Relationship between central corneal thickness and parameters of optic nerve head topography in healthy subjects

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PURPOSE. *To investigate the relationship between central corneal thickness (CCT) and topographic parameters of optic nerve head (ONH) in healthy eyes.*
METHODS. *Right eyes of 208 healthy subjects between 40 and 59 years of age with refractive error less than 1 D were enrolled in this cross-sectional study. Ultrasonic pachymeter was used to measure CCT, and the ONH parameters were obtained by using confocal scanning laser ophthalmoscope. Relationship of various topographic parameters to age and sex were also investigated. For statistical analysis Student t test, analysis of variance, Pearson and Spearman test, and partial correlation coefficients were used.*
RESULTS. *Mean CCT of subjects was 540.71±35.53 μm (462–621 μm), and the mean disc area was 2.37±0.44 mm^2 (1.28–3.66 mm^2). CCT showed negative correlations to disc area, rim area, rim volume, and retinal nerve fiber layer (RNFL) area. These correlations were found to be stronger in females. Negative correlations were demonstrated between age and the mean cup depth, maximum cup depth, RNFL thickness, and RNFL cross sectional area. Women had lesser rim volumes, but bigger cup to disk (C/D) area and linear C/D ratios compared to those of men.*
CONCLUSIONS. *In addition to its effect in the accuracy of intraocular pressure measurements, CCT has a structural relationship with the ONH in healthy nonglaucomatous eyes. Therefore, its effect on disc area might be especially important to explain the structural strength of the ONH in the pathogenesis of glaucoma. (Eur J Ophthalmol 2008; 18: 32-8)*

KEY WORDS. *Central corneal thickness, Optic nerve head topography, Disc area, Glaucomatous optic nerve damage*

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INTRODUCTION

Central corneal thickness (CCT) has a significant effect on intraocular pressure (IOP) measured by applanation tonometry (1). IOP may be underestimated in eyes with thin corneas and overestimated in eyes with thick corneas (2). Considerable evidence now supports that CCT has a major role in the diagnosis of glaucoma and progression of glaucomatous optic nerve degeneration. CCT measurements may show some differences depending on the type of glaucoma. Previously, CCT was reported to be higher in ocular hypertension (OHT) than in normotensive glaucoma; however, it was almost normal in patients with primary open angle glaucoma (POAG) (3, 4). It was also demonstrated that CCT could play an important role in the formation and progression of the visual field defects. Therefore, besides its effects on the accuracy of IOP measurements, it was argued that CCT might have some kind of effect on the optic nerve head resistance (5, 6). In a previous study including patients with POAG, an inverse correlation between CCT and the optic disc area was shown and the weakness of the optic nerve head in eyes with thin cornea could be explained with the assumption of thin structures of both lamina cribrosa and sclera which

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are the posterior continuations of a thin cornea (7). However, such a relationship could not be proven in a histomorphometric study done on enucleated eyes (8).

Heidelberg Retina Tomography (HRT) is a confocal scanning laser ophthalmoscope which has been widely used in follow-up of the changes in optic nerve head (ONH) topography since 1989. It was reported that topographic deterioration of ONH precedes formation of defects in visual fields (9). Meanwhile the effects of age, gender, laterality, refraction, and optic disc area on HRT parameters have been investigated in healthy subjects (10-17).

In the present study, we investigated the relationship between CCT and topographic analysis of the ONH with HRT II in healthy individuals to characterize the differences between the optic nerve parameters of the normal eyes with thin cornea and those with thick cornea.

MATERIALS AND METHODS

A total of 208 patients (aged 40–60 years) with nearsightedness were enrolled between April 2006 and February 2007. Individuals with a history of vascular, circulatory (diabetes mellitus, hypertension, and hypotension), autoimmune, and neurological diseases (including migraine), malignancy, chronic medication usage, glaucoma, uveitis, ocular surgery, or trauma were excluded. Only the right eye of each subject was evaluated in the study.

The ophthalmic examination included visual acuity measurement; slit lamp examination, fundus examination with +90 D lens, IOP measurement with Goldmann applanation tonometer, and gonioscopic examination with Goldmann three mirror lens. After the examination, subjects with visual acuity less than 10/10, refractive error more than 1 D (spherical or cylindrical), were excluded. Moreover, patients with an anterior chamber pathology that could affect IOP (pseudoexfoliation, pigment dispersion), congenital abnormality of optic nerve, prominent peripapillary atrophy, a linear cup to disc (C/D) ratio of greater than 0.4 or glaucomatous optic disc appearance, IOP more than 20 mm Hg, or abnormalities of iridocorneal angle (recession, excessive pigmentation, angle depth less than grade III according to Shaffer System) also were excluded.

ONH analysis of the patients was done by using a HRT II (Heidelberg Retinal Tomograph, Software Version 2.1, Heidelberg Engineering, Germany) scanning laser ophthalmoscope. No pupil dilatation was done and 15º angle view was used under the same intensity of dim room light. Images were taken and contour lines were drawn by the same experienced observer (A.B.C.). The accuracy in defining ONH circumference was performed by using minimum 6 points for drawing the contour line. Keratometric readings were used to exclude magnification effect. Subjects with standard deviation less than 30 µm and evaluated as within normal limits according to the Moorfields Classification were included in the study. Parameters calculated by HRT II hardware are disc area (mm^2), cup area (mm^2), rim area (mm^2), cup volume (mm^3), rim volume (mm^3), C/D area ratio, linear C/D ratio, mean cup depth (mm), maximum cup depth (mm), cup shape measure, height variation contour (mm), mean retina nerve fiber layer (RNFL) thickness (mm), and RNFL cross sectional area (mm^2).

CCT measurement was performed with ultrasonic pachymetry (Tomey AL-1000) following the instillation of one drop of propacaine hydrochloride (0.5%) to the right eye of each subject 5 minutes prior to measurement. Five consecutive measurements were taken while the patient was looking straight ahead. The examiner paid attention to apply the probe perpendicularly to the cornea without pressure. The mean of five measurements was calculated and recorded as the CCT value.

SPSS 13.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis with Student *t* test, analysis of variance, Pearson, Sperman, and partial correlation coefficient. Statistical significance was accepted as p 0.05 or less. Before we conducted the study, it was approved by the ethical committee of Ankara Ulucanlar Eye Research Hospital and the patients were all clearly informed about the study.

RESULTS

The study group consisted of 107 men and 101 women. Mean age was 49.11±6.29 (range 40–59). The mean age of men was 49.46±6.25 (range 40–59) and of women was 48.68±6.03 (range 40–59) (p=0.34). Mean CCT obtained was 540.71±35.53 µm (461–621 µm) and the mean IOP measured was 13.64±2.81 mmHg (9–19 mmHg). The mean CCT of men was 541.37±37 µm (462–613 µm) and women had a mean CCT of 539.37±54 µm (461–621 µm). The difference between the CCT measurements of the two sexes was not statistically significant (p=0.13). No correlation between the age and CCT of the subjects was observed (p=0.26, r=–0.28).

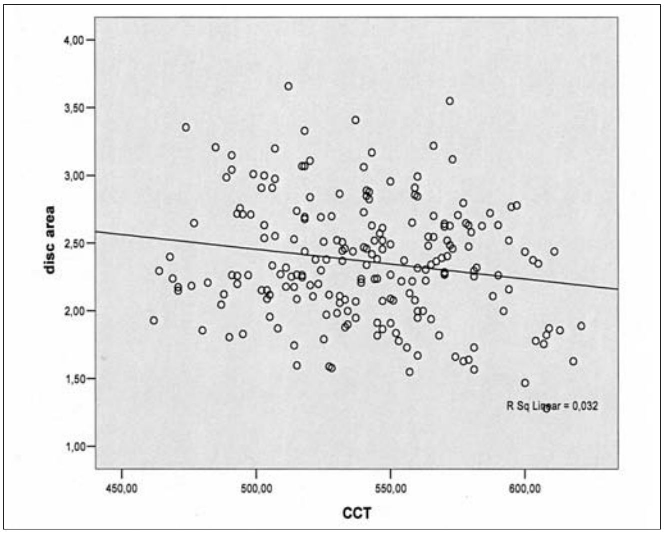

Fig. 1 - *Central corneal thickness versus disc area in healthy subjects (p=0.01, r=-0.178).*

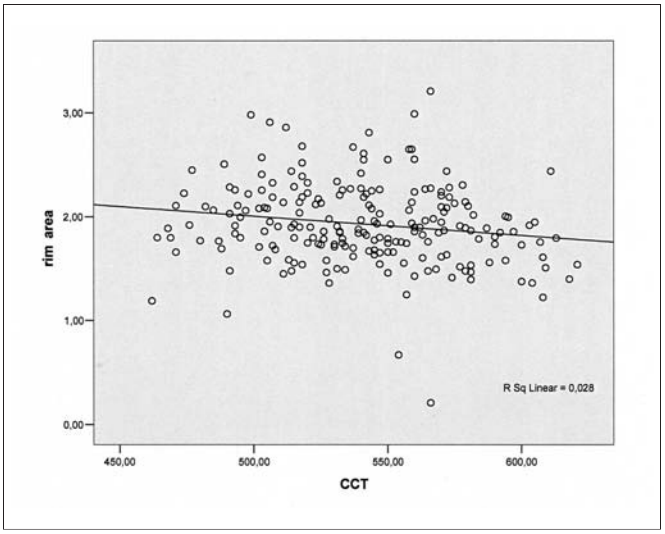

Fig. 2 - *Central corneal thickness versus rim area in healthy subjects (p=0.015, r=-0.168).*

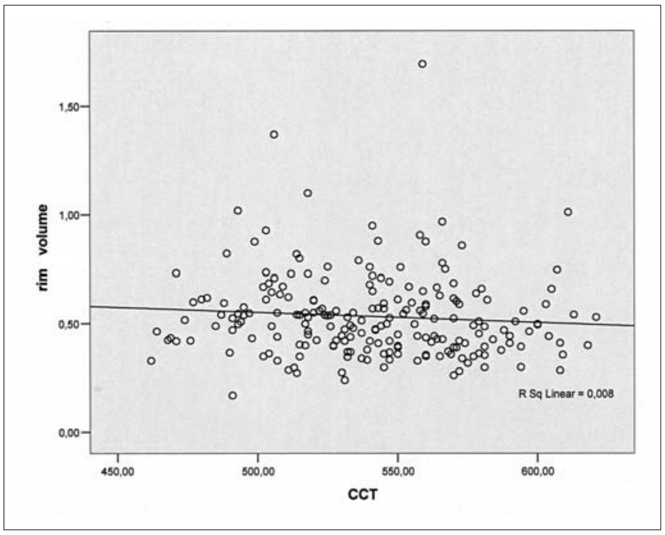

Fig. 3 - *Central corneal thickness versus rim volume in healthy subjects (p=0.049, r=-0.136).*

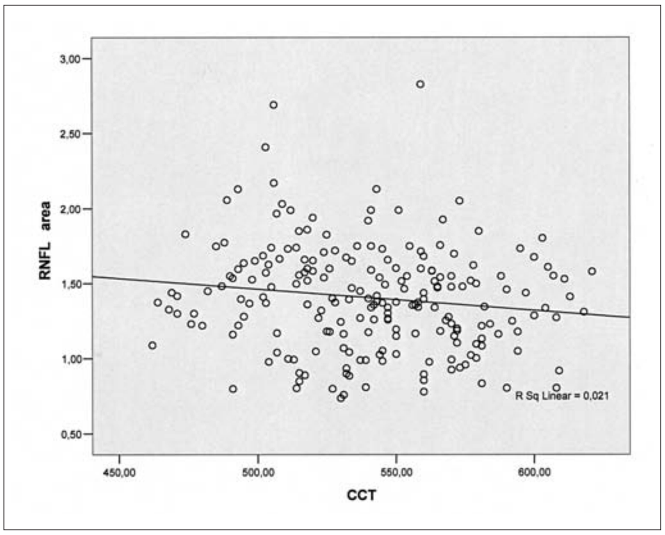

Fig. 4 - *Central corneal thickness versus RNFL area in healthy subjects (p=0.038, r=-0.144).*

The mean disc area of our subjects was calculated as 2.366±0.436 mm^2 (1.28–3.66 mm^2). The mean cup and rim areas were 0.42±0.3 mm^2 (0.01–1.67 mm^2) and 1.93±0.39 (0.21–3.21 mm^2), respectively, and the mean C/D area ratio was found to be 0.17±0.11 (0.01–0.41). The results of the ONH topographic study are shown in Table I.

In our study negative correlations were obtained between the CCT and those of disc area (p=0.01, r=–0.178) (Fig. 1), rim area (p=0.015, r=–0.168) (Fig. 2), rim volume (p=0.049, r=–0.136) (Fig. 3), and RNFL area (p=0.038, r=–0.144) (Fig. 4). However, other optic disc parameters showed no correlation with the CCT (Tab. II).

We also examined the correlations between age and the optic disc topographic parameters. According to the results obtained the mean cup depth (p=0.02, r=–0.160), maximum cup depth (p=0.03, r=–0.203), RNFL thickness (p=0.009, r=–0.180), and RNFL area (p=0.01, r=–0.177) exhibited negative correlations with age. (Tab. II). When the effect of age was controlled by partial correlation analysis, it was found that CCT had a negative correlation

TABLE I - GENDER-SPECIFIC AND ENTIRE GROUP OPTIC NERVE PARAMETERS

Topographic parameters	Sex	Mean	SD	p value
Disc area (mm^2)	M	2.3446	0.42669	0.56
	F	2.3887	0.44620	
	Total	2.366	0.43578	
Cup area (mm^2)	M	0.3853	0.31491	0.28
	F	0.4535	0.27457	
	Total	0.4184	0.29727	
Rim area (mm^2)	M	1.9282	0.43560	0.11
	F	1.9338	0.34462	
	Total	1.9309	0.39312	
Rim volume (mm^3)	M	0.5399	0.22127	0.04*
	F	0.5267	0.15533	
	Total	0.5334	0.19176	
C/D ratio	M	0.1579	0.11308	0.05*
	F	0.1831	0.09441	
	Total	0.1701	0.10494	
Linear C/D ratio	M	0.3658	0.16006	0.02*
	F	0.4073	0.13156	
	Total	0.3860	0.14797	
Mean cup depth (mm)	M	0.1599	0.07618	0.63
	F	0.1848	0.07837	
	Total	0.1720	0.07807	
Cup volume (mm^3)	M	0.0803	0.10825	0.90
	F	0.1009	0.09002	
	Total	0.0903	0.10011	
Maximum cup depth (mm)	M	0.4908	0.22319	0.68
	F	0.5816	0.23511	
	Total	0.5349	0.23299	
Cup shape measure	M	–0.2307	0.06132	0.11
	F	–0.2439	0.06805	
	Total	–0.2371	0.06486	
Height variation contour	M	0.3933	0.09951	0.25
	F	0.4178	0.18845	
	Total	0.4052	0.14959	
Mean RNFL thickness (mm)	M	0.2528	0.06133	0.83
	F	0.2637	0.05625	
	Total	0.2581	0.05903	
RNFL cross sect. area (mm^2)	M	1.3695	0.35997	0.86
	F	1.4417	0.33785	
	Total	1.4046	0.35044	

*Statistically significant; RNFL = Retinal nerve fiber layer

TABLE II - GENDER-SPECIFIC AND ENTIRE GROUP CORRELATIONS OF OPTIC NERVE HEAD PARAMETERS TO AGE AND CENTRAL CORNEAL THICKNESS

			Central corneal thickness					
	Age		Male		Female		Total	
	r	p	r	p	r	p	r	p
Disc area	–0.051	0.463	–0.103	0.289	–0.251	0.011*	–0.178	0.010*
Cup area	–0.097	0.163	–0.130	0.181	–0.028	0.782	–0.061	0.383
Rim area	–0.018	0.792	–0.045	0.642	–0.332	0.001*	–0.168	0.015*
Cup volume	–0.078	0.266	–0.091	0.351	0.082	0.413	–0.007	0.923
Rim volume	–0.033	0.631	0.038	0.70	–0.322	0.001*	–0.136	0.049*
C/D area	–0.105	0.132	–0.125	0.201	0.110	0.274	–0.023	0.739
Linear C/D	–0.126	0.069	–0.138	0.157	0.132	0.189	–0.023	0.746
Mean cup depth	–0.160	0.021*	–0.138	0.156	0.087	0.385	–0.030	0.667
Maximum cup depth	–0.203	0.003*	–0.128	0.190	0.115	0.252	–0.011	0.878
Cup shape measure	0.127	0.068	0.046	0.641	–0.086	0.392	–0.019	0.780
Height variation contour	–0.071	0.306	0.061	0.531	–0.142	0.156	–0.058	0.404
RNFL thickness	–0.180	0.009*	–0.021	0.830	–0.139	0.165	–0.078	0.261
RNFL area	–0.177	0.010*	–0.059	0.547	–0.235	0.018*	–0.144	0.038*

*Statistically significant; RNFL = Retinal nerve fiber layer with disc area (p=0.01, r=–0.178), rim area (p=0.02, r=–0.160), and RNFL area (p=0.032, r=–0.149).

Optic disc topographic parameters of the total group and each sex are given individually in Table I. The mean rim volume in men was found to be 0.54 mm^3, while it was measured as 0.52 mm^3 in women (p=0.04). C/D area ratio was calculated as 0.18 and 0.16 in women and men, respectively (p=0.05). Linear C/D ratio was found to be significantly higher in women than in men (0.41 and 0.37, respectively) (p=0.02). We further examined the relationship of CCT to the optic disc parameters in men and women, individually. It was demonstrated that the CCT and HRT parameters were in no means related in men. However, a significant relationship was noticed in women as negative correlations observed between CCT and disc area (p=0.011, r=–0.250), rim area (p=0.001, r =–0.332), rim volume (p=0.001, r=–0.322), and RNFL area (p=0.018, r=–0.235) (Tab. II).

DISCUSSION

The Ocular Hypertension Treatment Study Group reported that the risk of developing glaucomatous optic nerve damage in OHT was three times higher in eyes with CCT less than 555 μm than in eyes with CCT more than 585 μm (18). Additionally, early visual field defects and low RNFL thickness were also found to be more frequent in OHT patients with thin corneas (19, 20) Medeiros et al have found that thin CCT was a risk factor for the development of visual field defects in early stage glaucoma cases (6). In a large-scale study performed on 454 patients with POAG and OHT, Jonas et al have postulated a positive correlation between CCT and neuroretinal rim, expressing that the glaucomatous eyes with thinner corneas also have thinner neuroretinal rims (21). Hewitt and Franzco have reported that thicker corneas may offer a greater protective role against the optic nerve damage in POAG cases (22). Choi and coworkers have demonstrated in a study consisting of 75 NTG patients that CCT was a significant factor for localized RNFL loss (23). Therefore, it can be concluded that CCT has some sort of effect on optic nerve structure and eyes with thin corneas are more susceptible to IOP dependent glaucomatous optic nerve damage.

Cornea and sclera are continuous segments as a collagen coat of an eye. At the posterior segment, sclera is perforated forming lamina cribrosa which forms a barrier between intraocular space and cerebrospinal fluid, so that it plays a major role in optic nerve pathologies such as glaucoma (24, 25). From this point of view, Jonas et al investigated the association of lamina cribrosa thickness with CCT in 111 postmortem enucleated eyes; however, no correlation between CCT and lamina cribrosa was found (8). It is speculated that besides the effect of CCT on the resistance of optic nerve to IOP, eyes with thin corneas have decreased trabecular outflow facility and wide diurnal fluctuations because of structural changes in their trabecular meshwork (26).

HRT II gives three-dimensional optic nerve head measurement data, which are reproducible, highly sensitive, and objective (27). Therefore, in addition to the classic C/D area ratio, it gives much more detailed information about the optic nerve head and peripapillary retina.

In this study, our primary goal was to establish the possible relationship between CCT and optic disc parameters in healthy eyes. To neutralize the possible effect of refraction on the optic nerve parameters, eyes with refractive error less than 1 D (13) were used in correlation and to eliminate the probable role of laterality only the right eye of each individual subject was enrolled in the study (11, 12, 16).

We have found that CCT exhibited a negative correlation with disc area, rim area, rim volume, and RNFL area, showing that the eyes with thick corneas have smaller disc and rim areas as well as less rim volumes, and less RNFL cross sectional areas. Nevertheless, similar negative correlations between CCT and disc area, rim area, and RNFL area were still present when the effect of age was eliminated. Pakravan and coworkers have also reported a negative correlation between CCT and disc area in their study on cases with POAG, showing that eyes with thick corneas have smaller optic discs (7). Bigger discs could be considered to be more sensitive to increase the IOP than smaller discs and it was claimed that this sensitivity might be due to qualitative characteristics of extracellular matrix (28). When the disc size gets bigger, the ratio of lamina cribrosa pores to disc area increases, and therefore the connective tissue in the optic disc becomes less supportive. On the contrary, smaller disc size decreases the pore to disc area ratio and provides much greater tissue support (28).

In the present study, we have also found a negative correlation between age and the mean cup depth, maximum cup depth, mean RNFL thickness, and RNFL cross sectional area. These findings can be explained by the increase of the production of glial tissue and filling it into the cup during the progressive thinning of RNFL. Kergoat et al have demonstrated that as patients aged, RNFL became thinner and the disc area, cup area, and C/D ratio were all increased; however, the rim area stayed without changing (15). A significant correlation between the optic disc area and age was reported by Akar et al (10). Nevertheless, there are few studies suggesting that age has no effect on any of the optic disc parameters (14, 16, 29).

Our results showed that women have smaller rim volumes, higher C/D areas, and higher linear C/D ratios compared to those of men. Although Gundersen et al reported that the optic disc cup of women was wider and deeper than in men, these findings were not statistically significant (14). In another study, the height variation contour, mean RNFL thickness, and RNFL cross-sectional area of women was reported to be higher than those of men (30). However, Varma and coworkers have demonstrated that the optic disc parameters were not associated with sex (31). In our study, although CCT was not correlated with any of the optic disc parameters in men, a significant negative correlation was observed between CCT and the disc area, rim area, rim volume, and RNFL area in women. NTG, in which thin corneas are more prevalent, is two times common in women (32). This can be explained as the CCT being more effective on optic disc parameters in women than in men.

The small sample size of the cohort, limited age range of the subjects, and the dominance of a single ethnic group (white) could be considered as potential limitations of our study. Therefore, a longitudinal study with a much larger number of subjects including both normal controls and glaucoma patients of all age ranges and different ethnic groups is required to confirm our findings.

In addition to affecting the accuracy of IOP measurements and a person's susceptibility to glaucoma, we also found that CCT is related to morphology of the optic nerve head. Our findings support the notion that eyes with thinner corneas may have greater optic disc areas, which are more deformable and may render optic disc vulnerable to the effect of IOP.

Proprietary interest: None.

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