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Biomechanical changes of the cornea after orbital decompression in thyroid-associated orbitopathy measured by corvis ST

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This study aims to investigate the changes in ocular biomechanical factors in patients with inactive thyroid eye disease (TED) who undergo orbital decompression surgery. This observational prospective study include 46 eyes of 31 patients with inactive TED undergoing orbital decompression at a tertiary university hospital from October 2021 to September 2023. All participants underwent a full ophthalmic examination, and a biomechanical examination was performed using corvis ST at baseline, 1 month, and 3 months postoperatively. The study participants had a mean age of 45 ± 11.6 years, and 58.1% of them were female. The second applanation time (A2T) increased from baseline to postoperative month 1 and continued to increase to postoperative month 3 ($P < 0.001$). The first applanation velocity (A1V), highest concavity (HC) peak distance, and pachymetry parameters also increased from postoperative month 1 to postoperative month 3 ($P = 0.035$, $P = 0.005$, and $P = 0.031$, respectively). The HC time increased from baseline to postoperative month 3 ($P = 0.027$). Other changes were statistically insignificant. The P-values were adjusted according to biomechanically corrected intraocular pressure (bIOP). Baseline Hertel significantly influenced A2 time ($P < 0.001$). Our findings suggest that ocular biomechanical parameters may change following decompression surgery in patients with inactive TED. Specifically, an increase in A2T, A1V, and HC peak distance suggests a decrease in corneal stiffness, although the increased HC time contradicts this. It is recommended to postpone keratorefractive or intraocular lens implantation surgeries until corneal biomechanics stabilize after decompression surgery for optimal results.

Keywords Thyroid eye disease, Corneal biomechanical properties, Orbital decompression, Corvis ST

Thyroid eye disease (TED) is an autoimmune disease caused by the activation of orbital fibroblasts against thyroid receptors, which is triggered by autoantibodies. It is characterized by inflammation and enlargement of the extraocular muscles, fatty and connective tissue volume, which leads to orbital and periorbital congestion and tissue remodeling[1–4]. TED affects 2.9 to 16 per 100,000 worldwide and is more prevalent in women[5]. In most cases, the disease begins with an acute inflammatory or active phase, which typically lasts on average 6–24 months, although this period may vary significantly. TED can cause vision-threatening complications such as dysthyroid optic neuropathy (DON) and exposure keratopathy[6]. Active phase of the disease can be managed with steroid or targeted biologic therapies. Once the disease is thought to be relatively inactive and stable, surgical correction such as orbital decompression for proptosis and related complications can be considered[7]. The severity of TED is determined based on the degree of diplopia, proptosis, eyelid retraction and soft tissue changes, and their impact on the patient's quality of life, which is graded as mild, moderate to severe, or sight threatening[1].

Biomechanical properties are defined as the reaction of the biomechanical tissue to the applied force. Evaluating the corneal biomechanical response to an air puff applied to the cornea was first performed by Luce using ocular response analyzer (ORA, Reichert Ophthalmic Instruments, Depew, NY)[8,9]. The ORA was used to evaluate patients with TED and demonstrated that the ocular biomechanical properties often change in these patients[10–13].

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In the active phase of TED, inflammatory cytokines stimulate keratocytes, increase production of matrix metalloproteinases, and subsequent corneal stromal destruction, which may result in lower corneal hysteresis (CH) and corneal resistance factor (CRF)[14–18]. Also, deposition of glycosaminoglycans, fat hypertrophy, congestion, edema, and fibrosis cause alterations in orbital and periorbital tissue and possible rise in intraocular pressure (IOP)[19]. This tissue remodeling can result in decreased orbital compliance and ocular biomechanical attributes[20–22]. These changes can introduce bias in IOP measurement, particularly in patients with TED, who are at a higher risk of developing glaucoma[12,23,24]. Although the biomechanical changes in active TED in comparison to normal adults is well established, few studies have addressed its reversibility with medical or surgical treatments[25,26].

The corvis ST, developed by Oculus Optikgeräte Wetzlar in Germany, was first introduced at the AAO 2010 meeting as a novel non-contact tonometer (NCT) system. It is a dynamic Scheimpflug analyzer system that visualizes the response of the cornea to a concentric air puff and captures 140 images over a 32 ms duration. This allows for the calculation of a variety of corneal response parameters[27]. Novel parameters, such as whole eye movement (WEM), which accounts for periocular soft tissue compliance, and biomechanically corrected intraocular pressure (bIOP), which is least affected by ocular parameters, provide valuable insight into ocular biomechanics[28,29]. This prospective study aimed to evaluate alterations in ocular biomechanical parameters with Corvis ST in patients with quiescent TED who received orbital decompression surgery.

Methods

Study design and patient selection

This prospective observational study performed at a tertiary university hospital (Farabi eye hospital) from October 2021 to September 2023. The review board and Ethics Committee of our institute approved the study (IR.TUMS.FARABIH.REC.1400.087) and the investigation adhered to the ethical principles of the Declaration of Helsinki as amended in 2013. All participants gave their written informed consent prior to enrolment.

Patients with a diagnosis of inactive TED according to the EUGOGO consensus[30] and proptosis, who were candidates for surgical orbital decompression included. Surgery performed once the thyroid function and exophthalmometry was stable for at least 6 months[31]. All patients included were operated on by a single oculoplastic surgeon (S.M.R.) in our center. Performing medial only or both medial and inferior wall decompression with or without fat excision was selected based on the degree of proptosis. Exclusion criteria included: missing both follow-up visits, systemic diseases such as chronic kidney disease, pterygium, myopia < -5.00, hyperopia $> +3.00$, CAS (Clinical Activity Score) > 2, corneal erosion ($\geq$ grade 2 Oxford scheme)[32], dysthyroid optic neuropathy, previous refractive or intraocular surgery, and any corneal disease that could alter the biomechanical parameters.

Examinations and follow-up

All participants underwent a comprehensive history-taking and standard ophthalmic examination prior to surgery, which included autorefraction (KR-8800, Topcon, Tokyo, Japan), checking for corrected distance visual acuity (CDVA), margin to reflex distance 1 and 2 measurement (MRD1 and MRD2), Hertel exophthalmometry, slit-lamp biomicroscopy, and Corvis ST examination.

The Corvis ST parameters included A1 time (time of the first applanation), A2 time (time from start to the second applanation), highest concavity (HC) time (time of the highest displacement of the corneal apex), highest concavity deformation and deflection amplitude (HCDA: magnitude of the highest displacement of the corneal apex), A1 length (A1L: the length of the flattened segment in the first applanation), A2 length (A2L: the length of the flattened segment in the second applanation), A1 and A2 velocity (A1V and A2V: corneal velocity of movement during two applanations), HC peak distance (distance between bending points of the cornea at the highest concavity), HC radius (HCR, central concave curvature at the highest concavity), central corneal thickness (CCT) or pachymetry, and deformation amplitude (DA) ratio at 2 mm, integrated inverse radius, stiffness parameter A1 (SP-A1), Corvis biomechanical index (CBI), Ambrosio's relational thickness (ARTh), maximum whole eye movement (WEM), and biomechanically corrected IOP (bIOP)[33].

Preoperative examinations were performed within 2 weeks prior to surgery, and the patients were scheduled for two follow-up visits, the first at 1 month and the second at least 3 months after surgery, at which all examination were repeated. Patients who missed one of the follow-up visits were not excluded from the analysis.

Surgical intervention

After general anesthesia, to decompress the medial orbital wall, a medial transcaruncular orbitotomy was first performed. A conjunctival incision was made in the medial part and the tissue under the caruncle was dissected to the level of the periorbita. The exposed periorbita was then incised and the medial orbital wall was exposed with a periosteal elevator. Bone was then removed posterior to the posterior lacrimal crest and inferior to the ethmoidal arteries. As indicated in patients with severe proptosis requiring double wall decompression, an inferior transconjunctival orbitotomy was also performed in the same session. After exposing the inferior orbital rim, the periosteum was incised along the orbital rim. The periosteum was then lifted from the bone using a periosteal dissector. After accessing the orbital floor bone, the medial portion of the orbital floor was removed medial to the infraorbital nerve canal, which extended posteriorly to the posterior wall of the maxillary sinus. Bone was preserved 1 cm posterior to the inferior orbital rim and at the junction of the inferior and medial walls of the orbit. After sufficient bone was removed and bleeding was controlled, the conjunctiva was repaired with 8-0 Vicryl suture. Finally, the eye was bandaged with erythromycin ointment. The dressing was removed the day after surgery and the patient was discharged with chloramphenicol eye drops, betamethasone eye drops, artificial tear gel, and cephalexin capsules.

Statistical analysis

To present data we used mean, standard deviation, median and range, as well as percentile and percentage. We used generalized estimating equations (GEE), univariate and multivariable model analysis to compare the parameters and investigate the possible influential factors. To consider Type I error inflation based on multiple comparisons, we used the Sidak method. To investigate the effect of a factor on the alterations of the biomechanical parameters, we used its interaction with time within another GEE model. All statistical analysis performed by SPSS (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp). A P-value less than 0.05 was considered statistically significant.

Ethical approval

This research was approved by the ethics committee of Tehran University of Medical Sciences and adhered to the ethical principles of the Declaration of Helsinki, as amended in 2013.

Consent to participate

Written informed consent was obtained from all study participants.

Results

Forty-six eyes of 31 patients with inactive TED who were candidates for orbital decompression from October 2021 to September 2023, met the criteria to be included in this study. There were 18 females (58.1%) and 13 males (41.9%). Mean age was 45 ± 11.6 years (interquartile range 37–55 years). The right eye was operated in 52.2% of the cases. Mean disease duration was 4.4 years (interquartile range 1.5–3 years). Three eyes missed the first follow-up visit but completed the next session, and eight eyes missed only the second follow-up visit. The second follow-up ranged from 3 to 8 months (mean: 4.1 ± 1.7 months). Medial wall decompression alone was performed in 31 eyes (67.4%) and in the remaining 15 eyes (32.6%) both medial and inferior walls were decompressed. In addition, fat decompression was performed in 37 eyes (80.4%).

The MRD1, MRD2, and Hertel exophthalmometry measurements for all three visits are presented in Table 1. As expected, post-operative Hertel exophthalmometry and MRD2 are significantly decreased at 1 and 3 months, indicating the surgery's effectiveness in correcting proptosis (P < 0.001).

Some of the corneal biomechanical parameters measured by Corvis ST (CST) in the patients undergoing orbital decompression are presented in Tables 2 and 3. Pairwise comparisons between three measurements and the P-values with and without adjustment for bIOP are presented in these tables. According to Table 2, mean HC time increased from pre-op status to PO 1m and from there to PO 3m, but only the difference between pre-op and PO 3m was statistically significant (P = 0.027). The mean A1 time and A2 time parameters also increased in a stepwise fashion over the follow-up visits, which is consistent with the HC time parameter. However, only the A2 time parameter showed a significant increase from pre-op to PO 1m and PO 3m, and from PO 1m to PO 3m (P < 0.001).

Regarding the CST-derived parameters (Table 2), A1, HC and A2 deflection length increased from pre-op to PO 3m, but the changes were not significant. On the other hand, A1 velocity showed a significant increase from PO 1m to PO 3m (P = 0.035). Changes in the other parameters shown in Table 2 were not significant.

As shown in Table 3, changes in IOP or bIOP were not significant. Peak distance parameter despite a non-significant decrease from pre-op to PO 1m, showed a significant increase from PO 1m to PO 3m (P = 0.005). Pachymetry also showed a significant increase from PO 1m to PO 3m (P = 0.031). Whole eye movement length (WEM) has increased from pre-op to PO 1m and then decreased from PO 1m to PO 3m, but the difference was not significant. Changes in other parameters such as DA ratio 2mm, ARTh, SP-A1, and CBI were not significant.

Figure 1 displays box plots of biomechanical parameters that exhibited a significant difference. In the GEE model analysis, adjusted for all the bIOP, baseline Hertel, MRD1, MRD2, bone decompression site, and fat decompression simultaneously, the significant differences persisted. Changes in exophthalmos from baseline

Variable	Session	Mean ± SD	Median (range)	Pairwise comparison (A vs. B)	Mean diff (B-A)	95% CI		P-value
						Lower	Upper	
MRD1	Pre	6.1 ± 2.4	6.3 (1 to 11)	Pre vs. PO1	− 0.20	− 0.40	0.01	0.068
	PO1	5.9 ± 2.3	6 (1 to 10)	Pre vs. PO3	− 0.13	− 0.35	0.10	0.434
	PO3	5.9 ± 2.4	6 (1 to 11)	PO1 vs. PO3	0.07	− 0.09	0.22	0.656
MRD2	Pre	6.9 ± 1.3	7 (5 to 10)	Pre vs. PO1	− 0.93	− 1.14	− 0.73	**< 0.001***
	PO1	6 ± 1.3	6 (4 to 9)	Pre vs. PO3	− 0.99	− 1.20	− 0.78	**< 0.001***
	PO3	5.9 ± 1.2	6 (4 to 9)	PO1 vs. PO3	− 0.06	− 0.23	0.12	0.832
Hertel	Pre	24.2 ± 2.2	24.5 (20 to 29)	Pre vs. PO1	− 2.08	− 2.48	− 1.67	**< 0.001***
	PO1	22.2 ± 2.1	22 (18 to 28)	Pre vs. PO3	− 2.59	− 3.04	− 2.15	**< 0.001***
	PO3	21.5 ± 2.1	21.5 (18 to 25)	PO1 vs. PO3	− 0.52	− 0.82	− 0.22	**< 0.001***

Table 1. Clinical characteristics of the patients with TED receiving orbital decompression and the change after surgery. *MRD* margin to reflex distance, *Pre* pre operation, *PO1* 1 month post operation, *PO3* 3 months post operation, *SD* standard deviation, *CI* confidence interval. The comparison is based on GEE analysis. P-value less than 0.05 is considered significant, which is bold type in the table.

Variable	Session	Mean ± SD	Pairwise comparison (A vs. B)	Mean diff (B-A)	95% CI Lower	95% CI Upper	P-value	Adjusted P-value
A1 time [ms]	Pre	7.99 ± 0.79	Pre vs. PO1	0.003	−0.028	0.035	0.946	0.993
	PO1	8.06 ± 0.84	Pre vs. PO3	0.030	−0.009	0.069	0.801	0.193
	PO3	8.04 ± 0.82	PO1 vs. PO3	0.033	−0.001	0.066	0.964	0.055
HC time [ms]	Pre	16.32 ± 0.37	Pre vs. PO1	0.112	−0.077	0.301	0.315	0.403
	PO1	16.44 ± 0.44	Pre vs. PO3	0.174	0.015	0.334	**0.020***	**0.027***
	PO3	16.5 ± 0.31	PO1 vs. PO3	0.063	−0.111	0.237	0.787	0.772
A2 time [ms]	Pre	20.94 ± 0.5	Pre vs. PO1	0.159	0.052	0.266	0.212	**0.001***
	PO1	21.05 ± 0.54	Pre vs. PO3	0.423	0.287	0.559	**< 0.001***	**< 0.001***
	PO3	21.34 ± 0.53	PO1 vs. PO3	0.264	0.128	0.399	**< 0.001***	**< 0.001***
A1 deflection length [mm]	Pre	2.22 ± 0.38	Pre vs. PO1	−0.069	−0.225	0.086	0.688	0.636
	PO1	2.16 ± 0.37	Pre vs. PO3	0.018	−0.106	0.142	0.942	0.980
	PO3	2.24 ± 0.23	PO1 vs. PO3	0.087	−0.039	0.214	0.299	0.266
HC deflection length [mm]	Pre	5.97 ± 0.48	Pre vs. PO1	0.056	−0.121	0.232	0.999	0.836
	PO1	6 ± 0.49	Pre vs. PO3	0.083	−0.131	0.297	0.888	0.729
	PO3	6.02 ± 0.51	PO1 vs. PO3	0.028	−0.116	0.171	0.881	0.955
A2 deflection length [mm]	Pre	2.79 ± 0.59	Pre vs. PO1	−0.060	−0.299	0.178	0.980	0.907
	PO1	2.78 ± 0.61	Pre vs. PO3	0.056	−0.231	0.343	0.897	0.954
	PO3	2.87 ± 0.7	PO1 vs. PO3	0.116	−0.152	0.383	0.666	0.658
A1 velocity [m/s]	Pre	0.109 ± 0.018	Pre vs. PO1	0.00053	−0.00688	0.00794	1.000	0.997
	PO1	0.108 ± 0.016	Pre vs. PO3	0.00738	−0.00049	0.01524	0.097	0.074
	PO3	0.116 ± 0.017	PO1 vs. PO3	0.00684	0.00035	0.01334	**0.031***	**0.035***
A2 velocity [m/s]	Pre	−0.25 ± 0.04	Pre vs. PO1	0.0027	−0.0081	0.0134	0.745	0.911
	PO1	−0.24 ± 0.05	Pre vs. PO3	0.0059	−0.0046	0.0164	0.349	0.446
	PO3	−0.24 ± 0.04	PO1 vs. PO3	0.0033	−0.0071	0.0136	0.885	0.837

Table 2. Corneal biomechanical properties of the patients with TED receiving orbital decompression and the change after surgery, part 1. *HC* highest concavity, *Pre* pre operation, *PO1* 1 month post operation, *PO3* 3 months post operation, *SD* standard deviation, *CI* confidence interval. The comparison is based on GEE analysis and adjusted P-value is based on bIOP (biomechanically corrected intraocular pressure). P-value less than 0.05 is considered significant, which is bold type in the table.

to the last visit poorly correlated with the significantly changed Corvis parameters, including HCT ($R = 0.091$, $P = 0.31$), A2T ($R = 0.046$, $P = 0.61$), A1V ($R = 0.113$, $P = 0.21$), and HC peak distance ($R = -0.091$, $P = 0.321$). To investigate the effect of factors such as the site of bone decompression, fat decompression, baseline Hertel, change in exophthalmos from baseline to the last visit, MRD1, and MRD2 on the changes in biomechanical parameters that had a significant change, we used their interaction with time within another GEE model. Baseline Hertel significantly influenced A2 time ($P < 0.001$). The site of bone decompression had a significant interaction with pachymetry ($P = 0.006$). Fat decompression had no significant effect on the parameters. Other interactions were not significant.

Discussion

TED is a complex autoimmune disorder that causes molecular changes in the corneal stroma and ocular surface, as well as gross remodeling in orbital and periorbital tissues[1]. These gross changes persist even in the inactive phase, which may alter the ocular biomechanical properties. Previous studies have focused on differences between healthy subjects and patients with active TED, demonstrating a significant decrease in orbital compliance and biomechanical parameters[20,22]. However, limited information is available regarding the reversibility of these changes after medical or surgical treatments. In a prospective study, intravenous glucocorticoid therapy was found to be associated with increased WEM in patients with active TED[25]. Therefore, this study aimed to investigate changes in ocular biomechanical parameters in patients with inactive TED who underwent orbital decompression surgery.

The Corvis ST (CST) is a non-contact tonometer that utilizes a high-speed Scheimpflug camera to accurately and consistently measure ocular biomechanical properties. Numerous studies have utilized the CST to investigate changes in ocular biomechanics in patients with glaucoma. Although there are some discrepancies, they have shown that a longer A1T and HCT, shorter A2T, smaller magnitude of A1V and A2V, and smaller deformation amplitude in open angle glaucoma (OAG) eyes indicate a "stiffer cornea"[34–37]. This means that corneas that cave more slowly (longer A1T and HCT, and lower A1V) with smaller concavity (deformation and deflection amplitude) and return faster to the primary state (shorter A2T) are stiffer[34]. A study on normal eyes found that higher intraocular pressure (IOP) was associated with a stiffer cornea, as indicated by longer A1T, shorter A2T, smaller magnitude of A1V, A2V, and deflection amplitude max[38]. Prior to treatment, Miki et al. reported that

Variable	Session	Mean ± SD	Pairwise comparison (A vs. B)	Mean diff (B-A)	95% CI		P-value	Adjusted P-value
					Lower	Upper		
IOP-nct [mmHg]	Pre	21.6 ± 5.5	Pre vs. PO1	0.33	− 1.44	2.09	0.960	NA
	PO1	22.1 ± 6.2	Pre vs. PO3	0.58	− 1.24	2.39	0.832	NA
	PO3	21.9 ± 6.2	PO1 vs. PO3	0.25	− 1.12	1.62	0.962	NA
bIOP [mmHg]	Pre	21.61 ± 4.74	Pre vs. PO1	0.315	− 1.366	1.996	0.959	NA
	PO1	22 ± 5.19	Pre vs. PO3	0.334	− 1.373	2.040	0.954	NA
	PO3	21.77 ± 5.33	PO1 vs. PO3	0.018	− 1.251	1.288	1.000	NA
Pachymetry [μm]	Pre	505.4 ± 46.7	Pre vs. PO1	− 0.29	− 6.94	6.35	0.994	0.999
	PO1	503.5 ± 49.8	Pre vs. PO3	7.10	− 0.26	14.47	0.073	0.063
	PO3	506.8 ± 48.7	PO1 vs. PO3	7.40	0.50	14.30	**0.031***	**0.031***
Peak distance [mm]	Pre	4.86 ± 0.31	Pre vs. PO1	− 0.042	− 0.105	0.020	0.453	0.283
	PO1	4.83 ± 0.35	Pre vs. PO3	0.024	− 0.046	0.095	0.999	0.798
	PO3	4.87 ± 0.4	PO1 vs. PO3	0.067	0.016	0.118	0.305	**0.005***
Whole eye movement max [mm]	Pre	0.2 ± 0.07	Pre vs. PO1	0.0211	− 0.0039	0.0460	0.349	0.126
	PO1	0.22 ± 0.06	Pre vs. PO3	0.0092	− 0.0290	0.0473	0.985	0.919
	PO3	0.21 ± 0.1	PO1 vs. PO3	− 0.0119	− 0.0457	0.0218	0.827	0.783
DA ratio max (2 mm)	Pre	3.82 ± 0.55	Pre vs. PO1	0.065	− 0.118	0.248	0.998	0.779
	PO1	3.82 ± 0.66	Pre vs. PO3	0.076	− 0.039	0.191	0.984	0.308
	PO3	3.87 ± 0.54	PO1 vs. PO3	0.011	− 0.167	0.188	1.000	0.999
ARTh	Pre	459.8 ± 143.9	Pre vs. PO1	− 0.95	− 30.55	28.65	0.999	1.000
	PO1	469.4 ± 143.2	Pre vs. PO3	22.93	− 6.17	52.03	0.085	0.169
	PO3	475.3 ± 138.9	PO1 vs. PO3	23.88	− 6.27	54.03	0.152	0.166
SP-A1	Pre	131.01 ± 18.86	Pre vs. PO1	1.60	− 4.55	7.76	0.830	0.899
	PO1	131.47 ± 20.06	Pre vs. PO3	1.97	− 3.43	7.37	0.695	0.765
	PO3	131.17 ± 21.05	PO1 vs. PO3	0.37	− 5.36	6.10	0.999	0.998
CBI	Pre	0.29 ± 0.26	Pre vs. PO1	− 0.0108	− 0.0813	0.0597	0.913	0.977
	PO1	0.3 ± 0.29	Pre vs. PO3	− 0.0698	− 0.1555	0.0158	0.117	0.147
	PO3	0.27 ± 0.29	PO1 vs. PO3	− 0.0591	− 0.1305	0.0123	0.171	0.138

Table 3. Corneal biomechanical properties of the patients with TED receiving orbital decompression and the change after surgery, part 2. *IOP-nct* non-corrected intraocular pressure, *bIOP* biomechanically corrected IOP, *HC* highest concavity, *DA Ratio* deformation amplitude ratio, *ARTh* Ambrósio's relational thickness, *SP-A1* stifness parameter A1, *CBI* Corvis biomechanical index, *Pre* pre operation, *PO1* 1 month post operation, *PO3* 3 months post operation, *SD* standard deviation, *CI* confidence interval. The comparison is based on GEE analysis and adjusted P-value is based on bIOP. P-value less than 0.05 is considered significant, which is bold type in the table.

primary open angle glaucoma (POAG) eyes had a smaller A1T and A2T, larger HC peak distance, integrated inverse radius, and deflection amplitude ratio compared to normal eyes[39]. A meta-analysis of 15 case–control studies found significant heterogeneity among them. The results suggest that high-tension glaucoma patients have a stiffer cornea, as evidenced by smaller A2T and HC deformation amplitudes, while normal tension glaucoma patients have a softer cornea, as evidenced by lower A1T and HCT and higher HC peak distance, compared to normal controls[40].

We conducted CST measurement on patients prior to surgery, as well as 1 month and 3 to 8 months after surgery. The results indicate a significant increase in A2T in all pairwise comparisons from pre-op to post-operation visits, suggesting a softer cornea and increased orbital compliance after orbital decompression. Although there was an initial non-significant decrease, HC peak distance showed a significant increase over the next few months, indicating a more flexible cornea. The A1V value also showed a significant increase from PO 1m to PO 3m, indicating softer ocular biomechanics. However, these parameters were poorly correlated with changes in exophthalmos from baseline to the final visit, suggesting that biomechanical changes do not require a concomitant decrease in exophthalmos. Interestingly, pachymetry showed a non-significant primary decrease 1 month after surgery, which has significantly increased during the PO 3m visit. This increase remained even after adjusting for bIOP. However, changes in corneal thickness 3 months after decompression compared to before surgery were insignificant. These transient changes in the first months after surgery may be due to changes in the tear film and corneal hydration. Further studies with larger numbers of cases are needed to investigate the exact cause of these changes. In a previous study, it was found that thicker pachymetry and higher IOP were associated with a higher SP-A1 parameter, indicating a stiffer cornea[41,42]. On the other hand, HCT increased from pre-op to PO 3m visit, which is inconsistent with the other changes. These findings suggest that some of the biomechanical improvements resulting from decompression may regress over time, even in inactive TED. These discrepancies persisted even after adjusting for other factors. In a study published by Hsia et al., it was found that the A2 length significantly decreased 3 to 6 months after decompression, indicating a stiffer cornea[26]. However, our results do

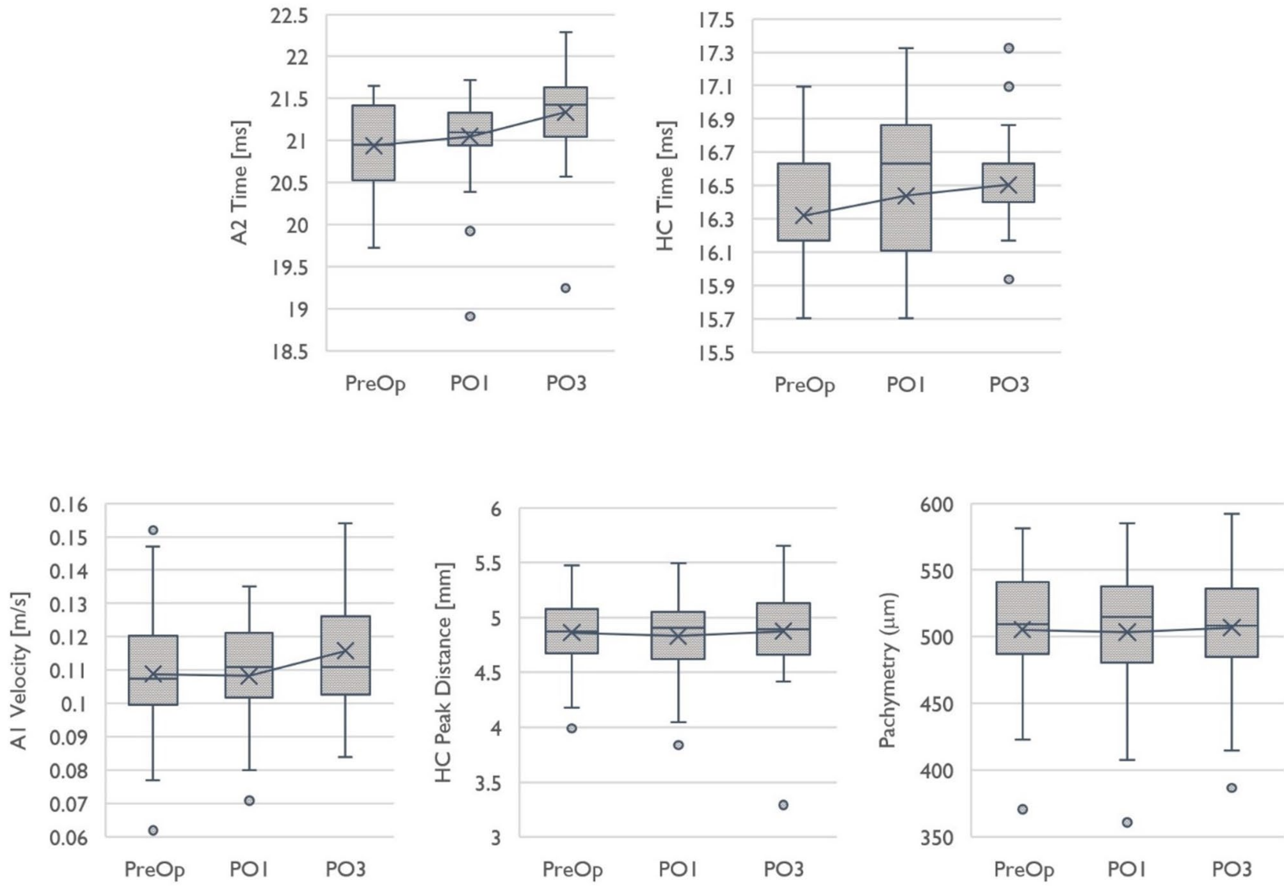

Figure 1. Preoperative, postoperative 1 m and 3 m Corvis measurements of the A2 time, HC time, A1 velocity, pachymetry, and peak distance in all eyes undergoing orbital decompression. *HC* highest concavity.

not support this finding. One possible explanation for this discrepancy could be the regression over time, which can be better monitored with multiple follow-up visits.

Previous studies have consistently reported altered corneal biomechanics in eyes with TED. These alterations are evidenced by lower corneal hysteresis and corneal resistance factor measurements using ocular response analyzer (ORA) and Corvis ST, suggesting lower damping ability when compared to normal eyes[43–45]. The cause of these changes may be related to the increased tear film osmolarity and inflammatory cytokines that are common in TED, leading to microstructural changes in the corneal epithelium and stroma, also may be related to the increased mechanical pressure in the orbital space (Supplementary Table 1).

Similar to the increase in intraocular pressure in glaucoma[34–40], an increase in orbital pressure applied externally to the globe can also affect corneal biomechanics, resulting in increased corneal stiffness and reduced mobility. However, previous studies have shown that in Graves' ophthalmopathy, the whole eye movement (WEM) is reduced compared to the normal population, indicating a decrease in mobility of the globe[44]. Performing decompression expands the orbital space and relieves pressure inside the orbit, resulting in a reduction of pressure on the globe. In confirmation of this point, one study has shown that the axial length increases after decompression surgery[45]. This reduction in pressure causes a decrease in corneal stiffness and an increase in flaccidity and mobility, which our study also confirms despite some discrepancies. For patients with thyroid ophthalmopathy who are candidates for keratorefractive surgery or intraocular lens implantation, it is advisable to consider these changes. It is recommended to delay such surgeries until the corneal biomechanics are stabilized after decompression surgery.

This study has several limitations that should be considered. It was a prospective observational study without a healthy control group, which may have introduced bias. Additionally, the sample size was restricted due to time and eligibility constraints, which may have rendered some differences statistically insignificant. Furthermore, the CST provides approximately 40 parameters, and multiple comparisons may have introduced bias. The study involved patients in an inactive phase who were eligible for surgical decompression. The inactivity of the disease by itself can alleviate the possible changes in ocular biomechanics, because previous studies have extensively addressed the biomechanical changes in active TED and their association with the inflammatory cytokines[20]. We performed CST measurements in two postoperative sessions, but the mean follow-up time at the last session was only 4.1 months, which is relatively short. Future studies should increase the duration of observation to gain a more accurate understanding of the course of these changes.

In conclusion, our findings indicate that ocular biomechanical parameters may change following decompression surgery in patients with inactive TED. Specifically, increased A2T, A1V, and HC peak distance suggest a decrease in corneal stiffness, although the increased HCT contradicts this. Pachymetry revealed a primary decrease one month after surgery, which has significantly increased over the next few months. To ensure optimal results, it is advisable to postpone keratorefractive or intraocular lens implantation surgeries until the corneal biomechanics have stabilized after decompression surgery. More research is needed to understand the exact magnitude of these subtle changes in A2T and A1V on refractive surgery outcomes. Ideally, studies would compare corneal biomechanics in TED patients who underwent decompression surgery with those who didn't, focusing on postoperative refractive surgery outcomes. In addition, further studies with longer follow-up are required to more clearly demonstrate the differences and provide a better understanding of ocular biomechanics in TED.

Data availability

The data set generated during this study is available upon reasonable request by contacting the corresponding author.

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Author contributions

Study design and material preparation were performed by Seyed Mohsen Rafizadeh and Mohammad Taher Rajabi. Data analysis was performed by Mahdi Soleymanzadeh. Seyed Mohsen Rafizadeh, Mohammadreza Nazari, Amir Reza Mafi, and Ghazal Ghouchani collected the data for this paper. The first draft of the manuscript was written by Mahdi Soleymanzadeh, and all authors commented on earlier versions of the manuscript. All authors read and approved the final version of the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

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