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Central Corneal Thickness of Normal Tension Glaucoma Patients in Japan

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Purpose: To compare central corneal thickness (CCT) of patients with normal tension glaucoma (NTG) with that of age-matched normal subjects, patients with open-angle glaucoma (POAG) and ocular hypertension (OH) subjects in Japan.

Methods: Central corneal thickness was measured in 79 NTG, 61 POAG, 73 OH, and 50 normal subjects with an ultrasonic pachymeter. One eye for 1 subject randomly selected in each group was used for inter-group comparison. The relationship between CCT and the maximum intraocular pressure (IOP) measured by Goldmann applanation tonometer with no ocular hypotensive medication (NTG, OH, and normal subjects) or under medication (POAG patients) was analyzed.

Results: The CCT of OH subjects (582 ± 32 μm; mean ± SD) was significantly greater than that of the other groups ($P < .001$), while no difference was seen in CCT among normal (552 ± 36 μm), NTG (548 ± 33 μm) and POAG (550 ± 33 μm) subjects. In normal subjects, CCT and the maximum IOP were significantly correlated but the correlation coefficient was small ($r = 0.420$, $P < .05$).

Conclusions: Central corneal thickness shows no significant difference among NTG, POAG, and normal subjects in Japan, while it is significantly greater in OH subjects. The CCT has little influence on the diagnosis of NTG in Japan. **Jpn J Ophthalmol 2000;44:643–647** © 2000 Japanese Ophthalmological Society

Key Words: Central corneal thickness, Goldmann applanation tonometry, intraocular pressure, normal tension glaucoma, ocular hypertension.

Introduction

Intraocular pressure (IOP) is a key index for the diagnosis and management of glaucoma. Goldmann applanation tonometry is most commonly used in clinical practice for IOP management. However, its accuracy is influenced by many ocular factors.[1] Especially, variation in corneal thickness might result in overestimation or underestimation of IOP measured by an applanation tonometer.[1–5] It has been reported that the measured IOP of ocular hypertension (OH) patients is likely to be overestimated because of their thicker corneas,[6–10] while the measured IOP of normal tension glaucoma (NTG) patients is likely to be underestimated because of their thinner corneas.[11–13] Population-based glaucoma surveys revealed a higher incidence of NTG in Japan than in Europe and the United States.[14–18] Since the corneal thickness was not measured in the glaucoma survey in Japan, one possible concern is that the reported higher incidence of NTG in Japan might actually have been influenced by the fact that Japanese NTG patients might have thinner corneas.

Central corneal thickness (CCT) has been measured by a photographic method, optical methods, a specular microscopic method, or ultrasonic methods and used for the evaluation of corneal thickness.[3,8–13,19–26] Recently, ultrasonic methods are most frequently used because of ease of use and good reproducibility.[20–22] There are several reports about the CCT in glaucoma patients,[9,27,28] but the number of subjects was limited and the results were not necessarily consistent among reports. The current study was carried out to compare CCT among Japanese

Received: May 11, 1999

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Published by Elsevier Science Inc.

0021-5155/00/$–see front matter
PII S0021-5155(00)00275-6

Jpn J Ophthalmol
Vol 44: 643–647, 2000

OH, primary open angle glaucoma (POAG), NTG patients and normal subjects in a larger, more adequate number of subjects.

Materials and Methods

Subjects

Central corneal thickness was measured in both eyes of a total of 263 subjects (NTG: n = 79, POAG: n = 61, OH: n= 73, and normal: n= 50) aged 62.0 ± 13.7 years (mean ± SD). Subjects were consecutive patients at the Department of Ophthalmology, University of Tokyo School of Medicine, who had made routine visits to either the Glaucoma Clinic or Comprehensive Ophthalmology Clinic.

The diagnosis of OH was based on the normal appearance of the optic nerve head, normal visual fields (Humphrey Field Analyzer, Humphrey Systems; Dublin, CA, USA, central 30-2 full threshold program) and an IOP >21 mm Hg measured by Goldmann applanation tonometer at least twice in at least 1 eye in the past. Normal tension glaucoma was diagnosed based on the following criteria: glaucomatous optic nerve head damage,[29] IOP not >21 mm Hg measured by Goldmann applanation tonometer including a 24-hour diurnal pressure curve without medication, visual field damage (Humphrey central 30-2 full threshold program) compatible with the optic nerve head findings and no other obvious causes for these changes. Diagnostic criteria for POAG are the same as those for NTG, except for an IOP >21 mm Hg measured by Goldmann applanation tonometer at least twice in at least 1 eye. The normal subjects were those with no history of elevated IOP or suggestion of glaucoma, and no other apparent ocular diseases except for mild to moderate senile cataract and/or refractive errors.

Subjects with a history of intraocular surgery, corneal disease, refractive error of more than 5 diopters of spherical equivalent and other ocular diseases were excluded.

Methods

The CCT was measured after tonometry with an ultrasonic pachymeter (DGH 500 Pachette™; DGH Technology, Exton, PA, USA) under local anesthesia between 10:00 AM and 1:00 PM. The speed of sound (1640 m/s) was used. All measurements were performed by one of the authors (L.L.W.), placing the pachymeter tip perpendicularly on the cornea and centered over the undilated pupil. An average of five consecutive readings was recorded. In subjects wherein both eyes fulfilled the diagnostic criteria, 1 eye for 1 subject was randomly selected and used for analysis.

Comparison of means was performed using the unpaired *t*-test with Bonferroni's correction for multiple comparison.

Results

The age, sex, and refraction (spherical equivalent) of all subjects are given in Table 1. Table 2 summarizes CCT and the maximum IOP recorded during the follow-up. The maximum IOP was recorded without glaucoma medication in all the subjects except POAG patients; they had received some treatment when they were first diagnosed with POAG.

The CCT of OH subjects (581 ± 32 μm, mean ± SD; n = 73; range, 508–677 μm) was significantly greater than that of the other groups ($P < .001$, unpaired *t*-test with Bonferroni's correction), while no difference was seen in CCT among normal subjects (552 ± 36 μm; n = 50; range, 491–643 μm), POAG (550 ± 33 μm; n = 61; range, 444–606 μm), and NTG patients (547 ± 33 μm; n = 79; range, 476–631 μm). The mean age of OH group was also significantly younger than that of other groups ($P = .003$), and the refraction was significantly more myopic in POAG than in normal subjects ($P = .045$).

There was no significant correlation between CCT and refraction, or age in the analyses using all the data, or each group's data ($P > .10$). The relation-

Table 1. Subject Characteristics

	Normal	NTG	OH	POAG
Age (years)*	66.3 ± 15.0	64.5 ± 10.6	55.0 ± 15.0†	63.5 ± 11.6
Sex (male/female)	23/17	37/42	36/47	25/56
Refraction (diopters)*	0.3 ± 2.0	−0.9 ± 2.0	−1.3 ± 2.1	−1.4 ± 2.0‡
Number of eyes	50	79	73	61

NTG: Normal tension glaucoma; OH: ocular hypertension; POAG: primary open angle glaucoma.
*Values are mean ± SD.
†Significantly smaller than others ($P = .003$).
‡$P = .045$.

Table 2. Central Corneal Thickness (CCT) and Maximum Intraocular Pressure (IOP) During Follow-up Period

	Normal	NTG	OH	POAG
CCT (μm)*	552 ± 36	548 ± 33	582 ± 32†	550 ± 33
Range (μm)	491–643	476–631	508–677	444–606
Maximum IOP (mm Hg)*	14.8 ± 2.3	17.2 ± 1.8	25.4 ± 3.5	24.9 ± 5.3

NTG: normal tension glaucoma; OH: ocular hypertension; POAG: primary open angle glaucoma.
*Values are mean ± SD.
†Significantly greater than others ($P < .001$).

ship between CCT and the maximum IOP was investigated in each group, in NTG + POAG patients, and in normal + OH patients. There was no correlation between CCT and the maximum IOP in each group except for the correlation between CCT and the maximum IOP in the normal subjects and in normal + OH patients. The correlation coefficients were $r = 0.423$, $P = .004$, and $r = 0.385$, $P < .0001$, respectively (Figures 1 and 2).

Discussion

The Goldmann applanation tonometer evaluates the IOP by flattening the cornea based on the Imbert-Fick law that the pressure of a sphere filled with liquid is equal to the pressure flattening the surface of the sphere.[1,3,30] However, applanation tonometry is influenced by many physical factors, such as corneal thickness or ocular rigidity, which offers resistance to applanation pressure.[1,3] The CCT is measured by various methods and is used as a representative value of corneal thickness.[3,8–13,19–26] The Goldmann applanation tonometer was designed to give accurate readings when CCT is 520 μm1,3,30. The CCT in normal cornea has great variation, however.[31,32] In the present normal subjects, the CCT varied from 491 to 643 μm.

Ultrasound pachymeters, which use pulsed ultrasound to measure CCT, are presently the most frequently used type of pachymeter because of ease of use, high reproducibility, and small inter-observer variation.[20–22] The coefficient of variation for this instrument was reported to be approximately 1%.[20–22] Salz et al[20] compared the Haag-Streit optical pachymeter and ultrasound pachymeters and concluded that ultrasound pachymeters had better reproducibility and smaller inter-observer or left and right eye variation than the Haag-Streit optical pachymeter. The CCT values measured with ultrasound pachymeters are, however, reported to be somewhat higher than those measured with optical pachymeters.[20,21] The difference might be attributed, in part, to the characteristics of the instruments and the problem of probe alignment. The probe width of the ultrasound pachymeter is usually 1.5–1.6 mm in diameter and there is a possibility of

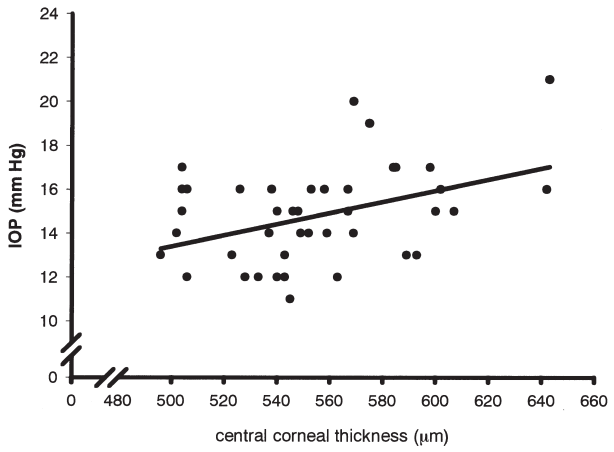

Figure 1. Relationship between central corneal thickness and maximum intraocular pressure (IOP) in normal subjects. Correlation coefficient was $r = 0.423$ and statistically significant ($P = .004$). Line indicates the linear regression line.

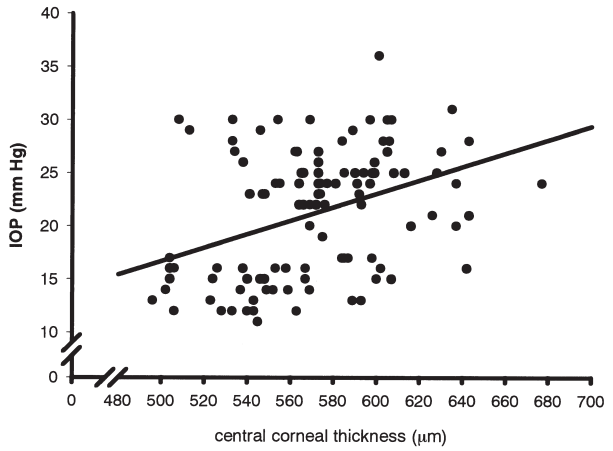

Figure 2. Relationship between central corneal thickness and maximum intraocular pressure (IOP) in ocular hypertension patients and normal subjects. Correlation coefficient was $r = 0.385$ and statistically significant ($P < .0001$). Line indicates linear regression line.

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overestimation of CCT measurement values caused by the position and angle of the probe, which is manually controlled by the observer.

Patients with OH have elevated IOP and do not have apparent optic nerve head damage. Many studies suggest that patients with OH have an increased CCT.[6–10] Our study also demonstrated a thicker CCT of 582 ± 32 μm in Japanese OH patients.

According to Ehlers et al,[5] Goldmann applanation pressure is over- or underestimated by approximately 5 mm Hg for every 70 μm deviation from 0.52 mm of CCT. They used an optical pachymeter to measure CCT,[5] however. Because the CCT values measured with ultrasound pachymeters were reported to be higher than those measured with optical pachymeters,[20,21] we calculated corrected values of IOP using 552 μm (the average value of normal subjects) instead of the 0.52 mm used by Ehlers et al[5]; $IOP_{corrected} = IOP_{measured} - 5/70\ (CCT_{measured} - 552)$. As a result, the maximum IOP of OH patients became <22 mm Hg in 32% of the measurements. Copt et al[13] did similar analysis using the Ehler method with the 0.52 mm of normal CCT value and concluded that 56% of OH patients had normal IOP after correcting for the effect of CCT. When we applied 0.52 mm instead of 552 μm to the correction of IOP, the percentage of OH patients whose maximum IOP became lower than 22 mm Hg was 54%, which was a value similar to that of Copt et al.[13] Conclusively, CCT must be considered an important variable in examining OH patients.

In contrast to OH patients, patients with NTG show glaucomatous optic nerve head damage and visual field defect in spite of normal IOP. Although not always confirmed,[28,33] several authors reported that CCT was significantly thinner in NTG patients than in POAG or normal subjects.[11–13] Do patients with NTG in Japan actually have thinner CCT? Our study demonstrated that CCT in patients with NTG in Japan showed no significant difference from that in patients with POAG or in normal subjects. By calculating the corrected maximum IOP in NTG patients, we found that only 9% of NTG patients had a corrected maximum IOP of ≥22 mm Hg. According to Copt et al,[13] 31% of NTG patients had IOP ≥22 mm Hg after correcting for the influence of CCT by using the normal CCT value of 0.52 mm. They suggested that the relatively higher prevalence of NTG in Japan[14] might be partly attributed to a thinner CCT in NTG patients. However, in our study, the calculation with the normal CCT value of 0.52 mm still gave us the lower percentage of 3% of NTG patients whose corrected maximum IOP was ≥22 mm Hg.

In summary, the CCT in NTG, POAG, OH, and normal subjects in Japan showed great variation. The OH subjects had significantly thicker corneas than the other groups but the CCT was not significantly different among NTG, POAG, and normal subjects. The CCT is thought to have little influence on the diagnosis of NTG in Japan.

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