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Corneal Aberrations in Keratoconus: A Pentacam Scheimpflug Imaging Study

Keratokonus ile Korneal Aberasyonların İlişkisinin Değerlendirilmesi

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Abstract

Objective: To investigate high-order corneal aberration alterations at different keratoconus (KC) stages using a Pentacam Scheimpflug camera (OCULUS, Wetzlar, Germany), and to compare data with healthy eyes

Material and Method: This retrospective comparative study investigated clinical data of 50 patients (100 eyes) with KC and 59 healthy individuals (118 eyes) who underwent corneal topography using the Pentacam Scheimpflug camera in our clinic. Demographic characteristics, total aberrations, HOAs, coma and spherical aberrations of all participants were extracted and recorded.

Results: Mean age in the KC group was 29.7±10.3 years and 32.1±12.4 years in the control group. These two groups were compatible in terms of age and sex (p=0.11; p=0.76, respectively,). Sixty-three eyes had mild, 23 had moderate, and 14 had sever KC. Differences in low-order astigmatism, trefoil, coma, tetra-foil, high-order astigmatism, high-order spherical aberration, and root mean square values between eyes with KC and healthy eyes were statistically significant (p<0.05). Additionally, there were statistically significant differences in the corneal aberrations between the keratometric classification groups.

Conclusions: There is direct proportionality between the KC stage and corneal HOA changes, which may be helpful for staging and improving the safety of refractive surgery.

Keywords: Corneal aberrations, corneal topography, irregular corneal astigmatism, keratoconus, pentacam scheimpflug camera

Öz

Amaç: Farklı keratokonus evrelerindeki yüksek dereceli kornea aberasyon değişikliklerini Pentacam Scheimpflug kamera ile araştırmak ve verileri sağlıklı gözlerle karşılaştırmak.

Gereç ve Yöntem: Bu retrospektif karşılaştırmalı çalışmada, kliniğimizde Pentacam Scheimpflug kamera kullanılarak kornea topografisi yapılan keratokonuslu 50 hasta (100 göz) ve 59 sağlıklı bireyin (118 göz) klinik verileri araştırıldı. Çalışmaya dahil edilen tüm katılımcıların demografik özellikleri, toplam aberasyonları, yüksek dereceli korneal aberasyonları, koma ve küresel aberasyonları kaydedilip analize edildi.

Bulgular: Keratokonus grubunda ortalama yaş 29.7±10.3 yıl ve kontrol grubunda 32.1±12.4 yıl idi. İki grupta yaş ve cinsiyet açısından uyumlu idi (sırasıyla p=0.11; p=0.76). Keratometrik sınıflandırmaya göre 63 gözde hafif, 23 gözde orta ve 14 gözde şiddetli keratoconus var idi. Düşük dereceli astigmatizma, yonca (trefoil), koma, tetra-folyo, yüksek dereceli astigmatizma, yüksek dereceli sferik aberasyon ve kök ortalama kare (root mean square) değerleri keratokonuslu gözler ile sağlıklı gözler arasındaki farklılıklar istatistiksel olarak anlamlı idi (P <0.05). Ayrıca keratometrik sınıflandırma grupları arasında kornea aberasyonlarında istatistiksel olarak anlamlı farklılıklar var idi.

Sonuç/Tartışma: Keratokonus evresi yüksek dereceli korneal aberasyon değişiklikleri ile ilişkilendirlmektedir. Bu ilişki özellikle refraktif cerrahinin evrelendirilmesi ve güvenliğinin iyileştirilmesinde yardımcı olabilir.

Anahtar Sözcükler: Korneal aberasyonlar, korneal topografi, düzensiz korneal astigmatizma, keratokonus, pentacam scheimpflug kamera

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INTRODUCTION

Keratoconus (KC) is a non-inflammatory or semi-inflammatory corneal disorder that generally shows bilateral and asymmetrical involvement. While its exact source has yet to be revealed, genetic, environmental and biomechanical factors are believed to be responsible.[1] Tear films of eyes with KC have been reported to have higher levels of inflammatory indicators that may support an inflammatory etiology.[2] Keratoconus, gradually leads to stromal thinning of the cornea and ectasia, irregular astigmatism and, subsequently, impaired vision.[3,4] Visual impairment deteriorates parallel to KC progression, which is characterized by high-order aberrations (HOAs).[5]

Keratoconus commonly begins during adolescence and gradually increases until the 3rd to 4th decade of life. Corneal topography along with slit-lamp biomicroscopic examination, retinoscopy, and pachymetry are used in the diagnosis of different forms of KC, including mild, moderate and advanced forms.[6] Scheimpflug imaging devices (OCULUS, Wetzlar, Germany) are also used to assess corneal height maps on both anterior or posterior corneal surfaces.[7,8]

Earlier studies in which investigation as to whether or not different ocular and corneal aberrations have distinguishing values, and if these parameters can be evaluated as almost identical or distinctive tools among KC relative to forme fruste KC and normal eyes, revealed an association between significantly higher ocular and corneal aberrations and KC.[9] Further, Jafri et al.[9] reported that the HOA vertical coma may be better data than videokeratoscopic inferior-superior asymmetry data in distinguishing early and suspected KC from normal eyes. In addition, it has been reported that HOAs in eye with KC were approximately 5.5 times higher than normal population levels, and approximately 53% of different HOA types alone were responsible for vertical coma in patients with KC.[10] Some researchers have therefore proposed that aberration data be used in the categorization of KC subtypes, which may be used during the selection of general optical corrections that are necessary for the correction of common HOA characteristics.[11-13] Gordon-Shag et al.[14] correspondingly emphasized that HOAs, particularly ocular ones, are very powerful tools in differentiating between eyes with KC and normal eyes.

As far as the current study is concerned, the authors posit parallel alterations of HOAs with respect to the progression of KC and whether or not these alterations will have any clinical consequences for the day-to-day activities of the patients concerned. The purpose of the current study was therefore to investigate HOA alterations in the eyes with different clinical stages of KC using the Pentacam Scheimpflug imaging system and to compare findings between study groups.

MATERIAL AND METHOD

Participants

In this retrospective comparative case-control study, the data of 100 eyes of 50 patients with KC and 118 normal eyes of 59 healthy individuals who applied to the Clinic of Ophthalmology at Training and Research Hospital between December 2018 and October 2019 were examined. The study protocol abided to ethical principles of the Declaration of Helsinki and was approved by the institutional review board of Muğla Sıtkı Koçman University Ethics Committee (no.2020/02-VII). Written informed consent was obtained from each participant.

Eyes with KC were classified into three groups based on the Amsler–Krumeich keratoconus classification system[12] that is, the average keratometry values: <47 D as mild; 47-52 D as medium; and >52 D as severe KC. Demographic characteristics, total aberrations, HOAs, coma and spherical aberrations of all participants were extracted and recorded. Patients with KC who were ≥18 years of age and without any systemic diseases were enrolled in the study. Exclusion criteria comprised of: presence of corneal scar and corneal dystrophies; prior corneal and/or anterior segment surgeries; usage of any systemic drugs; presence of collagen vascular diseases; usage of the contact lens; and pregnancy or lactation.

Ocular Examination and Anterior Segment Imaging

All participants underwent a comprehensive ophthalmologic examination, including measurements of the best-corrected visual acuity and Goldmann applanation tonometry and slit-lamp biomicroscopy of anterior and posterior segments before and after full pupil dilation.

In the meantime, corneal topographic imaging and aberrometry was performed using Pentacam Scheimpflug imaging device. The procedure was conducted between 9:00 am and 12:00 am in order to circumvent any feasible diurnal fluctuations. In addition, the use of contact lens was stopped at least two weeks before the study. Imaging procedures were taken at optimal compliance conditions along the visual axis, allowing the patients to look carefully at the central fixation light. Blinking was encouraged during the procedure to keep tear film layer intact. The eye movements of each patient were frequently monitored by the system, and the quality factor was automatically evaluated. The procedure was successfully carried out three times following two minutes of dark adaptation under dark scrutiny (2.2 Lux) and the resultant mean values were recorded.

Pentacam® HR device is a rotating Scheimpflug camera. Rotational imaging by Scheimpflug camera creates images in three-dimensional model. Creation of a complete view of the anterior segment of the eye takes no more than two seconds. The device's second camera was used to identify any possible ocular movements. Three-dimensional model of the anterior segment of the eye from 138.000 distinct heights was determined by Pentacam. Topography and pachymetry of the entire corneal front and back surfaces from limbus to limbus were also determined.

Analysis of the anterior segment of the eye included determination of the anterior chamber angle, anterior chamber volume, anterior chamber height, and measurement of the

function that can be applied manually anywhere in the anterior segment. Images of the corneal anterior and posterior surfaces, iris, and anterior and posterior surfaces of the lens were produced in a moving virtual eye. Lens and corneal densitometry values were automatically determined. Root mean square (RMS), coma, RMS trefoil, RMS total HOA, RMS astigmatism and global RMS aberrations were among the data collected.

Diagnosis

During diagnosis of KC, the corneal topography map, inferior-superior asymmetry, focal or inferior steepening, asymmetric bow tie with a skewed radial axis, anterior-posterior elevation pattern, and presence of more than one of the diagnostic signs essentially clinical manifestation of the Fleischer ring and Vogt's striae were considered.[15] The ocular, corneal and inner wave aberrations were measured by 6th row Zernike polynomial decomposition for a 6 mm diameter region with a central corneal peak. Further information on the Zernike polynomials has been analyzed in earlier publications.[16,17] The RMS of corneal, ocular, and internal aberrations was determined to measure amount of the HOAs. The lower the RMS value, the lower was the aberration of the optical system. In addition, groups that included low-order astigmatism, total trefoil, vertical coma, total coma, total tetra-foil, high-order astigmatism as well as total high-order spherical aberration were determined.

Statistics

The IBM SPSS Statistics software (Version 22; IBM Inc., New York, USA) was used in the statistical analysis. Data were expressed as mean±standard deviation. Chi-square test was used to compare categorical variables. Quantitative data were defined as mean±standard deviation. Kruskal-Wallis and Mann-Whitney tests were used accordingly. Spearman's correlation analysis was used to analyze association among values of the mean keratometry, posterior elevation, and RMS. P values <0.05 were considered to be statistically significant.

RESULTS

Participants were categorized into two groups: KC eyes with mean age of 29.7±10.3 years (females, 21; males, 29); and healthy eyes with mean age of 32.1±12.4 years (females, 26; males, 33). These groups were compatible regarding the age and sex parameters, respectively (p=0.11; p=0.76). The level of KC was mild in 63, moderate in 23, and severe in 14 eyes, based on the Amsler–Krumeich keratoconus classification system.

Keratometry values detected in the respective study groups are demonstrated in **Table 1**. There were statistically significant differences between eyes with KC and healthy eye in terms of low-order astigmatism, trefoil, coma, tetra-foil, HOA, high-order spherical aberration and RMS (p<0.05) There were also statistically significant differences in terms of corneal aberration among KC groups.

With regards statistical analysis of the corneal HOAs at various stages of KC, there was a general positive correlation between mean keratometry and RMS values. Specifically, the positive correlation between RMS total and mean keratometry values was statistically significant in all groups. There was also statistically significant positive correlation between RMS total coma and mean keratometry values in all groups (p<0.0001). The correlation between RMS trefoil and mean keratometry, however, was statistically significant in the medium KC group (p=0.04), and significant relative to that of all three groups (p<0.0001). The correlation between RMS astigmatism and mean keratometry was significant in all KC groups (p=0.02), and all RMS values had statistically significant positive correlation with mean keratometry in general (p<0.0001). There was also statistically significant correlation between spherical aberrations and mean keratometry in the moderate and severe KC groups (p<0.0001;p<0.001, respectively), and in comparison to the three groups (p<0.0001).

Table 1. Keratometry values detected in keratoconus and control groups

	KC; n=100	Group 1; n=63	Group 2; n=23	Group 3; n=14	Control; n=118	P1	P2
K1 (Diopter)	46.1±3.7	43.8±1.3	47.6±1.7	52.9±1.9	42.8±1.5	<0.001	<0.001
K2 (Diopter)	49.5±4.6	46.6±1.6	51.8±2.1	58.1±2.5	43.9±1.6	<0.001	<0.001
Km (Diopter)	47.6±4.1	45.1±1.2	49.7±1.7	55.5±1.9	43.4±1.5	<0.001	<0.001
LOA (µm)	-2.18±2.13	-1.74±1.83	-2.50±2.05	-3.58±2.86	-0.59±0.73	<0.001	0.041
Total trefoil (µm)	0.38±3.51	-0.011±0.14	0.21±1.08	2.39±9.15	-0.004±0.06	0.968	0.441
Total coma (µm)	0.15±0.27	0.13±0.15	0.31±0.33	0.006±0.43	-0.0001±0.05	<0.001	0.001
Total tetra-foil (µm)	0.027±0.55	-0.03±0.04	0.18±0.42	0.33±1.36	-0.03±0.04	0.808	0.280
HOA (µm)	0.18±1.38	-0.01±0.10	0.35±1.74	0.77±2.89	0.001±0.17	0.784	0.155
High-order spheric aberration (µm)	-0.19±0.78	0.06±0.38	-0.41±0.90	-0.95±1.21	0.21±0.11	<0.001	<0.001
Total high-order RMS (µm)	1.94±1.53	1.25±0.90	2.95±1.68	3.18±1.84	0.44±0.25	<0.001	<0.001

KC: Keratoconus, K1: Horizontal K, K2: Vertical K, Km: Average Keratometry, K1 post: Posterior Horizontal K, K2 post: Posterior Vertical K, Km Post: Average Posterior Keratometry, LOA: Low-Order Astigmatism, HOA: High-Order Astigmatism, RMS: Root Mean Square; P1=Comparison of Patients with Keratoconus and Controls, P2=Comparison of Patients with Keratoconus Patients Among Themselves (Group1-Group2-Group3), µm: Micrometer

DISCUSSION

This retrospective comparative study revealed correlation of ocular and corneal aberrations with KC versus healthy eyes. Nevertheless, the values of some aberration parameters, including vertical and total coma, total tetra-foil, and high-grade astigmatism were significantly different between the two groups. Similar to the study by Schlegel et al.[18] in which aberrometry was measured by OPD-Scan II, the current study revealed significantly higher optical aberrations, that is, ocular, corneal, and internal abnormalities in eyes with KC relative to normal eyes. Furthermore, in the current study, eyes with KC were more effectively differentiated from normal eye thanks to the use of the ocular HOA data, by which total HOAs, total coma and high-order astigmatism were significantly higher in eyes with KC. In the study published by Reddy et al.[19] the corneal aberrations, coma Z3-1 and Z31 extended to the uppermost viable specificity (100%, 63%, respectively) and sensitivity, while none of the topographic parameters did not reach this level of characteristic. In the presents study, however, sensitivity of almost all the ocular aberration parameters was obviously significant in differentiating eyes with KC from normal eyes. Therefore, some corneal aberrations such as vertical and total coma, and total trefoil considered to be highly potent aberration tools that can be used to differentiate eyes with KC from normal eyes.

There is currently a challenge in diagnosing cases of moderate and subclinical KC types. This is particularly important for eyes with a forme fruste KC that have not displayed any clinical signs of KC for a long time, as topographical indices and corneal curvature patterns may not be worthwhile in the diagnosis of disorder.[20] Gordon-Shaag et al.[14] and Hashemi et al.[21] suggested evaluation of the aberration parameters such as vertical asymmetry along with corneal topography in the assessment of patients with mild and subclinical KC forms. Correspondingly, the current study observed substantial differences between eyes with KC and normal eyes in terms of low-order astigmatism, trefoil, vertical and total coma, tetra-foil, HOA, high-order spherical aberration, and RMS values.

The aberrations parameters, including coma, trefoil, astigmatism, and global aberrations generally exacerbate in progressive KC. In one study published by Çolak et al.[22] following measurement of the corneal topographic parameters using Scheimpflug-Placido topography, statistically significant correlation between increased corneal curvature and total aberrations revealed during comparison of the corneal anterior surface aberrations between eyes with KC and normal eyes. Another study by Maeda et al.[17] which collated the wave-front aberrations of eyes with KC to normal eyes and assessed the properties of HOAs measured by the Hartmann-Shack sensor in eyes with KC, reported that increase in the ocular HOAs in eyes with KC was due to a resultant increase in the corneal HOAs. In the current study, during intra-group comparison of posterior height in eyes with different KC sub-groups, statistically significant differences were revealed in all HOA variables. Despite that, posterior height and RMS values in the mild, moderate, and severe KC sub-groups were positively correlated, the fact which can be explained by both the obvious differences in the HOA alterations and presence of high posterior heights. In addition, the current study observed correlation between the corneal HOAs and degree of KC using Scheimpflug camera, similar to the study published by Delgado et al.[23] Unlike earlier reports in the literature, the current study also revealed significant correlation between severity of coma aberration and RMS trefoil values in eyes with advanced KC. In consistent with the prior reports, a Pentacam study by Nakagawa et al.[24] reported higher corneal HOAs in eyes with KC relative to healthy eyes. All of these findings indicate that corneal HOAs can be used as a method for KC staging. In view of this, Alio et al.[12] also demonstrated that HOAs of the anterior corneal surface can be applied to diagnose stages of KC using videokeratoscopy and with corneal map analysis.

Optical aberrations in the eyes with KC have been studied in several clinical trials and in conjunction with the present research, increased HOAs, in particular coma and global aberrations, have been demonstrated.[9,19] Significantly increased HOAs lead to decreased visual acuity that is uncorrected with glasses or soft contact lenses.[25,26] In spite of that, intracorneal ring segments and phakic toric implantable lenses are effective methods based on the effect of reducing optical abnormalities in the patients with KC.[27]

The authors acknowledge the limitations of the present study. Due to our relatively limited sample size analysis, these observations should be considered carefully. Even more prospective trials comprising a greater number of patients would be worthwhile in order to assess the effectiveness of the ocular and corneal aberration measurements in the identification of different stages of KC and its subsequent implications in the everyday lives of the patients concerned.

CONCLUSION

Significant differences in low-order astigmatism, trefoil, coma, tetra-foil, high-order astigmatism, high-order spherical aberration, and RMS values have been identified in the current study. Significant changes in corneal aberrations among the keratometric classification categories have also been identified. In addition, corneal HOAs were consistent with corneal topographic parameters obtained from similar devices at various stages of the KC. Consequently, these changes may not just be of benefit to KC staging. They could also enhance the safety of refractive surgery.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study protocol abided to ethical principles of the Declaration of Helsinki and was approved by the institutional review board of Muğla Sıtkı Koçman University Ethics Committee (no.2020/ 02-VII).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was **obtained from patients.**

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