Corneal Thickness in Ocular Hypertension, Primary Open-angle Glaucoma, and Normal Tension Glaucoma

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Objectives: To determine the effect of central corneal thickness (CCT) on the measurement of intraocular pressure (IOP) and on the resultant reclassification of patients as having primary open-angle glaucoma (POAG), normal tension glaucoma (NTG), or ocular hypertension (OHT).

Methods: Intraocular pressure (Goldmann applanation tonometry) and CCT (ultrasound pachymetry) were measured in 22 patients with NTG, 49 with POAG, 44 with OHT and in 18 control subjects. The CCT was used to obtain a corrected value for the IOP and to reclassify the type of glaucoma.

Results: There was no significant difference in CCT between controls (552 ± 35 µm) and patients with POAG (543 ± 35 µm), but the CCT in the group with NTG (521 ± 31 µm) was significantly lower than that in the control group or the group with POAG (P<.001), and the CCT in the group with OHT (583 ± 34 µm) was significantly higher than in controls or patients with POAG (P<.001). Correcting IOP for corneal thickness, 31% of the patients with NTG could be reclassified as having POAG, and 56% of the patients with OHT as normal.

Conclusions: Patients with NTG have a thinner CCT than do patients with POAG or controls. Underestimation of the IOP in patients with POAG who have thin corneas may lead to a misdiagnosis of NTG, while overestimation of the IOP in normal subjects who have thick corneas may lead to a misdiagnosis of OHT.

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Intraocular pressure (IOP) is an important parameter in the diagnosis and follow-up of glaucoma. While Goldmann applanation tonometry is the preferred method of measurement of IOP, several factors, including corneal thickness, may influence its accuracy.1 A positive linear correlation between central corneal thickness (CCT) and IOP has been reported by Kruse Hansen and Ehlers.2,3 Intraocular pressure measured by applanation may be overestimated or underestimated in thick or thin corneas, respectively.

RESULTS

The study included 64 women (10 controls; 16 with NTG; 18 with POAG) and 69 men (8 controls; 6 with NTG; 26 with OHT; and 29 with POAG). Controls and patients with OHT were younger than patients with POAG and NTG (58.7 ± 25.9 and 60.3 ± 12.6 vs 68.8 ± 15.3 and 75.3 ± 10.1 years, respectively [mean ± SD]) (P<.001). The mean follow-up before the study was 8.5 ± 4.2 years for the patients with NTG, 9.6 ± 4.5 years for those with OHT, and 7.6 ± 3.7 years for those with POAG. The CCT, IOP, spherical equivalent, and number of glaucoma medications used in each group are given in Table 1. The mean SD for CCT readings was 5 µm. Patients with POAG and controls had equivalent mean corneal thick-
PATIENTS, MATERIALS, AND METHODS

One hundred fifteen white patients (49 with POAG, 22 with NTG, and 44 with OHT) seen in the glaucoma department of the Jules Gonin Eye Hospital, Lausanne, Switzerland, from June 1997 to January 1998 were included in the study; 18 control subjects were also recruited. All patients were informed concerning the study and gave their oral consent to undergo corneal thickness measurements.

Primary open-angle glaucoma was defined as an IOP of 22 mm Hg or higher in the presence of a typical glaucomatous disc and field changes and an open angle on gonioscopy. Normal tension glaucoma was defined as a typical glaucomatous disc and field changes with an IOP of 21 mm Hg or lower on diurnal measurement and an open angle on gonioscopy. Ocular hypertension was defined as an IOP of 22 mm Hg or higher with normal discs and visual fields and open angles on gonioscopy.

Patients with ocular disease other than glaucoma or OHT were excluded, as were those with myopia or hypermetropia of more than 3 diopters (D) or an astigmatism of more than 1 D.

The type of glaucoma, IOP measurement, refraction, corneal thickness, and number of glaucoma medications used were recorded. Intraocular pressure was measured in a standard manner with a calibrated Goldmann applanation tonometer. The average of 3 consecutive readings before initiation of glaucoma medication was recorded.

Central corneal thickness was measured with an ultrasonic pachymeter (DGH-1000, DGH Technology Inc, Frazer, Pa). All of the measurements were performed by the same examiner (A.M.). Each patient was asked to blink before CCT measurement to avoid any bias because of corneal drying. Ten measurements were made at the center of the cornea of each eye. The lowest CCT reading was used for analysis as it was thought to most likely reflect a perpendicular placement of the pachymeter probe and, therefore, to be the most accurate measurement.

A cycloplegic refraction was performed using an autorefractometer (Nidek AR-1100, Nidek, LTD, Tokyo, Japan). In each subject the mean spherical equivalent was considered for analysis. All measurements were carried out by an observer (R.-P.C.) masked to the diagnosis, and only 1 eye (randomly selected) of each patient was used for analysis. Comparison of means was performed using the Student t test.

Table 1. Values for Central Corneal Thickness, IOP, Spherical Equivalent, and Number of Glaucoma Medications for the Different Groups of Patients

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>NTG</th>
<th>OHT</th>
<th>POAG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central corneal thickness, µm</td>
<td>552 ± 35</td>
<td>521 ± 31</td>
<td>583 ± 34</td>
<td>543 ± 35</td>
</tr>
<tr>
<td>IOP, mm Hg</td>
<td>15.83 ± 2.82</td>
<td>17.25 ± 1.93</td>
<td>27.13 ± 3.84</td>
<td>23.33 ± 7.10</td>
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<tr>
<td>Spherical equivalent, diopters</td>
<td>0.53 ± 2.02</td>
<td>-0.37 ± 2.03</td>
<td>-0.12 ± 2.02</td>
<td>-0.63 ± 2.50</td>
</tr>
<tr>
<td>No. of glaucoma medications</td>
<td>0</td>
<td>1.54 ± 1.20</td>
<td>1.01 ± 0.93</td>
<td>1.63 ± 1.08</td>
</tr>
</tbody>
</table>

*NTG indicates normal tension glaucoma; OHT, ocular hypertension; POAG, primary open-angle glaucoma; and IOP, intraocular pressure. All values are given as mean ± SD.

ness measurements. The mean corneal thickness in the group with NTG was significantly lower than in patients with POAG or controls (P < .001). Central corneal thickness was significantly greater in groups with OHT than in groups with POAG or in controls (P < .001).

The refraction was not notably different between groups. Using the reported correction for corneal thickness, IOP in patients with NTG was underestimated by a mean of 2.2 mm Hg (Table 2); IOP in patients with OHT was overestimated by a mean of 2.3 mm Hg. When the IOP was corrected for corneal thickness, 7 patients (31%) who were diagnosed initially as having NTG had IOPs of 21 mm Hg or greater, and 25 patients (56%) who were diagnosed initially as having OHT had IOPs of 21 mm Hg or lower.

In this study, corneal thickness ranged from 484 to 700 µm. As Goldmann applanation tonometry is accurate for a corneal thickness of 520 µm, the maximum underestimation of IOP was 4.8 mm Hg, and the maximum overestimation was 10.5 mm Hg.

Goldmann and Schmidt first discussed the influence of variations in corneal thickness and scleral rigidity on applanation tonometry. Ehlers et al reported that the Goldmann tonometer provided accurate readings only when the CCT was 0.52 mm; they calculated that applanation tonometry overestimated or underestimated IOP by approximately 5 mm Hg for every 0.070 mm of deviation in corneal thickness. More recently Whitacre et al reported that thin corneas may result in a 4- to 9-mm Hg underestimation of IOP, and thick corneas may result in overestimation of the IOP by 6.8 mm Hg.

Our patients with NTG had considerably thinner CCT than did the group with POAG or the controls, while the group with OHT had notably thicker CCT than did patients with POAG or controls. We have shown that underestimation of IOP may result in some patients with POAG receiving a misdiagnosis and being treated for NTG. Indeed, when corneal thickness was taken into account, 7 (31%) of our patients thought to have NTG actually met the criteria for a diagnosis of POAG. Similarly, many patients diagnosed as having OHT (25 [56%] in our study) actually have normal IOP. In other words, 7 patients (31%) of the patients diagnosed as having NTG actually had POAG, and 25 (56%) of the patients diagnosed as having OHT really had an IOP that was within normal limits. Half of the patients diagnosed as having
OHT, but ultimately found to have normal IOP, had been undergoing treatment with one or more medications.

A high incidence of NTG has been reported in a nationwide survey conducted in Japan.\textsuperscript{10} It would be interesting to see if central corneal pachymetry performed on a sample of that population showed that the high incidence of NTG is more actually associated with thinner corneas.

It is recognized that only a minority of patients with OHT develop visual field loss.\textsuperscript{11,12} This may be because many of these individuals actually only have a thicker cornea, which leads to an overestimation of the IOP. There is also a potential bias in phase 3 pharmacologic studies, in which the effects of new compounds are often tested on patients with OHT, many of whom may actually be normal.

The correct diagnosis and management of patients with glaucoma is dependent on an accurate determination of IOP. Our study has shown that there is a potential for patients with POAG who have thin corneas to be given a misdiagnosis and treated inappropriately for NTG; similarly, normal individuals with thick corneas may be given a misdiagnosis and treated for OHT. We have shown that central corneal pachymetry is important to ensure accurate diagnosis and management of patients suspected of having some form of glaucoma. We suggest that measurement of CCT should be part of the routine workup of patients with glaucoma and those suspected of having glaucoma.

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\section*{REFERENCES}


\begin{table}
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\begin{tabular}{|c|c|c|}
\hline
 & NTG & OHT & POAG \\
\hline
IOP reading without glaucoma treatment & 17.25 ± 1.93 & 27.13 ± 3.84 & 23.33 ± 7.10 \\
Corrected IOP without glaucoma treatment & 19.45 ± 2.42 & 24.83 ± 2.53 & 23.87 ± 6.90 \\
IOP reading with glaucoma treatment & 13.13 ± 3.32 & 22.22 ± 4.16 & 18.59 ± 8.90 \\
Corrected IOP with glaucoma treatment & 15.33 ± 2.01 & 19.92 ± 4.22 & 19.23 ± 7.54 \\
\hline
\end{tabular}
\caption{Comparison of IOP Readings With and Without Treatment and Their Respective Correction for Corneal Thickness*}
\end{table}

* NTG indicates normal tension glaucoma; OHT, ocular hypertension; POAG, primary open-angle glaucoma; and IOP, intraocular pressure. Comparisons were made using the formula of Ehlers.\textsuperscript{8} Values are given as mean ± SD and measured in millimeters of mercury.