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Age-Related Changes in Human Corneal Epithelial Thickness Measured with Anterior Segment Optical Coherence Tomography

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Abstract

Corneal epithelium not only functions as a barrier that block the passage of foreign material, but also plays an important role in maintaining high optical quality. To evaluate the effect of age on human corneal epithelial thickness profile in a healthy population with a broad age range by anterior segment optical coherence tomography (OCT). This prospective, observational, noninterventional study included 160 eyes of 80 healthy individuals from those attending the outpatient clinics of 6 October's University hospitals. Patients were divided into four groups. Eye variations of epithelial thickness among age groups which in another means represents the effect of age on corneal epithelial thickness. The Minimum- Maximum (Right and Left) in group A, B, C and D was (7+1.0, -7+0.9), (-10+1.2, -11+1.1), (-17+1.4, -17+1.6), (-16+1.4, -17+1.7) respectively and total decline in CET in group A, B, C and D was (-7+0.9, -10.5+1.2, -17+1.5, -19.5+1.6) respectively. Age seemed to have no effect on corneal epithelial thickness of the central 2-mm and the superior or inferior limbus; while corneal epithelial thickness became thinner with increasing age at other corneal regions. Human corneal and limbal epithelial thickness profiles in normal corneas, measured by AS-OCT, could serve as a suitable basis for investigations into ocular surface pathology.

Keywords: Age-Related Changes, Human Corneal Epithelial Thickness, Optical Coherence Tomography.

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1. Introduction

As the outermost layer that covers the front of an eye, corneal epithelium not only functions as a barrier that block the passage of foreign material, but also plays an important role in maintaining high optical quality. Stem cells in the basal layer of Limbal epithelium hold a physiological significance in the renewal and metabolism of corneal epithelium, particularly under stress situations [1]. Optical coherence tomography (OCT) is an imaging modality that allows for noninvasive imaging of the morphology of biological tissue with micrometer scale resolution at imaging depths of 1 to 2mm below the tissue surface [2]. During these few years, OCT has become a useful clinical and research tool for imaging of the ocular surface [3]. In addition to the mostly used application for observing the optic disc and retinal choroidal structure, the usage in the anterior segment, especially cornea, was also widely developed [4]. The aim of this study was to evaluate the effect of age on human corneal epithelial thickness profile in a healthy population with a broad age range by anterior segment optical coherence tomography (OCT).

2. Patients and methods

This prospective, observational, non-interventional study included 160 eyes of 80 healthy individuals from those attending the outpatient clinics of 6 October's University hospitals. Patients were divided randomly into four, almost equally sized, groups on the basis of age: 18–29 years (group A), 30–44 years (group B), 45–59 years (group C), and 60–80 years (group D).

2.1. Inclusion criteria

Age group from 18 to 80 Y, no history of ocular surgery, K reading from 40 to 46 D and Completely clear cornea with absence of any other ocular or systemic disease.

2.2. Exclusion criteria

History of herpetic keratitis, concurrent corneal infections, or concomitant autoimmune diseases, severe dry eye, severe allergic conjunctivitis, Keratoconus or acute hydrops, intraocular pressure of >21 mm Hg, Pregnant or lactating females and Contact lens wearers.

2.3. Ethical consideration

The study was approved by the scientific ethic committee of faculty of medicine, Beni- Suef University. In addition, a written informed consent was obtained from individuals in agreement with the tenets of the Declaration of Helsinki.

2.4. Methods

All patients were subjected to the following procedure. All epithelial thickness (ET) measurements were performed between 2:00 PM and 5:00 PM to minimize the influence of diurnal variation. The use of any eye drops was prohibited from 2 hours before the examination. We used the Fourier-domain OCT system (RTVue-100; Optovue Inc., Fremont, CA, USA) with a cornea anterior module long adapter lens (1.96-mm scan depth and 6-mm scan width). The machine scans at an axial resolution of 5 lm, a beam width of 22 lm, a light source that is centered at 840 nm, and had a scan speed of 26,000 axial scans per second. A Pachymetry + Cpwr scan pattern was used to map the cornea over a 6-mm diameter area, the settings were 8 meridional B-scans, consisting of 1024 A-scans each 5-μm axial resolution. The subject was asked to fixate at a peripheral target to maintain the perpendicularity of the OCT beam at the surface of the targeted tissue, which was essential for obtaining accurate thickness values. Following correct fixation and centering on the pupil, each scan was acquired within 5 seconds. The OCT scan was aligned manually when both vertical and horizontal reflection stripes appeared simultaneously, which means the scan was centered on the corneal apex. The subject was asked to blink quickly, and the scan was triggered within 2 seconds. Any scan that proved to be of low quality or with evidence of signal blockage was excluded from the study. To avoid potential artifacts or interferences from other ocular examinations, OCT scans were performed first, on one eye (randomly selected) of each subject for three times. The ET map and data output was further redefined into a central zone (0–2 mm diameter), paracentral zone (2–5 mm diameter), and mid-peripheral zone (5–7 mm diameter). The ET measurement was repeated three times for each eye. The difference in central ET should be within 1 μm between these scans, and the average value was used for analysis. The regional thickness and topographic variability were compared between the 9 central and paracentral regions among the age groups.

3. Results and discussion

Table 1 showed that all patients were caucasian with sex representation in the form of 42 males (52.5%) and 38 females (47.5%). Age of patients ranged from 18 to 69 years with a mean of 44.87± 25.8 years. Table 2 showed that the K readings in the four age groups (A, B, C, and D) were 42±2.1, 42.5±3.1, 41.9±2.8, and 43.1±1.9 respectively and the overall K reading in the whole subjects was 42.37±2.47. The mean equivalent spherical refraction of all subjects ranged between +1.25 and −4.75 diopters with a mean of -2.1±2.57. Table 3 showed that the total corneal thickness in the central and paracentral (SN, N, IN, I, IT, T, ST, and S) regions for all eyes ranged 523-558 μm, 534-570 μm, 545-578 μm, 531-591 μm, 515-582 μm, 504-555 μm, 508-555 μm, 510-573 μm, and 544-581 μm respectively. The mean (±standard deviation) of the total corneal thickness in the central and paracentral (SN, N, IN, I, IT, T, ST, and S) regions for all eyes was (534+6.9), (553+ 9.1), (564+12.27), (557+18.0), (547+13.3), (534+12.9), (523+ 2.1), (543+ 8.9), and (571+14.0) respectively. Table 4 showed that the mean (±standard deviation) of the total corneal epithelial thickness in the central and paracentral (SN, N, IN, I, IT, T, ST, and S) regions for all eyes was (51+0.5), (52+2.3), (52+0.6), (52+ 2.1), (52+1.4), (52+1.1), (52+1.4), (51+0.6), and (52+1.2) respectively. The corneal epithelial thickness is the nearly the same in all corneal regions. Table 5 showed the within eye variations of epithelial thickness among age groups which in another means represents the effect of age on corneal epithelial thickness. The Minimum- Maximum (Right and Left) in group A, B, C and D was (7+1.0, -7+ 0.9), (-10+1.2, -11+1.1), (-17+1.4, -17+1.6), (-16+1.4, -17+ 1.7) respectively and total decline in CET in group A, B, C and D was (-7+0.9, -10.5+1.2, -17+1.5, -19.5+1.6) respectively. The study included 42 males (52.5%) and 38 females (47.5%) all subjects are Caucasian with total k readings of 42.37±2.47. There was no significant difference of K readings among subjects in the four groups (P > 0.05). Also, the mean equivalent spherical refraction of subjects included in groups A, B, C, and D had no significant difference (P > 0.05). While most of ocular refraction of the included subjects was biased toward myopia, the population was considered normal as all subjects were free of ocular pathology other than their refractive errors. Except for group C; which included four hypermetrope individuals, analysis of our results showed that the total central corneal thickness (TCCT) showed no significant difference among age groups (P >0.05). In contrast, there was significant difference in TCT between the central region and the other paracentral regions (P <0.001), and between different regions in the paracentral area (2-5mm) where P < 0.01. Further analysis showed that the cornea either in different groups or in the whole individuals is thicker in the superior and nasal haves than inferior and temporal haves respectively. Fares et al., (2012) reported that there was no significant difference between central corneal thickness readings measured by ultrasonic pachymetry and Pentacam. In contrast to our results, they reported a high positive correlation between the thickness at 3 mm and at 7 mm points. They noted a gradual increase in thickness from the center to the periphery with a high positive correlation between the mean thickness at the circles of 2, 4, 6, 8 and 10 mm [5]. In peer-reviewed literature, the average central CET measured by OCT system was (53.2 ± 2.9 μm); within the range (48.0–59.9 μm) [6,7,8,9,4,10,11,12,13]. In this study, the mean central corneal epithelial thickness of the included subjects was (51 + 0.5 μm) with an average of (51-52 μm). In contrast to Yang et al., (2014) and Li et al., (2012) the corneal epithelium had a uniform thickness profile with no significant difference among age groups (P > 0.05). However, irrespective to age, thickness of the central corneal epithelium remains the thinnest among all topographic corneal regions [4,14]. Micera et al., (2020) reported that an age-related change has been elicited in human corneal epithelium. However, few of these changes are well understood from clinical standpoint. Sometimes, it is difficult to distinguish age-specific alterations from degenerative modifications due to environmental and genetic factors [13].

Yang et al., (2014) showed that the differences of CET in 2- to 6-mm diameter area between under and over 40 years were ranged between 1.19 to 2.65 μm, which were slightly larger than the repeatability measurement fluctuations reported by Ma et al., (2013) They demonstrated that epithelial thickness in paracentral cornea decreased with aging. They added that these differences, though significant, were below the resolution of the AS-OCT device used [4,15]. In the current study, the differences of CET in the paracentral area (2- 5 mm diameter) ranged between 0 to 2 μm. The differences among the central, superior nasal, nasal, inferior nasal, inferior, inferior temporal, temporal, superior temporal, and superior map regions were (0), (0-2), (1), (1), (0-2), (0-1), (0-1), (0-2), (0-2) respectively. It showed no significant difference between the central region and the other paracentral regions (P > 0.05), and between different regions in the paracentral area (2-5mm) where (P >0.05). Interestingly, our study showed that age seemed to have no effect on central CET, which concurred with findings of Reinstein et al., (2008), Francoz et al., (2011), Kanellopoulos and Asimellis (2013), and Yang et al., (2014) [16,8,17,4]. As regards effect of aging on the corneal epithelial thickness in the paracentral area (2-5mm); this study showed that the difference between various topographic regions didn't exceed 1-2 μm with a non-significant correlation (P>0.05). Comparing the distribution of CET between Rt and Lt eyes in age groups of this study showed Rt \Lt mirror image in the incidence of increase or decrease of total corneal thickness and corneal epithelial thickness. Analysis of the minimal and maximal epithelial thickness in individuals among age groups of this study; showed a significant (P<0.001) correlation either in decrease of the minimal corneal epithelial thickness or increase of the maximal corneal epithelial thickness among individuals from one age group to its next. The total decline in corneal epithelial thickness (minimum epithelial thickness– maximum epithelial thickness) among age groups in this study was -7+ 0.9, -10.5+ 1.2, -17+ 1.5, and -19.5 + 1.6 in group A, B, C, and D respectively. This means that there is a progressive decline of corneal epithelial thickness in parallel to advancement of age in healthy corneas. However, the value of this decline in corneal epithelial thickness is slight in the last age group than that occurred in the previous three age groups. This means that the decline in corneal epithelial thickness is slight after 60 years. To explain such results, Yang et al implied that as the age increased, limbal epithelial stem cells (LESCs) kept a dynamic evolvement with attenuating proliferative potential, leading to degenerated capacity in maintaining the integrity and stability of the corneal epithelium. Thus, the old had thinner corneal epithelium compared with the young. Because the corneal epithelium is the most far from LESCs, this explanation can answer the question why the central corneal epithelium was less susceptible to age influences [4]. Our results showed no significant difference of epithelial thickness between different regions in the paracentral corneal area (P > 0.05). These results agree with those of Wang et al., (2003), Pérez et al., (2003), and Haque et al., (2008) who found that the epithelium was roughly uniform in thickness in the central 8 mm of the cornea [18,6,19]. Also, our results are in agreement with those of Patel et al., (2002) who concluded that the epithelial thickness was constant along the horizontal [20]. Although it was statistically insignificant, results of this study showed that the corneal epithelium is thicker superiorly and inferiorly than temporally and nasally and thicker superiorly than inferiorly. We attributed these results to the partial covering of superior and inferior cornea by eyelids which protects them from extrinsic environmental effects. Also, the more covering of the upper cornea (1-2mm) explains why the superior corneal epithelium is thicker than the inferior. In addition, observations showed that the inferior tear film was thinner than the superior in normal eyes [21].

Table 1: Demographic characteristics of the included subjects (n=80).

Race	
• Caucasian	80 subjects (100%)
• Negro	No
• Asian	No
• White	No
• Mongoloid	No
• Ausraloid	No
Age per years • Mean ±SD • (Range)	44.87± 25.8 (18—69)
Sex • Male • Female	42 (52.5%) 38 (47.5%)

Table 2: Refractive characteristics of the included subjects.

	Groups (n=20 subjects, 40 eyes)				**Total** (n=80 subjects, 160 eyes)
Age (years)	**A** (18–29)	**B** (30–44)	**C** (45–59)	**D** (60–80)	(18–80)
K readings	42±2.1	42.5±3.1	41.9±2.8	43.1±1.9	42.37±2.47
Equivalent spherical refraction	−3.15±2.2	−2.9±1.6	−2.1±1.9	−1.64±2.6	-2.1±2.57

Table 3: Comparison of total corneal thickness (mean values ± SDs; µm) within the 9 (central and paracentral) topographic regions among all individuals included in the study.

Regions / **Groups** n=20		**Central region (2mm)**	**Paracentral regions (3-5 mm)**							
			SN	**N**	**IN**	**I**	**IT**	**T**	**ST**	**S**
A		531±3.26	544± 3.52	571±7.2	557±3.1	542±3.9	529±6.5	524±3.7	541±5.2	563±12.5
B		528±4.9	560±9.3	552±4.9	535±4.1	520±4.2	509±4.8	515±6.6	530±13.7	566±6.5
C		544±12.1	555±9.1	556±10.9	559±2.1	576±3.9	552±2.7	551±4.4	562±9.81	588±6.5
D		531±3.5	552±3.1	577±4.1	578±3.9	550±4.5	531±2.6	525±2.3	539±3.9	566±2.5
Total n=80	**Mean**	534±6.9	553±9.1	564±12.27	557±18.0	547±13.3	534±12.9	523±2.1	543± 8.9	571±14.0
	Average	523:558	534:570	545:578	531:591	515:582	504:555	508:555	510:573	544:581

S: Superior, SN: superior nasal, N: nasal, IN: inferior nasal, I: inferior, IT: inferior temporal, T: temporal, ST: superior temporal. n=80 subjects, 160 eyes.

Table 4: Represents the total corneal epithelial thickness (µm) within the 9 (central and paracentral) topographic regions among all individuals included in the study.

Regions / **Groups**		**Central region (2mm)**	**Paracentral regions (3-5 mm)**							
			SN	**N**	**IN**	**I**	**IT**	**T**	**ST**	**S**
A		51±0.5	52±1.9	52±2.7	53±1.5	53±1.7	52±1.9	51±2.1	52±1.1	52±2.4
B		51±1.5	51±2.1	52±2.3	52±1.6	52±2.9	52±0.8	52±1.4	51±2.1	51±2.1
C		51±1.1	51±1.3	52±2.2	52±1.9	52±1.4	53±2.1	52±1.1	52±1.6	53±1.2
D		51±1.1	51±1.3	52±2.2	52±1.9	52±1.4	53±2.1	52±1.1	52±1.6	53±1.2
Total	**Average**	51:52	50:54	51:54	52:54	51:53	52:53	50:53	50:52	51:53
	Mean	51±0.5	52±2.3	52±0.6	52±2.1	52±1.4	52±1.1	52±1.4	51±0.6	52±1.2
	Range of difference	0	0-2	1	1	0-2	0-1	0-1	0-2	0-2

S: Superior, SN: superior nasal, N: nasal, IN: inferior nasal, I: inferior, IT: inferior temporal, T: temporal, St: superior temporal.

Table 5: Represents the mean of minimal and maximal values of corneal epithelial thickness (µm) among individuals included in the 4 groups of this study.

Groups	A		B		C		D	
	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt
Minimum	49±1.1	50±0.9	46±1.5	48±1.2	42±1.8	43±1.8	46±1.6	47±1.7
Maximum	56±0.9	57± 1.1	56±0.8	59±1.2	59±1.2	60±1.4	62±1.1	64±1.5
Min. – max.	-7±1.0	-7±0.9	-10±1.2	-11±1.1	-17±1.4	-17±1.6	-16±1.4	-17±1.7
Total decline in CET	-7± 0.9		-10.5± 1.2		-17± 1.5		-19.5± 1.6	

4. Conclusions

Age seemed to have no effect on corneal epithelial thickness of the central 2-mm and the superior or inferior limbus; while corneal epithelial thickness became thinner with increasing age at other corneal regions. Human corneal and limbal epithelial thickness profiles in normal corneas, measured by AS-OCT, could serve as a suitable basis for investigations into ocular surface pathology.

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