·Clinical Research·

Anatomical characterization of central, apical and minimal corneal thickness

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Abstract

• AIM: To anatomically locate the points of minimum corneal thickness and central corneal thickness (pupil center) in relation to the corneal apex.

• METHODS: Observational, cross-sectional study, 299 healthy volunteers. Thickness at the corneal apex (AT), minimum corneal thickness (MT) and corneal thickness at the pupil center (PT) were determined using the pentacam. Distances from the corneal apex to MT (MD) and PT (PD) were calculated and their quadrant position (taking the corneal apex as the reference) determined: point of minimum thickness (MC) and point of central thickness (PC) depending on the quadrant position. Two multivariate linear regression models were constructed to examine the influence of age, gender, power of the flattest and steepest corneal axes, position of the flattest axis, corneal volume (determined using the Pentacam) and PT on MD and PD. The effects of these variables on MC and PC were also determined in two multinomial regression models.

• RESULTS: MT was located at a mean distance of 0.909 mm from the apex (79.4% in the inferior-temporal quadrant). PT was located at a mean distance of 0.156 mm from the apex. The linear regression model for MD indicated it was significantly influenced by corneal volume (B =-0.024; 95% CI: -0.043 to -0.004). No significant relations were identified in the linear regression model for PD or the multinomial logistic regressions for MC and PC.

• CONCLUSION: MT was typically located at the inferior-temporal quadrant of the cornea and its distance to the corneal apex tended to decrease with the increment of corneal volume.

• KEYWORDS: corneal thickness; anatomy; glaucoma

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INTRODUCTION

The important role of the thickness of the cornea in glaucoma and its implications for refractive surgery have been established in several studies [1-7]. In a setting of glaucoma, corneal thickness has been identified both as a confounding factor for the gold standard method used to determine intraocular pressure (IOP), Goldmann applanation tonometry, and as an independent risk factor for the development and progression of glaucoma [1-7]. Today, a large number of anterior segment imaging instruments such as the Pentacam exist that provide accurate measurements of central corneal thickness (CCT). However, while much attention has been paid to the reliability and reproducibility of the instruments used to determine IOP, corneal refraction and topography, the systems available to measure CCT have not been subject to such rigorous validation. Ultrasound pachymetry is perhaps the most widely used method to determine CCT. Notwithstanding, other methods such as the Pentacam itself have offered highly reproducible results for this variable[8-10]. Besides the traditional measure of CCT, this device measures thickness at the thinnest point of the corneal and at the corneal apex[11-13].

The main purpose of this study was to anatomically locate the points of minimum corneal thickness and central corneal thickness (pupil center) in relation to the corneal apex as the reference point.

Table 1 Means, standard deviations and quartiles of the quantitative variables

Statistics	Mean	Std. deviation	Percentiles		
			25	50	75
Age (a)	67.33	14.722	59.00	73.00	79.00
Power steepest axis	44.828	1.5661	43.750	44.600	45.850
Power flattest axis	43.61	1.697	42.75	43.60	44.70
Corneal volume	59.767	4.8178	56.425	59.500	62.900
PT	562.21	41.410	530.00	559.50	595.50
MT	556.44	42.796	525.75	554.50	589.25
AT	563.55	41.833	531.00	561.00	595.25
PD	0.2716	0.15590	0.1651	0.2428	0.3585
MD	0.9093	0.54522	0.5923	0.8054	1.0433

Age (a): power of the flattest axis and steepest axis (diopters), corneal volume (mm^3); PT: Thickness at the pupil centre, μm; MT: Minimum corneal thickness, μm; AT: Thickness at the corneal apex, μm; PD: Distance from the corneal apex to PT, mm; MD: Distance from the corneal apex to MT, mm.

SUBJECTS AND METHODS

For this observational, cross-sectional study, 299 healthy volunteers were recruited among the staff and persons accompanying patients visiting the Ophthalmology Department of the Hospital Clínico San Carlos de Madrid, Spain. All volunteers were Caucasian of Spanish descent. The study protocol was approved by our institution's Review Board and complied with the guidelines of the Declaration of Helsinki (HSC-COSPTRAV-05). Informed consent was obtained from each participant before inclusion in the study.

Subjects were considered eligible for the study if they had no history of an ocular or a systemic disease other than high blood pressure and/or high blood cholesterol. General exclusion criteria were: a spherical equivalent greater than 3 diopters, 1 or more diopters of astigmatism, a best corrected visual acuity lower than 20/25, signs of early keratoconus according to topographic criteria provided by the Pentacam, opacities in the cornea or lens impairing optic nerve head visualization and alterations in optic nerve head morphology, such as oblique discs or peripapillary atrophy. We also excluded subjects who had undergone prior eye surgery and those with visual field defects. Only one eye was examined in each subject. If both eyes fulfilled all the inclusion and exclusion criteria, the eye to be entered in the study was randomly selected using an automated procedure (www. randomization.com).

All the study participants underwent a Pentacam (Pentacam, Oculus USA) examination to determine thickness at the corneal apex (AT), minimum corneal thickness (MT) and corneal thickness at the pupil center (PT). Then, using the pachymetric maps provided by the instrument, distances from the corneal apex to MT (MD) and PT (PD) were calculated. The following categorical variables were also established: point of minimum thickness (MC) and point of central thickness (PC) depending on the quadrant position of MT and PT respectively taking the corneal apex as the center (quadrants: superior-nasal, inferior-nasal, superior-temporal, inferior-temporal). Subject age and sex were also recorded. The normal distribution of the quantitative data was confirmed by the tests Saphiro-Wilk and Kolmogorov-Smirnov. For each quantitative variable (AT, MT, PT, MD and PD) mean, standard deviation and quartiles were determined. In addition, frequency distributions were calculated for each categorical variable (MC and PC).

Two multivariate linear regression models were constructed to examine the influence of age, gender, power of the flattest and steepest corneal axes, position of the flattest axis (grouped as 0°-30°, 30°-60°, 60°-90°, 90°-120°, 120°-150°, 150°-180°), corneal volume (determined using the Pentacam) and CCT (as PT) on MD and PD respectively. The effects of these variables on MC and PC were also determined in two multinomial regression models.

RESULTS

The means, standard deviations and quartiles of the quantitative variables determined are provided in Table 1. In Table 2, the distribution frequencies of MC and PC may be seen. Table 3 shows the mean distances of MT and PT from an imaginary line (defined by its abscissa and ordinate) centered at the corneal apex. The point of minimal corneal thickness, MT, occurred at a mean distance of 0.909 mm from the apex (79.4% in the inferior-temporal quadrant); at a mean distance of 0.468 mm towards the temporal side and of 0.458 mm towards the inferior with respect to the horizontal line passing through the apex. The central corneal point PT was located at a mean distance of 0.156 mm from the apex

Table 2 Frequency distribution of the quadrant position of PC and MC

Valid	PC (%)	MC (%)
Superior and nasal	8.7	1.6
Inferior and nasal	15.9	7.9
Superior and temporal	23.0	11.1
Inferior and temporal	52.4	79.4
Total	100.0	100.0

PC: Point of central thickness; MC: Point of minimum thickness.

Table 3 Means (mm), standard deviations and quartiles of the distances of PT (thickness at the pupil centre) and MT (minimum corneal thickness) from an imaginary line (defined by its abscissa and ordinate: x, y) centered at the corneal apex

Statistics	Mean	Std. deviation	Percentiles		
			25	50	75
PT.X	-0.1104	0.21161	-0.2500	-0.1250	0.0000
PT.Y	-0.0567	0.19581	-0.1600	-0.0700	0.0400
MT.X	-0.468	0.4661	-0.700	-0.530	-0.350
MT.Y	-0.4584	0.69356	-0.7050	-0.4300	-0.2100

PT.X: Distance of PT from the abscissa axis; PT.Y: Distance of PT from the ordinate axis; MT.X: Distance of MT from the abscissa axis; MT.Y: Distance of MT from the ordinate axis.

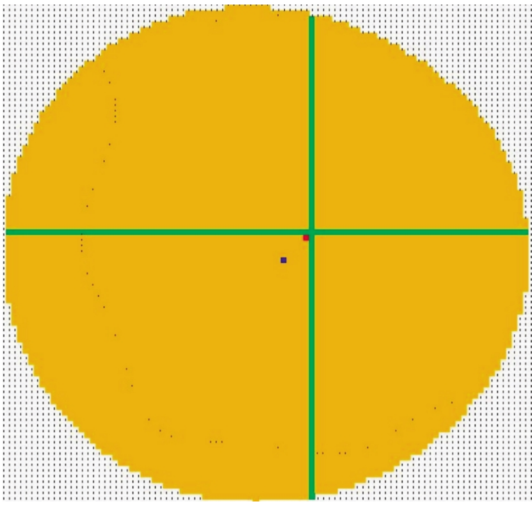

Figure 1 Characteristic locations of MT and PT in a right eye on a Pentacam pachymetric map The cornea is represented in yellow; the green lines corresponds to the Cartesian axis centered at the corneal apex; the red point represents the characteristic location of PT and the blue point the location of MT.

although this point showed more variation among subjects (Table 2). Figure 1 shows the characteristic locations of MT and PT in a right eye on a Pentacam pachymetric map.

The linear regression model for MD indicated it was significantly (adjusted R^2 =7.8%; P =0.005) influenced by corneal volume (B= -0.024; 95%CI: -0.043 to -0.004). No significant relations were identified in the linear regression model for PD or the multinomial logistic regressions for MC and PC.

DISCUSSION

Traditional methods used to measure corneal thickness such as ultrasound pachymetry have been gradually replaced by more modern anterior segment imaging systems such as the Pentacam. Besides providing a good estimate of CCT, the Pentacam has proved to be highly repeatable in its measurements and also offers other central pachymetry estimates including pupil center thickness as the CCT measure, minimum corneal thickness, and corneal apex thickness[8-10]. Moreover, this system can be used to determine the thickness of the peripheral cornea, which seems also to play an important role in a setting of glaucoma[11-14]. In a prior study, we noted that the factors minimal corneal thickness and apical corneal thickness were predictive of primary open-angle glaucoma (POAG) while CCT determined by ultrasound pachymetry was not[11].

Ultrasound pachymetry is perhaps the most widely used method to determine CCT and has been described as a highly reliable and reproducible method in several studies [15-17]. Nevertheless, other authos claim the Pentacam shows higher interobserver reproducibility[18]. This consideration highlights the potential importance of this device in corneal thickness measurements.

The relationship between corneal thickness and several variables such as age, refrantion and corneal hysteresis has been widely studied however there is an heterogeneous range of results. Thus some authors detect no significant variation in CCT with age [19-22]. On the contrary, significant correlation between age and CCT in emmetropic eyes have been reported (CCT tended to diminish with age)[23]. Consistent with this former report, a reduction in CCT with age in a sample of subjects from Thailand has been communicated and higher CCT in those subjects aged 40y than those aged 10-39y have been registered along with a significant negative correlation in peripheral corneal thickness[24,25]. With regard to ethnicity and age a study comparing Black American and Caucasian children, showed that the former have significantly thinner corneas detecting an increase in CCT with age in both race groups [26]. In a study in which high altitude hypoxic conditions were simulated, Karadag *et al* [27] observed that such conditions induced a significant increase in the CCT of subjects of a mean age of 32y but this was not detected in a group of subjects whose mean age was only 23y. Other studies have analyzed the relationship between refraction and corneal thickness: Linke *et al* [28] did detect weak yet significant correlation between CCT, refractive state or minimum corneal thickness and age. Kotecha *et al* [29] also studied the correlation between the biomechanical properties of the cornea using the ocular response analyzer and reported that the corneal constant factor (CCF), which increases with increasing corneal thickness, diminished with age. Finally, Gwin *et al* [30] detected a significant relationship between endothelial cell loss and an increasing CCT in the canine cornea.

Using the Pentacam, Khoramnia *et al* [13] determined CCT and minimal corneal thickness and noted that the latter point was located in the inferior-temporal quadrant in 92% of cases and observed the independence on age of corneal measurements.

Our approach was different in that we first characterized the anatomical location of the points of central and minimum thickness in relation to the corneal apex. This was done by determining their absolute distances from this point and their distances to an axis of coordinates centered at the apex. Both models of multivariate linear regression indicated that the distance between the point of minimal thickness and the corneal apex was correlated only with corneal volume, with a 0.024 mm reduction in this distance recorded for each 1 mm^3 increase in corneal volume. In contrast, central corneal thickness was not influenced by any of the possible predictive factors considered. Further, neither did these factors (age, sex, keratometric power and orientation along with CCT itself) have any effect according to our multinomial logistic regression on the location of the points of minimal and central corneal thickness in the different quadrants. When interpreting these results, however, it should be remembered that our study sample was comprised solely of healthy Spanish subjects. Hence, further work is needed to determine if our results could be extrapolated to other ethnic populations or patients with glaucoma or a corneal disease. Another issue that must be taken into account is the advanced mean age of our sample which was a consequence of the origin of our volunteers although the regression models did not found any impact of the age in the location of the corneal points studied. Our findings regarding the relatively constant position of MT, along with Koramnia *et al*'s [13] results and with the fact that the thickness of this point has shown some discriminating capacity between healthy subjects and patients with POAG, suggests this point could have anatomical entity.

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