Central Corneal Thickness of Normal-Tension Glaucoma and Non-Glaucoma Populations in Ethnic Chinese

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Background: The variations in central corneal thickness can influence intraocular pressure measurement. The aim of our study was to determine whether there is a difference in the central corneal thickness between normal-tension glaucoma (NTG) and non-glaucoma populations.

Methods: This prospective study included 33 consecutive patients with NTG and 33 age- and gender-matched healthy subjects as control subjects. The NTG patients were grouped according to the refractive error into group 1 (spherical equivalent +2.5 D ~ -6.0 D) and group 2 (spherical equivalent more than -6.0 D). Central corneal thickness was measured using a ultrasonic pachymeter. The mean central corneal thickness of the NTG and healthy subjects were compared using the student *t*-test and Nilcoxon Rank Sum test..

Results: The mean (±SD) central corneal thickness in the healthy subjects and NTG patients was 554.1 (±36.3) and 547.2 (±31.4) microns, respectively. There were no statistical significant differences between these two groups ($p=0.411$). The median central corneal thickness in the NTG group 1 and group 2 eyes was 545, and 547.5 microns, respectively. The difference was not statistically significant, either ($p=0.799$). Ten patients (30%) of NTG had high myopia (group 2), and their median age was 38.5 years old, which was significantly younger than that of the group 1 patients (50 years old, $p=0.0003$).

Conclusion: This study indicated that there were no significant differences of central corneal thickness between NTG patients and healthy subjects in our clinic. *(Chang Gung Med J 2004;27:50-5)*

Key words: **normal-tension glaucoma, central corneal thickness, myopia, intraocular pressure.**

In as early as 1957, Goldmann first mentioned that variations in central corneal thickness can influence intraocular pressure (IOP) measurement.[1] Many researchers have reported that IOP could be overestimated with a thick cornea and underestimated with a thin cornea.[2-7] In addition, the most apparent difference between normal-tension glaucoma (NTG) with the more common primary open-angle glaucoma (POAG)[8] is that the IOP is within the reference range. Therefore, our study was carried out to compare the central corneal thickness of NTG patients and non-glaucoma subjects to determine whether NTG represents a distinct disease entity or is simply POAG with thinner corneal thickness.

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Received: Jun. 3, 2003; Accepted: Sep. 3, 2003
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METHODS

This prospective study included 33 patients with NTG from January 2002 through December 2002 at the Department of Ophthalmology, Chang Gung Memorial Hospital. The criteria for the diagnosis of NTG included: (1) untreated IOP equal or less than 21 mmHg on at least two visits, (2) open angle on gonioscopic examination, and (3) documented glaucomatous optic nerve cupping with corresponding visual field defect on automated perimetry. Thirty-three subjects that were age matched and gender matched were selected as control subjects with the following criteria: (1) IOP equal or less than 21 mmHg on at least two visits, (2) no history of glaucoma or elevated IOP, (3) healthy optic nerve head, and (4) spherical equivalent range from +2.00 to -6.0 D, with no astigmatism of more than 1.75 D. In order to prevent that the refractive error might influence the results of IOP measurements, the NTG patients were grouped on the basis of the refractive error into group 1 (spherical equivalent +2.5 D to -6.0 D) and group 2 (spherical equivalent more than -6.0 D) prior to measurement. One eye per individual was randomly selected from the NTG patients and healthy subjects for the study. The eyes with corneal pathology or following ocular surgeries were excluded. IOP was measured using a Goldmann applanation tonometer. Central corneal thickness was measured 5 times using the DGH 500 ultrasonic pachymeter (PachetteTM, DGH Technology, Inc., Exton, Penn, USA). Optic nerve head was evaluated using direct ophthalmoscope and documented color disc photos. Visual field results were documented using a 30-2 program of the Humphrey analyzer. The mean central corneal thickness of the NTG patients and healthy subjects were compared by using the student *t*-test and Nilcoxon Rank Sun test. A p value less than 0.05 was considered statistically significant.

Table 1. Demographic Data of All Normal-Tension Glaucoma Patients

No.	Eye	Age (years)	Gender	IOP (mmHg)	CCT (microns)	SE (diopter)	C/D ratio
Group 1 (SE +2.5D ~ -6.0D)							
1	R	28	F	18	607	-1.00	0.7*0.8
2	R	30	M	15	545	+0.13	0.6*0.7
3	R	42	M	12	528	-0.25	0.7*0.9
4	L	43	F	17	607	-2.88	0.6*0.8
5	R	44	M	14	515	-2.63	0.7*0.8
6	R	45	F	15	565	+0.25	0.4*0.5
7	R	48	M	16	554	-5.38	0.9*0.9
8	L	49	M	10	509	+0.38	0.8*0.9
9	L	49	M	12	535	+2.50	0.7*0.8
10	R	49	M	9	491	-4.00	0.9*0.9
11	R	50	F	12	548	+0.88	0.9*0.9
12	R	50	M	9	511	-5.50	0.9*0.9
13	R	52	M	8	540	+0.38	0.8*0.8
14	L	52	M	13	574	+1.25	0.8*0.9
15	R	59	F	14	555	-0.25	0.8*0.9
16	R	62	M	10	515	+2.00	0.9*0.9
17	L	62	F	14	514	+0.25	0.8*0.9
18	L	62	F	18	573	-0.25	0.8*0.9
19	L	63	F	12	540	+1.63	0.7*0.8
20	R	65	M	15	546	+1.25	0.8*0.8
21	L	66	F	15	573	+1.25	0.7*0.8
22	R	67	M	13	541	-0.13	0.7*0.8
23	R	82	M	13	561	+2.63	0.5*0.7
median		50	14:9	13	545	0.25	
Group 2 (SE more than -6.0 D)							
1	R	27	F	15	571	-8.75	0.8*0.9
2	R	34	F	12	506	-7.38	0.8*0.9
3	L	34	M	13	605	-6.75	0.8*0.8
4	L	35	F	18	539	-8.38	0.9*0.9
5	L	37	F	12	540	-8.88	0.8*0.9
6	L	40	F	11	517	-6.00	0.8*0.8
7	R	41	F	18	587	-10.50	0.7*0.7
8	R	42	M	14	587	-8.50	0.4*0.5
9	R	42	F	12	502	-8.63	0.7*0.8
10	R	45	M	15	555	-8.88	0.8*0.9
median		38.5	3:7	13.5	547.5	-8.57	

Abbreviations: IOP: intraocular pressure; CCT: central corneal thickness; SE: spherical equivalent; C/D ratio: cup/disc ratio

RESULTS

The demographic data of all NTG patients are listed in Table 1. The mean (±SD) central corneal thickness in the healthy subjects and NTG patients was 554.1 (±36.3) and 547.2 (±31.4), respectively. No statistical differences were found between them ($p = 0.411$) (Power > 99.9%) (Table 2). The median central corneal thickness in the NTG group 1 and group 2 eyes was 545, and 547.5 microns, respectively, and no statistical differences were found either ($p = 0.799$). Thirty percent of NTG patients had high myopia (group 2) and their median age was 38.5 years old, which was significantly younger than that of the group 1 patients (50 years old, $p = 0.0003$) (Table 3).

Table 2. Gender, Age, IOP Readings, Central Corneal Thickness, and the Spherical Equivalent for the Normal-Tension Glaucoma Patients and Age- and Sex-Matched Healthy Subjects (Controls).

	Gender	Age (years)			IOP (mmHg)		CCT (microns)			SE (diopter)
	(M:F)	Mean (SD)	Range	*p*	Mean (SD)	Range	Mean (SD)	Range	*p*	Mean (SD)
NTG (n=33)	17:16	48.4 (12.8)	27-82	0.905	13.5 (2.7)	9-19	547.2 (31.4)	491-607	0.411*	-2.7 (4.2)
Controls (n=33)	17:16	48.7 (13.8)	29-86	--	13.7 (2.7)	8-18	554.1 (36.3)	470-617	--	-0.9 (2.0)

*Power > 99.9%

Abbreviations: IOP: intraocular pressure; CCT: central corneal thickness; SE: spherical equivalent

Table 3. Gender, Age, IOP Readings, Central Corneal Thickness, and Spherical Equivalent for All Normal-Tension Glaucoma Patients and Subgroups.

	Gender	Age (years)			IOP (mmHg)		CCT (microns)			SE (diopter)
	(M:F)	Median	Range	*p*	Median	Range	Median	Range	*p*	Median
NTG (N = 33)	17:16	48	27-82		13	9-19	545	491-607		-0.25
Group 1 (N = 23)	14: 9	50	28-82	--	13	9-19	545	491-607	--	0.25
Group 2 (N = 10)	3: 7	38.5	27-45	0.0003*	13.5	11-18	547.5	502-605	0.799	-8.75

Abbreviations: IOP: intraocular pressure; CCT: central corneal thickness; SE: spherical equivalent

* *p* value < 0.05, Nilcoxon Rank Sun Test

Group 1 (SE +2.5D ~ -6.0D)

Group 2 (SE more than -6.0D)

DISCUSSION

Goldmann applanation tonometry has been widely accepted as the "gold standard" for measuring IOP. It is based on the Imbert-Fick law, which assumes that the surface of the cornea is perfectly elastic, flexible, and infinitely thin.[9,10] In as early as 1957, Goldmann found that scleral rigidity and central corneal thickness influenced IOP measurement.[1] Later, many researchers[2-7,11,12] also reported the relation between central corneal thickness and IOP. Ehlers and associates[11] found that the differences between applanation readings and the actual IOP measured using manometry were linearly correlated with central corneal thickness. The authors concluded that a reduced corneal thickness of 0.45 mm produced an underestimation of IOP up to 4.7 mmHg, whereas an increased corneal thickness of 0.59 mm caused an overestimation of 5.2 mmHg, when the actual IOP is 20 mmHg. More recent studies have revealed that an increase of 0.18 to 0.23 mmHg[7,10] or 0.19 mmHg[12] in IOP with each 10-micron increase in central corneal thickness, which was considerably lower than the results of Ehlers et al. However, in this study, when we used Ehlers's estimation (0.7 mmHg per 10 microns) to adjust the IOP measurement, no patient with NTG had IOP of more than 21 mmHg (Fig. 1). Although the variation in central corneal thickness might influence the IOP measurement, the differences of readings could be clinically negligible except in cases of extremely thick or thick

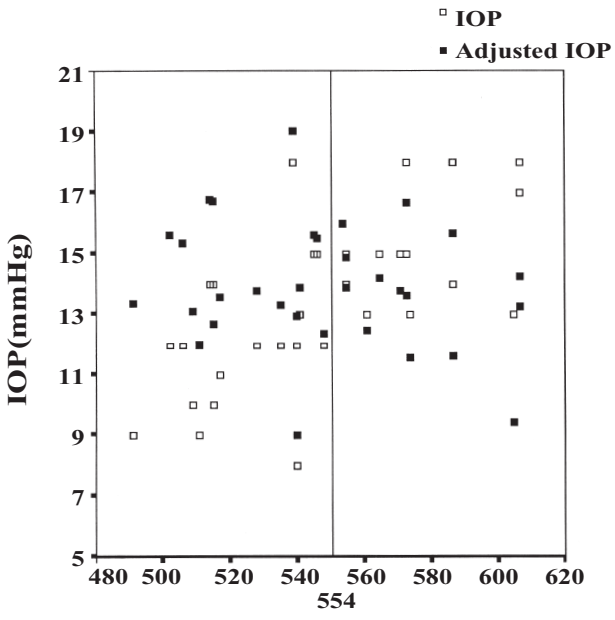

Fig. 1 The distribution of intraocular pressure (IOP) (before and after adjusting) using the estimate of Ehlers et al. The mean central corneal thickness as 554 microns. None of them more than 21 mmHg.

corneas. The statistical power of our study was larger than 99.9% (Table 2). Thus, our results indicated that the central corneal thickness of NTG patients were generally not thinner than those of healthy populations, which is in agreement with the results of some previous reports.[13-18]

However, other researchers have reported that the corneas of NTG patients were significantly thinner than those of healthy subjects or primary open-angle glaucoma (POAG) patients.[7,19-23] On the basis of their adjusted IOPs, these NTG patients could be grouped as POAG patients, suggesting that most NTG patients (except for those without thinner corneal thickness) are actually POAG patients. However, the differences between NTG and POAG in either mechanisms or clinical features have been reported in the literature.[24-30] Some have described that the optic disc heads differed in patients with NTG and POAG[24-26] and the optic disc bleeding[27,28] was increased in patients with NTG. Araie et al.[29] noted that the visual field defects differed between patients with NTG and POAG and suggested a difference between the regions of the optic disc were susceptible to damage in NTG and POAG. Zeiter et al.[30] also found visual field defect differences and suggested that vascular ischemia may have a larger role in the pathogenesis of optic nerve damage and visual field loss in patients with NTG than in those with POAG. Moreover, NTG but not POAG appears to be associated with migraine headache[31] and ocular vasospasm.[32,33] The differences in clinical findings and pathogenesis between NTG and POAG indicate that NTG and POAG are different disease entities. It is not reasonable that the NTG patients just have thinner cornea and must be grouped as POAG patients after adjusting IOPs, although actually a small portion of NTG patients with extremely decreased corneal thickness should be grouped as POAG patients. Because of the prevalence of NTG varied among different populations, we supposed that the different results among these studies may have resulted from the selection bias of the NTG patients. Our results agreed with the studies from China[13] and Japan[17] where NTG prevalence is higher. On the contrary, the studies with results contrary to ours may have enrolled in higher percentage of POAG patients with thinner corneal thickness (misdiagnosed as NTG patients), which resulted in the different results.

Since several researchers reported that the refractive status and corneal curvature could influence the results of IOP measurements,[10,23] our NTG patients were grouped according to the refractive status. Our results showed no differences of central corneal thickness between these two groups. However, we found that the patients with NTG and high myopia (spherical equivalent more than -6.0 D) were significantly younger. To our knowledge, this has not been previously mentioned, though many studies have noted the association between NTG and myopia.[8,34-37] The results of these studies have suggested that myopic eyes are more likely than healthy eyes to be within the reference range for IOP. Anatomical characteristics (including the oblique insertion of the optic nerve, thinner and weaker lamina cribrosa or relatively larger area of peripapillary atrophy,[38] which may result in interference in the blood supply, blockage of axonal transport or mechanical disruption at the lamina cribrosa and subsequently glaucomatous optic nerve head damage) may explain this likelihood. We suggested that the fragile optic nerve head of myopic eyes may be predisposed to develop juvenile glaucoma with intraocular pressure within the reference range. We must pay more attention to the optic nerve damage or visual field loss of these high myopic people whose optic discs are hard to evaluate.

In conclusion, this study showed no significant differences of central corneal thickness between NTG patients and healthy subjects. Adjusting IOP based on central corneal thickness did not result in high IOP readings for most NTG patients except in cases of extremely thick or thin corneas. In addition, the fragile optic nerve head of myopic eyes may predispose a patient to develop juvenile glaucoma with intraocular pressure within the reference range.

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中國人正常眼壓性青光眼病人之中心角膜厚度

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背 景： 角膜厚度之變異會影響眼壓之測量。本研究在比較正常眼壓性青光眼（normal-tension glaucoma）之病人的中心角膜厚度和正常人是否不同。

方 法： 本研究包括33位正常眼壓性青光眼病人及33爲年齡及性別相符的正常人作爲對照組。使用超音波角膜厚度儀測量中心角膜厚度。爲避免屈光度對眼壓測量之影響，我們將正常眼壓性青光眼病人依屈光度分成兩組，第一組爲球面度數介於+2.5至-6.0屈光度；第二組爲球面度數大於-6.0屈光度。使用t檢定來比較正常眼壓性青光眼和沒有青光眼的正常人之平均中心角膜厚度。

結 果： 沒有青光眼的正常人和正常眼壓性青光眼之平均中心角膜厚度（±變異數）分別爲554.1 (±36.3) 及547.2 (±31.4) 微米，在統計上並沒有差異，*p*值爲0.411。第一組及第二組病人之平均中心角膜厚度分別爲545及547.5微米，在統計上也沒有差異，*p*值爲0.799。所有正常眼壓性青光眼之病人中，有10位 (30%) 爲高度近視，歸類爲第二組，他們的平均年齡爲38.5歲，比第一組50歲的人來的低，在統計上有意義，*p*值爲0.0003。

結 論： 我們的結果顯示，正常眼壓性青光眼之中心角膜厚度和沒有青光眼的正常人並沒有不同。

(長庚醫誌 2004;27:50-5)

關鍵字：正常眼壓性青光眼，中心角膜厚度，近視，眼壓。

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受文日期：民國92年6月3日；接受刊載：民國92年9月3日。
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