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Anterior chamber parameters in early and advanced keratoconus. A meridian by meridian analysis

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ABSTRACT

Purpose: To explore anterior segment changes with keratoconus onset and progression to determine whether structural changes are predominantly corneal, limbal or both. To investigate these changes in different corneal meridians.

Method: Eighty-four eyes with keratoconus and 49 healthy eyes were included in the study. Eyes with keratoconus were divided in two groups according to the Amsler-Krumeich classification: stage I and stages II–IV. Scheimpflug images at three different meridians were used to evaluate the following parameters: anterior chamber depth from the endothelium (ACD_end) and corneal thickness (CT) (software provided), anterior chamber depth (ACD) and sagittal depth (SAGT) from the epithelium, and distance from the end point of SAGT to the anterior surface of the lens (DL) (measured manually), and [ACD – CT] and [SAGT – CT] (calculated). Changes in these parameters with ocular condition and meridian were analysed.

Results: Statistically significant larger values were found of ACD ($p = 0.012$) and DL ($p = 0.016$) with keratoconus onset and progression, with no differences in SAGT values. Besides, [ACD – CT] and [SAGT – CT] were significantly larger in keratoconus eyes ($p < 0.001$ and $p = 0.003$, respectively). Significant differences (all $p < 0.001$) were found in SAGT, [SAGT – CT] and DL among meridians. Changes in these parameters with keratoconus onset and progression were similar in all meridians.

Conclusion: Considering the results from the three meridians under investigation, it may be concluded that keratoconus onset has an impact on the anterior segment as a whole and not only on corneal structures. The DL distance is a useful parameter to describe limbal changes in keratoconus.

1. Introduction

Keratoconus is an ectatic corneal disorder, characterized by progressive thinning of the stroma and cone-like protrusion, which may lead to irregular astigmatism, myopia and severe visual impairment [1]. Although corneal topography has traditionally been the most sensitive method used to detect keratoconus [1], tomography (e.g., a Scheimpflug based imaging system such as the Pentacam, Optikgeräte Oculus GmbH, Wetzlar, Germany) is currently the best and most widely available technique to diagnose early keratoconus [2]. The Pentacam Imaging System, and other instruments, such as, the Visante (Carl Zeiss, Dublin, CA) anterior segment optical coherence tomographer (OCT), capture information of the anterior segment of the eye, from the anterior surface of the cornea to the lens, and assess several corneal and anterior chamber parameters [3]. Besides, relevant additional information may be obtained with the analysis, given the appropriate software, of the raw images provided by most of these devices.

Recent studies have used various instruments based on Scheimpflug photography to measure several anterior segment parameters in healthy and keratoconic eyes, including anterior chamber depth [4] and corneal sagittal height, and new parameters have been recently introduced, such as the DL distance, defined as the distance from the endpoint of the sagittal height to the anterior surface of the lens [5]. In addition, Scheimpflug images have been used to measure corneal peripheral angles in healthy and keratoconic eyes in different corneal meridians [6]. The findings of these and similar studies [7,8] suggest that keratoconus is accompanied by central and peripheral corneal involvement and by changes in the scleral shape, adjacent to the limbus. It has also been shown that the evaluation of corneal and anterior segment parameters may be useful for the characterization of the peripheral cornea, the limbal and the near limbus scleral zone, and, therefore, to gain a better understanding of the morphological changes in keratoconus [5–10].

The purpose of the present analysis was to further the exploration of

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the anterior segment geometry in keratoconus. We aimed at determining whether structural changes are predominantly corneal, limbal/scleral, or a combination of both, and at assessing possible differences amongst anterior segment meridians. This information may be useful when designing new contact lens fitting strategies for keratoconic eyes, either as an alternative or a complement to the traditional approach based on the assessment of corneal radii.

2. Material and methods

2.1. Study sample

The study sample included eyes with different stages of keratoconus. The same corneal specialist diagnosed and classified all the eyes according to the Amsler-Krumeich classification [1]. Eyes that had a history of ocular or refractive surgery, contact lens wear, ocular trauma or corneal pathology other than keratoconus were excluded from the study. In addition, a group of healthy eyes was included as a control group. All participants provided their written informed consent after explanation of the study procedures. The study followed the tenets of the Declaration of Helsinki (as revised in Tokyo in 2004) and was approved by an ethics review board.

2.2. Procedure

The Pentacam Scheimpflug System (software version 1:20), calibrated according to the recommendations of the manufacturer, was used to measure several anterior segment parameters. An experienced examiner captured three consecutive images from each eye, whereupon the mean of the measurements was used for statistical analysis.

The corresponding software was employed to determine the anterior chamber depth from the corneal endothelium (ACD_end) and central corneal thickness (CT). In addition, Scheimpflug images corresponding to the 0°–180°, 45°–225°, and 135°–315° meridians were selected to manually measure (with calipers) the anterior chamber depth from the epithelium (ACD) and the sagittal depth from the epithelium (SAGT) at each of these meridians. For this purpose, first, a line parallel to the lens was drawn from limbus-to-limbus at each meridian. The limbus was identified with the Pentacam software option “Show Pixel Edge” that marks the boundary of structures in Scheimpflug images. The length of this chord was considered as the corneal diameter for each meridian, and the one corresponding to the 0°–180° meridian was defined as the horizontal corneal diameter (HCD). Then, the corneal apex was located by drawing a second line parallel to the first one and tangential to the cornea. Thus defined, the apex represents the anterior corneal point of maximum vertical separation or elevation with reference to the limbus-to-limbus chord, which may not necessarily correspond to the point of maximum curvature or elevation with reference to a best fit sphere. Finally, starting from the corneal apex, measurements were conducted using a perpendicular vertical line to define two distances: from the apex to the anterior surface of the lens (ACD), and from the apex to the limbus-to-limbus line (SAGT). The values in mm of these distances, as illustrated in Fig. 1, were recorded.

Table 1
Anterior segment parameters assessed in keratoconus and healthy eyes (the source of each parameter, either provided by the software, measured on the Scheimpflug image, or derived from calculation from other parameters is shown).

Anterior Segment Parameters	Abbreviation
(provided by the Pentacam software)	
Anterior chamber depth from corneal endothelium	ACD_end
Central corneal thickness	CT
(measured on the Scheimpflug images)	
Anterior chamber depth from the epithelium	ACD
Sagittal depth from the epithelium	SAGT
Horizontal corneal diameter	HCD
(derived from other parameters)	
Distance to the lens[a] (ACD – SAGT)	DL
Measured anterior chamber depth from the endothelium	[ACD – CT]
Sagittal depth from the endothelium	[SAGT – CT]

[a] Distance from the endpoint of the sagittal height at the limbus-to-limbus chord to the anterior surface of the lens.

Subsequently, calculation was employed to determine several additional parameters, as previously described in the literature [5]: the distance DL, corresponding to the distance between the limbus-to-limbus chord at that meridian and the anterior surface of the lens, that is, ACD – SAGT; the anterior chamber depth from the endothelium [ACD – CT] and sagittal depth from the endothelium [SAGT – CT]. Table 1 shows a summary of all the previously described parameters.

It may be noted that the Pentacam system may not be free of error when conducting this type of measurements. Thus, on the one hand, the change in reflectivity used to determine the location of the limbus might not always represent the actual limbal location, as reflection actually denotes change in density, not geometric transition. On the other hand, absolute values of anterior chamber parameters measured through the cornea may not represent real values, as the Pentacam software provides a correction to account for light refraction. However, this source of error may be considered negligible in the framework of relative values, that is, when comparing the same parameter between different eyes.

2.3. Data analysis

Statistical analysis was conducted with the Minitab 17 Statistical Software (AppOnFly, Inc., San Francisco, CA). Data was first examined for normality with the Kolmogorov–Smirnov test, revealing the occurrence of a normal distribution. Accordingly, results are described as mean ± standard deviation (SD). The correlation between the values of [ACD – CT] at each meridian and the corresponding values of ACD_end was examined with a Pearson coefficient of correlation test. Age, HCD and CT values underwent a variance analysis (ANOVA),

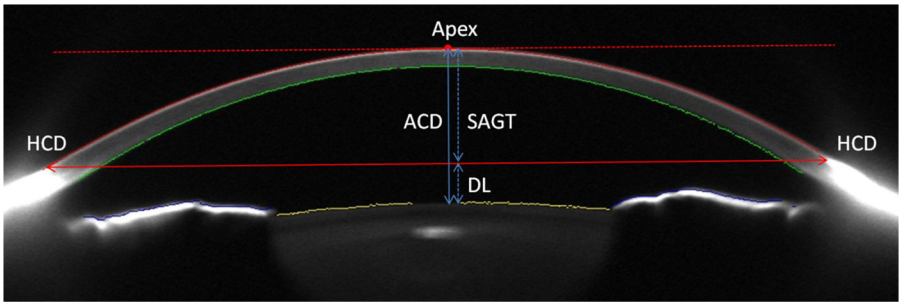

Fig. 1. Lines manually drawn and parameters measured on the Scheimpflug images for each meridian: corneal apex, limbus-to-limbus distance at the horizontal meridian (HCD), sagittal depth (SAGT) and anterior chamber depth from the epithelium (ACD). The DL distance is also shown.

considering "Ocular condition" as independent variable or factor: healthy eyes (A0); keratoconic eyes at Amsler-Krumeich stage I (A1) and keratoconic eyes at Amsler-Krumeich stages II–IV (A2). Finally, the parameters ACD, [ACD – CT], SAGT, [SAGT – CT] and DL underwent a two way ANOVA with “Ocular condition” (A0, A1 and A2) and “Meridian” (M0: 0°–180°; M45: 45°–225°; and M135: 135°–315°) as factors. Pair-wise analysis was performed with the Tukey test. A P value of 0.05 or less was defined as the cut-off point for statistical significance.

3. Results

3.1. Study sample demographics

Eighty-four eyes with keratoconus (40 right eyes and 44 left eyes) from 84 patients (47 females) were included in the study: 39 eyes (patients aged 32.9 ± 11.0 years) were at stage I (A1), and 45 eyes (patients aged 36.7 ± 16.2 years) were at stages II to IV (A2), including 23 eyes at stage II, 9 eyes at stage III, and 13 eyes at stage IV, according to the Amsler-Krumeich classification. In addition, 49 healthy (A0) eyes (23 right eyes and 26 left eyes) from 49 subjects (aged 32.4 ± 12.2 years; 25 females) were included as a control group. No statistically significant differences were found in neither age ($p = 0.253$) nor horizontal corneal diameter ($p = 0.069$) among the three groups.

3.2. Correlation analysis

Statistically significant linear correlations were found at each meridian between the [ACD – CT] values measured on the Scheimpflug images and the parameter ACD_end provided by the Pentacam software ($p < 0.001$ in all meridians). The coefficient of determination values were $R^2 > 0.94$ and the slopes of the regression equations were close to 1, with the *y*-intercept tending to zero (given x = [ACD – CT] and y = ACD_end, then $R^2 = 0.949$ and $y = -27.46 + 1.009x$ in M0, $R^2 = 0.943$ and $y = 28.12 + 0.9958x$ in M45, and $R^2 = 0.973$ and $y = 42.77 + 0.9938x$ in M135).

3.3. Corneal thickness

Corneal thickness values for each ocular condition group were: 554.7 ± 35.4 µm for A0, 517.5 ± 45.6 µm for A1 and 461.5 ± 65.9 µm for A2. An ANOVA test revealed statistically significant differences among groups, which were also found between each pair of groups with the Tukey test (all $p < 0.001$).

3.4. Ocular condition and Meridian analysis

With the onset and progression of keratoconus, statistically significant differences were found in ACD, DL, [ACD – CT] and [SAGT – CT], with larger values in the later stages of the condition. Conversely, no statistically significant group differences were found in SAGT. A summary of these measurements, the ANOVA results and the subsequent pair-wise analyses is provided in Table 2.

No significant differences were found in ACD and [ACD – CT] among meridians, in contrast with the parameters SAGT, DL and [SAGT – CT]. Thus, SAGT values were smaller in M45 and M135 than in M0. Accordingly, the DL distance was larger in M45 and M135 than in M0. A summary of these results and the corresponding ANOVA and Tukey analysis is shown in Table 3.

Finally, no interaction effect of the factors Ocular condition × Meridian was discovered for any of the parameters under evaluation ($p = 0.987$ for ACD; $p = 0.987$ for [ACD – CT]; $p = 0.537$ for SAGT; $p = 0.558$ for [SAGT – CT]; $p = 0.900$ for DL).

Table 2
Summary of anterior segment parameters obtained from Scheimpflug images for healthy (A0) and keratoconic eyes (A1: stage I; A2: stages II–IV). Results are displayed as mean ± SD. Outcomes of the ANOVA test are shown for each parameter. Statistically significant pair-wise differences are shown with different letters in the grouping columns.

Condition	(mean ± SD) (µm)	Grouping	(mean ± SD) (µm)	Grouping
	ACD ($p = 0.012$)		ACD – CT ($p < 0.001$)	
A0	3725 ± 403	A	3170 ± 400	A
A1	3838 ± 416	AB	3324 ± 419	B
A2	3872 ± 362	B	3421 ± 360	B
	SAGT ($p = 0.370$)		SAGT – CT ($p = 0.003$)	
A0	2999 ± 289		2444 ± 290	A
A1	3040 ± 287		2526 ± 306	B
A2	3005 ± 288		2554 ± 288	B
	DL ($p = 0.016$)			
A0	726 ± 355	A		
A1	798 ± 400	AB		
A2	867 ± 375	B		

Table 3
Summary of anterior segment parameters obtained from Scheimpflug images for each meridian (M0, M45, M135). Results are displayed as mean ± SD. Outcomes of the ANOVA test are shown for each parameter. Statistically significant pair-wise differences are shown with different letters in the grouping columns.

Meridian	(mean ± SD) (µm)	Grouping	(mean ± SD) (µm)	Grouping
	ACD ($p = 0.811$)		ACD – CT ($p = 0.840$)	
M0	3823 ± 392		3314 ± 398	
M45	3810 ± 394		3303 ± 406	
M135	3787 ± 413		3278 ± 421	
	SAGT ($p < 0.001$)		SAGT – CT ($p < 0.001$)	
M0	3169 ± 273	A	2660 ± 279	A
M45	2924 ± 258	B	2416 ± 272	B
M135	2916 ± 253	B	2407 ± 265	B
	DL ($p < 0.001$)			
M0	654 ± 387	A		
M45	886 ± 344	B		
M135	870 ± 358	B		

4. Discussion

The present study aimed at investigating the impact of keratoconus on the different anatomical structures of the anterior segment of the eye. To gain a better understanding of the corneal versus limbal alterations in keratoconus, the “anterior chamber depth” parameter was divided into a corneal portion, corresponding to the sagittal length from the epithelium (SAGT) and a limbal portion, defined as the distance DL, or the distance between the end point of SAGT and the anterior surface of the lens. This distance was defined and explored in detail in a previous publication [5], in which it was reported that the increase in anterior chamber depth observed in keratoconic eyes could be largely attributed to an actual increase in the DL distance, thus documenting a limbal impact of keratoconus, in addition to the previously observed corneal alterations. In the previous study, in which keratoconic and healthy eyes were compared, all measurements were conducted on Scheimpflug images corresponding to the horizontal or 0–180° meridian, defined as the HCD in this investigation. The purpose of the present study was to complement the previous investigation by exploring two oblique meridians, in addition to 0–180°, and to recruit a larger sample of patients including healthy, incipient and advanced keratoconus.

The present results provide validation to the consistency of the manual measurement method employed in the study. Thus, on the one

hand, as expected, the values of ACD in each meridian are very similar, with no statistically significant differences among them (Table 3). On the other hand, the correlation analysis revealed a strong statistically significant correlation between the values of [ACD – CT] measured on the Scheimpflug images in each meridian and the parameter ACD_end provided by the Pentacam software ($R^2 > 0.94$ and slopes close to 1 in the regression equations, with the independent terms tending to zero (< 1.7% of minimum [ACD – CT]).

4.1. Ocular condition

Measurements obtained from the corneal epithelium revealed that the increase in anterior chamber depth in keratoconic eyes, when compared with healthy eyes, appears to originate mainly from an increase in DL distance. Indeed, as may be observed in Table 2, the average ACD of the eyes with advanced keratoconus is 147 μm greater than the ACD of healthy eyes, a difference matching very closely the difference in DL distance (141 μm) between the same eye groups. In addition, the corneal portion represented by sagittal depth values (SAGT) did not show any statistically significant differences among eye groups (the maximum average difference was of 1.6%).

However, it must be noted that when corneal thickness is subtracted from ACD values, that is, when the reference point for measurements is the endothelium, the corresponding increase in anterior chamber depth from the endothelium [ACD – CT] in keratoconic eyes is associated with an increase in the values of both [SAGT – CT] and DL. Therefore, pooling measurements obtained in the three meridians under evaluation, it may be concluded that the changes produced by the emergence of keratoconus not only affect the corneal portion of the eye, but the entire anterior segment, as previously suggested [6,7]. Indeed, Piñero et al. [7], using the recently available corneo-scleral topographer Eye Surface Profiler (Eaglet Eye b.v., Houten, The Netherlands) also reported significant correlations between several corneal and scleral parameters, particularly in those patients presenting more advanced keratoconus. Our findings also show that the increase in [ACD – CT] and [SAGT – CT] values with keratoconus progression is not significant, and that the increase in the DL distance is only significant when comparing advanced keratoconus and healthy eyes.

The significant decrease in CT values with the onset and progression of keratoconus is not unexpected, as this parameter is used in the Amsler-Krumeich classification [1] to group keratoconic eyes according to the severity of the condition. In effect, the obtained CT values, ranging from 554.7 μm in healthy eyes to 461.5 μm in eyes with advanced keratoconus, are in agreement with those reported in previous studies [11,12]. It may be observed that the reduction in CT values balances the increase in internal sagittal depth [SAGT – CT] caused by the ectasia, resulting in unchanged external sagittal depth (SAGT) values.

4.2. Meridian

Anterior eye measurements at the different meridians revealed that SAGT values at the horizontal M0 meridian were significantly larger than those measured at the oblique meridians M45 and M135, which matched closely. Given a common reference plane at the anterior surface of the lens, the DL distances at the various meridians not unexpectedly presented the opposite behaviour, with values significantly larger, and similar, at the M45 and M135 meridians, and smaller at the M0 meridian. These findings provide evidence that the corneal-limbal transition in the horizontal meridian is located more posteriorly than in the oblique meridians. Thus, the base of the cornea is not contained in a single plane, although the similarity of the M45 and M135 SAGT values denotes a certain level of symmetry. The values of sagittal depth summarized in Table 3 are in agreement with those obtained by Hall and co-workers in a cross-sectional study of patients in the United Kingdom [13]. These authors used an OCT for their measurements, obtaining significantly larger sagittal depth values in the horizontal 3.17 ± 0.20 mm than in the vertical 3.09 ± 0.27 mm meridian.

4.3. Interaction ocular condition × Meridian

No significant interactions were revealed of the factors Ocular condition × Meridian in any of the parameters under evaluation. This finding gives support to a generalized involvement of the totality of the anterior segment of the eye in keratoconus, that is, keratoconus onset and progression has a similar impact in all meridians.

In conclusion, keratoconus onset leads to an increase in depth of the anterior chamber [ACD – CT] which is accompanied with larger values of both [SAGT – CT] and DL, that is, both corneal and limbal structures are affected by the disease, irrespective of the meridian under investigation. The DL distance was found to be a useful parameter to describe limbal changes in keratoconus, thus allowing for a more complete characterization of anterior segment changes. These findings may be of relevance when determining the best parameters for new contact lens designs, particularly in patients with more advanced forms of keratoconus in whom the correct selection of sagittal depth and landing zone angle may prove critical to fitting success.

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