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Corneal biomechanical responses detected using corvis st in primary open angle glaucoma and normal tension glaucoma

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Abstract

Structural differences have been reported between primary open angle glaucoma (POAG) and normal tension glaucoma (NTG), and biomechanical differences between POAG and NTG may account for why NTG patients are more vulnerable to lower intraocular pressure (IOP). This study compared the biomechanical properties of POAG and NTG patients using the Corvis scheimpflug technology (ST) non-contact Scheimpflug-based tonometer, and determined the factors associated with these properties.

In this retrospective cross-sectional study, 46 eyes with POAG, 54 eyes with NTG, and 61 control eyes were included. A non-contact Scheimpflug-based tonometer was used to examine and compare the corneal biomechanical responses in the POAG, NTG, and normal groups. We used univariate and multivariate regression analyses to determine the factors associated with the deformation amplitude in each group.

Baseline characteristics, including age, IOP, spherical equivalent, keratometry, axial length, and central corneal thickness, were similar among the 3 groups. Severity of glaucoma, as measured by mean deviation, was similar between POAG and NTG groups. Applanation 1 velocity and deformation amplitude were significantly smaller in POAG (0.13 ± 0.02 and 1.06 ± 0.14, respectively) than NTG (0.14 ± 0.01 and 1.13 ± 0.11, respectively) and normal groups (0.14 ± 0.02 and 1.13 ± 0.10, respectively). Radius of curvature was significantly larger in the POAG group compared to the normal group. In normal controls, IOP and keratometry were significant factors related to deformation amplitude. In POAG eyes, IOP was a statistically significant predictor of deformation amplitude. In NTG eyes, however, IOP , keratometry, and axial length were statistically significant predictors of deformation amplitude.

POAG eyes showed less deformable corneas compared to NTG and normal controls. IOP was significantly correlated with deformation amplitude in all groups. However, axial length was positively correlated with deformation amplitude only in NTG eyes. Characterization of the differences in biomechanical properties between POAG and NTG may contribute to a better understanding of the underlying pathophysiologies associated with these diseases.

Abbreviations: A1 = Applanation 1, CCT = central corneal thickness, IOP = intraocular pressure, NTG = normal tension glaucoma, ORA = ocular response analyzer, POAG = primary open angle glaucoma, RNFL = retinal nerve fiber layer.

Keywords: corneal biomechanics, normal-tension glaucoma, primary open-angle glaucoma

1. Introduction

Corneal biomechanical properties in glaucoma have attracted a great deal of attention because they may reflect the structural vulnerabilities associated with glaucoma, and hence provide valuable information regarding the pathophysiology of glaucoma.[1–5] The biomechanical properties of a tissue affect how it responds to stress, and may explain why some are more susceptible to glaucomatous damage than others. Sigal et al[6] showed that in stiff laminas, the sclera pulled the lamina taut as intraocular pressure (IOP) increased, whereas no such association was observed in the compliant lamina, and they speculated that the biomechanical and structural properties of the lamina cribrosa markedly influenced its response to variations in IOP.

The recent development of Corvis ST (Oculus, Wetzlar, Germany), a non-contact Scheimpflug-based tonometer, has enabled reliable in vivo measurement of corneal biomechanical properties,[7,8] and it has been shown to be capable of assessing the biomechanical properties in various ocular conditions, including post-refractive surgery,[7] keratoconus,[9,10] pseudoexfoliation,[11] and glaucoma.[11,12]

Primary open angle glaucoma (POAG) and normal tension glaucoma (NTG) are both progressive optic neuropathies that differ in definition only in the untreated IOPs: >21 mmHg in POAG and ≤ 21 mm Hg in NTG. Structural differences have been reported, such as thinner lamina cribrosa in NTG, and it is possible that biomechanical differences exist between POAG and NTG, which may account for why NTG patients are more vulnerable to lower IOP.[13]

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This study was performed to compare the biomechanical properties of POAG and NTG patients using the Corvis ST non-contact Scheimpflug-based tonometer, and to determine the factors associated with these properties.

2. Methods

This was a retrospective observational study performed at Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea. The study followed the tenets of the declaration of Helsinki for biomedical research and was approved by the Seoul St. Mary's Hospital Institutional Review Board. The study population consisted of 61 normal controls, 46 patients with POAG, and 54 patients with NTG. To fulfill the criteria for POAG or NTG, the patients had to have a normal anterior chamber on slit-lamp examination, open angle on gonioscopy, a glaucomatous optic disc (diffuse or focal thinning of the neuroretinal rim), and an abnormal visual field consistent with glaucoma confirmed by at least 2 reliable (fixation loss $<$ 20%, false-positive error $<$15%, and false-negative error $<$ 15%) visual field examinations. POAG patients had baseline IOP $>$21 mm Hg, and NTG patients had no recorded IOP $>$21 mm Hg. The normal control group included patients with no history of increased IOP or antiglaucomatous eye drops, non-glaucomatous optic nerve head, and no visible retinal nerve fiber layer (RNFL) defect, which were confirmed by 2 glaucoma experts (HLP and CKP). Patients were excluded if their cylinder correction was greater than 3 diopters or they had a history of any previous or current corneal disease, a history of ocular trauma or surgery, or previous refractive laser treatment. When both eyes were eligible for the study, 1 eye was randomly included in the analysis.

For each patient, a detailed review of ocular and medical histories, best-corrected visual acuity evaluation, IOP measurement with Goldmann applanation tonometry, Corvis ST measurement, dilated stereoscopic optic nerve head evaluation, stereoscopic optic disc photography, red-free RNFL photography (VX-10; Kowa Optimed, Tokyo, Japan), ultrasound pachymetry (Tomey Corporation, Nagoya, Japan) to measure the central corneal thickness (CCT), measurement of corneal curvature using an autorefractor (RK-5; Canon, Tokyo, Japan), axial length measurement, and achromatic automated perimetry using the 24-2 Swedish Interactive Threshold Algorithm (Humphrey Visual Field Analyzer; Carl Zeiss Meditec, Inc., Dublin, CA) were performed. IOP measurements with Goldmann applanation tonometry and Corvis ST were performed in random order. For each tonometer, the average of 3 measurements with a 3 to 5-minute interval between measurements was used for the analysis, and there was an interval of at least 30 minutes between tonometry.

2.1. Corvis ST measurements

The corneal biomechanical properties were obtained using Corvis ST (software ver. 1.2r1092; Oculus). First, the patient's cornea was centered appropriately (Fig. 1A), and then an air impulse at a pressure of 60 mm Hg was automatically emitted from the device from a distance of 11 mm. As the air impulse was emitted, the cornea moved inward through applanation (A1, Fig. 1B) or flattening of the cornea, into a concavity phase until reaching the highest degree of concavity (Fig. 1C). Then, the cornea returned gradually to its natural shape (Fig. 1E), passing through a second applanation (Fig. 1D). This deformation response of the central 8.5 mm of the cornea was recorded with an ultra-high-speed Scheimpflug camera, which takes 140 digital frames with a resolution of 640×480 pixels in 30 ms. IOP was measured based on time to A1. Corvis ST parameters are listed in Table 1.

2.2. Statistical analyses

To determine the significance of differences among groups, 1-way analysis of variance and Scheffé's multiple comparison were performed. To determine the factors associated with the deformation amplitude in each group, univariate and multivariate regression analyses were performed using SPSS (ver. 12.0.0 for Windows; SPSS Inc., Chicago, IL). In all analyses, $P < .05$ was taken to indicate statistical significance.

3. Results

A total of 161 patients (46 POAG, 54 NTG, and 61 normal controls) were included in the study. Age, IOP, spherical equivalent, keratometry, axial length, and CCT were similar among the POAG, NTG, and normal control groups. Severity of glaucoma, measured by mean deviation, was not significantly different between POAG and NTG patients (Table 1). A total of 32 and 38 patients in the POAG and NTG groups, respectively, used the prostaglandin analogues ($P = .930$). A1 velocity, radius of curvature, and deformation amplitude were significantly different among the 3 groups ($P = .007$, .032, and .010, respectively, Table 2). In post hoc analysis, A1 velocity was significantly lower in the POAG (0.13 ± 0.02 m/s) than the NTG (0.14 ± 0.01 m/s) and control groups (0.14 ± 0.02 m/s). The radius of curvature was significantly greater in the POAG (7.50 ± 0.99 mm) than in the control (6.99 ± 0.93 mm) group. In addition, deformation amplitude was significantly smaller in the POAG (1.06 ± 0.14 mm) than the normal (1.13 ± 0.10 mm) and NTG (1.13 ± 0.11 mm) groups.

Table 3 shows the results of univariate and multivariate regression analyses to determine the factors affecting the deformation amplitude of each group. Deformation amplitude in the normal control group was predicted by IOP ($P < .001$) and keratometry value ($P = .003$). In the POAG group, deformation was predicted by age ($P = .002$), IOP ($P < .001$), and mean deviation ($P = .001$) on univariate analysis and by IOP ($P < .001$) on multivariate analysis. In the NTG group, age ($P = .037$), IOP ($P < .001$), keratometry ($P = .007$), and axial length ($P = .048$) significantly affected deformation amplitude in both univariate and multivariate analyses.

4. Discussion

This study was performed to compare the corneal biomechanical factors between POAG and NTG eyes and to determine the associated factors. To the best of our knowledge, this is the first study to compare the biomechanical properties of the cornea with Corvis ST in patients with POAG and NTG.

Our study showed decreased deformation amplitude in POAG patients compared to NTG and normal controls (Table 2). Chronic elevation of IOP has been suggested to alter the biomechanical properties of ocular tissues, including the cornea. It has been reported that the optic nerve head is stiffened and less compliant in advanced glaucoma as a response to increased

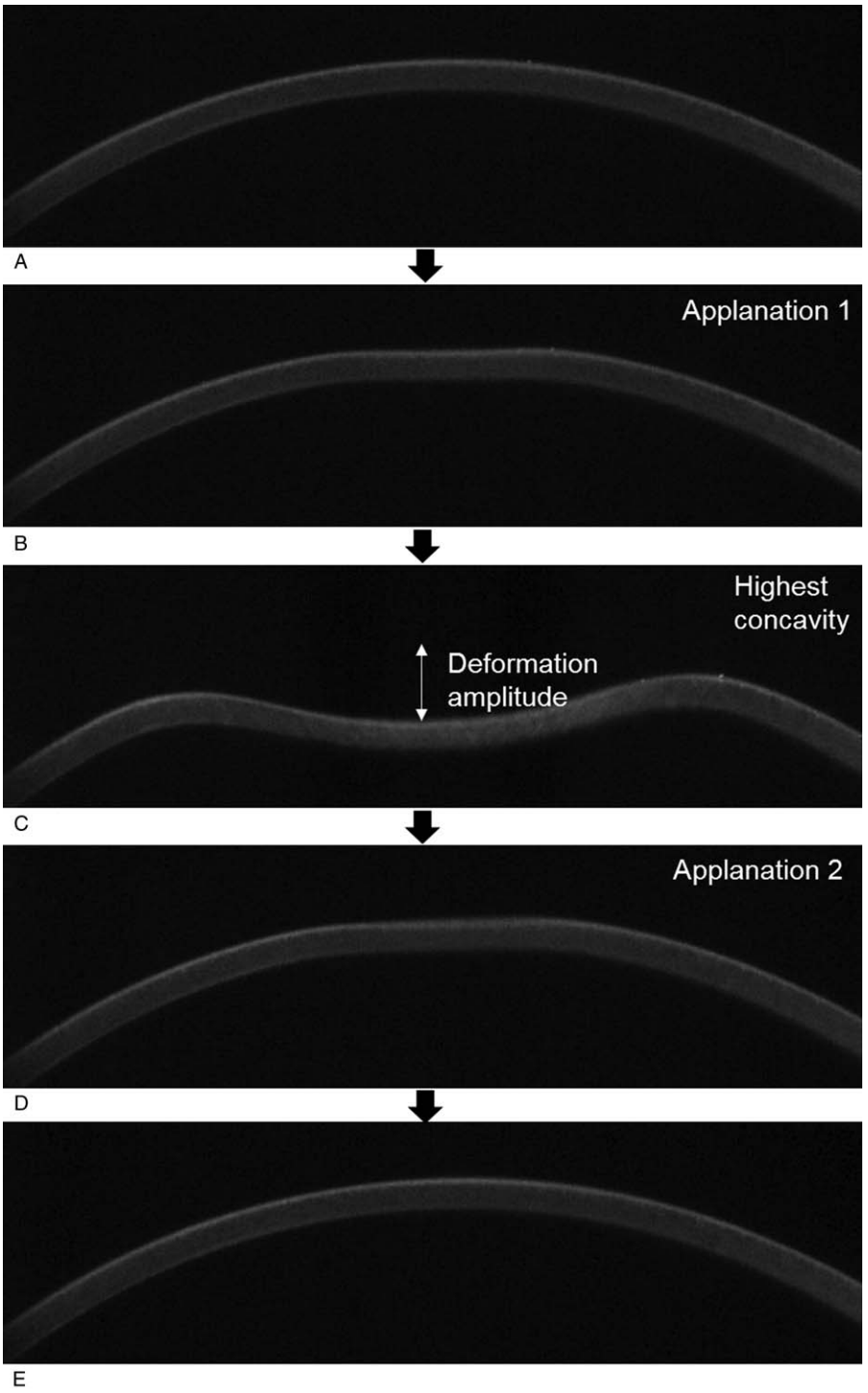

Figure 1. Corvis ST measurement. After centering the patient's cornea appropriately (A), an air impulse is emitted moving the cornea inward into applanation 1 (B). The cornea moves into a concavity phase reaching the highest concavity (C) at which point, the deformation amplitude is measured. Then the cornea passes through applanation 2 (D) then gradually returns to its natural shape (E).

IOP.[14,15] In POAG, chronic increases in IOP over a long period may have caused increased stiffening of the cornea, thus causing decreased deformation amplitude in POAG patients. Similar results have been reported by Ang et al[16] using the ocular response analyzer (ORA; Reichert Ophthalmic Instruments Inc., Depew, NY). In their study, POAG patients showed lower corneal hysteresis than NTG patients, suggesting altered corneal biomechanical properties in POAG patients.

If decreased deformation amplitude in POAG is the result of chronic IOP elevation in these patients, patients with advanced disease could be assumed to have smaller deformation amplitude. Interestingly, however, MD in POAG negatively predicted

Table 1

Baseline characteristics.

Baseline characteristic	Control (n = 61)	Glaucoma (*n* = 100)		*P*-value
		POAG (n = 46)	NTG (n = 54)	
Age, yr	56.19 ± 12.45	55.13 ± 15.65	57.77 ± 13.00	.481
Gender (male, %)	29 (47.5%)	25 (54.3%)	25 (46.3%)	.736
Intraocular pressure (mm Hg)	14.09 ± 2.33	14.71 ± 3.09	14.43 ± 1.75	.092
Spherical equivalent (D)	−1.43 ± 4.07	−2.11 ± 2.51	−2.17 ± 3.97	.506
Keratometry	44.29 ± 1.48	44.08 ± 1.67	43.67 ± 1.50	.108
Axial length (mm)	24.48 ± 1.93	24.58 ± 1.37	24.95 ± 1.83	.100
Central corneal thickness (μm)	540.07 ± 35.35	539.97 ± 30.82	534.20 ± 26.75	.644
Mean deviation (dB)	–	−5.21 ± 5.96	−4.96 ± 4.08	.652

Values are presented as means ± standard deviation.
NTG = normal tension glaucoma, POAG = primary open angle glaucoma.

Table 2

Corvis parameters in primary open angle glaucoma, normal tension glaucoma, and normal controls.

Corvis Parameter	Control (n = 61)	Glaucoma (n = 100)		*P*-value
		POAG (n = 46)	NTG (n = 54)	
Applanation 1				
Length (mm)	1.78 ± 0.43	1.77 ± 0.04	1.78 ± 0.06	.795
Velocity (m/s)	0.14 ± 0.02	0.13 ± 0.02[†,‡]	0.14 ± 0.01	.007[*]
Applanation 2				
Length (mm)	1.74 ± 0.31	1.73 ± 0.33	1.69 ± 0.32	.681
Velocity (m/s)	−0.35 ± 0.06	−0.34 ± 0.11	−0.36 ± 0.10	.586
Highest concavity				
Peak distance (mm)	4.03 ± 1.25	4.44 ± 1.10	4.12 ± 1.28	.214
Radius of Curvature (mm)	6.99 ± 0.93	7.50 ± 0.99[†]	7.28 ± 0.94	.032[*]
Deformation amplitude (mm)	1.13 ± 0.10	1.06 ± 0.14[†,‡]	1.13 ± 0.11	.010[*]

Values are presented as means ± standard deviation.
NTG = normal tension glaucoma, POAG = primary open angle glaucoma.
[*] $P < .05$ obtained via 1-way analysis of variance.
[†] $P < .05$ obtained via post hoc Scheffé's multiple comparisons between normal control and primary open angle glaucoma.
[‡] $P < .05$ obtained via post hoc Scheffé's multiple comparisons between primary open angle glaucoma and normal tension glaucoma.

deformation amplitude in the present study, indicating that more-advanced cases showed greater deformation amplitude (Table 3). This relationship was weak and not significant on multivariate analysis. It is difficult to explain why deformation amplitude is decreased in POAG compared to normal controls, but advanced POAG patients show greater deformation amplitude. Other factors may also have affected the corneal biomechanical properties in more-advanced POAG cases. One speculation is that the use of antiglaucomatous eye drops may have affected the biomechanical properties of the cornea, as other studies have reported altered biomechanical properties following use of antiglaucomatous medications.[17] Further research is warranted regarding the relationship between severity of glaucoma and biomechanical properties.

With regard to the factors that affect the deformation amplitude, IOP was a significant predictor of deformation amplitude in POAG, NTG, and normal controls, consistent with previous reports that IOP affects corneal deformation (Table 3).[9] In addition, keratometry was a significant positive predictor of deformation amplitude in normal and NTG patients, similar to a

Table 3

Univariate and multivariate regression analyses for deformation amplitude in primary open angle glaucoma, normal tension glaucoma, and normal controls.

Parameter	Normal control				POAG				NTG			
	univariate		multivariate		univariate		multivariate		univariate		multivariate	
	Coefficient	*P*-value	Coefficient	*P*-value	Coefficient	*P*-value	Coefficient	*P*-value	Coefficient	*P*-value	Coefficient	*P*-value
Age	0.002	.159			0.003	.002[*]	0.001	.246	0.004	.003[*]	0.002	.037[*]
Intraocular pressure	−0.028	< .001[*]	−0.029	< .001[*]	−0.038	< .001[*]	−0.036	< .001[*]	−0.032	< .001[*]	−0.031	< .001[*]
Central corneal thickness	0.000	.410			0.000	.775			−0.001	.403		
Spherical equivalent	−0.002	.660			−0.009	.321			−0.004	.401		
Keratometry	0.022	.002[*]	0.025	.003[*]	0.017	.232			0.033	.003[*]	0.029	.007[*]
Axial length	−0.007	.302			−0.001	.934			0.010	.027[*]	0.021	.048[*]
Mean deviation	–	–	–	–	−0.011	.001[*]	−0.004	.055	−0.007	.155		

[*] $P < .05$.

previous study by Ali et al[9] in keratoconus patients. Keratometry performed with an autorefractor measures the central 3 mm, Corvis records the central 8.5 mm, and deformation amplitude is measured at the center. Thus, steeper keratometry would result in greater deformation amplitude, but further research is required to determine why this relationship was significant in normal and NTG patients, but not POAG patients.

Previous ex vivo studies suggested that corneal stiffness increases with age.[18] Interestingly, deformation amplitude was positively correlated with age in NTG and POAG patients (Table 3). Consistent with our study, Leung et al reported that age was significantly positively correlated with deformation amplitude in glaucomatous eyes[19] and suggested that as ex vivo studies were performed on corneoscleral buttons, the measurement of pressure deformation response may not reflect the actual corneal biomechanical response in an intact globe.

Furthermore, axial length was a positive predictor of deformation amplitude only in the NTG group in the present study (Table 3). These findings differ from the results of previous studies. Nemeth et al[20] and Leung et al[19] found no significant relationship between axial length and deformation amplitude. However, Nemeth et al[20] performed measurement on normal corneas and Leung et al[19] included both normal and glaucomatous eyes in their analysis, which may account for the different results. Axial length has been shown to be a significant predictor of biomechanical properties measured by ORA.[21,22] Longer axial length was reported to be associated with lower corneal hysteresis in Chinese secondary school children, and the authors speculated that a more readily deformable corneoscleral coat is at greater risk for axial elongation.[22] In agreement with their findings, our study adds that more deformable corneas may be related with axial elongation, and this process may also be related to NTG.

To summarize, we reported the different corneal biomechanical properties in POAG and NTG patients. POAG patients showed a less deformable cornea than NTG and normal controls. Deformation amplitude was also shown to be affected by IOP in all groups, and axial length affected deformation amplitude only in NTG patients.

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