Investigation of the relationship between central corneal thickness and retinal nerve fiber layer thickness in ocular hypertension

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Abstract

Objectives: The purpose of the present study was to investigate the relationship between central corneal thickness (CCT), which is one of the most important risk factors for glaucomatous progression, and peripapillary retinal nerve fiber layer (RNFL) thickness in subjects with ocular hypertension (OHT).

Methods: A total of 66 eyes of 33 subjects with OHT (Group I) and 53 eyes of 27 healthy controls (Group II) were included in the study. All the participants underwent a complete ophthalmological examination, including CCT and RNFL thickness measurements using ultrasonic pachymetry (IOP-AC, Heidelberg Engineering, Germany) and Stratus optical coherence tomography (Stratus OCT Model 3000, Zeiss, ). The mean superior quadrant and inferior quadrant RNFL thicknesses were recorded. Possible relationships between the CCT and RNFL thicknesses were investigated.

Results: There was no statistically significant difference between the groups in terms of age and sex (p>0.05 for both). The mean CCT was 567.4±22.4µm in Group I and 542.2±27.9µm in Group II. The mean CCT was significantly thicker in Group I compared to Group II (p<0.05). There was no difference in the mean superior and inferior quadrant RNFL thicknesses of the subgroups with a CCT thicker than 555 µm. Subjects with OHT who had a CCT equal to or thinner than 555 µm showed a thinner inferior quadrant RNFL thickness compared to healthy individuals with thin corneas.

Conclusions: We found that OHT patients with thinner corneas (≤555 µm) had thinner mean and inferior quadrant RNFL thicknesses as compared to OHT patients with thicker corneas. In addition, OHT patients had a thinner inferior quadrant RNFL thickness compared to healthy controls.

Keywords: Central Corneal Thickness, Retinal Nerve Fiber Layer Thickness, Ocular Hypertension.

Introduction

Glaucoma is a slowly progressive, chronic optic neuropathy with characteristic visual field loss, optic nerve head changes with or without intraocular pressure (IOP) elevation (1,2). Retinal ganglion cell loss is the basis of glaucomatous damage, but damage cannot be detected using a conventional ophthalmic examination and visual field tests unless 20–30% of the ganglion cells are lost. The critical importance of early diagnosis of glaucoma has impelled investigators to develop diagnostic tools.

Optical coherence tomography (OCT) is a relatively new imaging technique, which provides high-resolution sections of biological tissues. New-generation OCT devices with enhanced resolution offer powerful imaging technology for medical diagnostics, and they can provide a type of optical biopsy. Retinal nerve fiber layer thickness (RNFL) measurements using OCT enable clinicians to diagnose glaucoma and progressive glaucomatous damage at an early stage.

Ocular hypertension (OHT) is defined as IOP of >21 mmHg in the absence of optic disc damage or abnormal visual field test results. The incidence of OHT is estimated at 7% in the population over 40 years old. According to the Ocular Hypertension Treatment Study, over a 5-year-period, patients with ocular hypertension and IOP levels of 24 mm Hg or more have a 10% overall risk of developing glaucoma (3). A low central corneal thickness (CCT), an IOP>25.75 mmHg, and a vertical cup-to-disc ratio of greater than 0.30 are the main risk factors for the development of glaucoma in patients with OHT. The risk of developing primary open angle glaucoma among OHT patients with a CCT ≤555 µm is three-fold higher than in those with a CCT>588 µm (3).

In the present study, we aimed to investigate the possible relationship between the CCT, which is the main risk factor for glaucoma progression in subjects with OHT, and the RNFL thickness in patients with OHT and age- and sex-matched healthy controls.
Table 1. The demographic data, CCT and RNFL thickness values of the groups.

<table>
<thead>
<tr>
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<th>Group I (OHT)</th>
<th>Group II (Control)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>53.6</td>
<td>56.4</td>
</tr>
<tr>
<td>Gender (Female/male)</td>
<td>25/8</td>
<td>17/10</td>
</tr>
<tr>
<td>Number of eyes</td>
<td>66</td>
<td>53</td>
</tr>
<tr>
<td>CCT (µm)</td>
<td>567.4±22.4</td>
<td>542.2±27.9</td>
</tr>
<tr>
<td>Mean RNFL thickness (µm)</td>
<td>101.2±9.5</td>
<td>98.1±11</td>
</tr>
<tr>
<td>Superior quadrant RNFL thickness (µm)</td>
<td>126.7±16</td>
<td>117.1±24.3</td>
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<tr>
<td>Inferior quadrant RNFL thickness (µm)</td>
<td>131±16.1</td>
<td>129.7±23</td>
</tr>
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CCT, Central corneal thickness; RNFL, retinal nerve fiber thickness; OHT, ocular hypertension.

Materials and Methods

The study included 66 eyes of 33 patients with OHT and 53 eyes of 27 healthy subjects who attended the Glaucoma Department of Third Eye Clinic, Ankara Numune Educational and Research Hospital between March 2010 and September 2011. The local ethics committee approved the study, and all the participants signed a consent form. Patients with a history of chronic eye disease, ocular surgery, topical and/or systemic drug use that could affect IOP were excluded from the study. The diagnosis of OHT was based on elevated IOP (>21 mmHg) in the absence of characteristic optic nerve loss and visual field loss in glaucomatous optic neuropathy.

All the participants underwent a complete ophthalmological examination, including best corrected visual acuity, IOP measurements using Goldmann applanation tonometry, slit-lamp biomicroscopy, gonioscopy, a dilated fundus evaluation, and a 30-2 full threshold visual field examination using a Humphrey field analyzer (HFA, Carl Zeiss-Meditec Inc., Dublin, CA, USA). In addition, CCT was measured using an ultrasonic pachymeter (IOP-AC, Heidelberg Engineering, Germany). Peripapillary RNFL measurements were performed in the fast RNFL thickness analysis mode using a Stratus OCT (Model 3000, Carl Zeiss Meditec, Dublin, CA) after pupillary dilation using tropicamide 1% (Tropamid, Bilim, Turkey). The mean superior and inferior quadrant RNFL thicknesses were recorded.

Group I consisted of patients with OHT without glaucomatous optic nerve damage and visual field loss. Healthy controls without IOP elevation were included in Group II. Both groups were divided into two subgroups according to their CCT (≤555 µm or >555 µm). The mean superior and inferior quadrant RNFL thicknesses in the subgroups in both groups were compared. For further analysis, Group I was divided into three subgroups: CCT ≤555 µm (thin), CCT 556–588 µm (average), and CCT >588 µm (thick). The mean RNFL thicknesses of the superior and inferior quadrants in these subgroups were then evaluated.

Statistical analysis

All statistical analyses were performed using SPSS 16.0 statistical software (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean ± standard deviation (SD). Nominal variables were presented as the frequency (%). Differences in the measured parameters between the two groups and the subgroups were analyzed by an independent samples t-test and one-way analysis of variance (ANOVA). When the ANOVA test results were significant, Tukey’s Honestly Significant Differences test was used. Categorical comparisons were made using a chi-square test. A probability value of p<0.05 indicated a statistically significant difference.

Figure 1. The mean, superior and inferior quadrants RNFL thicknesses in OHT group according central corneal thickness.

Results

Sixty-six eyes of 33 patients (25 female and eight male; mean age 53.6 years) with OHT and 53 eyes of 27 healthy subjects (17 female and 10 male; mean age 56.4 years) were included in the study. There was no statistically significant difference between the groups in terms of age and gender (p>0.05 for both). The mean CCT was 567.4±22.4 µm in Group I and 542.2±27.9 µm in Group II. There was a statistically significant difference in the mean CCT between the groups (p<0.05).
and thick corneas disease. Various devices, such as Heidelberg Retinal and to conduct further research on risk factors for this developing methods for the early detection of glaucoma diagnosis and treatment has led researchers to determining the prognosis. The importance of early diagnosis of glaucoma is very important in Glaucomatous damage is irreversible. Therefore, early preventable blindness in developing countries.

Glaucoma is one of the most important causes of blindness in the world, and it is an important cause of preventable blindness in developing countries. Glaucomatous damage is irreversible. Therefore, early diagnosis of glaucoma is very important in determining the prognosis. The importance of early diagnosis and treatment has led researchers to develop methods for the early detection of glaucoma and to conduct further research on risk factors for this disease. Various devices, such as Heidelberg Retinal Tomography (HRT) and scanning laser polarimetry, are available that can examine and analyze the optical nerve head and RNFL thickness at high resolution. It provides “optical biopsies” of the tissues due to its higher resolution compared to other devices. It is useful in visualizing the retinal layers, macula and optical nerve head. It aids not only the diagnosis of the disease but also the follow-up by enabling morphometric and quantitative measurements of the retina and optical nerves. In recent years, it has gained importance due to its utility in evaluating the RNFL thickness and optical nerve head, thereby enabling early diagnosis and follow-up of glaucoma patients.

Schuman et al. used OCT to compare the RNFL thicknesses of healthy individuals with those of patients with various stages of glaucoma (4). They found that the RNFL thickness was 95.9 µm in the normal case group, 80.3 µm in an early glaucoma group, and 50.7 µm in an advanced glaucoma group. They emphasized the association between RNFL thickness measurements and visual field loss. In another analysis of RNFL thickness using OCT, Mistiberger et al. found no significant differences between OHT and normal groups and significant thinning in the RNFL thickness in eyes where glaucoma was detected (5). They reported that the RNFL thickness measurements in their study were significantly correlated with visual field indexes (mean deviation and corrected pattern standard deviation).

In a study by Bowd and Weinreb (6), the RNFL thicknesses in patients with glaucoma were significantly thinner in comparison to the normal population. In addition, Saricaoglu et al. found that RNFL thickness were significantly thinner in comparison to both OHT and normal cases (7). According to the findings of these studies, the RNFL thickness becomes thinner in association with the progression of glaucoma, and it is thinnest in those with advanced stage disease. Therefore, the evaluation of RNFL thickness is an important parameter in both the diagnosis of glaucoma and the prognosis of the disease progression.

OCT measures the RNFL thickness in various locations around the optical disc. Previous studies showed that the most valuable measurement parameters in the differentiation of glaucoma are the mean RNFL thickness and the RNFL thickness values of the lower and upper quadrants (8,9). Leung et al. demonstrated that the best indicator in the differentiation of

<table>
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<th>Mean</th>
<th>Superieur quadrant</th>
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<tbody>
<tr>
<td>≤ 555</td>
<td>21</td>
<td>95±6.8 (82.2-106.8)</td>
<td>122±14.7 (104-161)</td>
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<td>556-588</td>
<td>34</td>
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<td>&gt; 588</td>
<td>11</td>
<td>111.4±10.3 (96.7-129.7)</td>
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<td>147.5±15.5 (113-175)</td>
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CCT, Central corneal thickness; RNFL, retinal nerve fiber thickness; OHT, ocular hypertension.

Discussion

The mean inferior quadrant and superior quadrant RNFL thicknesses were not significantly different between the groups (p>0.05 for all). Table 1 shows the demographic data, CCT, and RNFL thickness values of the groups in detail. When both groups were divided into two separate subgroups according to the CCT of ≤555 µm and >555 µm, there was no statistically significant difference among the subgroups with a CCT of >555 µm in the mean superior and inferior quadrant RNFL thicknesses (p>0.05). However, the subgroups with thinner corneas (≤555 µm) in the OHT and the control group showed a statistically significant difference in the inferior quadrant RNFL thickness (p<0.05) but not in the mean and superior quadrant RNFL thicknesses (p>0.05). When the OHT group was divided into three subgroups based on a CCT of ≤555 µm (thin), a CCT of 556–588 µm (average), and a CCT of >588 µm (thick), the inferior quadrant RNFL thickness was significantly less in the thin group compared to the other groups (p<0.05). Figure 1 and Table 2 show the mean superior and inferior quadrants RNFL thicknesses in the OHT group according to thin, average, and thick corneas.

Table 2. The mean, superior and inferior quadrants RNFL thicknesses in OHT group according to thin, average and thick corneas

<table>
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Although a high IOP is known to be the most important risk factor in the development of glaucoma, in some cases, such as OHT, can be observed without glaucomatous damage. Bron et al. used ultrasound pachymetry to evaluate the CCT in normal cases and in patients with OHT, glaucoma, and diabetes without glaucoma (10). They found that the CCT was significantly thicker in the OHT cases than in the other groups. Sen et al. detected significantly higher CCT values in OHT cases than in glaucoma and control groups (11). Arslan et al. also found that the CCT was thicker in OHT cases than in the normal population (12). In the present study, we found that the CCT values were significantly higher in OHT cases than healthy individuals.

Mumcuoglu et al. found no significant association between the CCT and RNFL thickness in their study in which they used ultrasound pachymetry to measure the CCT and scanning laser polarimetry (GDx-VCC), confocal scanning laser ophthalmoscopy (HRT II), and OCT (Stratus OCT; Carl Zeiss Meditec) to measure the RNFL thickness (13). Kaushnik et al. compared RNFL thicknesses by referencing the mean and the upper and lower quadrants RNFL thicknesses using OCT (14). Their study included 51 eyes of 51 OHT cases and 35 eyes of 35 healthy individuals as a control group, and they grouped the cases according to their CCT values. They found no significant difference between the OHT and the control groups in patients with thick corneas and a CCT above 555 μm. They also found that the RNFL thickness was significantly thinner in OHT cases with thin corneas and a CCT below 555 μm compared to the controls. When they compared the OCT cases within the group, the RNFL thicknesses were significantly thinner in those with a CCT below 555 μm in comparison to those with a CCT above 588 μm. Henderson et al. found that the RNFL thickness was significantly thinner in OHT cases with thin corneas than in OHT cases with thick corneas and a control group (15). However, they found that the RNFL thickness was significantly thinner in OHT cases with a CCT below 555 μm compared to the OCT cases with a CCT. Arslan et al. compared the RNFL thickness using Stratus OCT in OHT cases grouped as thin and thick corneas according to pachymetric measurements (12). Their study included 56 eyes of 32 cases. They found that the RNFL thickness was significantly thinner in the group with a CCT of 555 μm and below compared with those with a CCT above 588 μm (12).

Medeiros et al. detected early functional damage in OHT cases with thin corneas using wave automatic perimetry and frequency doubling perimetry in two separate studies (16,17). The patients in these studies probably had early glaucomatous damage that was undetectable with conventional methods. We designed our study on the basis that a thin CCT is a strong predictive factor for the development of glaucoma in OHT cases and that the risk of developing this disease is three times higher in OHT cases with a CCT of 555 μm or below in comparison to those with a CCT above 588 μm. (3). In the present study, we divided the OHT cases into three subgroups according to their CCT values (≤555μm, 556 µm, 588 µm, and ≥555 µm) and compared the RNFL thickness in these groups. There was no significant difference in the upper quadrant RNFL thickness, but both the mean and the lower quadrant RNFL thickness values were significantly thinner in the group with a CCT of 555 μm or below in comparison to the groups with a CCT between 556 and 588 μm and a CCT above 588 μm.

The literature data and our findings show that the thickness of the RNFL is thinner in those with a thin CCT, which is an accepted risk factor among OHT cases for the development of glaucoma. As emphasized in a previous study conducted with control groups (9), we found that the CCT thinning, which is accepted as the best indicator in the differentiation of glaucoma, was significant in the evaluation of the lower quadrant RNFL thickness.

Most OHT cases do not show glaucomatous changes during their lives without a need for a treatment. According to a report by the Ocular Hypertension Study group, the risk for the development of glaucoma is 4.4% in patients who receive treatment and 9.5% in those followed up without treatment. In other words, glaucoma has not been observed in 90% of cases followed up without treatment. Nevertheless, treatment reduces the risk of developing glaucoma (18). Therefore, OHT cases have to be followed up, with careful evaluation of the risk factors. Functional and structural tests are important in routine examinations, as well as in determining the patient groups that require close follow-up and treatment.

**Conclusion**

The use of the OCT technique to measure the RNFL thickness seems to be important in the detection of
early glaucomatous damage in OHT cases. Therefore, determination of the CCT and the RNFL thickness and interpretation of these two parameters, together with other risk factors, can be useful in the evaluation of OHT cases, in addition to routine ophthalmological examination methods. Based on this information, OHT cases with a thin CCT and a thin RNFL thickness can be followed up more closely to detect the development of glaucoma. In OHT cases with a high risk for the development of glaucoma, the decision about early commencement of treatment should be based on a detailed evaluation of the risk factors before damage develops.

References