Evaluation and Comparison of Posterior Corneal Elevation Parameters in Different Grades of Keratoconus by Pentacam

Reyhane Shariati Moghaddam[1], Asgar Doostdar[2], Payam Nabovati[2], Abbasali Yekta[3], Mohammad-Mehdi Sadoughi[4], Ali Mirzajani[2], Mehdi Khabazkhoob[5]

[1] Noor Research Center for Ophthalmic Epidemiology, Noor Eye Hospital, Tehran, Iran

[2] Department of Optometry, Rehabilitation Research Center, Iran University of Medical Sciences, Tehran, Iran

[3] Refractive Errors Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

[4] Department of Ophthalmology, Shahid Labbafinezhad Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[5] Department of Medical Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Received: 11 Jun. 2021; Accepted: 21 Jan. 2022

Abstract- To evaluate and compare posterior corneal elevation data and anterior segment parameters in different grades of keratoconus by Pentacam. 114 eyes of 114 keratoconic patients (85 men and 56 women) with a mean age of 31.6±4.7 years were evaluated with a Pentacam Scheimpflug camera. Keratoconic eyes were divided into 3 groups or grades according to the maximum keratometry reading: mild or grade I (K=50 or less than 50 diopters [D]), moderate or grade II (K=50.0 to 55.0 D), and severe or grade III (K=55.0 D or higher). The posterior corneal parameters were obtained posterior. There were no statistically significant differences between keratoconus grades in terms of sex (*P*=0.661). Also, there were no statistically significant differences between 3 grades in terms of age (*P*=0.214). There were statistically significant differences in anterior keratometry readings (K), anterior chamber depth (ACD), anterior chamber angle (ACA), and all pachymetric corneal measurements between all groups. With the progression of the disease, posterior K readings and all posterior elevation measurements were statistically different between the three grades. However, there were no significant differences in pupil diameter, anterior chamber volume (ACV), and corneal volume (CV) between the three grades of keratoconus. According to the results of this study, height data of posterior elevation, when combined with corneal anterior segment parameter, could provide a useful keratoconus severity classification tool.

Acta Med Iran 2022;60(3):165-170.

Keywords: Keratoconus; Severity; Posterior corneal elevation; Pentacam; Anterior segment parameters

Introduction

Keratoconus (KCN) is an ectatic corneal disorder characterized in most cases by progressive corneal thinning that leads to corneal protrusion, irregular astigmatism, and decreased vision (1). Biomicroscopic examination and placid disk-based corneal topography are widely used methods for the clinical detection of KCN. Placid disk-based corneal topography can only evaluate the anterior surface of the cornea. However, more recent techniques such as scanning slit topography and rotating Scheimpflug imaging present more versatile applications and evaluate both anterior and posterior corneal elevation and curvature data (2,3).

In recent years, many studies (2-6) showed that corneal posterior elevation measurements in clinical KCN patients differ from normal or subclinical patients. All these studies found that posterior corneal elevation was significantly higher in clinical KCN than subclinical and normal eyes. However, its efficacy seemed to be lower for discriminating subclinical KCN from normal corneas. Nevertheless, posterior corneal elevation has been described by many authors as the most effective indicator of keratoconus (4,7,8). On the other hand,

Corresponding Author: A. Doostdar
Department of Optometry, Rehabilitation Research Center, Iran University of Medical Sciences, Tehran, Iran
Tel: +98 2182401615, Fax: +98 2182401615, E-mail address: doostdar.a@iums.ac.ir

accurate measurement of anterior segment parameters is of great importance in keratoconus due to the progressive changes in corneal morphology. Keratoconus is considered a contraindication to refractive surgeries due to the corneal alteration caused by these procedures (9); inadequate visual satisfaction with spectacles and contact lens intolerance necessitate further therapeutic interventions. Some approaches for KCN treatment are corneal cross-linking treatment (10,11), intracorneal segmented rings (Intacs) (12-14), and phakic IOLs implantation (15,16). As the disease aggravates, treatment alternative options become more limited for KCN patients. Thus, a thorough evaluation of the changes in posterior corneal elevation data and anterior segment parameters may provide more sensitive and specific criteria in the diagnosis, progression monitoring, surgical follow-up, and surgical success rate of keratoconus patients. In addition, combining posterior height data with anterior corneal parameters could lead to a more comprehensive grading tool of keratoconus severity.

This study was designed to evaluate posterior corneal elevation data and anterior segment parameters in three different grades of keratoconus using the rotating Scheimpflug camera Pentacam.

Materials and Methods

This comparative study enrolled patients examined at the keratoconus section of Noor Eye Hospital. 114 eyes of 114 patients (85 men and 56 women, mean age 31.6±4.7) diagnosed with manifest keratoconus were studied using Pentacam. All participants were informed about inclusion in the study and consent was taken from all volunteers, and the protocol of the study was explained to them. All patients had a complete clinical examination that included uncorrected visual acuity, best-corrected visual acuity, manifest refraction, keratometry, fundus, and slit-lamp evaluations. Clinical keratoconus detection was based on: scissoring reflex on retinoscopy, oil drop reflex on ophthalmoscopy, localized steepening of the cornea, external signs (Munson sign, Rizzutti phenomenon), and following clinical slit-lamp findings: Vogt striae, Fleischer ring, corneal apical scars, stromal thinning. All participants in the present study filled the criteria for manifest keratoconus. Based on maximum keratometry reading, eyes were placed into 1 of 3 groups as follows: mild or grade I (K=50 or less than 50 diopters [D]), moderate or grade II (K=50.0 to 55.0 D), and severe or grade III (K=55.0 D or higher).

The participants with systemic or ocular diseases, positive history of ocular surgery, severe dry eye were excluded from the study due to the effect of these conditions on corneal morphology. Patients who wore RGP lenses were asked not to wear their contact lenses from one month before Pentacam imaging, and those with soft contact lenses were asked not to wear their contact lenses two weeks before the examination.

The corneal evaluation was performed using a Scheimpflug imaging system Pentacam. Patients were asked to sit on a chair. The chin was placed on the chinrest, and the forehead was pressed against the forehead strap. Patients were instructed to keep both eyes open and look into the black spot located in the middle of the blue fixation beam. When the perfect alignment was obtained, the Pentacam system automatically took the Scheimpflug images. The following posterior corneal data were obtained: posterior keratometry readings (max, min), central posterior corneal elevation, maximum posterior elevation (in 3mm zone), and maximum posterior elevation (in 5mm zone). Anterior corneal parameters were as follows: anterior k readings (max, min), thinnest corneal thickness (TCT), central corneal thickness (CCT), and apical corneal thickness (ACT) anterior chamber depth (ACD), corneal volume (CV), anterior chamber volume (ACV), and anterior chamber angle (ACA), pupil diameter (PD).

Statistical analysis was performed using SPSS software. The normality of all data samples was first checked by the Shapiro-Wilks test. When the parametric analysis was possible, 1-way analysis of variance (ANOVA) was used to compare anterior and posterior parameters between three groups of eyes. The Pearson correlation test was used to evaluate the correlation of parameters. Categorical variables were analyzed with the Chi-square test. All data were reported as means±standard deviation.

Ethical issues

The Ethics Committee of Iran University of Medical Sciences approved the study protocol, which was conducted in accord with the tenets of the Helsinki Declaration. All participants signed written informed consent.

Results

114 eyes of 114 volunteers with a mean age of 31.6±4.7 (21-40 years) were evaluated. 48 patients had mild keratoconus, 37 had moderate, and 29 had severe keratoconus. The Chi-square test revealed there were no

statistically significant differences between keratoconus grades in terms of patient sex (*P*=0.661). Also, the variance test showed there were no statistically significant differences between the three groups in terms of age (*P*=0.214). The demographics of the study population are shown in Table 1.

Table 1. Demographic features of the patients

Groups	Age (Y)	Sex (F/M)
	Mean±SD	%
Grade 1	30.80±4.93	42.9/41.2
Grade 2	32.39±4.56	28.6/35.3
Grade 3	31.83±4.46	28.6/23.5

ANOVA test results showed anterior K readings, ACA, and corneal thickness parameters (TCT, ACT, and CCT) were statistically significantly different between three groups of keratoconus grades. However, CV, ACV, and PD showed no significant difference between groups. Table 2 shows the mean anterior segment parameters between the three groups.

Posterior K readings, central posterior elevation, max posterior elevations (in 3 mm and 5 mm zones) were statistically different between the three grades. All posterior elevation parameters increased with the progression of keratoconus (*P*<0.001). The results of repeated measures ANOVA with controlling the effect of age and sex showed that all posterior elevation parameters were statistically significantly different between three grades of keratoconus. Table 3 shows the mean posterior corneal parameters in 3 keratoconus groups.

Table 2. Anterior segment parameters by group

	Grade 1	Grade 2	Grade 3	
	Mean±SD	Mean±SD	Mean±SD	*P*
Min K (D)	44.16±1.82	47.95±1.92	56.63±7.21	0.000
Max K (D)	46.20±2.22	51.79±1.54	62.35±7.41	0.000
CCT (µm)	497.08±39.52	459±29.80	418.86±52.33	0.000
ACT (µm)	492.78±42.29	448.78±30.07	392.81±61.54	0.000
TCT (µm)	480.98±43.66	442.09±36.61	377.14±67.50	0.000
CV (mm^3)	57.45±3.75	56.23±3.25	57.30±4.05	0.207
ACV (mm^3)	196.93±31.26	199.24±36.41	194.17±38.71	0.809
ACA (degrees)	38.21±5.22	37.54±4.87	36.16±5.93	0.189
ACD (mm)	3.28±0.27	3.39±0.32	3.62±0.40	0.000
PD (mm)	3.38±0.97	3.33±0.63	3.54±0.70	0.494

Table 3. posterior corneal parameters by group

	Grade 1	Grade 2	Grade 3	
	mean±SD	mean±SD	mean±SD	*P*
Min K (D)	-6.45±0.46	-7.17±0.44	-8.64±1.39	<0.001
Max K (D)	-6.96±0.58	-7.99±0.45	-9.81±1.27	<0.001
Central posterior elevation (µm)	17.98±15.41	37.76±20.01	75.31±45.76	<0.001
Maximum posterior elevation 3 (µm)	36.34±21.51	58±26.87	97.89±47.84	<0.001
Maximum posterior elevation 5 (µm)	39.27±20.98	59.72±27.71	101.17±47.46	<0.001

Discussion

The purpose of the current study was to determine and compare posterior corneal elevation data and anterior corneal segment parameters between three different grades of keratoconus using Pentacam.

There was no statistically significant difference between our three study groups in terms of gender and age. Though the mean age of our study participants was older than those enrolled in the study by Emre *et al.*, (17), they found no significant differences in sex and age of all three keratoconus groups. On the other hand, the mean age of our study was younger than those of Ishii *et al.*, (18) and Pinero *et al.*, (19); However, they also found the same results.

In our study, ACD showed a significant increase over the progression of the disease. Edmonds *et al.*, (20) compared ACD between normal and keratoconus individuals. They found ACD was affected by sex, age, and keratoconus. According to Kovacs *et al.*, (21), the anterior chamber was significantly deeper in keratoconus patients than normal eyes and was highly correlated with a posterior corneal elevation in the central cornea and 1 mm of the paracentral cornea. Fonts *et al.*, (22) evaluated CV, ACD, and CCT of mild keratoconus patients using pentacam. All their findings were statistically similar to our findings in mild KCN patients. Emre *et al.*, (17) compared anterior segment

parameters between three grades of keratoconus. They divided patients by mean K into three groups as follows: mild (K≤47 D, moderate (47<K<52), and severe (K≥52 D). In their study, ACD measurements were 3.2±0.3 mm, 3.3±0.3 mm, and 3.7±0.4 mm in mild, moderate, and severe KCN, respectively. In our study, we found ACD measurements to be 3.28±0.27 mm, 3.39±0.32 mm, and 3.63±0.4 mm in mild, moderate, and severe KCN, respectively. ACD data of their study seems to be in agreement with our findings. Precise measurements of ACD are highly important in the implantation of phakic intraocular lenses (pIOLs) for refractive treatment of keratoconus patients (15,16). Therefore, the progressive deepening of ACD could be considered a useful change.

As expected, pachymetric readings (CCT, TCT, and ACT) showed a significant decrease as the condition progressed. Similar to our study, Emre *et al.,* (17) showed a progressive decrease in TCT over the progression of keratoconus. Our TCT findings were 480.98±43.66 µm, 442.09±36.61 µm, and 377.14±67.5 µm compared to their measurements of 484.8±51.6 µm, 453.0±41.6 µm and 374.3±97.4 µm in mild, moderate and severe KCN, respectively. A decrease in corneal pachymetric values could be explained by progressive corneal thinning. Ishii *et al.,* (18) and Pinero *et al*., (19) also reported that in their studies, CCT and TCT decreased with the progression of the disease.

Our study results showed a progressive decrease in ACA from grade 1 to grade 3. Our study findings support those of Klayce and Smolek (23) and Emre *et al.,* (17) Klayce and Smolek found that flattening of the peripheral cornea is a consequence of the increase in central corneal curvature, and subsequently, ACA progressively decreases. However, ACA measurements of our study were slightly higher than those of Emre *et al.;* The discrepancy might be due to different grading systems or individual differences between these two studies. In our study, patients were categorized by maximum keratometry, while Emre *et al.,* divided patients by mean keratometry. Nilsson *et al.,* (24) compared ACA between keratoconus and normal subjects using Orbscan II and OCT. They concluded that ACA is unchanged in keratoconus. The difference could be due to different measurement techniques. Kovics *et al.,* (21) also found no significant difference between mild to moderate keratoconus patients and normal eyes in terms of ACA.

Our study showed no significant difference in CV findings between the three grades. In the studies of Pinero *et al*., (19), Emre *et al.,* (17), and Ambrosio (25), CV measurements showed a progressive decrease from grade 1 to grade 3. According to Fonts *et al.,* (22), CV measurement of patients with even mild KCN was statistically lower than those of the normal group suggesting that corneal volume loss may begin even in early stages. Henry and Bennett (26) stated that the presence of abnormal enzymes in the corneal epithelium leads to a simultaneous increase of collagenase enzymes and protease inhibitor enzymes in the corneal stroma. This causes the death of keratocytes and the subsequent decrease in stromal collagen, and as a result, the overall amount of corneal protein decreases, and stroma becomes thinner. Pinero *et al.,* (19) found corneal thinning was followed by no significant changes in the CV in grade 1. They claimed that the likely explanation could be the erratic and irregular distribution of corneal volume rather than the loss of tissue in the early stages of the disease. Meek *et al*., (27) conducted a study to map the collagen orientation and relative distribution of collagen fibers in keratoconus corneal buttons. They reported that the structure of the stromal lamellae was significantly changed in keratoconus in comparison to the normal cornea. The uneven distribution of collagen fibers was highly notable in the area of the corneal apex. Mollan *et al.,* (28) also stated stiffness and extensibility of corneal tissue seem to decrease in keratoconus as a result of abnormal collagen lamella. Mannion *et al.,* (29) compared the CV in keratoconic and normal eye using pentacam. According to their study, corneal volume was significantly decreased in keratoconus, especially in the central and paracentral corneal areas. The authors stated that a decrease in CV could be attributed to the loss of tissue in moderate and advanced stages of keratoconus. However, in the early stages, changes in corneal metabolic activity cause the tissue to extend, and in later stages, the stretching is followed by tissue loss. However, our study showed no significant changes in CV even in the advanced stages of the condition. Thus, this may suggest that corneal thinning is not the mere cause of changes in corneal volume. The possible explanation for the discrepancies between our study and these studies might be different grading systems or different ages, sex, and ethnicity in these studies, as mentioned before. Nevertheless, this is something that should be addressed in future studies.

In our study, ACV showed no significant difference between the three groups. Emre *et al.,* (17) reported that in contrast to the significant deepening of ACD, the progressive increase in ACV was not statistically significant. They claimed an increase in ACD might result in a subsequent increase in ACV. Kovacs *et al.,* (21) found there is no significant difference in ACV

between KCN patients and normal subjects in spite of a significant difference in ACD between the two groups. According to our findings, ACV showed no significant changes in spite of the deepening of the ACD with the progression of KCN, suggesting the different underlying changing processes during the progression of the disease.

In our study, anterior and posterior k readings showed a notable increase as the disease progressed. Tomidokoro *et al.,* (8) found that anterior and posterior k readings were significantly higher in KCN and KCN suspect patients. This could suggest that posterior corneal curvature changes begin even in the early stages of keratoconus. According to Pinero *et al.,* (19), anterior and posterior k readings were higher in KCN grade 2 (K<53) than grade 1 (K<48). However, all posterior k readings in their study were slightly higher than those of our study.

Recent studies considered the posterior corneal elevation to provide diagnostic values in the early detection of keratoconus (4,19). In our study, posterior elevation data showed a progressive increase with the progression of the disease. Maximum posterior elevation in the 5 mm zone had the highest, and central posterior elevation had the lowest readings. The significant difference between central posterior elevation and maximum elevations could be explained by decentration and misalignment of the corneal apex in relation to the center of the cornea. Most KCN patients show an inferotemporal decentration of the corneal apex (18). This could be the explanation for the considerable difference between the three posterior elevation data. Similarly, Ishii *et al*., (18) evaluated the correlation of corneal elevation with the severity of keratoconus by means of anterior and posterior topographic analysis. They used Amsler-Krumeich classification for grading keratoconus and found anterior and posterior corneal elevation to increase from grade 1 to grade 4. One possible explanation for the increase in posterior corneal elevation could be progressive anterior and posterior corneal steepening followed by decreased corneal pachymetry, especially in the central stroma.

In conclusion, height data of posterior cornea, when combined with corneal anterior segment parameters, could provide potential data for useful keratoconus severity classification.

References

1. YS r. Keratoconus. Surv Ophthalmol 1998;42:297-319.
2. Jafarinasab MR, Shirzadeh E, Feizi S, Karimian F, Akaberi A, Hasanpour H. Sensitivity and specificity of posterior and anterior corneal elevation measured by Orbscan in diagnosis of clinical and subclinical keratoconus. J Ophthalmic Vis Res 2015;101:10-5.
3. Schlegel Z, Hoang-Xuan T, Gatinel D. Comparison of and correlation between anterior and posterior corneal elevation maps in normal eyes and keratoconus-suspect eyes. J Cataract Refract Surg 2008;34:789-95.
4. de Sanctis U, Loiacono C, Richiardi L, Turco D, Mutani B, Grignolo FM. Sensitivity and Specificity of Posterior Corneal Elevation Measured by Pentacam in Discriminating Keratoconus/Subclinical Keratoconus. Ophthalmology 2008;115:1534-9.
5. Muftuoglu O, Ayar O, Ozulken K, Ozyol E, Akıncı A. Posterior corneal elevation and back difference corneal elevation in diagnosing forme fruste keratoconus in the fellow eyes of unilateral keratoconus patients. J Cataract Refract Surg 2013;39:1348-57.
6. Hashemi H, Beiranvand A, Khabazkhoob M, Mehravaran S, Emamian MH, Yekta A, et al. Corneal elevation and keratoconus indices in a 40- to 64-year-old population, Shahroud Eye Study. J Curr Ophthalmol 2015;27:92-8.
7. Miháltz K, Kovács I, Takács Á, Nagy ZZ. Evaluation of keratometric, pachymetric, and elevation parameters of keratoconic corneas with pentacam. Cornea 2009;28:976-80.
8. Tomidokoro A, Oshika T, Amano S, Higaki S, Maeda N, Miyata K. Changes in anterior and posterior corneal curvatures in keratoconus. Ophthalmology 2000;107:1328-32.
9. Colin J, Velou S. Current surgical options for keratoconus. J Cataract Refract Surg 2003;29:379-86.
10. Mazzotta C, Balestrazzi A, Traversi C, et al. Treatment of progressive keratoconus by riboflavin-UVA-induced cross-linking of corneal collagen: ultrastructural analysis by Heidelberg Retinal Tomograph II in vivo confocal microscopy in humans. Cornea 2007;26:390-7.
11. Wollensak G. Crosslinking treatment of progressive keratoconus: new hope. Curr Opin Ophthalmol 2006;17:356-60.
12. Hellstedt T, Mäkelä J, Uusitalo R, Emre S, Uusitalo R. Treating keratoconus with Intacs corneal ring segments. J Refract Surg 2005;21:236-46.
13. Colin J. European clinical evaluation: Use of Intacs for the treatment of keratoconus. J Cataract Refract Surg 2006;32:747-55.
14. Alió JL, Shabayek MH, Belda JI, Correas P, Feijoo ED. Analysis of results related to good and bad outcomes of Intacs implantation for keratoconus correction. J Cataract Refract Surg 2006;32:756-61.
15. Leccisotti A, Fields SV. Angle-supported phakic

intraocular lenses in eyes with keratoconus and myopia. J Cataract Refract Surg 2003;29:1530-6.
16. Budo C, Bartels MC, van Rij G. Implantation of Artisan toric phakic intraocular lenses for the correction of astigmatism and spherical errors in patients with keratoconus. J Refract Surg 2005;21:218-22.
17. Emre S, Doganay S, Yologlu S. Evaluation of anterior segment parameters in keratoconic eyes measured with the Pentacam system. J Cataract Refract Surg 2007;33:1708-12.
18. Ishii R, Kamiya K, Igarashi A, Shimizu K, Utsumi Y, Kumanomido T. Correlation of Corneal Elevation With Severity of Keratoconus by Means of Anterior and Posterior Topographic Analysis. Cornea 2012;31:253-8.
19. Piñero DP, Alió JL, Alesón A, Vergara ME, Miranda M. Corneal volume, pachymetry, and correlation of anterior and posterior corneal shape in subclinical and different stages of clinical keratoconus. J Cataract Refract Surg 2010;36:814-25.
20. Edmonds CR, Wung S-F, Pemberton B, Surrett S. Comparison of Anterior Chamber Depth of Normal and Keratoconus Eyes Using Scheimpflug Photography. Eye Contact Lens 2009;35:120-2.
21. Kovács I, Miháltz K, Németh J, Nagy ZZ. Anterior chamber characteristics of keratoconus assessed by rotating Scheimpflug imaging. J Cataract Refract Surg 2010;36:1101-6.
22. Fontes BM, Ambrósio R, Jardim D, Velarde GC, Nosé W. Corneal Biomechanical Metrics and Anterior Segment Parameters in Mild Keratoconus. Ophthalmology 2010;117:673-9.
23. Smolek MK, Klyce SD. Is keratoconus a true ectasia? An evaluation of corneal surface area. Arch Ophthalmol 2000;118:1179-86.
24. Nilsson M, Miller W, Cerviño A, Bergmanson JPG, Brautaset RL. Evaluation of the anterior chamber angle in keratoconus and normal subjects. Cont Lens Anterior Eye 2015;38:277-82.
25. Ambrósio R, Alonso RS, Luz A, Coca Velarde LG. Corneal-thickness spatial profile and corneal-volume distribution: Tomographic indices to detect keratoconus. J Cataract Refract Surg 2006;32:1851-9.
26. Bennet ES, Henry VA. Clinical manual of contact lenses. 4nd ed. Philadelphia: Lippincott Williams & Wilkins; 2013.
27. Meek KM, Tuft SJ, Huang Y, et al. Changes in collagen orientation and distribution in keratoconus corneas. Invest Ophthalmol Vis Sci 2005;46:1948-56.
28. Mollan SP, Wolffsohn JS, Nessim M, Laiquzzaman M, Sivakumar S, Hartley S, et al. Accuracy of Goldmann, ocular response analyser, Pascal and TonoPen XL tonometry in keratoconic and normal eyes. Br J Ophthalmol 2008;92:1661-5.
29. Mannion LS, Tromans C, O'Donnell C. Reduction in corneal volume with severity of keratoconus. Curr Eye Res 2011;36:522-7.