of hexagonal cells, reduced sub-basal nerve density and reduced corneal sensitivity. DM cause delay in cornea wound healing, alteration in stability and production of the tear film, edema, and recurrent erosion, which could influence a patient's vision quality.[3–5] DM can even increase central corneal thickness and affect intraocular pressure measures. [6]

An approach to investigating the mechanical function of the cornea is to measure its biomechanical behavior. [7] Cornea is a viscoelastic tissue. Viscoelasticity represents resistance against deformation. Viscosity shows the resistance against force and elasticity demonstrates the returning of the tissue to the original shape after removing the applied force.[8] These features lead into deformation, which could be reversible by time. Each corneal layer is of a specific role in this process depending on various factors, collagen's density and orientation for instance. [9] Researchers have investigated this feature under various conditions and diseases (such as glaucoma, dry eye, keratoconus), ageing, refractive surgery candidates, myopes, and emmetropes. [3] Comparing biomechanical behavior of cornea between older and younger ages, demonstrated a correlation between this feature and subjects' intraocular pressure regardless of the age.[10]

The biomechanical characteristic of cornea can help diagnose ocular diseases, such as glaucoma, ectasia, and keratoconus.[11] The first non-contact device that measured cornea biomechanics was the Ocular Response Analyzer (ORA). This device utilizes air puff and measures Intraocular pressure (IOP), corneal hysteresis (CH), and Corneal Resistance Factor (CRF).[12] Corneal hysteresis (CH) and Cornea resistance factor are indicative of cornea's viscosity and resistance, respectively. (4) Previous studies have measured the biomechanical response in DM with ORA and found an increase in CH and CRF.[13]

Corvis ST (CST) is a novel non-contact device that can evaluate the biomechanical properties of cornea, based on the dynamic changes of the cornea, employing high-speed Scheimpflug-camera. It has been proven that this device can measure intraocular pressure (IOP)[8], central corneal thickness (CCT), Deformation amplitude (DA) with acceptable accuracy, repeatability, and reproducibility. Corvis can help us screen the ketratoconic corneas using shape and biomechanical variables [14]. This device utilizes high-speed cameras to record 4330 images per second to depict the cornea's deflection response against pressure from a tiny air puff jet. The outputs from the device are time and length of the flattened cornea in the first and second applanation (A1&A2 time (ms) and A1&A2 length (mm)); corneal velocity during the first and second applanation (A1&A2 velocity (m/s)); time from the start until the highest concavity of cornea (HC-time (ms)); maximum deformation amplitude at the corneal apex(DA).[15]

Measuring the impact of DM on the cornea biomechanics using Corvis ST has recently attracted a great deal of scientific attention. In previous studies, researchers measured cornea biomechanics in diabetic patients and compared ORA to Corvis. They showed that DM could alter the parameters of each device. [16] In current study, we compared the data that was provided by Corvis-ST between diabetic and non-diabetic patients.

Materials And Method:

In this cross-sectional study, we assessed 28 diabetic patients vs. 62 non-diabetic control participants. All diabetic patients had type II diabetes, and were being treated with either oral medication or insulin. Inclusion criteria were intra-ocular pressure < 21 mmHg with applantation tonometry, best-corrected visual acuity (BCVA) of 20/40 or better, and refractive error of < 5 diopters of spherical equivalent and less than 3 diopters of astigmatism. History of the corneal disorder or systemic collagen diseases, wearing contact lens within 2 weeks prior to their enrollment in the study, irregular astigmatism, prior refractive surgery or any ocular surgery, glaucoma and/or chronic use of topical IOP-lowering medication were considered as exclusion criteria. The sampling method was simple and non-random. After explaining the study objectives the participants signed the written informed consent form.

Patients were examined, the visual acuity was measured with the best function recorded on Snellen acuity chart at 6 meters. Topcon KR800 automatic refractometer, refined by manual retinoscopy and subjective phoropter refraction, were used to assess the patients' refraction. After ophthalmic slit lamp biomicroscopy, corneal biomechanical evaluation was performed, using the OCULUS Corvis-ST device.

The OCULUS Corvis-ST device provides measures on corneal biomechanical response, using a high-speed Scheimpflug camera. This camera captures 4330 images of the air hitting the cornea in 1 second, with a light source of 455 nm wavelength. A 25 kPa pressure is forced on the cornea surface and is imaged in 30 milliseconds.

During the evaluation, the following parameters are measured by Corvis-ST:

1. Deformation amplitude (DA)- Maximum amplitude at the highest concavity

2. A1 length (mm)- Length of the flattened cornea at the first applanation
3. A2 length (mm)- Length of the flattened cornea at the second applanation
4. A1 velocity (m/s)- Speed of the corneal apex at the first applanation
5. A2 velocity (m/s)- Speed of the corneal apex at the second applanation
6. Highest concavity-time (HC-time) (ms)- Time from the start until HC is reached
7. Peak distance (PD) (mm)- Distance between the two peaks of the cornea at HC
8. SPA 1: stiffness parameter at first applanation 1
9. ARTH: Ambrosio relational thickness to the horizontal profile
10. CBI: Corvis biomechanical index
11. integrR: integrated radius

Statistical analysis:

SPSS 20 was used to perform the analysis. Kolmogorov-Smirnov test confirmed the normal distribution. To compensate for inter-ocular symmetry in each individual, for variables that did not prove to have a normal distribution, the marginal model of the Generalized Estimating Equation (GEE) and for variables with a normal distribution, linear mixed-effects model (MIXED) was used. Considering that the data in the present study had correlation (due to the measurement of patients' right and left eyes).

Results:

Table 1
depicts the normality of the variables determining the specific statistical test. The variables with a significant P value had normal distribution.

Parameter	P-value	Parameter	P-value
Age	0.001	**SPA**	0.2
Refraction	0.2	**ARTH**	0.001
years of diabetes	0.2	**DA ratio**	< 0.0001
IOP	0.06	**Integr R**	0.01
Applanation 1 Lenghth	0.03	**CBI**	< 0.0001
Applanation 2 Lenghth	0.004	**Highest Concavity**	0.2
Applanation 1 Velocity	< 0.0001	**DA**	0.2
Applanation 2 Velocity	0.2	**PD**	0.2
Thickness	0.04		

Table 1 **examining the normality of data**

The next table we performed the marginal model of the Generalized Estimating Equation (GEE) compensate for variables that did not prove to have a normal distribution, and for variables with a normal distribution, linear mixed-effects model (MIXED). Considering that, the data in the present study had correlation (due to the measurement of patients' right and left eyes).Table 2

Table 2
use of MIXED and GEE model

Parameter	Diabetes group (n = 62)	Control group (n = 28)	P-value
Sex			0.4***
Male	24(38.7)	8(28.6)	
Female	38(61.3)	20(71.4)	
Age	59.8 ± 9.3	36.6 ± 4.5	< 0.0001***
Refraction	-0.8 ± 1.7	-1.1 ± 0.7	0.2+
years of diabetes	8.5 ± 3.5	0	-
IOP	17.1 ± 3.3	16.4 ± 2.6	0.8**
Thickness	520.2 ± 32.3	531.9 ± 29.5	0.4*
Applanation 1 Lenghth	2.3 ± 0.3	2.3 ± 0.3	0.5*
Applanation 2 Lenghth	1.6 ± 0.5	1.7 ± 0.4	0.8*
Applanation 1 Velocity	0.1 ± 0.04	0.1 ± 0.02	0.6*
Applanation 2 Velocity	-0.3 ± 0.04	-0.3 ± 0.04	0.1**
Highest Concavity	7.8 ± 1.2	7.7 ± 0.6	0.7**
DA	1.07 ± 0.1	1.03 ± 0.08	0.4**
PD	4.9 ± 0.3	4.9 ± 0.2	0.4**
SPA	108.6 ± 17.7	101.9 ± 15.2	0.6**
ARTH	486 ± 162.8	485.3 ± 81.3	0.7*
DA ratio	4.2 ± 0.6	4.2 ± 0.4	0.02*
Integr R	7.1 ± 1.2	7.4 ± 0.9	0.5*
CBI	0.1 ± 0.3	0.09 ± 0.2	0.2*

Considering IOP, gender, age, and CCT as confounders, our results indicated that Applanation 2 Velocity was significantly different between the two groups at -0.3 ± 0.04 (P value = 0.02). Hence, having diabetes affects the Applanation 2 Velocity. Other Corvis variables were of no significant differences between the two groups, which are represented in Table 3.

Table 3
results considering confounders

Parameter	Diabetes group (n = 62)	Control group (n = 28)	P-value
Sex			0.4***
Male	24(38.7)	8(28.6)	
Female	38(61.3)	20(71.4)	
Age	59.8 ± 9.3	36.6 ± 4.5	< 0.0001***
Refraction	-0.8 ± 1.7	-1.1 ± 0.7	0.2+
years of diabetes	8.5 ± 3.5	0	-
IOP	17.1 ± 3.3	16.4 ± 2.6	0.3+
Thickness	520.2 ± 32.3	531.9 ± 29.5	0.1***
Applanation 1 Lenghth	2.3 ± 0.3	2.3 ± 0.3	0.2*
Applanation 2 Lenghth	1.6 ± 0.5	1.7 ± 0.4	0.4*
Applanation 1 Velocity	0.1 ± 0.04	0.1 ± 0.02	0.4*
Applanation 2 Velocity	-0.3 ± 0.04	-0.3 ± 0.04	0.02**
Highest Concavity	7.8 ± 1.2	7.7 ± 0.6	0.5**
DA	1.07 ± 0.1	1.03 ± 0.08	0.3**
PD	4.9 ± 0.3	4.9 ± 0.2	0.3**
SPA	108.6 ± 17.7	101.9 ± 15.2	0.8**
ARTH	486 ± 162.8	485.3 ± 81.3	0.9*
DA ratio	4.2 ± 0.6	4.2 ± 0.4	0.07*
Integr R	7.1 ± 1.2	7.4 ± 0.9	0.7*
CBI	0.1 ± 0.3	0.09 ± 0.2	0.2*

Discussions:

According to the obtained results, there was a significant difference concerning the biomechanical properties of the cornea, expressed as Applanation 2 Velocity, between the diabetic and non-diabetic patients, which was measured utilizing OCULUS Corvis-ST device.

Hun Lee et al. proved that corneal biomechanical parameters are correlated with IOP regardless of subjects' age. Therefore, after considering IOP and age as a confounder, we can assume that the

significant difference of Applanation 2 velocity between two groups is due to diabetes mellitus and age difference did not affected the outcome. [10]

AsLee R et al. reported that highly myopic eyes (spherical refractive error higher than − 6.0 D) have greater deformation amplitude. Hence, we chose to compare patients with lower rates of myopia to eliminate the effect of this confounder. [17]

Ying Hon and Andrew K.C. Lam found that CCT and DA were the most repeatable parameters measured with Corvis-ST. Our study detected no significant differences between the diabetic patients *and* non-diabetic ones with respect to DA (P-value:0.07) and CCT (P-value:0.1).[18] However, in order to validate this result, a higher number of diabetic patients are required to confirm our findings. Examining the thickness of cornea using confocal microscopy could also help to achieve better results with respect to the changes in the thickness and shape of the corneal cells in diabetic patients, which should be considered in future researches.

Although DA was not statistically significant between the two groups, the results of the diabetic patients were slightly higher than that of non-diabetic patients.

Increased AGE formation in the cornea is the leading reason for corneal changes. Perez-Rico C et al. proved that diabetes, specifically uncontrolled ones, is correlated with corneal changes from the AGE formation. The current study exhibited that in most Corvis ST parameters, particularly DA, A1, and A2 times and A1 and A2 velocity, there was a significant difference between the diabetic patients and non-diabetic patients. [19] Our study is in line with their findings, indicating that the A2 velocity was significantly different between the two groups.

Thomas A Fuchsluger et al. used Corvis-ST to compare healthy patients to patients with keratoconus eyes. They found that A2 velocity was a viable variable for this difference. [15] Similarly, we found that in this parameter, diabetic patients were significantly different compared to non-diabetic patients.

Furthermore, in Consuelo Perez-Rico's research, A2 velocity in diabetic and non-diabetic patients was significantly different, which confirms our results.

Conclusion:

In conclusion, A2 velocity was significantly different between the diabetic patients *and* non-diabetic patients, which is an indication of increased corneal biomechanics amongst diabetic patients. Researchers have proved that Corvis-ST parameters are correlated with IOP regardless of subjects' age. Therefore, after considering IOP and age as confounder, we can assume that the significant difference of Applanation 2 velocity between two groups is due to diabetes mellitus and age difference did not affected the outcome. The average age of the control group was lower than that of the diabetic patients, which is due to the prevalence of the type 2 diabetes in the elderly. The cornea's thickness and structure were almost the same in the two groups; hence, the amount of internal pressure in the eye, which is

confounded by the thickness of the cornea, did not significantly differ between the two groups. Therefore, it could be suggested that in order to obtain more accurate results in the future studies, researchers should evaluate corneal biomechanics among same age group. the number of samples in the two groups should be the same and the amount of corneal thickness should be performed employing other devices, such as confocal biomicroscope.

Declarations

Authors' contributions

All the authors contributed in the preparation of this article.

Declaration of Competing Interest

None declared.

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