



Relationship Between Optic Nerve Head and Nerve Fiber Layer with Central Corneal Thickness in Primary Open Angle Glaucoma: A Three-Dimensional Optical Coherence Tomography Study

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Abstract

Introduction: To evaluate the relationship between optic nerve head (ONH) parameters and retinal nerve fiber layer (RNFL) thickness with central corneal thickness (CCT) in primary open angle glaucoma (POAG) patients using three-dimensional spectral domain optical coherence tomography (3D SD-OCT).

Methods: In this cross-sectional study, 144 eyes of 144 patients (79 female, 65 male) with POAG were studied. Patients were classified into thick cornea group (Group 1) and thin cornea group (Group 2). Group 1 represented eyes with CCT ≥ 540 μm and Group 2 with CCT < 540 μm . Topographic measurements of the ONH and peripapillary RNFL thickness was performed using 3D-OCT. The outcomes were correlated with the CCT of the subjects.

Results: The mean age of the study population was 63.6 ± 12.7 years (47–69 years). There was no statistically significant difference between the two groups in terms of age, sex, spherical equivalent refractive error, and mean intraocular pressure ($p=0.52$, $p=0.45$, $p=0.34$, $p=0.65$, respectively). The mean CCT of subjects was 556.6 ± 34.37 μm (468–635 μm), and the mean disc area was 2.52 ± 0.47 mm^2 (1.76–3.99 mm^2). CCT showed a negative correlation with cup area ($p=0.03$), cup-disc area ratio ($p<0.005$), horizontal cup-disc ratio ($p=0.04$), and cup volume ($p<0.005$) and a positive correlation with rim area ($p=0.025$), rim volume ($p=0.015$), and inferior RNFL ($p<0.005$). No significant difference in optic disc area, vertical cup-disc ratio, average RNFL, and superior RNFL existed between the two groups ($p=0.81$, $p=0.516$, $p=0.13$, $p=0.14$, respectively).

Discussion and Conclusion: POAG patients with thin corneas may be at greater risk of glaucomatous damage as measured by a cup-disc ratio, neuro-retinal rim, and RNFL.

Keywords: Central corneal thickness; optic nerve; primary open angle glaucoma; retinal nerve fiber.

Corneal thickness is a predictive factor of the formation and progression of optic nerve damage in glaucoma.^[1, 2] Several studies have reported that thinner corneas may lead to low intraocular pressure (IOP) readings, which hide the risk of developing POAG, whereas thick corneas may cause a false POAG diagnosis.^[3-5] However, the factors contributing to the vulnerability of eyes with thin corneas in

glaucoma has not been elucidated.^[6]

Circumpapillary nerve fiber layer and optic nerve head (ONH) parameters are essential parameters in glaucoma diagnosis and progression. It has been found that the structure of the sclera directly affects the severity of retinal ganglion cell and ONH injury resulting from increased IOP.^[7] Because the sclera and cornea are composed of a com-

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plementary connective tissue layer, the structural change of the cornea may reflect the change of lamina cribrosa. In some studies, the corneal thickness was found to be correlated with the anterior scleral thickness in POAG^[8] and the scleral bed was thin in excavated optic nerves.^[9] Biomechanical properties of the cornea are believed to reflect the structural vulnerability of the eye and increase glaucoma susceptibility. Therefore, it has been suggested that corneal thickness has an effect on ONH resistance as well as on IOP measurement.

The purpose of this study was to determine whether thin corneas are associated with specific ONH parameters and peripapillary retinal nerve fiber layer (RNFL) thickness. The assessment of the relationship between biomechanical properties of the cornea and optic nerve may provide an additional insight in understanding the advanced damage in glaucomatous eyes with thin corneas.

Materials and Methods

The study was a retrospective, cross-sectional study on documented patients with POAG in glaucoma practice. The study and data collection confirmed to all local laws and complied with the principles of the Declaration of Helsinki. In total, 144 eyes of 144 patients (79 female, 65 male) with newly diagnosed POAG were included in the study. All eyes had open-angle observed by gonioscopy, and the patients fulfilled at least two of the following criteria: glaucomatous optic neuropathy, IOP >21 mmHg on at least three occasions, and glaucomatous visual field defects. Eyes were divided into two groups on the basis of their median central corneal thickness (CCT) and classified into thick cornea group (Group 1) and thin cornea group (Group 2). Group 1 represented 82 eyes with CCT $\geq 540 \mu\text{m}$ and Group 2 represented 62 eyes with CCT $< 540 \mu\text{m}$. Each patient underwent a complete ophthalmic examination with glaucoma diagnosis confirmed by at least two visual fields with standardized reliability indices (Humphrey stat pac 2 parameters of <5% probability for mean deviation, and either corrected pattern standard deviation of <5% probability or glaucoma hemifield test "outside normal limits"). Visual field was tested using the 30-2 Swedish interactive threshold algorithm standard strategy of the Humphrey Field Analyzer (Carl Zeiss Meditec AG, Jena, Germany).

Inclusion criteria were best corrected visual acuity not worse than 20/60, refractive errors $\leq \pm 3.0$ D sphere and $\leq \pm 1.5$ D cylinder, and good OCT image quality. Exclusion criteria were secondary glaucoma, history of previous ocular surgery, corneal or retinal diseases, and systemic comorbidities that may affect the visual field.

IOP was measured using Goldmann applanation tonometry, and at least two IOP measurements were applied. CCT was measured with Nidek ultrasonic pachymetry UB-1000. ONH with RNFL imaging was performed by the Topcon 3D SD-OCT 2000 (Topcon Corporation, Tokyo, Japan). Eyes were dilated with 0.5% tropicamide, and OCT images were obtained by the same technician. Images with signal strength >40 were used for analyses.

For each eye, average, superior, and inferior peripapillary RNFL thicknesses were evaluated and automatically calculated by OCT using existing software. 3D SD-OCT 2000 (software Version 8.00; Topcon Corporation) automatically detects the disk center by referring to the infrared reflectance image. On the basis of the inputted refractive information, the software adjusts the circle diameter for the circle scan and corrects papillary diameter, area, and volume, while also calculating magnification compensation, which enables accurate scanning. The machine automatically detects the edge of the optic disk as the end of the retinal pigment epithelium/choriocapillaris. Among the parameters measured by ONH analysis, the following were examined: optic disc area, cup area, cup-disc area ratio, horizontal cup-disc ratio, vertical cup-disc ratio, cup volume, rim area, and rim volume.

SPSS 11.5 for Windows was used for statistical analysis. All OCT parameters were compared with the two groups as defined according to the corneal thickness value. Significance between groups was determined using independent-samples T-tests. Pearson correlation analysis was used for the correlation coefficient regarding relationship to CCT.

Results

The study included 144 eyes of 144 patients with POAG. Of these, 79 subjects were female, and 65 subjects were male. The range of age was 47–69 years. The demographic and ophthalmic characteristics of patients with POAG classified into thin cornea group and thick cornea group are shown in Table 1. There were no significant differences in mean

Table 1. Demographic and clinical characteristics of patients with Primary Open-Angle Glaucoma (POAG)

	CCT <540 μm (n=62)	CCT $\geq 540\mu\text{m}$ (n=82)	p*
Age (years)	61.3 \pm 13.5	63.3 \pm 12.5	0.52
Sex			
Male/Female	28/34	40/42	0.45
Spherical equivalent (D)	1.8 \pm 1.0	1.4 \pm 0.9	0.34
Mean IOP (mmHg)	14.1 \pm 1.0	16.2 \pm 2.6	0.65

CCT: central corneal thickness; D: diopters; *Independent-samples T-tests.

Table 2. Optic nerve head parameters in patients with POAG classified by central corneal thickness

Optic nerve head parameters	CCT <540µm (n=62)	CCT ≥540µm (n=82)	p*
Optic disc area (mm ²)	2.23±0.27	2.03±0.29	0.81
Cup area (mm ²)	1.49±0.53	0.58±0.15	0.03
Cup:disc area ratio	0.71±0.14	0.63±0.13	<0.005
Horizontal cup-disc ratio	0.89±0.10	0.84±0.09	0.04
Vertical cup-disc ratio	0.88±0.10	0.86±0.13	0.51
Cup volume (mm ³)	0.63±0.26	0.51±0.27	<0.005
Rim area (mm ²)	0.72±0.36	0.86±0.33	0.025
Rim volume (mm ³)	0.06±0.05	0.08±0.10	0.015

CCT: Central corneal thickness; *Independent-samples T-tests; POAG: Primary Open-Angle Glaucoma.

age, sex, spherical equivalent refractive error, and mean IOP between the two groups (p=0.52, p=0.45, p=0.34, and p=0.65, respectively).

Regarding ONH parameters by OCT, there was a statistically significant difference as measured by cup area (p=0.03), CDAR (p<0.005), HCDR (p=0.04), cup volume (p<0.005), rim area (p=0.025), and rim volume (p=0.015) between the two groups (Table 2). The study also found statistically significant relation between thin CCT and inferior RNFL thickness (p<0.005) (Table 3). There was no significant difference in optic disc area (p=0.81), vertical cup-disc ratio (p=0.51), average RNFL (p=0.13), and superior RNFL (p=0.14) between the two groups. There was a statistically significant negative correlation between thin CCT and cup area (r=-0.240), CDAR (r=-0.432), HCDR (r=-0.032), and cup volume (r=-0.410) while a significant positive correlation was observed with rim area (r=0.043), rim volume (r=0.024), and inferior RNFL thickness (r=0.353) (Table 4).

Discussion

In this study, we aimed to evaluate the relationship between CCT and quantitative measurements of the ONH and nerve fiber layer. We found that glaucomatous eyes with thin corneas were associated with larger and deeper optic disc cups and that they may be at greater risk of RNFL loss.

Studies regarding the association of corneal thickness and optic disc morphology in glaucoma patients have been reported previously. Gunvant et al.^[10] found that thinner corneas are associated with increased cup depth and volume, and this may reflect an increased susceptibility to glaucomatous optic neuropathy in ocular hypertensive patients. Kniestedt et al.^[11] showed that a significant negative correlation exists between the cup-to-disc ratio, and CCT and decreased corneal thickness was found to be in-

Table 3. RNFL thickness in patients with POAG classified by central corneal thickness

RNFL Thickness	CCT <540µm (n=62)	CCT ≥540µm (n=82)	p*
Average±SD	90.6±8.7	98.5±13.8	0.13
Superior±SD	99.5±13.8	108.3±11.2	0.14
Inferior±SD	80.7±13.5	89.4±13.4	<0.005

RNFL: Retinal nerve fiber layer; CCT: Central corneal thickness; SD: Standard deviation; *Independent-samples T-tests.

Table 4. Statistically significant parameters related to thin central corneal thickness

OCT parameters	Correlation Coefficient (r)*
Cup area (mm ²)	-0.240
Cup-disc area ratio	-0.432
Horizontal cup-disc area (mm ²)	-0.032
Cup volume (mm ³)	-0.410
Rim area (mm ²)	0.043
Rim volume (mm ³)	0.024
Inferior RNFL (µm)	0.353

OCT: Optical coherence tomography; RNFL: Retinal nerve fiber layer; *Pearson correlation coefficient.

dicative of more advanced disease. Herndon et al.^[12] suggested that corneal thickness is a significant determinant of glaucomatous damage in open-angle glaucoma as measured by cup-disc ratios of the initial examination. Jonas et al.^[13] confirmed this relation showing a significant positive relationship between the thin cornea and rim area at the time of glaucoma diagnosis. However, the progression of glaucomatous optic nerve neuropathy was found to be independent of corneal thickness. Lesk et al.^[14] found that open-angle glaucoma and ocular hypertension with thinner corneas show significantly greater shallow of the cup, and it is suggested that patients with thin central cornea maybe less able to respond to IOP reduction due to the damaged vasculature of the lamina cribrosa.

In the present study, there was a significant positive correlation between thin CCT and neuroretinal rim area in patients with POAG. In addition, thin CCT was associated with an increased cup to disc ratio. These findings agree with previous studies, which suggest that glaucomatous optic nerve damage correlates significantly with a thin central cornea.^[13, 15]

Copt et al.^[16] showed that patients may be misdiagnosed as normal tension glaucoma when the corneal thickness is not measured in patients with POAG with thin corneas, and inappropriate treatment is given. Although our study

evaluated the pachymetric values when diagnosing open-angle glaucoma, our results suggested that there was an increased sensitivity to glaucomatous damage in the presence of thin corneas.

In a population-based study, the corneal thickness was not related to optic disc parameters evaluated by stereoscopic optic disc photographs.^[17] In a similar study with scanning laser ophthalmoscopy and scanning laser polarimetry, corneal biostructure has been reported to have a positive correlation with rim area and RNFL measurement.^[18] Therefore, the relationship between the biomechanical properties of the cornea and the optic nerve parameters is controversial.

In our study, a significant positive correlation was found between the CCT and inferior RNFL. Kaushik et al.^[15] found that the RNFL in ocular hypertensives with CCT ≤ 555 μm was significantly thinner than in those with thick corneas measured by OCT. Henderson et al.^[19] showed that OHT patients with thinner corneas had significantly lower RNFL thickness measurements than OHT patients with thicker corneas and healthy subjects measured by scanning laser polarimetry. The common result of these studies is that ocular hypertensives with thinner corneas represent a subgroup either having preclinical glaucoma or a susceptibility to glaucomatous damage in the presence of high IOP and thin RNFL. This may explain the correlation between the thin cornea and glaucomatous damage in our open-angle glaucoma series.

In summary, the present study showed that patients with thin corneas have a higher risk of glaucoma detection. This relationship may be due to the underestimation of the intraocular pressure until the time when the patient is referred to the glaucoma specialist.

Our study has some limitations. The study is based on patients referred to a glaucoma clinic; therefore, there may be a selection bias because patients with thin corneas may be referred late due to false low intraocular pressure measurements. In addition, CCT measurements may have a daily variation; thus, a single CCT measurement may not represent CCT as well.^[20]

In conclusion, patients with thinner corneas are likely to develop greater glaucomatous optic nerve damages than those with thicker corneas. Corneal thickness is a significant predictor of glaucomatous damage as measured by a cup-disc ratio and neuroretinal rim in patients with POAG. Measurement of corneal thickness in glaucomatous patients is important to recognize high-risk patients for the development of glaucomatous damage and to ensure that ophthalmologists can treat these patients earlier.

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