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CLINICAL STUDY

Corneal thickness and visual field damage in glaucoma patients

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Abstract

Purpose **To verify whether there was a significant correlation between central corneal thickness (CCT) and visual field damage in patients with primary open angle glaucoma (POAG).**

Methods **A total of 99 eyes with POAG were consecutively recruited. Patients were classified as glaucomatous based on visual field and optic nerve head damage. All underwent applanation tonometry, Humphrey perimetry, and measurement of CCT with ultrasonic pachymetry. Based on CCT value, the sample was split at the mode in two groups (group 1 $<535\,\mu$m, $n=49$; group 2 $\geq 535\,\mu$m, $n=50$).**

Results **Entire cohort: mean CCT 554 μm $\pm$ 45.03; mean deviation (MD) -6.68 dB $\pm$ 7.32; pattern standard deviation (PSD) 5.33 $\pm$ 3.75; intraocular pressure (IOP) 17.91 $\pm$ 4.16 mmHg with treatment. Group 1: CCT was 504.8 μm $\pm$ 30.8; MD -9.01 dB $\pm$ 8.72; PSD 6.38 $\pm$ 3.99; IOP 18.02 mmHg $\pm$ 4.66. Group 2: mean CCT 574.6 μm $\pm$ 35.03; MD -4.39 dB $\pm$ 4.70; PSD 4.25 $\pm$ 3.19; IOP 17.79 mmHg $\pm$ 3.57. A significant difference was found between the two groups for both MD and PSD. Linear regression analysis showed a significant correlation between CCT and PSD ($P<0.001$).**

Conclusions **Our data show that patients with a thinner cornea had a worse MD and PSD. As a thinner CCT causes an underestimation of the true IOP, there may be a delay in the diagnosis of POAG or an inadequate estimate of the clinical course despite apparently desirable IOP applanation readings.**

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Introduction

The term glaucoma refers to a group of diseases that have in common a characteristic optic neuropathy with associated visual field loss, for which elevated intraocular pressure (IOP) is one of the primary risk factors.[1] The 'normal' IOP is a statistical description of the range of IOP in the population, and is not applicable to the individual subject.[2] Today, different methods to measure the IOP are available.

The most widely used instrument, considered the international gold standard, is the Goldmann applanation tonometer. Hans Goldmann applied the Imbert–Fick principle which states: 'the existing pressure in a sphere containing a liquid, whose wall is constituted by a very thin and perfectly elastic membrane, can be measured by an external compression sufficient to transform a portion of spheric surface in a plain surface'. This theoretical sphere is dry, thin-walled, and readily flexible, all features not applicable to the cornea.

The force necessary to flatten the cornea during tonometry can be influenced not only by the IOP but also by corneal characteristics such as central corneal thickness (CCT) , corneal shape and hydratation,[3] rigidity of the sclera and the globe.

Goldmann himself, in his first report described some of the possible sources of measurement error.[3] He specifically outlined that the theoretical basis for his instrument was calculated for a mean CCT of 500 μm and that the accuracy could vary if CCT was significantly different from this value.

Nowadays, CCT is considered as a possible explanation for glaucoma cases where clinical findings do not match.[4] A positive correlation between IOP readings and corneal thickness was found in patients attending a general clinic.[5]

Recently Henderson *et al*[6] demonstrated that ocular hypertension (OHT) patients with

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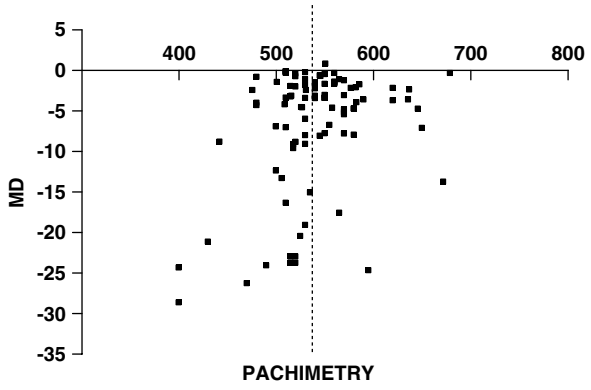

Figure 1 Scattergram of MD (*y*-axis) and CCT (*x*-axis). Entire group, $n=99$; the dotted line separates the two groups.

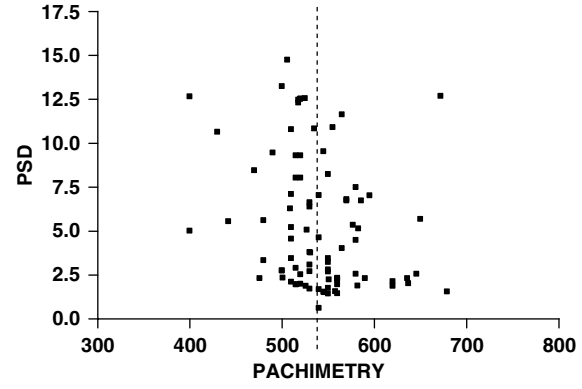

Figure 2 Scattergram of PSD (*y*-axis) and CCT (*x*-axis). Entire sample, $n=99$; the dotted line separates the two groups.

thinner CCT had a significant lower retinal nerve fibre layer thickness measurements compared with both OHT patients with thicker CCT and normal patients, thus suggesting that different CCT values might be associated with different probability of developing glaucoma damage.

The Ocular Hypertension Treatment Study specified some clinical and demographic factors that might represent risk factors for the development of open angle glaucoma. Among them thinner CCT was found to be a significant risk factor.[7] The aim of our study was to verify whether there was a correlation between CCT and standard threshold perimetry indices in patients with primary open angle glaucoma (POAG).

Materials and methods

In total, 99 consecutive eyes with POAG treated with IOP-lowering medications for at least 5 years were prospectively recruited. All subjects were Caucasians, had a normal cornea at the slit-lamp, had no signs or history of corneal surgery or disease, and were phakic. Visual fields were assessed by a Humphrey Field Analyzer 750 (HFA, Humphrey, Inc., San Leandro, CA, USA), 24-2 SITA (Swedish Interactive Threshold Algorithm) standard, program full threshold. Mean deviation (MD) and pattern standard deviation (PSD) were considered in this study.

Patients were classified as having POAG when a typical abnormal optic nerve head or typical damage of the visual field and open angle at gonioscopy were present.

The findings necessary to classify patients as having abnormal OHN were the optic rim notch, diffuse generalized loss of optic rim tissue, vertical cup/disc diameter ratio, asymmetry unexplained by side differences in optic disc size, and/or disc haemorrhage.

The Spaeth's gonioscopy grading system was used.

A visual field test was considered glaucomatous when abnormal Glaucoma Hemifield test was confirmed on two consecutive tests, or three abnormal points confirmed on two consecutive tests with $P<5\%$ probability of being normal, one of which should have $P<1\%$, all not being contiguous with the blind spot and CPSD $<5\%$ if the visual field is otherwise normal, confirmed on two consecutive tests.[8] Any defect or suspected defect had to be confirmed by repeated testing. Patients were excluded when either visual field testing was considered unreliable (false-negative and false-positive responses $>30\%$ and fixation losses $>20\%$).

Patients were not excluded on the basis of gender, race, or age. All patients had former experience of visual field examination and all visual fields were performed by the same perimetrist. The refractive error ranged from -7 to $+7$ diopters.

Each patient underwent a biomicroscopic and a visual field examination, CCT and IOP measurements.

CCT was measured with ultrasonic contact pachymetry (Quantel Medical, model: POCKET, France). Pachymetry values were always obtained by an observer masked to the perimetry data. Patients were instructed to look straight ahead at a fixation target located at 3 m. After having pushed the button to initiate corneal thickness measurements, the probe tip was gently positioned to touch the patient's cornea at its centre. The Pachymeter probe had to be perpendicular to the apex of the cornea. If the measurement was valid, a value appeared on the digital display. The mean value of three consecutive measurements was used for the statistical analysis. All measurements were taken by the same physician.

IOP was evaluated with Goldmann applanation tonometry (Haag-Streit, Switzerland).

All patients were in a sitting position and a topical anesthetic drop with fluorescein was instilled in both eyes. Each patient positioned the head on the chin-rest of

a Haag-Streit slit-lamp biomicroscope and a Goldmann applanation measurement was performed. Patients were asked not to move their eyes, not to blink, and to continue breathing normally while looking at a target point on the slit-lamp, in order to keep the visual axis parallel to the probe.

The entire cohort of eyes was divided in two groups ranked on CCT values, separated at the mode. In group 1, the CCT value was less than 535 μm, whereas in group 2 CCT value was greater than or equal to 535 μm.

The results were analysed by descriptive analysis and when the distribution of the data was normal, *t*-test and Pearson's *r* coefficient were used to compare and correlate CCT, MD, and PSD. When the distribution of the data was non-normal, Mann–Whitney test and Spearman coefficient were used. A linear regression analysis was used.

The IRB approved the study without the need for a specific informed consent as pachymetry is noninvasive and considered as a routine part of a tertiary care glaucoma evaluation.

Results

The mean refractive error of the included patients was -1.7 ± 4.7 (mean $\pm$ SD) diopters and the mean age was 63 ± 16 years. The mean value of CCT for the entire sample was 554 μm $\pm$ 45; MD, -6.68 ± 7.32 dB, PSD 5.33 ± 3.75, and IOP 17.9 ± 4.16 mmHg with treatment.

Figure 1 shows the Scattergram of MD (y-axis) and CCT (x-axis); Figure 2 shows the Scattergram of PSD (y-axis) and CCT (x-axis).

Table 1 Correlation between CCT and other parameters

	r^2	P-*value*
MD	0.21	0.039
PSD	−0.29	0.006
IOP	0.09	0.40

CCT, central corneal thickness; IOP, intraocular pressure; MD, mean deviation; PSD, pattern standard deviation.
Entire sample, $n = 99$.

Table 1 shows the correlation between CCT and the other parameters of the entire sample calculated with linear regression.

Table 2 shows the comparison between group 1 ($n = 49$) and group 2 ($n = 50$). The mean MD value for the group 1 was significantly lower ($P < 0.001$) compared to the mean MD value of group 2 (-9.01 ± 8.72 and -4.39 ± 4.70 dB, respectively).

The mean PSD value for the group 1 was significantly higher ($P < 0.05$) than the mean PSD value of group 2 (6.38 ± 3.99 and 4.25 ± 3.19, respectively).

No differences were found in the IOP between the two groups.

Table 3 shows the linear regression analysis of age *vs* MD or PSD for the entire sample and for the two groups. No correlation was found among these parameters.

The refractive error was -2.1 ± 5.2 diopters in group 1 and -1.3 ± 4.2 diopters in group 2.

Discussion

In 1975, Ehlers measured the 'real' or 'manometric' IOP using a cannulation method in a group of 29 normal eyes undergoing cataract surgery and correlated corneal thickness to measurement errors of Goldmann applanation tonometry.[9] The IOP value measured with

Table 3 Linear regression of age *vs* MD or PSD, both in the entire sample and in the two groups

Group	*PSD*	*MD*
Entire		
r^2	0.004	0.002
P	0.695	0.822
Thin		
r^2	0.022	0.044
P	0.53	0.40
Thick		
r^2	0.154	0.080
P	0.146	0.328

MD, mean deviation; PSD, pattern standard deviation.

Table 2 Comparison between group 1 ($n = 49$) and group 2 ($n = 50$)

	Group 1 (<535 μm) n = *49*		*Group 2 (>535 μm)* n = *50*		t-*test*
	Mean	*SD*	*Mean*	*SD*	P-*value*
CCT (μm)	504.8	30.8	574.6	35.03	<0.001
MD (dB)	−9.01	8.72	−4.39	4.70	0.0014
PSD (dB)	6.38	3.99	4.25	3.19	0.0076
IOP (mm Hg)	18.02	4.66	17.79	3.57	0.957

CCT, central corneal thickness; IOP, intraocular pressure; MD, mean deviation; PSD, pattern standard deviation.

Goldmann tonometer was equal to the manometric one when CCT value was about 520 μm. Deviations from this value resulted in overestimation or underestimation of IOP that could be calculated as 7 mmHg every 100 μm of thickness; CCT was significantly correlated with the IOP measured by applanation tonometry, but no correlation was found between the IOP measured with applanation tonometry and the corneal radius. In 1978, Johnson *et al*[10] published the data of a patient with CCT of 900 μm that despite hypotonic therapy did not lower its IOP In 1991, Graef[11] demonstrated that different CCT caused different readings of IOP both with applanation tonometry and Reichert noncontact tonometry (NCT II). In 2004, Brandt *et al*[12] published data suggesting that CCT measurements may be useful in the management of glaucomatous patients. Nowadays, many studies have demonstrated that CCT vary significantly in the general population and that this difference may cause misclassification of patients whenever Goldmann applanation tonometry IOP value is used for diagnostic definitions.[9–14] There is general agreement on the finding that patients with ocular hypertension have thicker central corneas,[15,16] whereas cases of normal pressure glaucoma have thinner than average central corneas.[17,18] The relationship between pachymetry values and the risk of glaucoma damage is still controversial. No correlation between the thickness of the central cornea, of the peripapillary retinal nerve fibres,[19] and of the lamina cribrosa[20] was found in nonglaucomatous human eyes; it is not known whether hystomorphometry of the lamina cribrosa or peripapillary nerve fibre layer thickness in glaucomatous eyes would show a relationship with corneal thickness. There is no consensus on the influence of pachymetry values on the likelihood of progression of glaucomatous damage in established glaucoma. Kim and Chen[21] and Herndon *et al*[22] proved the association of thinner central cornea values with VF progression in glaucoma patients.

Jonas *et al*[23] and Chauhan *et al*[24] found an association among lower CCT and worse base line VF, but the lower CCT was not associated with progression of glaucomatous optic nerve neuropathy.

In our study, a significant correlation was found between CCT and both MD and PSD, with thinner corneas significantly associated with worse damage. When we analysed the correlation in the two groups, the significance was less for PSD probably because of its nonlinear behaviour, for the 50% reduction of the number of eyes in the each group, or for the different distribution of the values. When the entire cohort was divided into two groups on the basis of CCT, a significant difference was found for both MD and PSD. Ocular hypertensives and POAG cases with very early damage were not included. Our data suggest that a thinner cornea, causing a systematic underestimation of the true IOP, could very well lead to a late diagnosis and as a consequence to greater progression of damage despite apparently 'safe' treated IOP. On the other hand, patients with a thick cornea despite a possibly lower risk of progression are more likely to be treated.

Our data did not show any correlation between CCT and IOP probably because all patients were already treated with IOP-lowering medications; this type of correlation was outside the purpose of this study.

In our study, no correlation was found between age and CCT and between age and VF indices.

It is assumed that CCT does not change during adult life. Whether this applies to glaucoma patients undergoing chronic topical treatment is not known yet.

A simple exam as pachymetry might be useful to obtain a prognostic factor for the onset of glaucoma or for the severity of glaucomatous damage. Thin central corneas were shown to be a strong factor associated with progression from OH to POAG[7,16,25] or for the appearance of early defects with nonconventional perimetry in OHTs.[26,27]

In summary, our data show a definite inverse relationship between the central corneal pachymetry value and the damage of the visual field.

Should the correlation between corneal thickness and progression of disease be confirmed longitudinally for POAG, the pachymetry value could become helpful also for cross-sectional evaluations even without an IOP-correcting algorithm.

Our study has limitations. It was of sectional nature and therefore does not allow direct estimation of the influence of CCT on the progression of disease.

Study selection criteria limited the sample to patients with unquestionable glaucoma damage, not yielding data on glaucoma suspects or ocular hypertensives.

Our data support the existence of a *de facto* relationship between CCT and stage of glaucoma damage. Whether this is related to IOP-measuring error or to intrinsic ocular factor associated with thinner CCT remains to be assessed and warrants further studies.

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