Relationship between central corneal thickness and ganglion cell complex thickness in mild to moderate myopia

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Abstract

Background: Myopia is not only refractive error, but also an eyesight-threatening disease. To search for a relationship between the central corneal thickness (CCT) and ganglion cell complex (GCC) thickness in patient with myopia.

Methods: The prospective cross-sectional study comprised 122 eyes of 122 subjects with mild to moderate myopia. The participants were divided into two groups according to the CCT; thicker than 555 micrometer (Group 1) or thinner than 555 micrometer (Group 2). CCT was measured using the optical biometer machine. All subjects received a slit-lamp examination and optical coherence tomography. The retinal nerve fiber layer (RNFL) thickness and GCC thickness were automatically quantified.

Results: The retinal GCC and GC-IPL thickness were decreased in Group 1 compared with Group 2 (p=0.002 and p=0.007, respectively). The RNFL thickness was statistically significantly decreased only in the superior-temporal quadrant (p=0.041). There was a significantly positive correlation between CCT and GCC and GC-IPL thickness (r=0.222, p=0.014, and r=0.203, p=0.025, respectively). There was no correlation among CCT and RNFL thickness (p 0.05).

Conclusion: There was a relationship between the CCT and GCC thickness in eyes with mild to moderate myopia.

Background

Patients with myopia have a higher tendency to develop glaucoma [1]. The relationship between these two common ocular disorders may be related to the easily deformable lamina cribrosa due to myopia. Myopic findings consist of elongated axial length and increased vitreous cavity depth together with changes in connective tissue which can increase the vulnerability of the optic nerve head to the glaucomatous damage [2].

Central corneal thickness (CCT) is a substantial parameter in the diagnosis and treatment of glaucoma patients [3–5]. Thicker corneas result in artificially higher intraocular pressure readings [6]. It has been proposed that a thinner cornea is linked to the altered biomechanical and structural characteristics of the posterior sclera and the lamina cribrosa, which may cause a higher vulnerability of the retinal ganglion cell (RGC) to the glaucomatous damage [7]. Previous studies evaluating the correlation between the myopia and the CCT have shown conflicting results [8].

Glaucoma is an optic neuropathy that can affect all components of the ganglion cell complex (GCC). The ganglion cell layer (GCL) thickness is measured over the macular region, owing to the fact that over 50% of the ganglion cells are localized at this location and the RGC bodies are 10 to 20 times the diameter of their axons [11–13]. Due to tilting of the optic disc and peripapillary atrophy, the retinal nerve fiber layer (RNFL) measurements may be prone to errors in patients with myopia. Therefore, the thickness of the ganglion cell layer (GCL) and inner plexiform layer (IPL) may have a good ability to detect glaucoma, besides the RNFL thickness [11].

In this study, the aim was to search for a relationship between the CCT and the retinal GCC thickness in non-glaucomatous myopic eyes.

Methods

This prospective cross-sectional research was in accordance with the principles of the Declaration of Helsinki and was approved by the local ethics committee. Signed consent forms were obtained from the subjects. Only one eye of each participant was included according to the criteria described below. If both eyes met the criteria, a random eye was selected.

Patients with myopia less than -6.00 D and astigmatism less than -2.00 D were included. Patients with an axial length over 26 mm, irregular corneal astigmatism, ocular surface inflammation, previous ocular intervention, history or signs of glaucoma or ocular hypertension, optic nerve disease or neurodegenerative disease, and media opacity affecting OCT image quality were excluded from the study.

All patients underwent a full ophthalmologic evaluation including best-corrected visual acuity measurement, automated kerato-refractometer (Topcon Co., Tokyo, Japan), biomicroscopy, intraocular pressure measurement, and fundoscopy. The CCT measurement was performed with an optical biometry device (Lenstar LS 900, Hagg-Streit AG, Koeniz, Switzerland)). Based on the evidence from the Ocular Hypertension Treatment Study (OHTS), the participants were divided into 2 groups; CCT over 555 µm (Group 1) and below 555 µm (Group 2) [7].

Heidelberg spectralis OCT device (software version 6.3.3.0, Heidelberg Engineering Inc., Germany) was used for the GCC and RNFL measurements in the patient groups. Before capturing the images, keratorefractive values of the subjects were entered into the software of the OCT device to estimate optical magnification. Heidelberg spectral domain-OCT applies an automatic modification process to reverse the ocular magnification effect, developing individual scan lengths based on 3 parameters (refraction, keratometry and axial length). All measurements were made by an observer masked to the study groups. The OCT images were recorded under dim light conditions between 9:00 am and 12:00 pm in the same room.

A scan circle with a diameter of 3.45 mm was centered at the optic disc. Nine B-scan images were captured and automatically averaged. More attention was paid to obtain good-quality scans with focused images, proper adjustment of the disc margins, and signal strength ≥20. The RNFL thickness parameters measured were; average RNFL thickness (a-RNFL thickness), superior-temporal (ST), temporal (T), inferior-temporal (IT), inferior-nasal (IN), nasal (N), and superior-nasal (SN) quadrant RNFL thicknesses (Figure 1).

The GCC protocol was used to measure the macular GCC thickness from the inner limiting membrane (ILM) to the inner plexiform layer (IPL). Layer segmentation was executed automatically using the new software for the Spectralis OCT, and it was checked to be adequate in the 61 B-scans of each imaged eye using the criteria of Ishikawa et al.[11] (Figure 1).

The statistical analyses were done using SPSS (Statistical Package for Social Sciences; version 15.0). A Shapiro-Wilk test was used to detect normal distribution. The differences between the groups were evaluated by Student T and Mann-Whitney U tests. Spearman correlation coefficients for the results were calculated. The data adjusted for age and corrected means were estimated with standard error and 95% confidence interval. Multiple linear regression models were created to evaluate the relationship among the RNFL, GCC, GC-IPL thicknesses and age, CCT, axial length (AL), and spherical refraction values. "Enter method" was used as the variable selection method. The standardized and non-standardized regression coefficients of the models were presented together with the p values, and the risk factors affecting these variables were investigated. The statistical significance was set at a level of 5% ($p<0.05$).

Results

In total, 122 eyes of 122 participants were included in the study. The mean age was 26.63±8.26 in Group 1 (n=60) and 25.25±7.94 in Group 2 (n=62). While 66.6% of Group 1 was female, this rate was 62% in Group 2. There were not any significant differences among groups in terms of age and gender ($p>0.05$).

The mean CCT was 517.48±23.2 micrometer in Group 1 and 572.29±21.62 micrometer in Group 2 (p 0.001). The mean spherical refraction was 2.74±1.34 D in Group 1 and 2.68±1.22 D in Group 2 (p=0.959). The mean AL was 24.47±0.97 mm in Group 1 and 24.73±0.92 mm in Group 2 (p=0.183). Mean intraocular pressure was 15.45±2 mmHg in Group 1 and 16.88±2.1 mmHg in Group 2 (p=0.665). The mean C/D ratio was 0.28±0.07 in Group 1 and 0.30±0.07 in Group 2 (p=0.146). The clinical and demographic characteristics of the participants are given in Table 1.

Table 1
Clinical and demographic characteristics of the patient groups.

	Group 1	Group 2	p-value
Age (years)	26.63±8.36	25.25±7.95	0.287
Spherical refraction (D)	2.74±1.34	2.68±1.22	0.959
Cylindrical refraction (D)	0.69±0.68	0.67±0.63	0.985
CCT (µm)	517.48±23.2	572.29±21.62	0.001
IOP (mmHg)	15.45±2	16.88±2.1	0.665
Cup to disc ratio	0.28±0.07	0.30±0.07	0.146
AL (mm)	24.47±0.97	24.73±0.92	0.183
CCT: Central corneal thickness; IOP: Intraocular pressure, AL: Axial length			

The retinal GCC thickness was found to be statistically significantly decreased in Group 1 compared with Group 2 (p=0.002). The GC-IPL thickness was also statistically significantly decreased in Group 1 compared with Group 2 (p=0.007). When two groups were compared in terms of RNFL thickness, no statistically significant difference was found except for the superior-temporal quadrant (p=0.041). Table 2 presents the comparison of the GCC, GC-IPL and RNFL thickness between Group 1 and Group 2.

Table 2
Comparison of GCC, GCC-IPL and RNFL thickness in the groups

(µm±SD)	Group 1	Group 2	p-value
GCC thickness	44.36±9.35	50.03±10.18	0.002*
GCC-IPL thickness	33.28±7.81	37.43±8.42	0.007*
a-RNFL thickness	99.88±10.09	99.51±9.13	0.998
T-RNFL thickness	74.83±11.09	74.48±12.03	0.634
ST-RNFL thickness	142.56±17.02	135.88±18.02	0.041*
SN-RNFL thickness	111±18.84	112.08±23.46	0.890
N-RNFL thickness	70.98±13.52	69.67±13.16	0.510
IN-RNFL thickness	106.41±21.15	114.12±26.32	0.281
IT-RNFL thickness	147.5±19.41	145.11±19.15	0.764
GCC: Ganglion cell complex; GC-IPL: Ganglion cell-inner plexiform layer;			
a-RNFL: Average RNFL; Temporal (T); superior-temporal (ST); superior-nasal (SN); nasal (N); inferior-nasal (IN); inferior-temporal (IT)			
*: Statistically significant p-value			

The CCT was statistically significantly correlated with the GCC and GC-IPL thicknesses (r=0.222, p=0.014, and r=0.203, p=0.025, respectively). There was no statistically significant correlation between the CCT and the RNFL thicknesses (p 0.05).

Table 3 lists the multiple linear regression analysis between the RNFL, GCC, GC-IPL thicknesses and the mean age, CCT, AL, and spherical refraction values.

Table 3
Standardized coefficients () and statistical significance values (p) from multiple linear regression models

β															
	ST-RNFL thickness		SN-RNFL thickness		T-RNFL thickness		N-RNFL thickness		IN-RNFL thickness		IT-RNFL thickness		a-RNFL thickness		GCC thi
	β	p	β	p	β	p	β	p	β	p	β	p	β	p	β
Age (years)	-0,008	0.93	0,046	0,613	-0,197	0,036*	0,126	0,159	0,087	0,319	0,01	0,917	0,026	0,76	0,101
AL (mm)	-0,211	0.05*	-0,263	0.014*	0,048	0,654	-0,19	0,068	-0,267	0,009*	-0,219	0.043*	-0.314	0.002*	0.371
Spherical refraction	0,014	0.897	-0,053	0.615	-0.146	0.18	-0.148	0.159	-0.141	0.167	-0.028	0.797	-0.001	0,987	-0.132
CCT (µm)	-0,128	0.163	0.033	0.711	-0.091	0.328	-0.033	0.708	0.185	0.034*	-0.005	0.957	-0.156	0.124	0.222

AL: Axial length, CCT: Central corneal thickness

Discussion

To our knowledge, this is the initial research to demonstrate the relationship between CCT and GCC and GC-IPL thickness in otherwise healthy mild to moderate myopic eyes. Eyes with mild to moderate myopia with thinner corneas revealed significantly decreased GCC and GC-IPL thickness. Except for the superior-temporal quadrant, there was no significant difference for RNFL thickness.

Considering that myopia is a significant risk factor for the glaucoma, studies have shown that it can increase the risk of glaucoma development by 2 to 3 folds and also the risk is associated with the amount of myopia [14]. Chen et al. proposed that evaluating glaucoma in high myopic patients using only a database including low myopic measures could lead to misdiagnosis and that GCC thickness determined by a high myopic database should be used [15]. Wang et al. and Scuderi et al. have reported that macular GCC thickness has increased diagnostic power than the RNFL thickness in glaucoma patients with high myopia [16, 17].

The structural or elastic properties of the cornea were shown to be significant indicators for the overall structural and elastic characteristics of the eye. In eyes with OHT, lower CCT is an independent risk factor for conversion to glaucoma [7, 18]. In eyes with known glaucoma, lower CCT seems to be a risk factor for progression [19–21].

Previous studies have shown that the RNFL could be thinner in high myopic patients than in mild myopic patients [22, 23]. Zhao et al. also found that as the amount of myopia increased, there was a thinning of the RNFL [22]. Similarly, Sezgin Akçay et al. analyzed the GCC and RNFL thickness in patients with varying amount of myopic refraction [23]. They showed that both RNFL and GCC thickness were decreased in eyes with high myopia. They also noted that there was no significant correlation between the GCC layer and the axial length in moderate myopia group. Henderson et al. evaluated the relationship among CCT and RNFL thickness in healthy eyes and did not find any correlation [24]. They also searched for a relationship between the RNFL thickness and CCT in patients with ocular hypertension. The authors used scanning laser polarimetry with improving the accuracy of the technique for diagnosing glaucoma. The patients with OHT with thinner corneas had significantly thinner RNFL than the patients with thicker corneas and healthy control subjects. Arranz-Marquez et al. measured the CCT and RNFL thickness in healthy subjects with mild to moderate myopia [25]. The mean spherical refractive error in their study group was greater than in our study group (-3.4±1.9 D and -2.74±1.34 D, respectively). They also found that there was a positive significant correlation between the mean RNFL thickness and CCT.

There are very few studies conducted to analyze the thickness of the retinal GCL in myopic eyes. In patients with amblyopia, Park and Oh measured increased thickness in the inner nuclear layer, IPL and GCL, particularly in myopic eyes, and reported that these findings may be attributable to the genetic factors [26]. Zereld et al. investigated the effect of refractive errors on the retinal thickness and found that the foveal thickness in the inner and outer retinal layers were increased, while the thickness in the inner and outer retinal layers of the parafoveal and perifoveal regions were decreased in moderate to high myopic eyes [27]. They linked the retinal thinning measured in myopic eyes to the myopic elongation of the eye. In a very recent study, Ganekal et al. found that average GC-IPL and GC-IPL thickness of all sectors were significantly decreased in high myopic group compared to low myopic group [28]. None of the previous studies included corneal thickness as a parameter. In our study, the GCC and GC-IPL thickness were significantly decreased in myopic eyes with thin corneas, without a generalized RNFL thinning. The CCT was statistically significantly correlated with the GCC and GC-IPL thicknesses.

Here, we may propose two different mechanisms; first, decreased GCC thickness can be related to the increased risk of progression of glaucoma in myopic eyes with thin corneas. Second, the decreased GCC thickness in myopic patients with thin corneas may itself be a risk factor for the development of glaucoma. The decreased GCC thickness measurement in mild to moderate myopic eyes with thin corneas may therefore turn to a high risk group. As the thickness of the GCC is an established representative of early glaucomatous damage, the finding of decreased GCC thickness in myopic eyes supports the population-based studies. Longitudinal studies with longer follow-ups are needed to address this in future.

Our study had some limitations. First, including more participants with a wider range of the CCT, RNFL, and GCC thicknesses might have allowed for stronger correlations and analysis of subgroups. Second, the cut-off value for CCT was 555 micrometer. The reason for using this value was based on OHTS Group data. We did not include a healthy control group as it has already been shown that healthy patients with thin corneas or varying myopia had GCC and RNFL changes.

Conclusions

In conclusion, current study showed that the GCC and GC-IPL thicknesses were decreased in eyes with myopia and thinner corneas. Therefore, before evaluating the thickness of the GCC and GC-IPL in glaucoma patients, not only the amount of myopia but also the CCT should be taken into the consideration as well. Still, prospective population-based studies are needed to reveal the effect of the CCT on the GGC and RNFL thicknesses in myopic eyes.

Abbreviations

CCT: Central corneal thickness, GCC: Ganglion cell complex, RNFL: Retinal nerve fiber layer, GC-IPL: Ganglion cell -inner plexiform layer, a-RNFL thickness: average RNFL thickness, ST: superior-temporal ,T: temporal, IT: inferior-temporal, IN: inferior-nasal, N:nasal, SN: superior-nasal

Declarations

Ethics approval and consent to participate: Kırşehir Ahi Evran University Faculty of Medicine clinical research ethics committee. Decision no:2021-12/145. Written informed consent was obtained from all participants.

Consent for publication: Written consent was obtained from the participants for the publication of their clinical findings.

Availability of data and material: The datasets generated and/or analysed during the current study are available in the [Özkan kocamış] repository.

Conflict of interest: The authors declare that they have no conflict of interest.

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Authors' contributions: ÖK: Data collection, Report preparing, ET: Data collection, GÖ: Data collection, KÖ: Report preparing

All authors have read and approved the manuscript.

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Figures

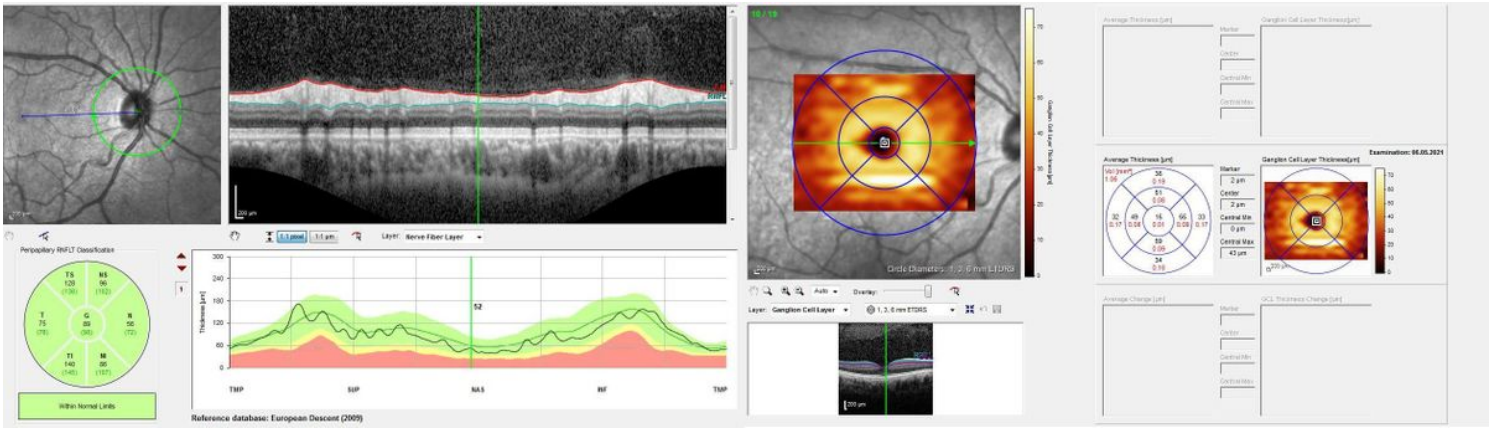

Figure 1

The RNFL thickness parameters measured were; average RNFL thickness, superior-temporal, temporal, inferior-temporal, inferior-nasal, nasal, and superior-nasal quadrant RNFL thicknesses