SCIENTIFIC REPORT

Central corneal thickness and correlation to optic disc size: a potential link for susceptibility to glaucoma

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Aims: To evaluate a possible relationship between central corneal thickness (CCT) and optic disc area in patients with primary open-angle glaucoma (POAG).

Methods: Patients with POAG underwent eye examination, optic disc imaging with the Heidelberg Retina Tomograph II (HRT II) and ultrasound corneal pachymetry. Exclusion criteria were prior ocular surgery and low-quality HRT II images (HRT standard deviation (SD) >50). Pearson's correlation coefficients were calculated to assess the associations between CCT and optic disc area.

Results: 212 eyes of 137 patients with POAG were examined. In all, 66 (48%) subjects were women, 104 (76%) were Caucasian, 26 (19%) African-American and 7 (5%) other races. 72 eyes remained after excluding those with prior intraocular surgery and low-quality HRT II images. In a univariate analysis of this group, CCT was inversely correlated with optic disc surface area (Pearson's correlation coefficient $r = -0.284$, $p = 0.036$, $n = 72$). Mean (SD) disc area was 2 (0.53) mm² ($n = 160$). Caucasians had significantly smaller discs ($p < 0.001$) than other races (Caucasian 1.9 (0.47) mm² ($n = 119$), African-Americans 2.4 (0.54) mm² ($n = 31$), other races 2.3 (0.45) mm² ($n = 10$)).

Conclusion: CCT is inversely correlated to optic disc area. Although thicker corneas have been recognised to cause slight overestimation of true intraocular pressure (IOP), they may also indicate the presence of a substantially smaller, and thus more robust, optic nerve head. People with thinner corneas which slightly underestimate the true IOP may also have larger and more deformable optic discs.

Recent publications have shown an association between central corneal thickness (CCT) and the risk of glaucoma.^{1,2} These reports have focused on the concern that thinner-than-average corneas may underestimate the true IOP whereas thicker-than-average corneas may overestimate the true IOP. This effect has been found to be in the order of 1 mm Hg correction for every 25 μ m deviation from a CCT of 550 μ m.^{3,4}

This factor alone, however, would not appear sufficient to explain the markedly increased susceptibility to glaucoma found in those with thinner corneas.

The cornea and optic disc both fill scleral "portholes" of the eye, and due to the continuity of the cornea, sclera and optic disc lamina, we may consider the possibility that CCT may be extrapolated to characteristics of the optic disc itself, including disc area and deformability, factors that may relate more significantly to the risk of developing glaucoma.

We undertook this study to evaluate a possible link between CCT and optic disc area in patients with primary open-angle glaucoma (POAG).

METHODS

The study population consisted of patients with documented POAG being followed prospectively in a longitudinal study at

the Wilmer Ophthalmological Institute Glaucoma Clinic. All patients gave informed consent, and all procedures were reviewed by the Johns Hopkins Institutional Review Board (Baltimore, Maryland, USA). All patients underwent a complete eye examination by a glaucoma specialist, with the diagnosis of glaucoma confirmed by the following information: two or more visual fields with recognised abnormalities (Humphrey Stat Pac 2 parameters of <5% probability for mean deviation, and either corrected pattern SD <5% probability, or glaucoma hemifield test "outside normal limits"), with corroborating disc abnormalities evaluated by a glaucoma specialist.

Subjects underwent disc imaging with a confocal scanning laser ophthalmoscope (Heidelberg Retina Tomograph II (HRT II); Heidelberg Engineering, Dossenheim, Germany). Subjects whose HRT II images had a standard deviation ≤ 50 were included for final analysis. CCT was measured using an ultrasonic pachymeter (DGH-500 Pachette; DGH Technology, Exton, Pennsylvania) using the average of three measurements. Subjects with previous intraocular surgery were also excluded from final evaluation. The SPSS V.13.0 computer program was used to generate Pearson's correlation coefficients. The χ^2 test was used for proportions, and analysis of variance was used to compare the means.

RESULTS

One hundred and thirty seven patients with POAG consented to participate in the study. Of these, 66 (48%) subjects were women, 104 (76%) were Caucasian, 26 (19%) were African-American and 7 (5%) were from other racial groups. The mean (SD) age was 67.9 (12) years.

Seventy two eyes were eligible after excluding those with any prior intraocular procedures or HRT images with SD >50. These 72 eyes belonged to 53 patients (28 women, 37 Caucasian, 11 African-American, 5 other races). In this group, we found a statistically and clinically significant inverse correlation between CCT and optic disc area by generating a Pearson correlation coefficient ($r = -0.284$, $p = 0.036$, $n = 72$; fig 1).

In an analysis stratified by race, we found a similar inverse relationship in Caucasians ($r = -0.3$, $p = 0.031$, $n = 52$). In African-Americans, a non-significant positive correlation was found ($r = +0.479$, $p = 0.098$, $n = 13$), whereas in our "other races" mixed group a non-significant negative correlation was noted ($r = -0.252$, $p = 0.586$, $n = 7$).

To evaluate CCT alone, and maximise the number of cases, we performed an analysis excluding eyes with prior surgeries, but including those with lower quality HRT images (as CCT measurements are independent of HRT). The mean (SD) CCT was 528.7 (35.2) μ m. There were no differences in CCT between men and women ($p = 0.564$). African-Americans had thinner corneas than Caucasians or those of other racial groups

Abbreviations: CCT, central corneal thickness; POAG, primary open-angle glaucoma; HRT II, Heidelberg Retina Tomograph II

Figure 1 Central corneal thickness versus disc area in eyes with primary open-angle glaucoma ($r = -0.284$, $p = 0.036$, $n = 72$).

(Caucasians $532 (32) \mu\text{m}$ ($n = 59$), Africans $512.2 (42) \mu\text{m}$ ($n = 16$) and other races $536.7 (37.2) \mu\text{m}$ ($n = 9$)), although the difference did not reach significance ($p = 0.10$; table 1).

To maximise the number of cases for evaluation of disc parameters, we excluded those with low-quality HRT images ($\text{SD} > 50$) and included eyes that had previously undergone surgery (as surgery does not affect the disc area). The mean (SD) disc area was $2 (0.5) \text{mm}^2$, shown stratified by race in table 1.

There was no significant difference in mean disc area between men and women ($p = 0.476$). Caucasians had significantly smaller discs than other racial groups (Caucasians $1.9 (0.47) \text{mm}^2$ ($n = 119$), African-Americans $2.4 (0.54) \text{mm}^2$ ($n = 31$), other races $2.3 (0.45) \text{mm}^2$ ($n = 10$); $p < 0.001$). Pairwise comparison was done adjusting for multiple comparisons. There were significant differences between the mean disc areas of Caucasians and African-Americans ($p < 0.001$), and Caucasians and other races ($p = 0.02$), but not between African-Americans and other races ($p = 0.5$).

We also used a logistic regression model to look for potential confounding by age or sex. No significant differences were noted between the univariate and multivariate analyses (data not shown).

DISCUSSION

Anatomical and biometric evaluations of the optic disc and corneal thickness with correlations to various parameters, including sex, age, race, height, iris colour, keratometry, anterior chamber depth, lens thickness, refraction, axial length, IOP and various types of glaucoma have been made.^{5–13} A single study of central corneal thickness with thickness of the lamina cribrosa in human cadavers, however, did not allow for

conclusive results due to histological artefacts in preservation techniques and sectioning.¹⁴ We undertook this study to evaluate a possible link between CCT and optic disc area.

After excluding eyes with prior intraocular surgeries and low-quality HRT images, we found a significant negative correlation between CCT and optic disc area in a population of patients with primary open-angle glaucoma ($r = -0.284$, $p = 0.036$, $n = 72$).

This correlation was negative and significant in Caucasians ($r = -0.3$, $p = 0.031$, $n = 52$), positive but insignificant in African-Americans ($r = 0.479$, $p = 0.098$, $n = 13$), and negative and insignificant in other races ($r = -0.252$, $p = 0.586$, $n = 7$). Considering the number of excluded patients and the low power associated with our non-Caucasian subgroups, we believe that data available are insufficient to comment further on any potential associations between CCT and disc area in non-Caucasian subgroups. Any potential differences between races would need to be evaluated in a larger group of patients.

We found that the mean optic disc area was smaller in Caucasians than in African-Americans and in other races (Caucasians $1.9 (0.47) \text{mm}^2$ ($n = 119$), African-Americans $2.4 (0.54) \text{mm}^2$ ($n = 31$), other races $2.3 (0.45) \text{mm}^2$ ($n = 10$); ($p = 0$)), and we also found CCT to be thinner in African-Americans compared with Caucasians and other races (Caucasians $532 (32) \text{mm}^2$ ($n = 59$), African-Americans $512.2 (42) \text{mm}^2$ ($n = 16$), other races $536.7 (37.2) \text{mm}^2$ ($n = 9$)), although our findings did not reach statistical significance ($p = 0.10$).

Indeed, it has been well established that, on average, African-Americans have thinner corneas than Caucasians¹⁵ and in separate studies, that African-Americans have larger optic discs than Caucasians.^{5, 16} The hypothesis that the two conditions should be related and co-exist in the same individuals has not been dealt with, yet is both logical and anatomically plausible. As the cornea and optic disc each constitute and fill what we may consider to be scleral “portholes” of the eye, and because of the structural continuity of central cornea with posterior sclera, scleral canal and lamina, we wished to verify an implicit relationship between CCT and optic disc area.

Optic disc size influences the susceptibility of axonal damage in glaucoma. The particular propensity of the inferior and superior disc areas to excavation and axonal damage is associated with the higher lamina cribrosa pore-to-disc area ratio and thinner connective tissue support in these regions. However, with decreasing disc size, the pore-to-disc area ratio also decreases, providing greater tissue support.^{17–19} Moreover, given equal tissue characteristics, Laplace’s Law dictates that the deformability of a disc with smaller radius is less than that of one with larger radius. As our findings indicate that CCT is inversely associated with optic disc area, CCT may also be correlated with the optic nerve’s susceptibility to IOP-induced damage.

It is well understood that the presence of a thicker CCT can cause slight overestimation of actual IOP by applanation

Table 1 Ocular findings

Maximum	Minimum	SD	Mean	Number	Different races	Parameter
605	450	32.01	531.9	59	Caucasians	CCT (μm)
583	458	42.04	512.2	16	African-Americans	
597	499	37.16	536.7	9	Other races	
3.23	0.75	0.47	1.9	119	Caucasians	Disc area (mm^2)
3.55	1.33	0.54	2.4	31	African-Americans	
3.28	1.91	0.45	2.3	10	Other races	

methods, whereas thinner CCT can cause slight underestimation.^{3,4} However, our results in Caucasians indicate that thicker corneas often exist in eyes with smaller optic nerve heads that are more resistant to the effects of even increased IOP, serving, thus, to counterbalance the potential concerns of higher intraocular pressure. The corollary, however, is more ominous. Eyes with thinner and more deformable corneas causing underestimation of the true IOP may have larger and more deformable optic discs, making them more susceptible to glaucomatous damage. Thus, there is the oft-noted predisposition for African-Americans, with thinner corneas and larger discs, to develop glaucoma with IOPs equivalent to those of Caucasians.

In other words, the more significant and real implication of thinner corneas may be as a marker for more deformable discs, prone to the effects of increased IOP, whereas increased corneal thickness may simply indicate more rigid, resistant globes including optic disc laminae.

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