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Original research

Anterior segment characteristics in normal and keratoconus eyes evaluated with a combined Scheimpflug/Placido corneal imaging device

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Abstract

Purpose: To assess the anterior segment parameters of keratoconus (KC) eyes at different stages of the disease by a new Scheimpflug camera combined with Placido disk corneal topography (Sirius, CSO, Italy) in a sample of the Iranian population.
Methods: A total of 225 eyes of 225 individuals comprising 41 suspect KC, 40 mild KC, 71 moderate KC, 48 severe KC and 25 normal eyes were assessed for the following parameters: corneal thickness at the apex (CTA), thinnest corneal thickness (TCT), anterior chamber depth (ACD), corneal volume (CV), corneal keratometry (K), corneal asphericity (Q), and corneal elevation in the anterior and posterior surface. Also, the Zernike coefficients for the corneal aberrations including total root mean square (RMS), RMS Coma, RMS spherical aberration (SA), RMS Astigmatism, Baiocchi Calossi Versaci front index (BCV_f), and BCV back index (BCV_b) were noted for all eyes. Data was analyzed using analysis of variance (ANOVA) and post hoc Bonferroni test for comparison of the means of the five groups. P-value was considered significant if it was <0.05.
Results: The TCT, CTA and posterior corneal elevation were significantly different between all comparison groups ($P < 0.05$). ACD values showed inconsistent differences between groups. Mean value of CV in comparing normal eyes vs suspect KC group, normal eyes vs mild KC, and normal eyes vs moderate KC revealed statistically significant change ($P < 0.05$). Also, weak non-significant positive correlation was demonstrated between K and CV ($r = 0.08$). There were statistically significant differences in total RMS, RMS coma, BCV_f, and BCV_b for most groups ($P < 0.05$).
Conclusion: Posterior corneal elevation, corneal thickness and high order aberrations are important indices that need to be considered to diagnose different grades of keratoconus.

Keywords: Cornea; Keratoconus; Topography

Introduction

Detection of suspect keratoconus among refractive surgery candidates is important because keratorefractive procedures may lead to post-surgery ectasia in these eyes. The increasing volume of patients interested in refractive surgery and the new treatment options available for keratoconus have generated a higher interest in achieving a better characterization of this pathology.[1] Keratoconus is a bilateral non-inflammatory progressive disorder characterized by corneal ectasia and thinning.[2−4] Detecting moderate and advanced keratoconus is not difficult using corneal topography, biomicroscopic, retinoscopic and pachymetric findings.[3] Several indices have been proposed to help in the diagnosis of keratoconus and subclinical keratoconus with different topography systems.[5−13] They include quantitative descriptors such as the keratometry (K), inferior−superior (I−S) value, astigmatism (KISA)% index proposed by Rabinowitz and Rasheed[8] and the Keratoconus

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Prediction Index and Keratoconus Index proposed by Maeda et al[14] Smolek and Klyce,[7] developed a neural network classification based on corneal topography indices. Other detection schemes based on Zernike decomposition of the anterior corneal surface have been described by Schwiegerling et al[15] and Langenbucher et al[16] With the Scheimpflug imaging system, corneal elevation in the anterior and posterior corneal surface are being investigated and research debated which of the corneal surfaces had higher sensitivity in detecting keratoconus.[11,17–20] Incorporating corneal thickness, corneal volume, and corneal curvature using a Scheimpflug camera have been evaluated in several other articles.[21,22] The Sirius system is a relatively new Scheimpflug-Placido topographer that combines a single-Scheimpflug rotating camera with Placido disk topography to measure and image the anterior eye segment. Within a single scan, it can simultaneously acquire more than 30,000 points on the anterior and posterior corneal surface and 25 radial sections of the cornea and anterior chamber.[23] Evaluation of keratoconic and normal eyes to determine all tomographic parameters including keratoconus indices, pachymetric graph values, and the posterior corneal elevation values may help to identify at-risk corneas. The purpose of our study was to evaluate and compare changes in the anterior segment of keratoconus eyes at different stages of the disease, the anterior and posterior corneal surface parameters, thickness profile data, and data from enhanced elevation maps of keratoconic and normal eyes with the Sirius Scheimpflug-Placido corneal tomography and to determine the sensitivity of these parameters in discriminating early keratoconus from normal eyes.

Methods

This study is a retrospective study of 200 patients (200 eyes) who were seeking refractive surgery in Bahman Hospital and had been diagnosed as clinical keratoconus. Twenty-five normal volunteer subjects (25 eyes) were included as a control group. This study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee, Tehran University of Medical Sciences, Iran. All patients included in the study were informed about the purpose of the study and provided informed consent. Subjects were recruited from consecutive patients who were admitted to the private hospital (Bahman Hospital, Tehran, Iran) for ocular examination between October 2014 and October 2015. For analysis, keratoconus eyes have been classified into 4 subgroups according to Amsler-Krumeich classification.[24] Keratoconus suspect is a catchall term to indicate a patient with inferior or central steepening on topography with abnormal localized steepening or an asymmetrical bow-tie pattern, a normal-appearing cornea on slit-lamp biomicroscopy, and at least 1 of the following signs: steep keratometric curvature (>47.00 D), oblique cylinder greater than 1.50 D, central corneal thickness less than 500 mm, or clinical keratoconus in the fellow eye.[12,13,17,25,26] Eyes were considered normal if they had no ocular pathology, no previous ocular surgery, no significant refractive error, and no irregular corneal pattern. For this study, only one eye of each subject was chosen for the study according to a random-number sequence (dichotomic sequence 0 and 1). Exclusion criteria were: previous ocular surgery, corneal scarring, trauma, pregnancy or lactation, glaucoma, and causes of ocular astigmatism other than corneal i.e. lenticular astigmatism such as early cataract, lens subluxation, or lenticonus. Individuals with connective tissue disease, such as Marfan or Stickler syndrome, were also excluded from the study. In the current study, a comprehensive ocular examination including Scheimpflug-Placido topography (Sirius, CSO, Italy) using software version 1.0.5.72 was performed on all eyes. The Sirius is a new topography device that combines a monochromatic rotating Scheimpflug camera and a Placido disk. The scanning process acquires a series of 25 Scheimpflug images (meridians) and 1 Placido top-view image to analyze the anterior segment by obtaining 25 radial sections of the cornea and anterior chamber. Anterior surface data from Placido and Scheimpflug images are merged using a proprietary method. All other measurements for internal structures are derived solely from Scheimpflug data. A 475 nm ultraviolet-free blue light–emitting diode light is used to measure 35,632 points for the anterior corneal surface and 30,000 points for the posterior cornea. The system acquires the radius curvature measurements in the flat and steep meridians on a 3.0 mm-diameter field of the central cornea. The corneal power and astigmatism were calculated using the 1.3375 keratometric refractive index. Corneal aberrometry is obtained using the ray-tracing technique.[23,27] Measurements were performed by a single optometrist. The patient's eye was aligned along the visual axis using a central fixation light. Patients were instructed to blink between shots to keep eyes moist. The images were obtained with the automatic mode. Eye movement of the subject was constantly monitored by the system, and quality factor was automatically evaluated. In case of a poor-quality scan with movement artifacts and irregularities (e.g. due to misalignment or blinks during the scan), 1 more measurement was taken. In eyes with scans not attainable, artificial tears were added to allow better acquisition. In this study, the following parameters were evaluated: corneal thickness at the apex (CTA), the thinnest corneal thickness (TCT) defined as the thinnest point in the corneal thickness map, anterior chamber depth (ACD) defined as the distance from the corneal endothelium to the anterior surface of the lens capsule, corneal volume (CV) reported as the volume of the cornea in a diameter of 9 mm, centered on the anterior corneal apex, K in both the anterior and posterior corneal surface as well as steep and flat keratometry, corneal asphericity (Q) reported as the asphericity data provided by the Sirius and taken from 8 mm central cornea with reference to the anterior corneal apex, corneal elevation in both the anterior and posterior corneal surfaces with aspherotoric surface as a reference, and total root mean square (RMS) as quantitative comparisons of aberrations between different eyes. The compensation between corneal and internal aberrations was defined as: (total eye aberration RMS) that is calculated out to the 6th Zernike order for a 6.0-mm pupil diameter, RMS Coma, RMS spherical aberration (SA), RMS Astigmatism, Baiocchi Calossi Versaci front index (BCV_f) and BCV back

Table 1
Demographic features of patients.

Feature	Normal N = 25	Suspect N = 41	Mild KC N = 40	Moderate KC N = 71	Severe KC N = 48
Age Mean ± SD	28.7 ± 7.0	25.4 ± 8.3	24.9 ± 9.6	27.2 ± 7.5	28.6 ± 6.7
Sex Male%	56%	58.5%	45%	52.1%	41.6%
Eye Rt/Lt	14/11	19/22	21/19	38/33	26/22

KC: Keratoconus, Rt: Right, Lt: Left.

index (BCV_b), vertical trefoil $c3^{-3}$, vertical coma $c3^{-1}$, horizontal coma $c3^{+1}$, primary spherical aberration $c4^0$, and second order vertical coma $c5^{-1}$. BCV_f, which is expressed in micrometers, was obtained by properly combining these coefficients (from the anterior corneal surface) and weighting them by a function of the coma axis. Likewise, a linear combination of $c3^{-3}$, $c3^{-1}$, $c3^{+1}$, $c4^0$, $c5^{-1}$, and information about the coma axis on the posterior Zernike decomposition were used to define the BCV_b. Also, repeatability of the BCV_f and BCV_b indices and the anterior and posterior corneal powers (in central 3.0 mm zone) were recorded. Data were analyzed using Intercooled STATA version 9.2 for Windows (StataCorp, College Station, Texas (TX)). All statistical tests were two-tailed, and $P < 0.05$ was considered statistically significant. The baseline characteristics of age and anterior segment parameters were compared among the groups using one-way analysis of variance (ANOVA) (with least significance difference *post hoc* comparison to compare anterior segment parameters between the different groups) whereas sex differences among the groups were compared using the chi-square test. When the data were not normally distributed, Kruskal−Wallis test and Mann−Whitney test were used. Pearson correlation coefficients (r) were used to assess the correlation of the steep anterior keratometry and other anterior segment parameters. The correlations were considered weak, moderate, or strong according to the following criteria: strong for r between 0.7 and 1.0, moderate for r between 0.3 and 0.7, and weak for r below 0.3. For this study, subjects were separated into ten groups. G1 compared normal eyes vs. suspect keratoconus (KC), G2 compared normal eyes vs. mild KC, G3 compared normal eyes vs. moderate KC, G4 compared normal eyes vs. severe KC, G5 compared suspect KC vs. mild KC, G6 compared suspect KC vs. moderate KC, G7 compared suspect KC vs. severe KC, G8 compared mild KC vs. moderate KC, G9 compared mild KC vs. severe KC, and G10 compared moderate KC vs. severe KC. Comparisons between all groups were performed separately to the effective factors between the groups reduced.

Results

A total of 225 individuals comprising 41 (18.22%) suspect KC, 40 (17.77%) mild KC, 71 (31.55%) moderate KC, 48 (21.33%) severe KC, and 25 (11.11%) normal eyes were analyzed. Demographic features of patients with normal eyes as a control group along with the suspect KC and the other three groups of KC are stated in Table 1. There were no significant differences in sex ($P = 0.28$) or age ($P = 0.47$) among the five groups. Tables 2 and 3 show anterior segment characteristics and corneal aberrations, respectively. According to Tables 2 and 3, all parameters showed statistically significant differences between all groups ($P < 0.0001$, one-way ANOVA). As expected, the thinnest corneal thickness and corneal thickness at the apex were significantly different in all comparison groups ($P < 0.05$). In comparing suspect KC against the mild KC, most of the parameters, except for the anterior corneal power reading, were not statistically significant ($P > 0.05$). As presented in Table 4, the comparing of corneal volume in normal eyes vs suspect KC group (G1), normal eyes vs mild KC (G2), and normal eyes vs moderate KC group (G3) was statistically significant (P = 0.03, 0.001, and 0.002, respectively). ACD values between the five groups showed inconsistent differences. Posterior corneal elevation between all groups, except for G5, was significant ($P = 0.0001$). According to Table 5, comparisons of corneal aberrations parameters such as total RMS, RMS coma, BCV_f, and BCV_b for most groups, except for Group 5 (G5), were statistically significant ($P = 0.0001$). Correlation of steep anterior keratometry in all parameters, except for corneal volume, were significant. As expected, steep keratometry revealed a negative correlation with the thinnest corneal point and thickness at the

Table 2
Anterior segment parameters and their comparisons between groups.

Parameters mean ± SD	Normal N = 25	Suspect N = 41	Mild KC N = 40	Moderate KC N = 71	Severe KC N = 48
Thinnest location (μm)	525.7 ± 38.7	486.4 ± 41.2	475.1 ± 40.4	443.5 ± 49.2	384.2 ± 57.1
CTA (μm)	578.1 ± 62.0	529.4 ± 56.2	507.1 ± 61.5	473.9 ± 53.6	421.1 ± 68.9
ACD (mm)	3.1 ± 0.2	3.2 ± 0.3	3.2 ± 0.3	3.3 ± 0.2	3.6 ± 0.3
CV (mm^3)	56.6 ± 3.9	52.3 ± 4.0	53.6 ± 4.0	53.9 ± 4.1	55.2 ± 4.7
Anterior mean K	42.2 ± 1.1	42.5 ± 1.3	45.0 ± 1.19	47.2 ± 1.9	55.5 ± 6.1
Posterior mean K	−5.9 ± 0.3	0.45 ± 5.9	1.1 ± 6.2	0.7 ± 6.8	0.1 ± 8.6
Anterior elevation	4 ± 2.2	9 ± 9.1	12 ± 9.9	17 ± 12.2	32 ± 20
Posterior elevation	9.7 ± 3.6	17.8 ± 11.7	18.9 ± 9.3	28.2 ± 17.6	54.7 ± 28.9

CTA: Corneal Thickness at the Apex, ACD: Anterior Chamber Depth, K: Keratometry, KC: Keratoconus, CV: Corneal volume.

Table 3
Corneal aberrations parameters and their comparisons between groups.

Parameters mean ± SD	Normal N = 25	Suspect N = 41	Mild KC N = 40	Moderate KC N = 71	Severe KC N = 48
Corneal asphericity (Q)	0.2 ± 0.1	0.3 ± 0.3	0.5 ± 0.4	0.9 ± 0.6	1.7 ± 0.8
Total RMS	0.4 ± 0.2	0.5 ± 0.4	0.7 ± 0.6	1.2 ± 0.7	3.4 ± 2.5
RMS Spherical aberration	0.1 ± 0.1	0.1 ± 0.1	0.2 ± 0.2	0.2 ± 0.2	0.7 ± 0.7
RMS coma	0.2 ± 0.1	0.3 ± 0.2	0.5 ± 0.6	0.9 ± 0.7	2.2 ± 1.5
RMS Astigmatism	0.1 ± 0.7	1.6 ± 1.4	2.3 ± 2.6	4.1 ± 3.4	6.6 ± 5.6
BCV_f	0.2 ± 0.2	0.8 ± 0.8	1.1 ± 0.9	2.3 ± 1.6	5.4 ± 3.0
BCV_b	0.1 ± 0.2	0.9 ± 0.8	1.3 ± 1.3	2.5 ± 1.7	5.0 ± 3.2

RMS: Root Mean Square, BCV_f: Baiocchi Calossi Versaci front index, BCV_b: Baiocchi Calossi Versaci back index, KC:Keratoconus.

apex (Table 6). There was a strong positive correlation between the steep anterior keratometry and all corneal aberrations (P = 0.0001).

Discussion

Accurate and precise determination of the anterior ocular segment is fundamental to many clinical and research applications in ophthalmology[27−33]. The Sirius device is non-contact and easy to use and showed good repeatability of the anterior segment measurements in healthy eyes as well as those after refractive surgery or with keratoconus.[27,32,33] As far as we are concerned, this is the first retrospectively designed comparative study of the differences and agreement of the measurement of the anterior segment using the Scheimpflug-Placido Sirius topographer in monitoring and determining the management of KC in an Iranian population. There have been numerous attempts by various authors to differentiate subclinical KC from normal eyes.[28] The detection of KC at the earliest preclinical stages is typically very difficult. The term suspect KC typically refers to the early stage of KC where there are no noticeable signs on slit-lamp biomicroscopic examination, but subtle changes can be detected via topographic and pachymetric features, similar to clinical KC.[24,29,31] This early detection may aid in early management decisions of the disease (by methods such as collagen cross-linking) and thus improve quality of life by virtue of delaying (if not eliminating) the need for subsequent corneal transplantation. This study showed that several indices derived from Sirius measurements, including pachymetric readings and the anterior and posterior corneal power along with the posterior corneal elevation, are helpful in discriminating eyes in different degrees of keratoconus from normal eyes. The TCT and posterior corneal elevation seem to be the best indices in discriminating suspect keratoconus from normal eyes. As progressive corneal thinning is a well-known pathophysiological feature of KC, decrease of CCT and TCT are important signs of KC progression in the current study and would be beneficial in monitoring KC.[20] These findings are in agreement with the Piñero et al[22] study that showed that the mean CCT and TCT in a suspect KC group were significantly lower than normal eyes and higher than the KC group. Schlegel et al.'s[12] study used the Orbscan IIz slit-scanning topography on 60 normal myopic patients and 48 suspect keratoconus patients. They found that the differences between the suspect keratoconus group and normal eyes group were statistically significant for corneal pachymetric values. In contrast, Rao et al[34] did not find significant differences in the mean central and thinnest point pachymetry values between suspect keratoconus patients and the control group, while Nilforoushan et al[13] reported that the suspect keratoconus group had thinner pachymetry using the Pentacam imaging. In the current study, we reported that in corneal thickness at apex and at the thinnest location between the suspect keratoconus and keratoconus eyes compared with normal eyes, there were significant differences. In our study, the value of ACD in the normal group is slightly lower than those of Edmonds et al[35] (3.13 ± 0.29 versus 3.18 ± 0.32 mm). Our results showed a progressively increasing and significant change in ACD values in mild, moderate, and severe KC eyes, with the highest values

Table 4
Multiple comparisons of anterior segment parameters between groups.

Parameters	G1	G2	G3	G4	G5	G6	G7	G8	G9	G10
ACD	0.84	0.34	<0.001	0.006	1.00	0.62	<0.0001	1.00	<0.0001	<0.0001
Thinnest location	<0.0001	<0.0001	<0.0001	<0.0001	1.00	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
CTA	<0.0001	<0.0001	<0.0001	<0.0001	0.18	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
CV	0.03	0.001	0.002	0.71	1.00	1.00	1.00	1.00	0.12	0.19
Anterior mean K	1.00	<0.0001	<0.0001	<0.0001	0.001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Posterior mean K	<0.0001	<0.0001	<0.0001	<0.0001	1.00	1.00	1.00	1.00	1.00	1.00
Anterior elevation	0.0001	0.0001	0.0001	0.0001	0.16	0.0001	0.0001	0.0001	0.0001	0.0001
Posterior elevation	0.0001	0.0001	0.0001	0.0001	0.12	0.0001	0.0001	0.0001	0.0001	0.0001

CTA: Corneal Thickness at the Apex, ACD: Anterior Chamber Depth, K: keratometry, CV: Corneal Volume, G1 compared normal eyes vs. suspect KC, G2 compared normal eyes vs. mild KC, G3 compared normal eyes vs. moderate KC, G4 compared normal eyes vs. severe KC, G5 compared suspect KC vs. mild KC, G6 compared suspect KC vs. moderate KC, G7 compared suspect KC vs. severe KC, G8 compared mild KC vs. moderate KC, G9 compared mild KC vs. severe KC, and G10 compared moderate KC vs. severe KC.

Table 5
Multiple comparisons of corneal aberrations parameters between groups.

Parameters	G1	G2	G3	G4	G5	G6	G7	G8	G9	G10
Total RMS	0.0007	0.0001	0.0001	0.0001	0.03	0.0001	0.0001	0.0001	0.0001	0.0001
Corneal asphericity (Q)	1.00	0.02	<0.0001	<0.0001	0.29	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
RMS Spherical aberration	0.51	0.48	0.002	0.0001	0.15	0.01	0.0001	0.0003	0.0001	0.0001
RMS coma	0.0001	0.0001	0.0001	0.0001	0.009	0.0001	0.0001	0.0001	0.0001	0.0001
RMS Astigmatism	0.98	0.001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
BCV_f	0.0001	0.0001	0.0001	0.0001	0.06	0.0001	0.0001	0.0001	0.0001	0.0001
BCV_b	0.0001	0.0001	0.0001	0.0001	0.20	0.0001	0.0001	0.0001	0.0001	0.0001

RMS: Root Mean Square, BCV_f: Baiocchi Calossi Versaci front index, BCV_b: Baiocchi Calossi Versaci back index.

in the latter group. These results are in agreement with the results of the study by Abolbashari et al[36] Corneal volume was recently investigated as an additive screening factor for keratoconus. It is noteworthy that CV has been proposed as a new index in diagnosing KC in the screening of refractive surgery patients. In the present study, the corneal volume measurements in eyes with mild to moderate keratoconus were significantly lower than those in a group of normal eyes, which was similar to most reported studies.[21,22,37,38] Pinero et al[22] reported inconsistent findings and found no significant difference in CV between control, subclinical, and clinical KC eyes or at varying stages of KC and suggested that in the early stages of the disease, redistribution of CV occurred, but without associated tissue loss, whereas in our study, there was a weak non-significant positive correlation between K value and CV ($r = 0.08$). Gordon-Shaag et al[39] reported that corneal higher order aberrations were significantly higher in keratoconic than normal eyes, but the results for suspect keratoconus were mixed. Corneal aberrometry has been established as a potential diagnostic tool for keratoconus. Several authors have reported significant amounts of higher order aberrations in this ectatic disease, especially vertical coma and coma-like aberrations.[24,30,39] This tendency was also observed in our study. We found that the values of the corneal higher order aberrations were significantly higher in the group of keratoconic eyes than normal eyes group. In spherical aberration, there was no difference between normal eyes, suspect KC, mild KC, and moderate KC, but spherical aberration was significantly higher in the severe group of KC. The study performed by Alio et al[24] showed that higher order aberrations of the anterior corneal surface can be used to detect grades keratoconus.[24] Also, our study demonstrated a progressive increase in BCV_f, BCV_b values (which are a combination of corneal high order aberrations) in suspect keratoconus and keratoconus eyes than normal eyes. Fam and Lim showed that the anterior corneal elevation parameters are clinically relevant measures for detecting keratoconus and suspected keratoconus eyes.[11] Previous studies reported that the anterior and posterior elevation were the most effective parameters for the diagnosis of keratoconus.[17,34] In the current study, we found that the posterior corneal elevation measured with the Sirius system is higher in subclinical keratoconus and keratoconus than normal corneas. In conclusion, the anterior segment measurements provided by the Sirius Scheimpflug camera–Placido corneal topography system were highly repeatable and can be used in clinical routine and for research purposes as a valuable tool in diagnosing KC, especially KC suspect and early KC.

Table 6
Correlation between steep anterior keratometry and other parameters.

Parameters	Correlation co-efficient	P-value
ACD (mm)	0.51	<0.0001
Thinnest location (μm)	−0.71	<0.0001
CT at apex (μm)	−0.57	<0.0001
Corneal volume (mm^3)	0.08	0.12
Anterior flat K	0.93	<0.0001
Posterior flat K	0.03	0.38
Posterior steep K	0.02	0.69
Anterior elevation	0.32	0.05
Posterior elevation	0.72	<0.0001

ACD: Anterior chamber depth, CT: Corneal thickness, K: Keratometry.

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