Correlation between Central Corneal Thickness and Visual Field Defect, Cup to Disc Ratio and Retinal Nerve Fiber Layer Thickness in Primary Open-Angle Glaucoma Patients

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Objective: *To assess the correlation between central corneal thickness (CCT) and visual field parameters, cup-to-disc ratio and retinal nerve fiber layer (RNFL) thickness in primary open-angle glaucoma (POAG) patients in Songklanagarind Hospital.*

Material and Method: *A Retrospective analytical study of the medical records of primary open-angle glaucoma patients, between January 2006 and April 2008, were reviewed. All subjects underwent a complete eye examination. The CCT measurement was performed by ultrasonic pachymeter. Mean deviation (MD), pattern standard deviation (PSD), cup-to-disc ratio, and the RNFL thickness of each patient were collected. The correlation coefficient between CCT and MD, PSD, cup-to-disc ratio and RNFL thickness was analyzed.*

Results: *Twenty-six POAG patients (47 eyes) were eligible for the study. Mean age was 60.96±7.44 years. Average CCT was 511.15±29.66 μm. Mean MD and PSD were -10.01± 8.20 and 7.52±4.43 decibel respectively. Mean cup-to-disc ratio was 0.71±0.17. Mean RNFL thickness of superior, inferior, temporal, nasal quadrants and all quadrants were 101.60±28.68, 87.15±32.56, 60.64±14.14, 61.83±13.96 and 77.80±17.58 μm, respectively. There were significant correlations between CCT and MD (r = 0.532, p<0.001), PSD (r = -0.288, p = 0.05), cup-to-disc ratio (r = -0.478, p = 0.001), and average RNFL thickness (r = 0.487, p = 0.001).*

Conclusion: *There were significant correlations between CCT and visual field parameters, cup-to-disc ratio, and RNFL thickness.*

Keywords: *Central corneal thickness, Mean deviation, Pattern standard deviation, Retinal nerve fiber layer thickness, Optical coherence tomography*

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Glaucoma is a chronic progressive optic neuropathy, which is represented by decreased peripapillary retinal nerve fiber layer (RNFL) thickness, followed by optic neuropathy and visual field defect[1-3]. Currently, glaucoma diagnosis can be achieved through structural and functional evaluations. Structural evaluation includes optic disc and RNFL assessment, and functional evaluation is obtained through perimetry.

Some studies have found a correlation between RNFL thickness and visual field defect in early glaucoma patients although RNFL loss would be detected before visual field defect[1,4,5]. Thus, thinning of RNFL is important for glaucoma diagnosis and treatment.

Nowadays, many implements have emerged to encourage glaucoma diagnosis and monitoring glaucoma progression. One of these innovations, which help to assess RNFL, is optical coherence tomography (OCT). This technology is based on low coherence interferometry to create an optic disc image for peripapillary RNFL thickness evaluation. The outstanding properties of OCT are non-contact equipment, high resolution, and the provision of a cross-sectional image that is good for quantitative evaluation of the optic disc and RNFL[6]. Moreover, it is not only convenient to operate, but also a time saving procedure.

Central corneal thickness (CCT) effects glaucoma diagnosis, treatment, and follow-up because it has an impact on intra-ocular pressure (IOP)

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measurement by Goldmann applanation tonometer. Thicker corneas provide falsely elevated IOP and thinner corneas give a falsely lower value[7]. According to the Ocular Hypertension Treatment Study (OHTS), CCT appears to be a strong predictive factor for the development of primary open-angle glaucoma (POAG) in ocular hypertension patients[8].

Therefore, knowing the correlation between CCT and RNFL thickness should be beneficial for early glaucoma detection and treatment.

Material and Method

A retrospective analytical study reviewed the medical records of POAG patients in Songklanagarind Hospital between January 2006 and April 2008. The study was approved by the institution's Ethics Committee. The inclusion criteria were age between 18 and 80 years, spherical refraction within ±5.0 diopters, and cylinder correction within ±3.0 diopters. POAG was defined according to the following criteria: glaucomatous optic neuropathy, glaucomatous visual field defects with a pattern of standard deviation <5%, or a glaucoma hemifield test (GHT) showing outside normal limit with an iridocorneal angle that was opened. Glaucomatous optic neuropathy included one of these findings: cup-disc ratio >0.5, asymmetrical cup-disc ratio >0.2, notching of the neuroretinal rim, vertical elongation of the optic cup, or RNFL loss.

Subjects were excluded if they had any history of corneal disease, previous ocular or refractive surgery, ocular laser, contact lens use, optic nerve disease, retinal disease, or other conditions that concealed a retinal evaluation (e.g., vitreous hemorrhage).

The following data were obtained for analysis: demographic data, such as age, sex, and ethnicity, and past medical history. Each subject underwent a comprehensive ophthalmic examination, including best-corrected visual acuity, slit-lamp biomicroscopy, intra-ocular pressure (IOP) measurement by Goldmann applanation tonometry, gonioscopy and optic nerve head and peripapillary RNFL evaluation by 78 or 90-diopter lens. All participants were also performed automated perimetry using 30-2 or 24-2 Swedish Interactive Threshold Algorithm (SITA), mean CCT measurement by ultrasonic pachymeter (Tomey SP-3000), and peripapillary RNFL thickness assessment using the optical coherence tomography technique (OCT) (Stratus OCT model 3000, software ver. 4.0; Carl Zeiss Meditec, Dublin, CA, USA) through fast RNFL thickness scanning.

Correlation between CCT and other parameter including RNFL thickness, cup to disc ratio, mean deviation (MD), and pattern standard deviation (PSD) were determined by Pearson's correlation coefficient (r) (SPSS Version 13.0; SPSS, Chicago, IL, USA). The results were considered significant at $p<0.05$.

Results

Twenty-six POAG patients (47 eyes) were eligible for the study. Demographic data and descriptive statistics are presented in Table 1. Mean age of patients was 60.96±7.44 years. Nearly fifty-eight percent of the patients were male. The distribution of RNFL thickness from thickest to thinnest was superior, inferior, nasal, and temporal respectively. Regarding to visual field parameters, there were statistically significant correlation between CCT and MD (r = 0.532; $p<0.001$), CCT and PSD (r = -0.288; $p = 0.05$) (Fig. 1, 2). The correlation coefficient between CCT and cup-to-disc ratio also had statistically significant correlation (r = -0.478; $p = 0.001$) (Table 2, Fig. 3). Table 3 showed the correlation coefficient between CCT and RNFL thickness. There were

Table 1. Demographic data of enrolled patients

Data	Total (n = 26 patients, 47 eyes)
Age (years)	60.96±7.44
Male	15 (57.69%)
Type of POAG	
Normal tension glaucoma (NTG)	23 (48.94%)
High tension glaucoma (HTG)	23 (48.94%)
Pseudoexfoliation glaucoma	1 (2.12%)
IOP (mmHg)	16.40±3.91
Cup-disc ratio	0.71±0.17
CCT (μm)	511.15±29.66
RNFL thickness (μm)	
Superior quadrant	101.60±28.68
Inferior quadrant	87.15±32.56
Temporal quadrant	60.64±14.14
Nasal quadrant	61.83±13.96
Average	77.80±17.58
Visual field (dB)	
MD (SD)	-10.01±8.20
PSD (SD)	7.52±4.43

POAG = primary open angle glaucoma; IOP = intraocular pressure; CCT = central corneal thickness; RNFL = retinal nerve fiber layer; MD = mean deviation; PSD = pattern standard deviation

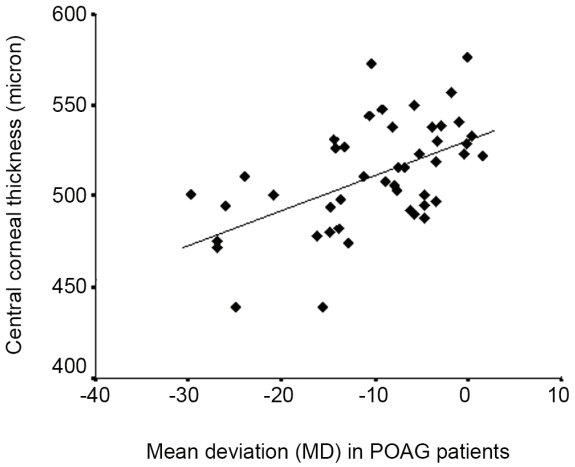

Fig. 1 Scatter plot of CCT versus mean deviation (MD) in POAG patients.

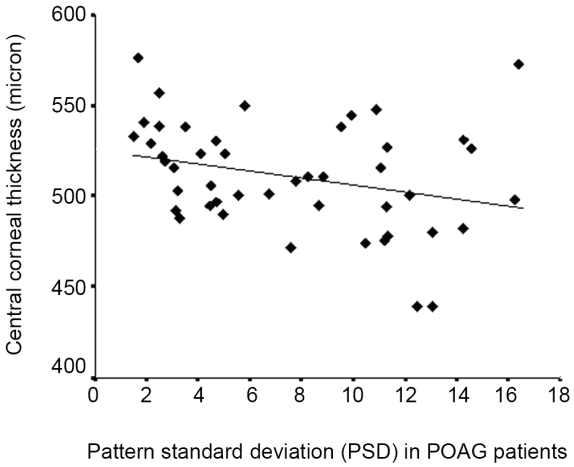

Fig. 2 Scatter plot of CCT versus pattern standard deviation (PSD) in POAG patients.

statistically significant correlations between CCT and RNFL in all quadrants and average RNFL with highest correlation for average RNFL (r = 0.487; $p = 0.001$) (Fig. 4).

Discussion

Detecting glaucoma progression is very important for glaucoma management. Not only regular and careful IOP monitored but also identified risk factors in each patient were crucial for stabilization of deterioration of vision in glaucoma patients. Thin central corneal thickness (CCT) is an independent risk factor for conversion of ocular hypertention to POAG and glaucoma progression[8,9].

Many studies found the relationship between thin CCT and severity glaucomatous visual field defect that consistency with this study's results[10-12]. However, a study by Cao et al reported a contradicted result[13]. The present study found no relationship between thin CCT and visual field progression in treated POAG patients who had asymmetric CCT between both eyes. The difference of these results might cause by different glaucoma staging, studied population, and study design.

The association between CCT and cup-to-disc ratio was previously documented by some studies. The results of those studies showed negative correlation between CCT and cup-to-disc ratio that meant patient who had thinner CCT trended to have more severe glaucomatous optic neuropathy (larger cup-to-disc ratio)[10,14,15]. In the present study, the result also showed negative correlation between CCT and cup-to-disc ratio that was comparable with previous studies.

The significant moderate correlation between CCT and average RNFL thickness in POAG patients in the present study was comparable with the previous report by Kaushik et al, that ocular hypertensive patients with thin corneas (CCT ≤555 μm) had thinner

Table 2. Correlation between CCT and cup to disc ratio, MD, and PSD

CCT (n = 47 eyes)	Cup to disc ratio (n = 47 eyes)	MD (n = 47 eyes)	PSD (n = 47 eyes)
Pearson's correlation coefficient (r)	-0.478	0.532	-0.288
p-value	0.001	<0.001	0.05

Table 3. Correlation between CCT and RNFL thickness

CCT	RNFL thickness (μm)				
	Superior quadrant	Inferior quadrant	Temporal quadrant	Nasal quadrant	Average
Pearson's correlation coefficient (r)	0.413	0.328	0.471	0.355	0.487
p-value	0.004	0.025	0.001	0.014	0.001

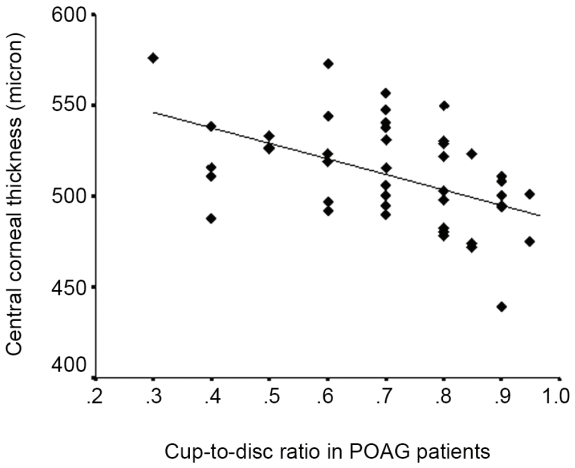

Fig. 3 Scatter plot of CCT versus cup-to-disc ratio in POAG patients.

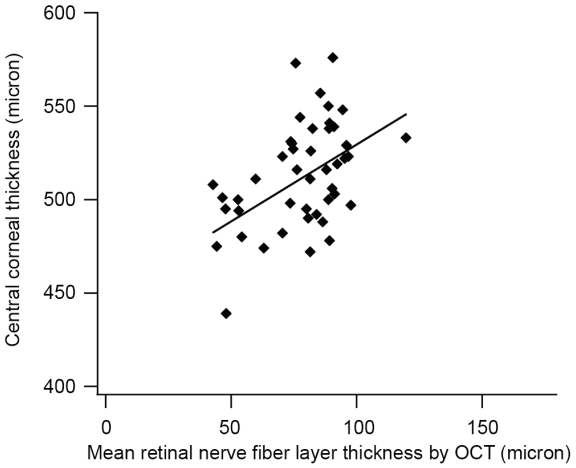

Fig. 4 Scatter plot of CCT versus mean RNFL thickness by OCT in POAG patients.

RNFL thickness compared to subjects with thick corneas[16]. Additionally, this correlation was found also in the study by Henderson et al, which thinner RNFL was associated with thinner CCT in OHT patients by using a scanning laser polarimeter to assess RNFL thickness[17]. These results implied that thinner CCT indicates more glaucoma severity.

In a recent study, the inferior part of the peripapillary RNFL had the strongest correlation with CCT in OHT patients[16]. Moreover, the inferior quadrant of the RNFL was also the best discriminator for glaucoma[18-20]. There was no solid evidence that can explain these findings, only the observation that the inferior quadrant OCT-measured RNFL defect corresponding with superior visual field defect was a common finding in early stage of POAG[21-24]. However, the most powerful correlation between RNFL and CCT found in the present study was average segment. The dissimilarity might originate in the racial differences, which effected RNFL thickness[25-27].

Previously, there were some hypotheses about the association between the changing of CCT and peripapillary RNFL thickness in glaucoma patients. One interesting hypothesis proposed a correlation between CCT and extracellular matrix alteration in lamina cribosa[28]. This hypothesis was supported by another study by Girkin et al, who described the influences of thin CCT on aqueous humor drainage and diurnal IOP fluctuation by using the embryological relationship among the cornea, trabecular meshwork, iris, and lamina cribosa. If there was corneal structural change, it should be related to trabecular meshwork transformation in glaucoma patients[29].

However, the present study also had limitations because it was a retrospective study. Outcome measures collected from medical records might be impeded, for example, and optic disc evaluations relied on the experience of ophthalmologists, CCT measurement depended on technician skill, and RNFL assessment using OCT was effected by each patient's conditions (e.g., a cataract reduced measure reliability due to decreased signal strength). The subjects in the present report could not reflect glaucoma characteristics of the population as a whole, because the sample size was small, and there were barely any other ethnicities than Thai. Nevertheless, some data that were recruited for analysis might lack of independency (two eyes from one patient). Although the correlation coefficient (r) showed significant correlation, the correlations of most of the analyses showed only low to moderate correlation thus careful interpretation was recommended. Even so, these findings yielded profits in the management for glaucoma patients.

Conclusion

From the correlation between CCT and visual field parameters, cup-to-disc ratio and RNFL thickness, these can be inferred that thin CCT is a factor associated with POAG. Thus, thin CCT patients should be observed closely for early glaucomatous changing.

What is already known on this topic?

The relationship between thin CCT and glaucoma progression both structural and functional were established. Among these relationships, there

were some contradictions of the results between studies, especially between thin CCT and structural change. One of the hypotheses that might explain these results was the ethnic distribution in the studied subjects. In the previous reports, most of studied subjects were white and/or black patients. Hence, knowing more about the relationship of thin CCT and glaucoma damage in Thai ethic would enlighten for glaucoma management in Thai people.

What this study adds?

Among Thai glaucoma patients, the relationship between thin CCT and structural and functional damage were same as previous evidences. However, the most powerful correlation between thin CCT and RNFL thickness was average RNFL thickness that contradicted from previous report. This result might be useful for glaucoma progression monitoring in Thai patient.

Potential conflicts of interest

None.

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ความสัมพันธ์ระหว่างความหนาของกระจกตาส่วนกลาง และความผิดปกติของลานสายตา สัดส่วนของจานประสาทตาและความหนาของเส้นใยประสาทจอตา ในผู้ป่วยโรคต้อหินแบบมุมเปิดปฐมภูมิ

บุญชัย หวังศุภดิลก, ลชญาช์ โอพาพิริยกุล

วัตถุประสงค์: *เพื่อทราบความสัมพันธ์ระหว่างความหนาของกระจกตาส่วนกลาง และความผิดปกติของลานสายตา สัดส่วนของจานประสาทตาและความหนาของเส้นใยประสาทจอตา ในผู้ป่วยโรคต้อหินแบบมุมเปิดปฐมภูมิ ในโรงพยาบาลสงขลานครินทร์*

รูปแบบการศึกษา: *การศึกษาเชิงวิเคราะห์แบบศึกษาย้อนหลัง (retrospective analytical study)*

วัสดุและวิธีการ: *เก็บข้อมูลจากแฟ้มประวัติผู้ป่วยที่ได้รับการวินิจฉัยเป็นโรคต้อหินแบบมุมเปิดปฐมภูมิ ตั้งแต่เดือนมกราคม พ.ศ. 2549 ถึง เดือนเมษายน พ.ศ. 2551 วินิจฉัยโดย ลักษณะจานประสาทตาและลานสายตาผิดปกติเข้าได้กับโรคต้อหิน ทุกคนได้รับการตรวจตาโดยละเอียด ร่วมกับวัดความหนาของกระจกตาส่วนกลางโดยเครื่องวัดด้วยคลื่นเสียงความถี่สูง และวัดความหนาของเส้นใยประสาทจอตารอบจานประสาทตาโดยเครื่อง optical coherence tomography (OCT) ข้อมูลที่ได้นำมาวิเคราะห์หาความสัมพันธ์ระหว่างความหนาของกระจกตาส่วนกลาง และ mean deviation (MD), pattern standard deviation (PSD), cup to disc ratio และความหนาของเส้นใยประสาทจอตา*

ผลการศึกษา: *มีผู้ป่วยโรคต้อหินแบบมุมเปิดปฐมภูมิที่เข้าได้กับการศึกษาทั้งหมด 26 ราย (47 ตา) มีอายุเฉลี่ย 60.96±7.44 ปี ค่าเฉลี่ยความหนาของกระจกตาส่วนกลาง คือ 511.15±29.66 ไมครอน ค่าเฉลี่ย mean deviation และ pattern standard deviation คือ -10.01±8.20 และ 7.52±4.43 เดซิเบล ตามลำดับ ค่าเฉลี่ย cup to disc ratio คือ 0.71±0.17 ค่าเฉลี่ยความหนาของเส้นใยประสาทจอตาด้านบน ด้านล่าง ด้านนอก ด้านใน และรวมทุกด้าน เท่ากับ 101.60±28.68, 87.15±32.56, 60.64±14.14, 61.83±13.96 และ 77.80±17.58 ไมครอน ตามลำดับ และความหนาของกระจกตา ส่วนกลางมีความสัมพันธ์กับ mean deviation (MD) ($r = 0.532$, $p<0.001$), pattern standard deviation (PSD) $r = -0.288$, $p = 0.05$), cup to disc ratio ($r = -0.478$, $p = 0.001$) และความหนาของเส้นใยประสาทจอตาเฉลี่ย ($r = 0.487$, $p = 0.001$) อย่างมีนัยสำคัญทางสถิติ*

สรุป: *ความหนาของกระจกตาส่วนกลาง มีความสัมพันธ์กับ mean deviation, pattern standard deviation, cup to disc ratio และความหนาของเส้นใยประสาทจอตาอย่างมีนัยสำคัญทางสถิติ*