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Association between Corneal Deformation Amplitude and Posterior Pole Profiles in Primary Open-Angle Glaucoma

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Purpose: To investigate the relationships between corneal deformation amplitude and posterior pole profiles, including β-zone parapapillary atrophy (βPPA), optic disc tilt ratio, torsion degree, and disc-foveal angle, in patients with glaucoma.

Design: Cross-sectional study.

Participants: A total of 107 patients with glaucoma.

Methods: Each patient underwent measurement of deformation amplitude with Corvis ST (Oculus Optikgeräte GmbH, Wetzlar, Germany), color optic disc photography, red-free retinal nerve fiber layer photography, axial length measurement, and 24-2 standard automated perimetry. From fundus photographs, the βPPA area, optic disc tilt ratio, torsion degree, and disc-foveal angle were obtained. Pearson's correlation was used to determine the relationships between deformation amplitude and posterior pole profiles. To determine the factors associated with the posterior pole profiles, univariate and multivariate regression analyses were performed.

Main Outcome Measures: Deformation amplitude, βPPA area, optic disc tilt ratio, torsion degree, and disc-foveal angle.

Results: The study included 50 men (46.7%) and 57 women (53.3%). The mean age was 55.38±14.14 years. The mean tilt ratio, torsion degree, and disc-foveal angle were 1.16±0.14, 10.26±7.63°, and 7.60±3.64°, respectively. The mean βPPA area was 18 211.00±28 725.53 pixels. The βPPA (r = 0.391, $P < 0.001$) and tilt ratio (r = 0.408, $P < 0.001$) had significant relationships with deformation amplitude after adjusting for intraocular pressure (IOP). Torsion degree and disc-foveal angle showed no significant relationship with deformation amplitude. The βPPA area was associated with deformation amplitude and axial length in both univariate ($P = 0.008$ and 0.006, respectively) and multivariate ($P = 0.035$ and <0.001, respectively) regression analyses. The tilt ratio was associated with deformation amplitude in univariate regression analysis ($P = 0.002$), but not in multivariate regression analysis. Axial length was significantly associated with the tilt ratio in both univariate ($P < 0.001$) and multivariate ($P < 0.001$) regression analyses.

Conclusions: Deformation amplitude was associated with PPA area and tilt ratio in patients with glaucoma, although in our data set βPPA area and tilt ratio were not associated with visual field mean deviation. *Ophthalmology 2016;■:1–6 © 2016 by the American Academy of Ophthalmology.*

Supplemental video is available at www.aaojournal.org.

Although intraocular pressure (IOP) is an important risk factor for glaucoma, several population-based studies have reported glaucoma in patients with a normal IOP range, and some patients do not develop glaucoma despite an abnormally high IOP.[1,2] Biomechanical properties of the optic nerve head and peripapillary scleral connective tissue have been postulated to determine how these structures respond to IOP, which may account for why some patients are more susceptible to glaucomatous damage.[3]

Posterior pole profiles have been reported to be linked to glaucomatous damage. Parapapillary atrophy (PPA) has been shown to be associated with the development and progression of glaucoma and with glaucoma severity.[4–6] It has also been reported that the location of largest PPA correlates with the location of the most rapid visual field (VF) progression.[7] In addition, disc-foveal angle and disc torsion have been shown to be associated with the location of the glaucomatous damage.[8,9] All of these changes may be related to the biomechanical properties of the optic nerve head and posterior scleral tissues. However, there is no clinical method to measure these properties in vivo. If corneal biomechanical property could reflect the characteristics of the posterior profiles, including PPA and disc tilt/torsion, it may be possible to predict the susceptibility to glaucomatous damage using the corneal deformation amplitude.

The relationship between the corneal hysteresis and the susceptibility of the optic nerve head to glaucomatous damage has been described. Corneal hysteresis has been associated both with increased deformation of the optic

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nerve head surface in patients with glaucoma during IOP elevation[10] and with VF progression.[11−14] However, the relationship between corneal deformation amplitude and vulnerability of the optic nerve head or the peripapillary sclera has not been described.

The objective of the following study was to demonstrate the relationships between corneal deformation amplitude and anatomic alterations of the posterior pole profiles and to identify the factors that may be associated with the posterior pole profiles in patients with glaucoma.

Methods

The study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Seoul St. Mary's Hospital. The medical records of patients with established glaucoma who visited the glaucoma clinic at Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, in July 2015, were reviewed retrospectively. Glaucoma was defined as a normal anterior chamber based on slit-lamp examination, an open angle on gonioscopy, a glaucomatous optic disc (diffuse or focal thinning of the neuroretinal rim), and an abnormal VF consistent with glaucoma that was confirmed by at least 2 reliable VF examinations (<20% of fixation loss, <15% of false-positive error, and <15% of false-negative error). Patients were excluded if they had a corneal disease, a history of a 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.

Each patient underwent a medical history review and a complete ophthalmic examination including best-corrected visual acuity, Goldmann applanation tonometry, refraction (RK-5; Canon, Tokyo, Japan), slit-lamp biomicroscopy, gonioscopy, measurement of deformation amplitude with Corvis ST (ver. 1.2r1092; Oculus Optikgeräte GmbH, Wetzlar, Germany), dilated stereoscopic optic nerve head evaluation, color optic disc photography, red-free retinal nerve fiber layer (RNFL) photography (VX-10; Kowa Optimed, Tokyo, Japan), ultrasound pachymetry (Tomey, Nagoya, Japan), axial length measurement, and achromatic automated perimetry using the 24-2 Swedish Interactive Threshold Algorithm (Humphrey Visual Field Analyzer; Carl Zeiss Meditec, Dublin, CA).

Corvis ST Measurements

The corneal deformation amplitude was obtained using Corvis ST. First, the patient's cornea was appropriately centered, and then an impulse of air at a pressure of 25 kPa was automatically emitted from the device from a distance of 11 mm. The response of the central 8.5 mm of the cornea was recorded with an ultra-high-speed Scheimpflug camera, which took 140 digital frames with a resolution of 640×480 pixels in 30 msec. As the air impulse was emitted, the cornea moved inward into a concavity phase until it reached the highest degree of concavity. At this time, the deformation amplitude, defined as the amount of corneal displacement at highest concavity, was measured by the device. For each eye, 3 measurements were made and averaged.

Posterior Pole Profiles: β-Zone Parapapillary Atrophy Area, Optic Disc Tilt Ratio, Torsion Degree, and Disc-Foveal Angle

Color optic disc and red-free RNFL photographs were taken using a nonmydriatic retinal camera (Nonmyd 7; Kowa Optimed). We used a previously described method to control the head tilt.[15,16] Patients were seated at the camera with their foreheads placed against the forehead rest and their chins on the chin rest. The chin rest was adjusted so their eyes were aligned with the reference mark on the forehead rest support. The patient was then instructed to look at the internal fixation target in the fundus camera and to keep their heads upright throughout the examination. The red-free RNFL images were examined in random order by 2 glaucoma specialists (Y.J. and H.-Y.L.P.) blinded to clinical information, using ImageJ software (ver. 1.48; http://imagej.nih.gov/ij/download.html, National Institutes of Health, Bethesda, MD). The average values of the 2 examiners were used.

The β-zone parapapillary atrophy (βPPA), defined as the inner crescent of chorioretinal atrophy with visible sclera and choroidal vessels, was determined by tracing the disc and βPPA margin using a mouse-driven cursor, and the area was automatically calculated in pixels using ImageJ software (Fig 1A). The tilt ratio was used to determine the optic disc tilt, defined as the ratio between the longest and shortest diameters of the optic disc (Fig 1A).[17] The disc-foveal angle was the angle between the optic disc and the fovea and was defined as the angle between the reference line connecting the disc center and the fovea and a horizontal line through the disc center, as previously described (Fig 1B).[15,16] If the fovea was located inferior to the optic disc, the disc-foveal angle had a positive value. Optic disc torsion was defined as the angle between the axis of the longest diameter of the optic disc and the vertical meridian, which was at right angles to the reference line[8,9] (Fig 1C). The absolute value of the measured torsion degree was used.

Statistical Analyses

Pearson's correlation was used to determine the relationships between deformation amplitude and posterior pole profiles after adjusting for IOP at the time of Corvis ST measurements and the use of topical carbonic anhydrase inhibitors (CAIs). To determine factors associated with the posterior pole profiles, univariate and multivariate regression analyses were performed using SPSS (ver. 17.0; SPSS Inc, Chicago, IL). In all analyses, $P < 0.05$ was taken to indicate statistical significance.

Results

A total of 107 eyes of 107 patients with glaucoma were included in the study. Baseline characteristics are shown in Table 1. There were 50 men (46.7%) and 57 women (53.3%). The mean age was 55.38±14.14 years. The mean tilt ratio, torsion degree, and disc-foveal angle were 1.16±0.14, 10.26±7.63°, and 7.60±3.64°, respectively. The mean PPA area was 18 211.00±28 725.53 pixels.

Table 2 and Figure 2 show the relationships between deformation amplitude and posterior pole profiles after adjusting for IOP and the use of CAI. The βPPA ($P < 0.001$ and 0.002, respectively) and tilt ratio ($P < 0.001$ for both models) had significant relationships with deformation amplitude after adjusting for IOP and after adjusting for both IOP and CAI. Torsion degree and disc-foveal angle showed no significant relationship with deformation amplitude. In addition, deformation amplitude had a significant relationship with axial length ($r = 0.291$, $P = 0.007$).

To identify the parameters affecting the posterior pole profiles, univariate and multivariate regression analyses were performed. The βPPA area was associated with deformation amplitude and axial length in both univariate ($P = 0.008$ and 0.006, respectively) and multivariate ($P = 0.035$ and <0.001, respectively) regression analyses (Table 3). The VF mean deviation showed a negative