Does graves' ophthalmopathy affect anterior segment parameters?

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Abstract

Aim: To evaluate whether anterior segment parameters (ASPs) differ between patients with Graves's ophthalmopathy (GO) and healthy individuals.

Materials and Methods: In a case-control study, 62 patients with GO and 45 healthy sex- and age-matched individuals were compared for ASPs obtained from Scheimpflug camera imaging (Sirius, Florence, Italy). The ASPs were anterior chamber depth (ACD), anterior chamber volume (ACV), iridocorneal angle (ICA), corneal volume, corneal curvatures (K1, K2, and Kmean), and white-to-white, apical, and thinnest corneal thickness.

Results: Mean white-to-white corneal distance, corneal volume, ACD, ACV, ICA, K1, K2, and Kmean were similar between patients and controls (p = 0.815, p = 0.285, p = 0.522, p = 0.102, p = 0.275, p = 0.114, p = 0.566, p = 0.137, p = 0.405, and p = 0.447, respectively). There was a negative correlation between mean Hertel measurement and mean ACD (r = - 0.284, p = 0.003), ACV (r = - 0.283, p = 0.003), and ICA (r = - 0.295, p = 0.002).

Conclusion: The ASPs were not associated with significant alterations between patients with GO and controls.

Keywords: Anterior chamber; anterior segment parameters; corneal topography; Graves' ophthalmopathy; thyroid eye disease

INTRODUCTION

Graves' disease (GD) is an autoinflammatory thyroid disease attributed to the interaction of autoantibodies with thyroid-stimulating hormone receptors (TSHRs) (1,2). Among known causes of hyperthyroidism, GD ranks highest, with an estimated yearly incidence of 2 to 5 patients with hyperthyroidism per 10,000 (3). Beyond that, approximately 40% of patients with GD experience Graves' ophthalmopathy (GO) (4,5). Although the mechanism of orbital involvement in GD is debated, the most widely accepted idea is the triggering of orbital inflammatory cells, especially fibroblasts, by autoimmune (6,7). Rundle and Wilson have described that clinical process as biphasic, in which the active (i.e., inflammatory) phase involves the progression of orbital symptoms, lasting 6 to 18 months, followed by an inactive phase (8,9). If the volume of tissue in the orbit increases with the assembly of glycosaminoglycans and inflammation, then GO becomes more clinically significant (1,3,10). Eyelid retraction and exophthalmos frequently result from that development, whereas diplopia and optic neuropathy occur less often (1).

To date, literature addressing GO and GD has concentrated on changes in extraocular structures and orbital fibrocytes, often with reference to studies investigating GO's pathogenesis and treatment strategies for the condition (11,12). The exaggerated enlargement of the orbital adipose tissue moves the globe forward, which may affect both the anterior (changes in meibomian glands) and posterior segments (optic nerve, retinal vessels, choroid) (11,13,14). Other studies have demonstrated that the cornea's biomechanical properties are altered in GO, while choroidal thickness is increased (9,15). However, research evaluating anterior segment parameters (ASPs), including anterior chamber depth (ACD), anterior chamber volume (ACV), and iridocorneal angle (ICA), remains sparse. Therefore, we sought to evaluate ASPs in patients with GO by using Sirius Scheimpflug camera imaging to measure white-to-white corneal distance (WTW), apical corneal thickness (ACT), thinnest corneal thickness (TCT), corneal volume (CV), and keratometry (K1, K2, and Kmean).
MATERIALS and METHODS

Study population and design
A cross-sectional, case-control study was performed in the Department of Ophthalmology at Ataturk Training and Research Hospital in Katip Celebi University, Izmir, Turkey. The Institutional Review Board approved the methods, and the research protocol adhered to the tenets of the Declaration of Helsinki. Patients previously diagnosed with GD by the hospital’s Department of Endocrinology, in the disease’s euthyroid phase, defined as thyroid stimulating hormone (TSH) of 0.35–4.94 μIU/mL and thyroxin hormone (T4) of 0.7–1.48 ng/dL were referred to the Department of Ophthalmology for a routine ophthalmological examination. After being informed about the aim and possible side effects of the study, all participants provided their written, informed consent to participate. An experienced ophthalmologist (XX) diagnosed the patient as GO if he/she had clinical and/or MRI findings. The clinical signs were the eyelid abnormalities (e.g., lid lag, movement abnormalities), proptosis, chemosis, corneal staining, and conjunctival hyperemia. The classical MRI finding was enlargement of the extraocular muscles sparing the tendons.

The VISA classification or vision (i.e., dysthyroid optic neuropathy), inflammation (i.e., congestion), strabismus (i.e., motility restriction), appearance (i.e., exposure), (Table 1) was used to identify the phase of GO (16,17).

<table>
<thead>
<tr>
<th>Clinical Findings</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caruncular edema</td>
<td>0–1</td>
</tr>
<tr>
<td>Retrobulbar pain</td>
<td>0–2</td>
</tr>
<tr>
<td>Chemosis</td>
<td>0–2</td>
</tr>
<tr>
<td>Eyelid edema</td>
<td>0–2</td>
</tr>
<tr>
<td>Conjunctival injection</td>
<td>0–1</td>
</tr>
<tr>
<td>Eyelid injection</td>
<td>0–1</td>
</tr>
<tr>
<td>Diurnal variation</td>
<td>0–1</td>
</tr>
<tr>
<td>Total</td>
<td>0–10</td>
</tr>
</tbody>
</table>

Table 1. VISA inflammation score

As controls, 45 healthy sex- and age-matched individuals were also recruited to participate. Only one eye (right eye) was selected to prevent double-organ bias (type 1 error) for both the patients and the control group. The ocular inclusion criteria for the study included a refractive error of ±3.00 diopters (D), an axial length of 22 ± 2 mm, intraocular pressure (IOP) of less than 22 mmHg, no previous ocular diseases or surgeries, and no history of uveitis, retinal disease, and also dense corneal opacities.

Each participant underwent a comprehensive ophthalmic examination administered by BA for best-corrected visual acuity using LogMAR, IOP (Goldmann applanation tonometer, Haag-Streit Inc., Köniz, Switzerland), the existence of exophthalmos with a Hertel exophthalmometer, and the evaluation of the anterior segment and fundus from dilated pupillae by slit lamp biomicroscopy with a +90 D lens. For each participant, Placido were measured with Placido disc corneal topography and Scheimpflug camera imaging (Sirius, CSO Inc., Florence, Italy).

Sirius Scheimpflug camera measurements
The Sirius topography device couples an illumination system and a rotating Scheimpflug camera combined with a Placido disc, in a system used for noninvasive, 3D anterior segment evaluation (18). In our study, 3D anterior chamber analysis modules were used, and to achieve standardization, all images were taken under mesopic conditions. Each participant underwent three measurements to avoid miscalculations due to poor imaging quality, and of the three measurements, the image with the highest quality was retained for further analysis. The quantitative values of WTW (mm), ACT (μm), TCT (μm), ACD (mm), ACV (mm³), ICA (°), CV (mm³), and K₁, K₂, and K_mean (D) were obtained from topography.

Statistical Analysis
The Statistical Package for the Social Sciences version 24.0 for Windows (IBM Inc., Armonk, NY, USA) was used for statistical analysis, and descriptive statistics were recorded in M ± SD, frequency, and ratio. The Kolmogorov–Simirnov test, evaluated the distribution of variables, quantitative values were compared between the groups with a t test and Mann–Whitney U test, and a χ² test was used to compare qualitative variables. Last, correlation analysis was performed using Spearman correlation coefficients. Any p value less than 0.05 was considered statistically significant.

RESULTS
Demographical and the other characteristics of the groups are demonstrated in Table 2.

The mean age of patients with GO and controls were 38.74 ± 1.17 (23-67) and 38.44 ± 1.20 (24-60) years, respectively (p = 0.863). Among other results, patients exhibited significantly increased exophthalmometry measurements than controls (19.2 mm vs. 16.8 mm, respectively, p < 0.001).

Sirius Scheimpflug camera measurements
In patients group the ASPs were not statistically different from the control group (Table 2).

There was a negative correlation between mean Hertel measurement and mean ACD (r = -0.284, p = 0.003), ACV (r = -0.283, p = 0.003), and ICA (r = -0.295, p = 0.002).
DISCUSSION

Although some studies have shown that, aside from the eyelids and orbit, the choroid, retina, and optic nerve may be disturbed, (9,19,20) no such study has evaluated the anterior segment in patients with GO (PubMed search: Graves, Ophthalmopathy, Anterior segment parameters). Thus, in our research, we evaluated ASPs with Sirius topography in patients with GO and found that the ASPs in patients versus controls did not significantly differ.

In the literature, relatively few studies have involved assessing changes in the anterior segment that are linked to orbital inflammation. In a case report, Zborowski-Gutman et al. revealed that orbital pseudotumors precipitate angle-closure glaucoma, and after treatment for inflammation, the eyes were quite, and the IOP has remained normal (21). In response, those authors postulated that the iris diaphragm might have been forced forward by the swollen uvea. Adding to those findings, Bernardino et al. (22) used MRI and ultrasound biomicroscopy to reveal the anterior displacement of the iris diaphragm in three patients with orbital pseudotumors with angle-closure glaucoma. All three patients had uveal effusions, and after the treatment of their pseudotumors, their IOP returned to normal.

We suggest that in patients with GO, expanded orbital soft tissues and engorged extraocular muscles may apply pressure to the globe, thereby increasing episcleral venous pressure (EVP) and possibly causing uveal effusion. The effusion of the ciliary body may displace the iris diaphragm more anteriorly, and some changes in ASPs, especially ACD, ACV, and ICA, may occur. The negative correlation between those values and Hertel measurements found in our study ran parallel to our expectations.

Onaran et al. (23), who evaluated the effect of orbital decompression surgery on episcleral venous outflow in patients with GO found that EVP decreased after surgery. Moreover, Cagiltay et al. (24) found that the choroid was thicker in patients with mild GO, and in view of those results, they speculated that venous obstruction and congestion may cause choroidal thickening in such patients. The most likely reason for the similarity of ASPs in our study was that patients have not affected by venous congestion leading a disturbance with the ASPs. However, as with this study’s limitation we did not evaluate choroidal thickness.

Kim et al. (25) observed that after orbital decompression surgery, the axial length significantly increased, and a myopic shift occurred; however, neither the lens’s thickness nor the ACD changed significantly. Also evaluating changes in the cornea and finding no difference before versus after surgery, they postulated that the refractive change may be affected by changes in the posterior segment, especially the posterior portion of the muscle insertion site. Our results were similar to theirs insofar as ACD and other corneal parameters were approximately the same in both patients with GO and controls. We suggest that the anatomical position of the

<table>
<thead>
<tr>
<th>Table 2. Characteristics of two groups</th>
<th>Patients (n:62)</th>
<th>Controls (n:45)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>38.74±9.25</td>
<td>38.44±8.07</td>
<td>0.863</td>
</tr>
<tr>
<td>Gender (male- %)</td>
<td>43.5</td>
<td>44.4</td>
<td>0.927**</td>
</tr>
<tr>
<td>BCVA, (logmar)</td>
<td>-0.005±0.02</td>
<td>-0.006±0.02</td>
<td>0.676</td>
</tr>
<tr>
<td>IOP (mmHg)</td>
<td>15.8 ± 1.8</td>
<td>15.9 ± 1.5</td>
<td>0.868</td>
</tr>
<tr>
<td>White-to-white (mm)</td>
<td>11.83±0.41</td>
<td>11.87±0.42</td>
<td>0.666</td>
</tr>
<tr>
<td>Corneal volume (mm3)</td>
<td>58.90±4.53</td>
<td>58.78±3.82</td>
<td>0.888</td>
</tr>
<tr>
<td>Anterior chamber depth (mm)</td>
<td>3.33±0.37</td>
<td>3.45±0.38</td>
<td>0.102</td>
</tr>
<tr>
<td>K1 (D)</td>
<td>43.59±1.40</td>
<td>43.14±1.72</td>
<td>0.137</td>
</tr>
<tr>
<td>K2 (D)</td>
<td>44.59±1.50</td>
<td>44.41±1.91</td>
<td>0.582</td>
</tr>
<tr>
<td>Kmean (D)</td>
<td>44.09±1.41</td>
<td>43.76±1.69</td>
<td>0.278</td>
</tr>
<tr>
<td>VISA inflammatory score</td>
<td>4.32±1.21</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Disease duration (years)</td>
<td>3.4 ± 1.4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Thinnest pachymetry (μm)</td>
<td>541.5 (450-620)</td>
<td>542 (487-610)</td>
<td>0.796</td>
</tr>
<tr>
<td>Apical pachymetry (μm)</td>
<td>573 (504-805)</td>
<td>567 (514-673)</td>
<td>0.285</td>
</tr>
<tr>
<td>Anterior chamber volume</td>
<td>137.5 (78-215)</td>
<td>144 (81-214)</td>
<td>0.275</td>
</tr>
<tr>
<td>Iridocorneal angle(*)</td>
<td>39.5 (23-56)</td>
<td>43 (25-54)</td>
<td>0.114</td>
</tr>
<tr>
<td>Exophthalmometry (mm)</td>
<td>19.2 (16.5-21)</td>
<td>16.8 (16-18.5)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

SD, standard deviation; BCVA, best corrected visual acuity; IOP, intraocular pressure; D, diopters; VISA, vision, inflammation, strabismus, appearance; ’ Student’s t-test; “ chi-square; ’’ Mann-Whitney-U; boldface, significant value, p < 0.05.
ciliary body is not prone to influence only from vectoral forces of engorged muscles but also effusion that rotates the ciliary body anteriorly so that the ASPs change.

**LIMITATIONS**

As for our study's limitations, we could not evaluate the anatomical position of the ciliary body. In response, we suggest evaluating the ciliary body in patients with GO with ultrasound biomicroscopy or at least MRI. The other limitation was that the patients were all in their euthyroid phase. Further studies should be undertaken with patients in different stages of GO.

**CONCLUSION**

In sum, despite literature showing significant changes in the posterior segment of the globe, our pilot study, aimed at evaluating ASPs in patients with GO, revealed that their ASPs did not differ significantly from those in controls.

*Competing Interests: The authors declare that they have no competing interest.*

*Financial Disclosure: There are no financial supports.*

*Ethical Approval: Izmir Katip Celebi University Clinical Research Ethics Committee approved the study (20.02.2020-19).*

**REFERENCES**