DOI:10.14744/bej.2022.08941
Beyoglu Eye J 2022; 7(3): 193-198

Original Article

The Effect of Thyroid Eye Disease on Corneal Biomechanical Properties

Melis Cansu Comert,[1] Sezen Yilmaz,[1] Ayse Yildiz Tas,[2] Afsun Sahin[2]

[1]Koç University, Faculty of Medicine, Istanbul, Türkiye
[2]Department of Ophthalmology, Koç University Hospital, Istanbul, Türkiye

Abstract

Objectives: The aim of this study was to identify corneal biomechanical parameters measured by ORA in patients with TED compared to the healthy group. The NOSPECS classification of patients is used to assess the relation between biomechanical changes and disease severity.

Methods: We included 22 TED patients, diagnosed with TED for more than five years, and 43 healthy participants. The NOSPECS classification was assessed as mild (grade 1-3) and severe (grade 4-6) disease. For each group, corneal hysteresis (CH), corneal resistance factor (CRF), central corneal thickness (CCT), Goldmann-correlated intraocular pressure (IOPg) and corneal compensated intraocular pressure (IOPcc) parameters were measured by ORA.

Results: The mean age was 38.8±11.6 years for the TED patients and 42.9±15.58 years for the control group. For TED patients and healthy volunteers, the mean levels of CRF, CH, and CCT were measured as follows: 10.43±2.04 vs 10.28±1.91mmHg, p=0.67; 10.18±1.81 vs 10.21±1.68 mmHg, p=0.90; 550.31±35.73 vs 545.23±37.91 µm, p=0.47, respectively. These values were not significant between groups, but they were significantly higher in females compared to males in TED patients [CRF;10.68 (IQR: 9.49-12.14) vs 8.96 (IQR: 8.04-9.92) mmHg, p=0.002, CH; 10.43 (IQR: 9.48-11.25) vs 8.58 (IQR: 7.90-9.95) mmHg, p=0.003 and CCT; 554.25 (IQR: 536.05-579.52) vs 527.40 (IQR: 492.25-545.90) µm, p=0.014]. CRF values were negatively correlated with NOSPECS score (r=-0.317, p=0.036) and significantly higher CRF was observed in mild patients compared to severe disease (11.43 (IQR: 10.14-12.87) vs 9.46 (IQR: 8.75-10.28) mmHg, p=0.008).

Conclusion: We found a significant gender effect on corneal biomechanical parameters of TED patients. CRF, CH and CCT values were significantly higher in females compared to males with TED. The clinical severity score of TED showed negative correlation with CRF. CRF value might be a useful parameter in follow-up of TED patients in clinical practice.

Keywords: Corneal biomechanical parameters, corneal resistance factor, NOSPECS classification, thyroid eye disease, ocular response analyzer

Introduction

Thyroid eye disease (TED) affects 25–50% of individuals with Graves' disease (1). TED can appear at any time over the course of the disease but it is most common in people in their fifth and seventh decades (2). Autoimmune activation leads to retro-orbital inflammation, orbital fibroblast overproduction of glycosaminoglycans, and adipose tissue hyperplasia in the etiology of TED (2-5). Clinical signs of TED emerge as a result of these pathophysiological alterations, as well as cytokine production and structural modifications (3). Clinical signs and symptoms of TED range from mild

How to cite this article: Comert MC, Yilmaz S, Yildiz Tas A, Sahin A. The Effect of Thyroid Eye Disease on Corneal Biomechanical Properties. Beyoglu Eye J 2022; 7(3): 193-198.

Address for correspondence: Afsun Sahin, MD. Department of Ophthalmology, Koç University Hospital, Istanbul, Türkiye
Phone: +90 532 137 39 49 **E-mail:** op.dr.afsahin@gmail.com

Submitted Date: December 01, 2022 **Accepted Date:** May 09, 2022 **Available Online Date:** August 05, 2022

ocular and extraocular discomfort to restrictive myopathy, severe proptosis, lid retraction, and exposure keratitis (6). One of the most important manifestations of TED is corneal changes as the disease progresses. The corneal involvement of TED has not been fully understood yet. Using confocal microscopy, corneal pachymetry, and fluorophotometry, previous investigations produced some data on corneal microstructural changes in TED (7-9). While it is suggested that hyperthyroidism or severity of TED had no effect on central corneal thickness, the average permeability value of the corneal epithelium in TED was significantly higher than the control. The nerve density was reduced, and the tortuosity of the nerve fibers was raised, compared to healthy controls, in the TED group's corneal in vivo confocal microscopy parameters.

Corneal structural alterations in TED patients studied from different perspectives with different examination methodologies and using various examination procedures. However, it needs to be further evaluated to establish the best of our knowledge. In our study, we investigated the effect of microstructural changes on corneal biomechanical properties of TED patients with an ocular response analyzer (ORA) (Reichert Ophthalmic Instruments, Buffalo, USA).

The ORA was introduced to measure corneal biomechanical properties using an air jet that generates pressure on the cornea and aims to provide information on corneal hysteresis (CH) and corneal resistance, which gives the value of CH, corneal resistance factor (CRF), central corneal thickness (CCT), and non-contact intraocular pressure measurement as well as Goldmann-correlated intraocular pressure (IOP_g) and corneal compensated intraocular pressure (IOP_{cc}) (5).

Several classification systems have been conceived to assess the clinical manifestations of TED. The vision, inflammation, strabismus, and appearance (VISA), the European Group of Graves' Orbitopathy (EUGOGO), and NOSPECS classification are widely used grading systems to assess the activity and severity (10,11). NOSPECS classification is composed of no TED signs (N), only eyelid sign (O), soft-tissue involvement (S), proptosis (P), extraocular motility restriction (E), corneal involvement (C), and sight loss (S). It is one of the oldest and widely used classification systems which was introduced by Werner in 1969 (12). This classification grades exclusively the clinical severity of TED objectively and practically. On the other hand, the EUGOGO and VISA classification also evaluate disease activity in their scoring systems. Therefore, we obtained the NOSPECS classification in our study to evaluate only the clinical severity.

Despite the fact that the previous studies also focused on corneal biomechanical changes in TED, there is relatively little information on the link between disease severity score and corneal biomechanics. The major goal of this study, from this perspective, was to investigate altered biomechanical properties of the cornea in patients with TED and to determine their relationship with clinical severity, as measured by the NOSPECS classification.

Methods

Twenty-two patients with TED and 43 age- and sex-matched healthy participants were included in this study. Patients who have been diagnosed with thyroid disease for more than 5 years by an endocrinologist and healthy volunteers were included in the study. For both patients and healthy control groups, we excluded high refractive error cases. Spherical equivalent between −3.00 D and +3.00 D was included in the study. Subjects with diabetes mellitus, glaucoma, cornea, or ocular surface disorders, contact lens usage, or history of ocular surgery were excluded from the study. The study followed the tenets of the Declaration of Helsinki and was approved by the local ethics committee. All the patients with TED were routinely followed by the endocrinology department and were under treatment for their thyroid disease. All subjects underwent complete detailed ophthalmologic examination including visual acuity, biomicroscopy, and fundoscopy.

All subjects underwent ORA in primary position (13) for the measurement of CH, CRF, CCT, IOP_g, and IOP_{cc} parameters. All ORA measurements were obtained using the same calibrated instrument by a single masked person. All ORA examinations were performed between 09.00 AM and 12.00 PM to reduce the effects of diurnal variation in corneal biomechanics. Testing was performed according to the equipment manual of ORA. Three measurements with a minimum waveform score of 6.0 were obtained for each subject.

The clinical severity of TED was assessed with the NOSPECS classification as shown in Table 1. Soft-tissue and extraocular muscle involvements were evaluated with an MRI or CT scan. Best-corrected visual acuity (Snellen chart), color vision (Ishihara plates), and optic disk evaluation with a

Table 1. NOSPECS classification[12]

Class	Clinical features
0	No signs and symptoms
1	Only signs, no symptoms
2	Soft-tissue involvement with signs and symptoms (i.e., tearing, conjunctival and eyelid edema, foreign body sensation)
3	Proptosis (rop mm)
4	Extraocular motility restriction
5	Corneal involvement
6	Sight loss (optic nerve involvement)

fundus examination were done to evaluate optic nerve involvement. We grouped the patients according to their NOSPECS classification as mild (Grades 1–3) or severe (Grades 4–6) disease.

All the statistical analyses were performed using the software, SPSS version 26.0 (SPSS Inc., Chicago, USA). The parameters used in the study were expressed as means ± standard deviation and median (interquartile range [IQR]). The analysis was conducted with the normality test for continuous variables and the non-parametric test for the data that cannot meet normality criteria. Demographic features of the TED group and control were analyzed using a Student's t-test for age and Yates' continuity correction Chi-square test for sex. The Student's t-test was used to determine the significance of the difference between the TED and control groups. P<0.05 was considered statistically significant with a 95% confidence interval (CI). Mann–Whitney U non-parametric test is applied to both the diseased and healthy control groups individually with gender grouping variables. The same test was used to identify statistical significance between mild and severe NOSPECS groups. Spearman correlation analysis was used by assuming NOSPECS as a continuous variable to evaluate NOSPECS relation with ORA parameters. Same method was used to run correlation analysis between IOP_{cc}, IOP_g, CH, and CRF values in both the TED and healthy control groups. A post hoc power analysis is conducted for TED gender groups with the program G*Power.

Results

The mean age was 38.8±11.6 years for the TED patients and 42.9±15.58 years for the control group (p=0.095). There was no significant difference in sex and age between groups. The mean values of CRF, CH, CCT, IOP_{cc}, and IOP_g were measured for the TED patients and control group as follows: 10.43±2.04 versus 10.28±1.91 mmHg, p=0.67; 10.18±1.81 versus 10.21±1.68 mmHg, p=0.90; 550.31±35.73 versus 545.23±37.91 μm, p=0.47; 16.81±3.41 versus 16.26±3.16 mmHg, p=0.36; and 16.20±3.66 versus 15.59±3.42 mmHg, p=0.35, respectively. These values were not statistically different between groups (Table 2). However, when we compared female and male TED subjects, the median values of parameters were, respectively: CRF (10.68 [IQR: 9.49–12.14] vs. 8.96 [IQR: 8.04–9.92] mmHg, p=0.002), CH (10.43 [IQR: 9.48–11.25] vs. 8.58 [IQR: 7.90–9.95] mmHg, p=0.003), and CCT [554.25 [IQR: 536.05–579.52] vs. 527.40 [IQR: 492.25–545.90] μm, p=0.014) (Table 3). Males showed significantly lower values in biomechanical parameters compared to females in the TED group. In the healthy control group, no such difference was seen: CRF (9.70 [IQR: 8.30–11.170] versus 10.50 [IQR: 9.38–11.68] mmHg, p=0.653), CH (9.93 [IQR: 9.03–11.63] vs. 10.00 [IQR: 9.03–11.18] mmHg, p=0.822), and CCT (530.80 [IQR: 513.35–554.15] vs. 550.40 [IQR: 519.30-585.40] μm, p=0.087). IOP_{cc} and IOP_g values did not show any significant difference between males and females, respectively, in both the TED (IOP_{cc} (15.73 [IQR: 14.40–20.07] vs. 17.23 [IQR: 15.07–19.02] mmHg, p=0.685), IOP_g (15.44 [IQR: 13.81–19.84] vs. 15.13 [IQR: 13.54–16.23] mmHg, p=0.118)) and healthy groups (IOP_{cc} (16.06 [IQR: 14.36–17.90] vs. 16.10 [IQR: 14.76–19.08] mmHg, p=0.447), IOP_g (14.80 [IQR: 12.13–17.95] vs. 15.76 [IQR: 14.10–17.90] mmHg, p=0.207)). IOP_g values of both the TED and healthy groups showed statistically significant positive correlation with CRF values (r=0.636, p<0.001 and r=0.667, p<0.001). In addition, IOP_{cc} values of both the TED and healthy groups showed statistically significant negative correlation with CH values (r=−0.365, p=0.015 and r=−0.414, p=0.005). CRF values of patients were negatively correlated with NOSPECS score (r=−0.317, p=0.036), which means that CRF value de-

Table 2. Demographic features and corneal parameters of participants

	TED patients	Healthy controls	p
n	22	43	
Female/male (n)	17/5	26/17	0.085
Mean age±SD (year)	38.8±11.6	42.9±15.58	0.095
Corneal resistance factor (CRF) (mmHg) (mean±SD)	10.43±2.04	10.28±1.91	0.672
Corneal hysteresis (CH) (mmHg) (mean±SD)	10.18±1.81	10.21±1.68	0.908
Central corneal thickness (CCT) (μm) (mean±SD)	550.31±35.73	545.23±37.91	0.472
Goldmann-correlated intraocular pressure (IOP_g) (mmHg) (mean±SD)	16.20±3.66	15.59±3.42	0.354
Corneal compensated intraocular pressure (IOP_{cc}) (mmHg) (mean±SD)	16.81±3.41	16.26±3.16	0.362

Demographic features of the TED group and control were analyzed using a Student's t-test for age and Yates continuity correction Chi-square test for sex. The Student's t-test was used to determine the difference of corneal parameters between groups. Data expressed as means ± standard deviation (SD) and p<0.05 considered statistically significant.

Table 3. Comparison of corneal parameters between female and male TED patients

	Female patients	Male patients	P
Corneal resistance factor (CRF) (mmHg) (median (IQR))	10.68 (IQR: 9.49–12.14)	8.96 (IQR: 8.04–9.92)	0.002
Corneal hysteresis (CH) (mmHg) (mean±SD)	10.43 (IQR: 9.48–11.25) versus	8.58 (IQR: 7.90–9.95)	0.003
Central corneal thickness (CCT) (μm) (median (IQR))	554.25 (IQR: 536.05–579.52)	527.40 (IQR: 492.25–545.90)	0.014
Goldmann–correlated intraocular pressure (IOPg) (mmHg) (median (IQR))	15.44 (IQR: 13.81–19.84)	15.13 (IQR: 13.54–16.23)	0.118
Corneal compensated intraocular pressure (IOP_{cc}) (mmHg) (median (IQR))	15.73 (IQR: 14.40–20.07)	17.23 (IQR: 15.07–19.02)	0.685

Difference in corneal parameters between genders was analyzed by Mann–Whitney U (MWU). Data expressed in median (IQR) and P<0.05 considered statistically significant.

creased with the increased severity of disease, whereas CH, CCT, IOP_{cc}, and IOP_g did not. The correlation analysis of CH, CCT, IOP_{cc}, and IOP_g with NOSPECS score resulted as follows: CH (r=−0.202, p=0.190), CCT (r=−0.096, p=0.545), IOP_{cc} (r=−0.177, p=0.249), and IOP_g (r=−0.279, p=0.067). A significantly higher CRF was calculated in mild compared to severe disease: 11.43 (IQR: 10.14–12.87) versus 9.46 (IQR: 8.75–10.28) mmHg, p=0.008. A post hoc power analysis showed for female and male TED patients, based on means, the effect size (d) of CRF as 1.086 with a power (1-β err prob) of 0.83 and the effect size (d) of CH as 1.0 with a power (1-β err prob) of 0.77 using G*Power software.

Discussion

In our study, we found a relationship between CRF values of biomechanical corneal parameters and the clinical severity of TED. Despite the fact that no significant differences in any of the biomechanical measures existed between the TED and control groups, CRF values declined as disease severity increased, according to the NOSPECS classification.

Corneal alterations are one of the most critical, but poorly understood, symptoms of TED. ORA, an in vivo system that uses standard air-puff tonometry to induce stress on the cornea and records the level of corneal deformation to evaluate ocular biomechanics, can be used to measure changes in biomechanical corneal properties in these individuals (5,14).

Despite our findings that ORA measurements were not statistically different between the TED and healthy groups, such significance in terms of CH was identified by Karabulut et al., Moghimi et al., and Kuebler et al. for Graves' disease, and by Kırgız et al. for Hashimoto's thyroiditis (15-18). Kuebler et al. also discovered that CRF differed significantly between the TED and healthy groups (18). In comparison to our analysis, these studies feature an older patient population and a lower female-to-male ratio in the control group. We can explain why our results differ from those of earlier studies when it relates to demographic diversity. Two of those studies included Hashimoto's thyroiditis patients in their patient groups, which could indicate differences in pathophysiological pathways, leading to different outcomes than our study. These earlier research, on the other hand, did not link ORA findings to NOSPECS clinical severity grading. In that aspect, there is a need to investigate the relation between ORA measurements and this clinical severity.

In comparison to the control group, we found that IOP_{cc} and IOP_g in Graves' patients are not substantially different. Some studies have found that people with Graves' disease have higher IOP values than the general population, implying that higher IOP values are more common among Graves' patients (19-21). Although there was no statistical difference in mean or median values between the sick and healthy groups, there was statistically significant gender influence in some biomechanical measures of the TED group.

In further analysis, we found that CRF, CH, and CCT values were significantly higher (p<0.015) in females compared to males in the TED group, while there is no gender difference within the control group. The studies of Ortiz et al. and Shah et al. were consistent with our control group findings, showing no difference in biomechanical properties observed between men and women in the healthy group, however, gender role on corneal biomechanics in TED has not been fully identified in the literature (22,23). In our study, female-to-male ratio of TED calculated 3.4:1 while in previous incidence studies, female-to-male ratio was around 6.14:1 (24). The demographics of our TED patients are distributed in favor of female gender compared to male as given above. Since the natural demographics of the disease also show female dominance, we did not consider this disparity as a limitation, but our biggest limitation is its low sample size. Through Cohen's G*Power analysis system, we justified that our sample size is enough to meet widely accepted power (1-β err prob) of 0.80 (25). Thyroid orbitopathy is more prevalent among females whereas it is known to have a worse disease course among males (2,26). In our study, in Graves' patient group, significantly lower CRF and CH values were found in

the male population compared to females. Those parameters can be a predictive parameter for bad prognostic expectations in the male patient population. However, preclinical data from Schlüter et al. revealed in the mouse model that gender is not solely a predisposing factor for the development or progression of TED (27). Altogether, the TED is affected not only by gender but sex-related factors as an explanation for significant severity in men.

The ORA measures CH parameter accurately which represents cornea's ability to take in and free energy comes from the ejected high-speed airflow (5). The previous studies showed significantly lower CH values in patients diagnosed with glaucoma compared to control and describe it as predict glaucoma progression risk (28,29). In our study, the TED group showed mean IOP in normal range, which might be an explanation for our conclusion of insignificant CH values between the diseased population compared to the control group. Pniakowska et al. revealed decreasing CH and increasing IOP_{cc} of Graves' patients and explicated IOP_{cc} as a marker of the early subclinical stages of glaucoma in patients with TED (30). Similarly, we observed a significant negative correlation between CH and IOP_{cc} of patients which supports this hypothesis. In addition, it is suggested that corneal biomechanical properties appear to be compromised with varying degrees of myopia and axial length (AL). AL is an important indicator of the development of myopia and a major factor, leading to visual impairment. In literature not only increasing level of myopia (31-33) but also AL (34,35) is associated with lower CH. It is known that that AL is the largest determinant of myopia and a great number of reports have shown a negative relationship between AL and myopia (36,37). In our study, only emmetropic or mild myopic patients and controls were selected but AL of eyes was not measured. Due to its strong correlation with refractive error, not measuring AL was not considered as a limitation in our study.

In our study, we found a significant association between CRF value and clinical severity, when we grouped patients as mild (Classes 1–3) and severe (Classes 4–6) disease based on their NOSPECS score. CRF was calculated significantly higher in patients with moderate disease than in patients with severe disease, and CRF value decreased with increasing TED disease severity score in correlation analysis. This considerable difference could indicate that as the disease advances, the cornea's viscoelastic response declines. This finding may be used in the clinical practice as a follow-up parameter of TED patients. There was not any previous study that investigated the association between corneal biomechanical properties and NOSPECS classification in TED patients. However, Karabulut et al. used another grading system called VISA to classify TED patients based on VISA/exposure (15). Karabulut et al. showed no significant difference between CRF value and VISA, but they showed a negative correlation ($P = 0.007$) between CH value and VISA of TED patients (15). On the other hand, we showed a negative correlation between CRF value and NOSPECS classification. This discrepancy may be caused because of different TED severity classification rather than NOSPECS used in Karabulut's study.

We acknowledge that there are some limitations in this study. More subjects would only improve the significance. Adding another classification system would have allowed for a great comparison and remove the objectivity of using only one classification system. Further studies may be needed to support our findings to prove it as a reliable parameter in the follow-up of TED patients.

Conclusion

We showed that TED progression affects the biomechanical properties of the cornea by decreasing CRF. This parameter indicates that the viscoelastic response of the cornea decreases while disease progresses. Based on our findings, CRF might be a useful parameter in the follow-up of TED patients in clinical practice.

Disclosures

Ethics Committee Approval: Koç University Committee on Human Research (2021.246.IRB1.079 - May 2021).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – A.S.; Design – M.C.C., S.Y., A.Y.T.; Supervision – A.S.; Resource – A.S.; Materials – A.S.; Data collection and/or processing – M.C.C., S.Y., A.Y.T.; Analysis and/or interpretation – M.C.C., S.Y., A.Y.T.; Literature search – M.C.C., S.Y.; Writing – M.C.C., S.Y.; Critical review – A.S., M.C.C., S.Y., A.Y.T.

References

1. Lazarus JH. Epidemiology of Graves orbitopathy (GO) and relationship with thyroid disease. Best Pract Res Clin Endocrinol Metab 2012;26:273–9. [CrossRef]
2. Perros P, Crombie AL, Matthews JN, Kendall-Taylor P. Age and gender influence the severity of thyroid-associated ophthalmopathy: A study of 101 patients attending a combined thyroid-eye clinic. Clin Endocrinol (Oxf) 1993;38:367–72. [CrossRef]
3. Bahn RS, Heufelder AE. Pathogenesis of Graves ophthalmopathy. N Engl J Med 1993;329:1468–75. [CrossRef]
4. Dolman PJ. Evaluating Graves orbitopathy. Best Pract Res Clin Endocrinol Metab 2012;26:229–48. [CrossRef]
5. Luce DA. Determining in vivo biomechanical properties of the cornea with an ocular response analyzer. J Cataract Refract Surg 2005;31:156–62. [CrossRef]
6. Tanda ML, Piantanida E, Liparulo L, Veronesi G, Lai A, Sassi L, et al. Prevalence and natural history of Graves orbitopathy

in a large series of patients with newly diagnosed Graves hyperthyroidism seen at a single center. J Clin Endocrinol Metab 2013;98:1443–9. [CrossRef]
7. Khalil HA, Van Best JA, De Keizer RJ. The permeability of the corneal epithelium of Graves ophthalmopathy as determined by fluorophotometry. Doc Ophthalmol 1989;73:249–54. [CrossRef]
8. Villani E, Viola F, Sala R, Salvi M, Mapelli C, Curro N, et al. Corneal involvement in Graves orbitopathy: An in vivo confocal study. Invest Ophthalmol Vis Sci 2010;51:4574–8. [CrossRef]
9. Unal M, Onol M, Konuk O, Aktas Z, Aksoy S. Hyperthyroidism and severity of orbital disease do not change the central corneal thickness in Graves ophthalmopathy. Eur J Ophthalmol 2008;18:125–7. [CrossRef]
10. Bartalena L, Baldeschi L, Boboridis K, Eckstein A, Kahaly GJ, Marcocci C, et al. The 2016 European thyroid association/european group on Graves orbitopathy guidelines for the management of Graves orbitopathy. Eur Thyroid J 2016;5:9–26. [CrossRef]
11. Barrio-Barrio J, Sabater AL, Bonet-Farriol E, Velazquez-Villoria A, Galofre JC. Graves ophthalmopathy: VISA versus EUGOGO classification, assessment, and management. J Ophthalmol 2015;2015:249125. [CrossRef]
12. Werner SC. Modification of the classification of the eye changes of Graves disease. Am J Ophthalmol 1977;83:725–7. [CrossRef]
13. Nardi M, Bartolomei MP, Romani A, Barca L. Intraocular pressure changes in secondary positions of gaze in normal subjects and in restrictive ocular motility disorders. Graefes Arch Clin Exp Ophthalmol 1988;226:8–10. [CrossRef]
14. Hodgson NM, Rajaii F. Current understanding of the progression and management of thyroid associated orbitopathy: A systematic review. Ophthalmol Ther 2020;9:21–33. [CrossRef]
15. Karabulut GO, Kaynak P, Altan C, Ozturker C, Aksoy EF, Demirok A, et al. Corneal biomechanical properties in thyroid eye disease. Kaohsiung J Med Sci 2014;30:299–304. [CrossRef]
16. Kirgiz A, Cabuk KS, Yetmis M, Atalay K. Corneal biomechanical properties in patients with Hashimoto's thyroiditis. Adv Clin Exp Med 2019;28:109–12. [CrossRef]
17. Moghimi S, Safizadeh M, Mazloumi M, Hosseini H, Vahedian Z, Rajabi MT. Evaluation of corneal biomechanical properties in patients with thyroid eye disease using ocular response analyzer. J Glaucoma 2016;25:269–73. [CrossRef]
18. Kuebler AG, Wiecha C, Reznicek L, Klingenstein A, Halfter K, Priglinger S, et al. Comparison of different devices to measure the intraocular pressure in thyroid-associated orbitopathy. Graefes Arch Clin Exp Ophthalmol 2019;257:2025–32. [CrossRef]
19. Cockerham KP, Pal C, Jani B, Wolter A, Kennerdell JS. The prevalence and implications of ocular hypertension and glaucoma in thyroid-associated orbitopathy. Ophthalmology 1997;104:914–7.
20. Ohtsuka K, Nakamura Y. Open-angle glaucoma associated with Graves disease. Am J Ophthalmol 2000;129:613–7. [CrossRef]
21. Behrouzi Z, Rabei HM, Azizi F, Daftarian N, Mehrabi Y, Ardeshiri M, et al. Prevalence of open-angle glaucoma, glaucoma suspect, and ocular hypertension in thyroid-related immune orbitopathy. J Glaucoma 2007;16:358–62. [CrossRef]
22. Ortiz D, Pinero D, Shabayek MH, Arnalich-Montiel F, Alio JL. Corneal biomechanical properties in normal, post-laser in situ keratomileusis, and keratoconic eyes. J Cataract Refract Surg 2007;33:1371–5. [CrossRef]
23. Shah S, Laiquzzaman M, Bhojwani R, Mantry S, Cunliffe I. Assessment of the biomechanical properties of the cornea with the ocular response analyzer in normal and keratoconic eyes. Invest Ophthalmol Vis Sci 2007;48:3026–31. [CrossRef]
24. Bartley GB, Fatourechi V, Kadrmas EF, Jacobsen SJ, Ilstrup DM, Garrity JA, et al. The incidence of Graves ophthalmopathy in Olmsted County, Minnesota. Am J Ophthalmol 1995;120:511–7.
25. Faul F, Erdfelder E, Lang AG, Buchner A. G* Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 2007;39:175–91.
26. Lin MC, Hsu FM, Bee YS, Ger LP. Age influences the severity of Graves ophthalmopathy. Kaohsiung J Med Sci 2008;24:283–8.
27. Schluter A, Flogel U, Diaz-Cano S, Gortz GE, Stahr K, Oeverhaus M, et al. Graves orbitopathy occurs sex-independently in an autoimmune hyperthyroid mouse model. Sci Rep 2018;8:13096. [CrossRef]
28. Sullivan-Mee M, Billingsley SC, Patel AD, Halverson KD, Alldredge BR, Qualls C. Ocular response analyzer in subjects with and without glaucoma. Optom Vis Sci 2008;85:463–70. [CrossRef]
29. Congdon NG, Broman AT, Bandeen-Roche K, Grover D, Quigley HA. Central corneal thickness and corneal hysteresis associated with glaucoma damage. Am J Ophthalmol 2006;141:868–75.
30. Pniakowska Z, Klysik A, Gos R, Jurowski P. Corneal biomechanical changes and intraocular pressure in patients with thyroid orbitopathy. Int J Ophthalmol 2016;9:439–43.
31. Shen M, Fan F, Xue A, Wang J, Zhou X, Lu F. Biomechanical properties of the cornea in high myopia. Vision Res 2008;48:2167–71.
32. Qiu K, Lu X, Zhang R, Wang G, Zhang M. Corneal biomechanics determination in healthy myopic subjects. J Ophthalmol 2016;2016:2793516. [CrossRef]
33. Inceoglu N, Emre S, Ulusoy MO. Investigation of corneal biomechanics at moderate to high refractive errors. Int Ophthalmol 2018;38:1061–7. [CrossRef]
34. Wong YZ, Lam AK. The roles of cornea and axial length in corneal hysteresis among emmetropes and high myopes: A pilot study. Curr Eye Res 2015;40:282–9. [CrossRef]
35. Bueno-Gimeno I, Espana-Gregori E, Gene-Sampedro A, Lanzagorta-Aresti A, Pinero-Llorens DP. Relationship among corneal biomechanics, refractive error, and axial length. Optom Vis Sci 2014;91:507–13. [CrossRef]
36. Young TL, Metlapally R, Shay AE. Complex trait genetics of refractive error. Arch Ophthalmol 2007;125:38–48. [CrossRef]
37. Mallen EA, Gammoh Y, Al-Bdour M, Sayegh FN. Refractive error and ocular biometry in Jordanian adults. Ophthalmic Physiol Opt 2005;25:302–9. [CrossRef]