Original Article

Corneal Epithelial Thickness in Normal Corneas with Low and High Toricity

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Abstract

Purpose: To compare the corneal epithelial thickness along the flat and steep meridians of corneas with low and high toricity.

Methods: This was a prospective observational comparative study on healthy subjects with normal corneas seeking preoperative evaluation for refractive surgery at a university-based hospital. Subjects with up to 2 diopters (D) of corneal with-the-rule astigmatism were defined as low corneal toricity (CT), whereas cylinder > two-dimensional was considered as high CT. The anterior segment optical coherence tomography was conducted to measure the epithelial thickness along the principle meridians of CT over a diameter of 9 mm. At the eye level, outcome variables (corneal and epithelial thicknesses in low- and high-astigmatism groups) were assessed using generalized estimating equation models.

Results: Included were 98 eyes (49 subjects): 46 eyes (23 subjects) with low CT and 52 eyes (26 subjects) with high CT. Two groups were similar with respect to the age ($P = 0.82$), sex ($P = 0.49$), and spherical equivalent ($P = 0.11$). Although the corneal thickness at steep and flat meridians was not different between two groups, high-CT group had significantly thinner epithelium at inferior 2.5–3.5 and 3.5–4.5 mm zones ($P = 0.01$ and 0.04) as well as superior 2.5–3.5 mm zone ($P = 0.03$) along the steep meridian. Two groups were similar with respect to epithelial thickness of flat meridian (all $P > 0.05$).

Conclusion: The epithelium of steep meridian was thinner in the high-CT group compared to the low-CT group.

Keywords: Anterior segment optical coherence tomography, Astigmatism, Corneal epithelium

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Introduction

The epithelial thickness distribution contributes to the corneal refractive power.[1] The corneal epithelium is a moldable, active outermost layer of the cornea that maintains the high optical quality of the eye.[2,3] The thickness of the corneal epithelium is not homogeneous. It tends to be highly reactive to irregularities and changes its thickness to compensate for irregular underlying corneal stroma in an attempt to maintain a smooth optical surface.[4] The phenomenon of epithelial remodeling has been described following photorefractive keratectomy, laser-assisted *in situ* keratomileusis, orthokeratology, and eyes with keratoconus.[5-7]

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In healthy corneas, some studies reported a nonuniform distribution of epithelium although the deviations were not considerable.[7-12] In one of these studies, no correlations were found between corneal epithelial thickness, astigmatism axis, and corneal front curvature.[12] However, no previous study assessed the patterns of the epithelial map along the steepest and flattest meridians in various amounts of corneal toricity (CT). Moreover, the question remains whether epithelial remodeling occurs in low and/or high regular CT. Therefore, the current study evaluated the distribution of total corneal and epithelial thickness in subjects with low

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and high CT using an anterior segment optical coherence tomography (AS-OCT) system.

Methods

It is a prospective comparative study on healthy subjects with normal corneas seeking preoperative evaluation for refractive surgery at the University Hospital, from September 2020 to November 2021. Consecutive recruitment of participants was performed. This study followed the tenets of the Declaration of Helsinki and was approved by the Ethic Committee (IR. TUMS.FARABI.REC.1400.007). Informed consent was also obtained from patients. The inclusion criteria for subjects were as follows: (1) 18 ≤ age ≤45 years, (2) myopic spherical refractive error <−2.00 diopters (D) of the sphere, (3) with-the-rule (WTR) astigmatic refractive error, and (4) central corneal thickness ≥500 µm. WTR astigmatism was considered when the axis of the cylinder was located between 0° and 22.5° or 157.5° and 180°. We recruited participants whose both eyes were concordant with the inclusion and exclusion criteria. We chose subjects with WTR astigmatism because of the lower prevalence of normal cornea with against-the-rule (ATR) and oblique astigmatisms and the higher possibility of corneal disease among them which makes sampling from this population difficult. The exclusion criteria included: patients with dry eye, any corneal opacity, corneal scars, previous ocular surgery or trauma, corneal pathology such as keratoconus, recent contact lens wear (within 1 month), systemic diseases with corneal involvement, and any history of corneal surgeries including keratorefractive surgery and pterygium. All participants underwent a thorough ophthalmic examination, including measurement of uncorrected visual acuity (UCVA), best-corrected visual acuity (BCVA), subjective refraction, tonometry, funduscopy, and slit-lamp biomicroscopy.

The Sirius corneal topographer (CSO, Costruzione Strumenti Oftalmici srl, Florence, Italy) was used to measure the corneal curvature and CT. Simulated keratometry was used to define CT as the difference between steep (Ks) and flat (Kf) keratometry values (Ks-Kf). The cornea with CT > two-dimensional (2D) (median of CT of the study population) was considered as high CT. The low CT was defined as CT ≤2 D. The Ks and Kf values and their meridians were also obtained at 3, 5, and 7 mm diameters centered on the corneal apex.

The total corneal and epithelial thickness maps of a central 9 mm diameter area were obtained using RTVue-XR AS-OCT (Optovue, Inc., Fremont, CA) with commercial software (software version 2016.1.0.90). The OCT machine has a 5 µm axial resolution at a speed of 26,000 A-scans per second width and a light source with a wavelength of 830 nm. The corneal vertex was determined by the saturated, specular reflection which was used as the center of the OCT scan. The epithelial maps were divided into 25 zones, automatically: one central zones of 2-mm diameter (C), eight zones at 2- to 5-mm paracentral area (superior [S], superotemporal [ST], temporal [T], inferotemporal [IT], inferior [I], inferonasal [IN], nasal [N], and superonasal [SN]), eight zones at 5- to 7-mm midperipheral area (S, ST, T, IT, I, IN, N, and SN), and eight zones at 7- to 9-mm diameter peripheral area. Superior-inferior and temporal-nasal sectors were compatible with steep and flat corneal meridians, respectively. The quality of all scans was checked, and only those without obvious artifacts were used. The average thickness of each zone was calculated and displayed automatically in the corresponding region. Moreover, the uniformity indices of the epithelial thickness maps were the minimum thickness, the maximum thickness, and the differences of the minimum and maximum points (min–max) which were recorded and analyzed. All eyes were scanned during the hours of 8:00 AM to 1:00 PM to eliminate the effect of diurnal variation. All measurements (AS-OCT imaging and Sirius topography) were performed by a well-trained operator.

Statistical analysis

Statistical analyses were performed with SPSS for Windows software version 22.0 (SPSS Inc., Chicago IL, USA). Quantitative data were described with means (standard deviation) and percentages in continuous and numerical data, respectively. Shapiro–Wilk test was used to assess whether variables had a normal distribution. At the eye level, outcome variables (corneal and epithelial thicknesses in low-and high-astigmatism groups) were assessed using generalized estimating equation models to account for including both eyes from the patients. Results were considered significant at $P < 0.05$. In each direction (superior, inferior, nasal, and temporal), significant P values were adjusted for < 0.0125 for intragroup comparisons [Figure 1].

Results

Included were 98 eyes (49 subjects) including 46 eyes (23 subjects) with low CT and 52 eyes (26 subjects) with high CT. Two groups were similar with respect to age, sex, UCVA, and BCVA [Table 1]. Although the spherical equivalent of two groups was similar, the low-CT group was more myopic ($P = 0.009$) with a lower cylinder ($P < 0.001$).

Table 2 illustrates the corneal and epithelial thicknesses at various zones in two groups. Superior zones had the thinnest corneal epithelium in both groups, followed by temporal zones [Figure 1]. The thickness of the epithelium of both groups decreased from center to periphery in all directions except inferior and nasal parts [Figure 1]. In nasal and inferior parts, the epithelium of low- and high-CT groups remained stable up to 2.5–3.5 mm distance from the vertex, respectively [Figure 1].

The corneal thickness at steep and flat meridians was not different between the two groups in all sectors except the 3.5–4.5 mm inferior zone [Table 2]. The general pattern of epithelium thickness was also similar between the two groups in steep [Figure 2] and flat [Figure 3] corneal meridians.

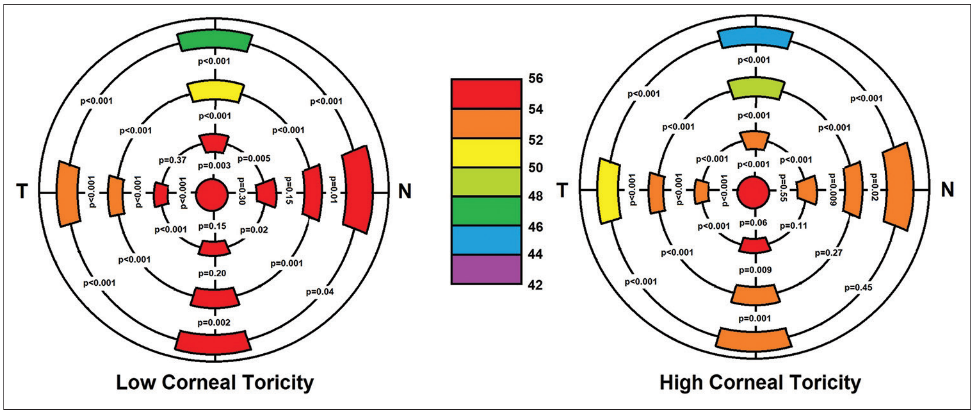

Figure 1: Topographic maps of the average epithelial thicknesses for healthy eyes with low (left map) and high (right map) corneal toricity. The color scale represents the thickness in μm. *P* values were reached by generalized estimation equation analysis and adjusted for <0.0125 as a significant value due to multiple comparisons. N: Nasal, T: Temporal

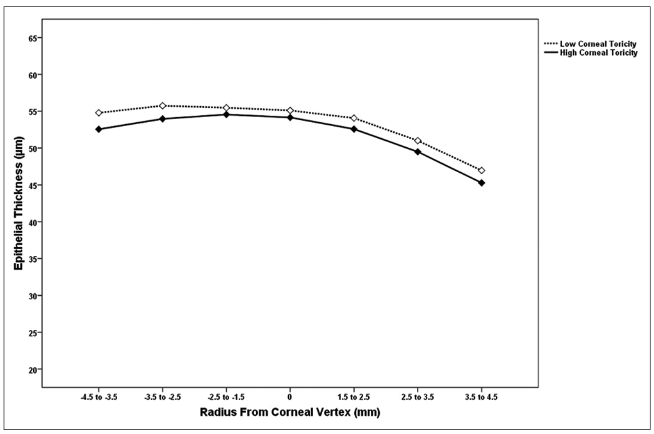

Figure 2: Comparison of average epithelial thicknesses of the corneal steep meridian for healthy eyes with low and high corneal toricity. "−" represents inferior to corneal vertex, "+" represents superior to corneal vertex

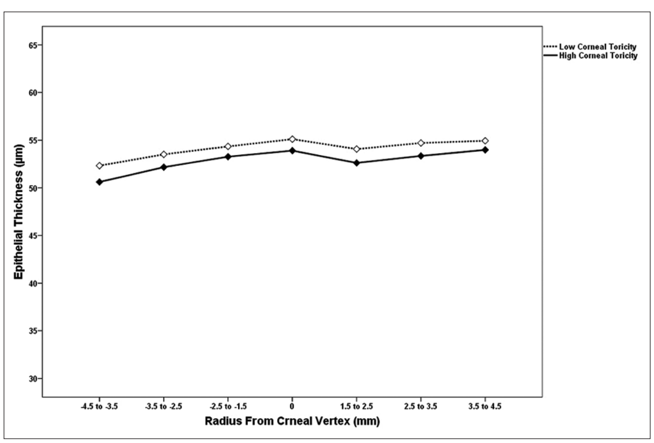

Figure 3: Comparison of average epithelial thicknesses of the corneal flat meridian for healthy eyes with low and high corneal toricity. "−" represents temporal to corneal vertex, "+" represents nasal to corneal vertex

However, the high-CT group had significantly thinner corneal thickness at the inferior 3.5–4.5 mm zone of the steep meridian ($P = 0.02$) [Table 2]. High-CT group also had thinner epithelium than the low-CT group at inferior 2.5–3.5 and 3.5–4.5 mm zones ($P = 0.01$ and 0.04) of the steep meridian as well as superior 2.5–3.5 mm zones ($P = 0.03$) [Table 2].

Discussion

CT exists in a significant proportion of the general population. Previous studies have demonstrated the CT of ≥0.25 and >0.50 D in over 90% and 30% of people younger than 55, respectively[13-15] However, the prevalence of high CT (>2D) drops to <10%.[13-15] The prevalence and amount of CT also increase considerably with age.[13]

The current study compared the epithelial thickness profiles of the steep and flat meridians between the corneas with low and high toricity. This study showed that the epithelium was thinner along the steep meridian of subjects with high CT compared to subjects with low CT, especially in inferior zones. Meanwhile, the two groups did not differ in terms of epithelial thickness of flat meridian.

Limited studies evaluated the epithelial thickness profile in healthy corneas.[7-12,16] All of them highlighted the nonuniform profile of corneal epithelium.[7-12] Reinstein *et al*.[16] characterized the corneal epithelial thickness over a 10 mm diameter area of healthy virgin eyes using a very high-frequency digital ultrasound system.[16] They reported that the corneal epithelium was thinner in the superior to inferior meridians. Moreover, they found the corneal epithelium was thicker nasally than temporally.[16] Therefore, the thinnest epithelium of the study population was in the ST region.[16] Although recent studies[7-12] mapped epithelial thickness distribution using spectral domain-OCT (SD-OCT), they reported similar results to Reinstein's study.[16] Moreover, Wu and Wang found no correlations between corneal epithelial thickness, astigmatism axis, and corneal front curvature.[12] In line with previous studies, we also observed the thinnest epithelium in the superior, temporal, and superior temporal zones. There are several theories for vertical asymmetry in epithelial thickness.

Table 1: Baseline demographic data, refraction and corneal topography of 23 subjects (46 eyes) with low corneal toricity (low-corneal toricity: not more than 2.00 diopter) and 26 subjects (52 eyes) with high corneal toricity (high-corneal toricity; >2.00 diopter)

Variables	Total	Low-CT	High-CT	*P*
Age (years)	31.14±6.52	30.91±7.65	31.35±5.48	0.82[†]
Female, *n* (%)	26 (53.1)	11 (47.8)	15 (57.7)	0.49[‡]
UCVA, logMAR	0.53±0.21	0.56±0.22	0.50±0.20	0.29[§]
BCVA, logMAR	0.01±0.03	0.001±0.007	0.02±0.04	0.02[§]
Subjective refraction				
Sphere (D)	−1.25±0.72	−1.48±0.57	−1.04±0.78	0.009[§]
Cylinder (D)	−2.05±1.27	−1.28±0.38	−2.79±1.37	<0.001[§]
Spherical equivalent (D)	−2.28±0.82	−2.12±0.53	−2.43±1.00	0.11[§]
Flattest keratometric value (D)	42.87±1.46	42.79±1.38	42.94±1.53	0.67[§]
Steepest keratometric value (D)	45.18±1.78	44.31±1.38	46.01±1.72	<0.001[§]
CT (D)	2.31±1.00	1.51±0.35	3.07±0.82	<0.001[§]

[†]Independent *t*-test, [‡]Chi-square test, [§]Feneralized estimation equation. UCVA: Uncorrected visual acuity, BCVA: Best-corrected visual acuity, D: Diopter, CT: Corneal toricity

Table 2: Corneal total and epithelial thickness of 23 subjects (46 eyes) with low and 26 (52 eyes) subjects with high-corneal toricity

Variables	Distance from vertex (mm)	Total (μm), mean±SD				Epithelial (μm), mean±SD			
		Total	Low-CT	High-CT	*P*[†]	Total	Low-CT	High-CT	*P*[†]
Central thickness		545.61±29.58	536.69±13.62	525.28±22.58	0.16	54.49±3.65	55.42±4.01	54.45±3.22	0.21
Maximum thickness		658.69±23.75	667.42±20.41	650.86±24.12	0.02	58.18±5.15	58.92±5.87	57.66±4.02	0.22
Minimum thickness		539.36±28.86	530.92±13.79	520.59±31.95	0.19	46.49±5.15	48.65±3.32	46.17±5.36	0.01
Maximum–minimum difference		133.22±16.73	136.50±17.72	130.28±15.52	0.20	11.43±5.69	10.27±5.02	11.48±6.39	0.39
Steep meridian	−4.5– −3.5	653.77±24.88	661.83±20.38	643.83±26.32	0.02	53.52±4.06	54.52±4.03	53.28±4.13	0.01
	−3.5– −2.5	625.11±32.81	629.67±27.92	621.04±36.46	0.41	54.72±4.16	55.62±4.29	53.72±3.85	0.04
	−2.5– −1	584.41±33.57	589.85±31.70	579.18±34.80	0.21	54.91±3.99	55.47±4.00	54.37±3.93	0.28
	1–2.5	560.33±30.12	566.15±26.73	554.76±32.34	0.14	53.10±3.99	54.06±4.06	52.18±3.74	0.06
	2.5–3.5	593.96±31.70	594.81±21.13	587.15±31.94	0.12	50.01±3.91	50.74±3.20	49.40±4.34	0.03
	3.5–4.5	628.43±31.10	627.86±23.53	613.07±30.82	0.43	46.12±4.56	46.72±4.24	45.97±4.02	0.09
Flat meridian	−4.5– −3.5	615.70±36.04	613.48±27.25	587.03±28.04	0.06	51.45±3.53	52.69±3.78	51.72±3.40	0.05
	−3.5– −2.5	586.50±34.86	588.24±21.57	578.43±38.77	0.16	52.82±3.64	53.45±3.94	52.26±3.49	0.14
	−2.5– −1	559.05±30.99	565.02±27.01	553.33±33.66	0.14	53.79±3.72	54.34±3.85	53.27±3.55	0.27
	1–2.5	573.10±31.03	579.23±29.41	567.22±31.70	0.12	54.45±3.73	54.94±3.72	53.98±3.72	0.32
	2.5–3.5	606.46±31.03	607.38±21.77	598.40±29.98	0.13	54.01±3.57	54.71±3.56	53.35±3.48	0.13
	3.5–4.5	642.69±27.90	642.86±25.68	626.55±25.70	0.14	53.32±3.75	54.06±3.74	52.61±3.66	0.11

[†]Generalized estimation equation, for steep meridian, "-" represents inferior to corneal vertex, "+" represents superior to corneal vertex; For flat meridian, "-" represents temporal to corneal vertex, "+" represents nasal to corneal vertex. CT: Corneal toricity, SD: Standard deviation

First, the constant force of the upper eyelid on the superior and temporal zones of the cornea is the most probable cause.[17,18] On the other hand, the pooling of the tear film in the inferior meridian may cause a falsely thick reading.[19] Hashmani *et al*.[9] proposed that less contact time of the tear film to the superior meridian leads to faster desquamation of the epithelium and subsequent thinning over time.

No previous study has considered the amount of CT and axis of astigmatism in the evaluation of the epithelial distribution profile. Zhou and Stojanovic[10] compared the epithelial thickness along the steepest and flattest meridians between subjects with keratoconus and those with healthy corneas with corneal astigmatism ≥2 D using SD-OCT. They defined the steepest and flattest meridians based on Scheimpflug topography and then obtained the thickness profile along the meridians. They found that the epithelium of patients with keratoconus was thin at midperipheral area over the cone in addition to increasing of thickens superior.[10] In healthy subjects, the epithelial thickness map had a nearly homogeneous distribution along the steepest and flattest meridians with only small deviations.[10] Similarly, Li *et al*.[11] and Rocha *et al*.[7] also studied the epithelial thickness distribution in keratoconus and compared them to healthy eyes. However, they did not match groups based on the amount of astigmatism.[7,11] Rocha *et al*.[7] also reported small deviations along the main meridians of healthy corneas. In the current study, we found thinning of the epithelial layer along the steep meridian of high CT subjects where the elevation of the cornea decreases. This proposed that the epithelium enhances and contributes to increase the CT in normal eyes with regular astigmatism. Therefore, the epithelial thickness distribution of normal high CT corneas may behave differently from keratoconus and other corneal ectatic disorders.

The profile of the epithelial thickness may help ophthalmologists in various areas, especially increasing the accuracy of corneal refractive surgery.[20,21] Some corneal refractive surgeries with excimer laser are performed through the corneal epithelium, such as phototherapeutic keratectomy and transepithelial photorefractive keratectomy.[22] Considering the contribution of the corneal epithelium in corneal refraction, the profile of the epithelium may improve the design and accuracy of the abovementioned surgeries. Moreover, an epithelial thickness map may also reflect the shape and profile of the underlying stromal surface (by subtraction from the pachymetry map). This will change the amount of stromal tissue removal in transepithelial topography-guided surface ablation at areas with thinner epithelium and thus optimize the procedure.[23,24]

This study has some limitations. Small sample size and using binocular data might prevent us from showing significant results in some sectors. Moreover, corneas with oblique and ATR toricity were not assessed in the current study.

In conclusion, this study described the profile of the corneal epithelial thickness in healthy eyes with low and high CT and showed they were different. Although subjects with high and low CT had similar epithelial thickness along the flat meridian, the epithelial distribution of the two groups was different. The epithelium of eyes with high CT was thinner than eyes with low CT along the steep meridian.

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Conflicts of interest
There are no conflicts of interest.

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