Correlations between Corneal Biomechanics and Glaucoma Severity in Patients with Primary Open Angle Glaucoma

Dana DASCALESCU; Catalina CORBU; Mihaela CONSTANTIN; Miruna CRISTEA; Catalina IONESCU; Miruna CIOBOATA; Liliana VOINEA

a Clinical Hospital of Ophthalmologic Emergencies, Bucharest, Romania
b Oftaclinic Clinic, Bucharest, Romania
c Emergency University Hospital, Bucharest, Romania

ABSTRACT

Objectives: To investigate the relationship between corneal biomechanical changes and glaucoma severity in primary open angle glaucoma patients.

Design: Correlation study.

Material and methods: Our study included 70 glaucomatous eyes; they were divided in groups using Glaucoma Staging System Based on Humphrey Visual Field. Ocular Response Analyzer (ORA) was used in order to determine corneal hysteresis (CH) and corneal resistance factor (CRF); ultrasonic pachimetry (Ocuscan) to measure central corneal thickness (CCT) and Humphrey Visual Analyser to determine mean deviation (MD), pattern standard deviation (PSD) and visual field index (VFI). For statistical analysis we used descriptive analysis and linear regression using IBM SPSS Statistics Standard.

Outcomes: Out of the 70 eyes with primary open angle glaucoma examined that had visual acuity 0.7 or better, 35 were included in stage 1 (MD 0.01dB -> -6dB), 21 in stage 2 (MD -6.01dB -> -12dB) and 14 in stage 3 (MD -12.01dB -> -20dB). A considerable statistic correlation was found between CH and VFI both in the entire group of primary open angle glaucoma patients (r=0.44, p<0.001), and in stages 1 (r=0.44, p<0.009), 2 (r=0.51, p<0.01) and 3 (r=0.52, p<0.05).

Conclusions: The study shows a moderate correlation, statistically significant, between corneal hysteresis and visual field index in glaucoma patients. Ocular response analyzer can be considered an useful instrument in evaluation of primary open angle glaucoma patients.
INTRODUCTION

Glaucoma is known as being the leading cause for irreversible blindness in the world (1).

In 2013, the prevalence of POAG in the world among people 40 to 80 years old was estimated to 64.3 million. It is also recognized the fact that in the future is expected a growth of the prevalence of the disease to about 76.0 million in 2020 and 111.8 million people in 2040 (2).

Glaucoma represents an optic neuropathy associated with damage of the visual field and ganglion cell loss in the absence of other ocular disease (3).

The progression and the prognosis of the disease depend on a multitude of risk factors whose importance may be different. One of the most important risk factors which influences the development of the disease is represented by the intraocular pressure (IOP) and its daily fluctuations (3). In fact, the intraocular pressure is the only modifiable risk factor involved in glaucoma progression (3,4).

The accuracy of the IOP’s measurements is, in its turn, influenced by many factors among which the geometrical (thickness and curvature) and biomechanical properties of the cornea (5-11). A decreased CCT represents a factor of negative prognosis of the disease.

OBJECTIVES: Our goal is to determine the mean values for CH, CCT and VFI in POAG patients considering the 3 stages of severity, as well as the correlation between CH and VFI.

MATERIAL AND METHODS

For this study were selected patients diagnosed with primary open angle glaucoma. Each patient underwent a detailed ophthalmologic examination which included anamnesis, visual acuity with and without correction, slit lamp examination of the anterior pole, intraocular pressure measurement using Goldmann applanotonometer, ORA, gonioscopy, automated perimetry using HFA (24-2 strategy) and stereoscopic fundus examination.

The primary open angle glaucoma was diagnosed based on glaucoma optic neuropathy (using Optic Coherence Tomography quantifying retinal nerve fiber layer thickness) and damage of the visual field (using Humphrey perimeter and determining Glaucoma Hemifield Test: Outside normal Limits or low MD), best corrected visual acuity 0.7 Snellen or more.

Optical glaucoma neuropathy involves a vertical C/D ratio 0.6 or more or asymmetry of the excavation between the two eyes 0.2 or more and/or presence of deficit in the retinal nerve fiber layer or peripapillary hemorrhages.

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldman</td>
<td>12 mmHg</td>
<td>22 mmHg</td>
</tr>
<tr>
<td>CH</td>
<td>9.00</td>
<td>14.9</td>
</tr>
<tr>
<td>CRF</td>
<td>7.9</td>
<td>15.4</td>
</tr>
<tr>
<td>CCT</td>
<td>495 μm</td>
<td>632 μm</td>
</tr>
<tr>
<td>MD</td>
<td>-5.06 dB</td>
<td>-0.21 dB</td>
</tr>
<tr>
<td>PSD</td>
<td>0.58</td>
<td>4.43</td>
</tr>
<tr>
<td>VFI</td>
<td>90%</td>
<td>100%</td>
</tr>
</tbody>
</table>

TABLE 1. The average values of the parameters determined on these three stages of glaucoma severity.
We included into the study 70 eyes that fulfilled the inclusion criteria; they were divided into 3 groups, based on POAG stadialization described by Richard P. Mills (14) as follows: the first group included 35 eyes with a mild perimetric defect and with MD between 0dB and -6dB, the second group includes 21 eyes with moderate perimetric defect and MD between -6.01dB and -12dB and the last group eyes with advanced perimetric defect and MD between -12.01dB and -20dB. All patients undertook ultrasonic pachimetry (Alcon® OcuScan® RxP Ophthalmic Ultrasound System) to measure the central corneal thickness; ten measurements were taken for each eye, the lowest and highest values being deleted and thus, we determined the average of the remaining values. Ocular Response Analyzer was used to determine the CH and CHF.

Five recordings for each eye; in the study we used the best measurement for each eye with waveform score over 7. The intraocular pressure was determined with Goldman applanotonometer, with two measurements for each eye, using the average value. The visual field was performed using the Humphrey Field Analyzer II (Carl Zeiss Meditec Inc, Dublin, California) strategy 24-2.; we only considered the reliable examinations (fixation errors, false positive and false negative errors under 20%).

Ocular Response Analyser® (Reichert Ophthalmic Instruments, NY) is an instrument capable of establishing in vivo the corneal biomechanical properties, being the only instrument which can measure the corneal hysteresis (12,13). The ORA measurement provides four variables: corneal compensated intraocular pressure (IOPcc), Goldmann intraocular pressure (IOPg), corneal hysteresis (CH) and corneal resistance factor (CRF).

ORA uses a by-directional applanation process that makes the cornea move inward-outward. The difference between the two pressure values as a result of the viscous dumping represents corneal hysteresis (12). Corneal hysteresis is a parameter that reveals the corneal capacity to absorb and dissipate energy (13) and it measures the corneal viscoelastic properties (12). In normal eyes CH varies between 9-11 (17). Low values for CH can be associated to a thin cornea or a high IOP. Recent studies show that a lower CH is associated to a more advanced glaucoma (13-16). CRF is an indicator of the global resistance of the cornea. CRF is associated to CCT, being higher in patients with thicker corneas (10,12,19).

Visual field index is an indicator of the rate of progression on the visual field. The parameter is expressed in percent. VFI is approximately 100% in normal fields and gets lower as the disease progresses, dropping to 0% in absolute glaucoma (3,18). In a patient diagnosed with glaucoma, a reduction in VFI in consecutive visual fields shows progression, while constant VFI can be found in stationary glaucoma (3).

For statistical analysis we used descriptive analysis and frequency tests, means and linear regression.

**RESULTS**

In these 70 eyes with POAG we found a negative correlation, statistically significant, between CH and IOP: \( r = -0.56, p < 0.0001 \) (Figure 1) and between CH and PSD: \( r = -0.56, p < 0.0001 \). A positive correlation, statistically significant, was found between CH and CCT: \( r = 0.62, p < 0.0001 \), between CH and MD: \( r = 0.27, p < 0.02 \) and between CH and VFI: \( r = 0.66, p < 0.0001 \) (Figure 2).

A negative correlation between CH and IOP was found in stages 2 and 3 of glaucoma severity, being statistically significant, but not in stage 1 (Table 2).

At the same time, CH correlates with CCT, this time being a positive correlation in all stages, according to Table 3.

According to our study, mean values for the visual field parameters in glaucomatous eyes were: -7.15±5.79 for MD, 4.31±3.42 for PSD and 84.55±21.27 for visual VFI.

The visual field coefficients correlate with the corneal hysteresis as follows: in stage 1 pos-

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD from 0 to -6 dB</td>
<td>MD from -6.01 dB to -12 dB</td>
<td>MD from -12.01 to -20 dB</td>
</tr>
<tr>
<td>Correlation coefficient</td>
<td>( r = 0.24 )</td>
<td>( r = -0.52 )</td>
</tr>
<tr>
<td>Statistical value</td>
<td>( p &lt; 0.16 )</td>
<td>( p &lt; 0.01 )</td>
</tr>
</tbody>
</table>

**TABLE 2.** The correlation between CH and IOP in the three stages of the glaucoma severity.

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD from 0 to -6 dB</td>
<td>MD from -6.01 dB to -12 dB</td>
<td>MD from -12.01 to -20 dB</td>
</tr>
<tr>
<td>Correlation coefficient</td>
<td>( r = 0.52 )</td>
<td>( r = 0.72 )</td>
</tr>
<tr>
<td>Statistical value</td>
<td>( p &lt; 0.008 )</td>
<td>( p &lt; 0.06 )</td>
</tr>
</tbody>
</table>

**TABLE 3.** The correction between CH and CCT in the three stages of the severity of the glaucoma.
The eyes have a variable tolerance to high values of the intraocular pressure. Thus, there are eyes which present losses of the nervous fibers at low IOP, while others can tolerate a significant growth of the IOP without showing a loss of nervous fibers. To support this statement, there are studies showing that those patients with normotensive glaucoma have a lower value of the CH (16).

Our study reveals that eyes with lower values for CH are the eyes with more advanced disease proving once again that CH is an indicator of the progression in glaucoma patients. Also, in all three stages of disease severity CH is correlated positively to VFI, lower levels of CH are correlated to lower levels of VFI and higher levels of CH are correlated to higher levels of VFI.

The relationship between CH and CCT has already been documented, but this study reveals once again a positive correlation between these two parameters in all three stages of glaucoma severity.

As recent studies show, a low CH is associated to a more rapid progression of the glaucoma (16), our study revealing that CH correlates positively to VFI and CCT in eyes with mild, moderate and severe disease. Also, the mean CH and VFI is significantly lower in advanced glaucoma group showing once again that those eyes that have lower CH levels have a higher risk of glaucoma progression over time.

CONCLUSION

Dealing with patients suspected of glaucoma or already diagnosed with glaucoma has many faceplates: we have to consider the IOP, the cup, the rim, the visual field parameters and the RNFL. Sometimes, it is still difficult to diagnose glaucoma or to evidence progression; corneal biomechanical parameters (CH and the CCT) might be useful instruments for diagnosis.

Corneal biomechanical profile determined by the corneal structure and thickness (mainly CH) can be considered an useful parameter in the diagnosis and follow up glaucoma patients. CH is significantly lower in patients with advanced disease than in patients with mild disease. CH is positively correlated with CCT and VFI in all three stages of glaucoma.

Abbreviations

CH = corneal hysteresis
CRF = corneal resistance factor
IOP = intraocular pressure
**REFERENCES**

12. Ocular Response Analyzer- Introduction to Ocular Response Analyzer ; Reichart Technologies