Comparison of Different Topographic Reference Surfaces in Keratoconus Cases

Keratokonus Olgularında Farklı Topografik Referans Yüzeylerin Karşılaştırılması

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Abstract

Objective: To compare the sensitivity and specificity of corneal elevation maps obtained from different topographical reference surfaces used in the diagnosis of keratoconus.

Materials and Methods: In this prospective study, 40 eyes of 23 patients with keratoconus (keratoconus group) and 40 eyes of 25 refractive surgery candidates without keratoconus (control group) were included. Flat keratometry (K1), steep keratometry (K2) and apex curvature keratometry (Kmax) values were obtained for both groups using the Scheimpflug camera system. Both anterior and posterior elevation maps were obtained from the spherical, aspherical and aspherotoric reference surfaces by assessing an 8 mm central corneal area. Topographic data were used to determine a more sensitive and specific corneal elevation mapping method to use in the differentiation of normal and keratoconic corneas.

Results: The ROC curve analysis showed that posterior elevation measured from the aspherical and aspherotoric surfaces had a higher area under the ROC curves (0.987, 0.973 respectively) than the value obtained from the spherical reference surfaces. According to the data obtained from the ROC curve analysis, the posterior elevation maps obtained from the aspherical and aspherotoric reference surfaces had the highest sensitivity (97.5% for both) and the posterior elevation map obtained from the aspherical reference surface had the highest specificity (90%).

Conclusion: The highest sensitivity and specificity values were obtained from the aspherical and aspherotoric reference surfaces compared to the spherical reference surface. When compared to the anterior elevation values, the posterior elevation values were found to be more sensitive and specific. Therefore, aspherical and aspherotoric reference surfaces and a posterior elevation map are seen more accurately in the differentiation of keratoconus and normal cornea.

Keywords: Cornea; Keratoconus; Scheimpflug camera; Reference surface selection; Corneal topography.

Öz

Amaç: *Keratokonus tanısında kullanılan topografik referans haritalama yöntemlerinin duyarlılık ve özgüllüğünün karşılaştırılması amaçlanmıştır.*

Gereç ve Yöntemler: *Keratokonuslu 23 hastanın 40 gözü (keratokonus grubu) ile keratokonus olmayan ve rastgele seçilen refraktif cerrahi adayı 25 hastanın 40 gözü (kontrol grubu) Scheimpflug (Sirius CSO-Italy) topografi cihazı ile analiz edildi. Her iki grup için düz keratometri (K1), dik keratometri (K2) ve apeks eğrilik keratometri (Kmax) değerleri elde edildi. Sferik, asferik ve asferotorik referans yüzeyler kullanılarak ön ve arka korneal elevasyon haritaları (8 mm'lik santral korneal alanda) elde edildi. Normal ve keratokonuslu kornealarım ayrımında daha duyarlı ve daha özgül olan korneal elevasyon haritalama yöntemini belirlemek için topografik veriler kullanıldı.*

Bulgular: *ROC eğri analizlerine göre; asferik ve asferotorik yüzeylerden elde edilen posterior elevasyon verilerinin her ikisinin de keratokonusu saptamadaki duyarlılığı (97,5%), sferik referans yüzeyden elde edilen verilere göre anlamlı olarak daha yüksekti. Asferik referans yüzeyin keratokonus tanısında en yüksek özgüllüğe (90%) sahip olduğu sonucuna ulaşıldı.*

Sonuç: *Çalışmaya göre yüksek duyarlılık ve özgüllük değerleri asferik ve asferotorik referans yüzeylerden elde edildi. Posterior elevasyon değerleri ile anterior elevasyon değerleri kıyaslandığında posterior yüzeyin daha değerli olduğu görüldü. Bu yüzden asferik ve asferotorik referans yüzeyin keratokonusu saptamada posterior elevasyon ile birlikte daha doğru sonuçlar vereceği sonucuna ulaşıldı.*

Anahtar Kelimeler: *keratokonus; kornea; korneal topografi; referans yüzey seçimi; scheimpflug kamera*

INTRODUCTION

Keratoconus is the progressive ectasia of the cornea and causes a decrease in visual acuity by leading to high myopia and astigmatism. An accurate and more sensitive and specific method is crucial for diagnosis, follow-up the prognosis of the disease and planning the treatment options. The efficiency of diagnosis is more important in refractive surgery cases that may develop postoperative ectasia.[1-2]

Corneal topography is currently the gold standard diagnostic method in keratoconus cases. Although some limitations; placido disc-based corneal topographies have been widely used for a long time. Placido-disc based topographies only evaluate the anterior corneal surface and measurements are greatly affected by the angle and position of the surface.[2] Many studies on keratoconus have revealed that the morphological changes also occur on the posterior corneal surface.[3-5] It is now known that the morphological changes begin to occur primarily on the posterior corneal surface.[5] Corneal elevation change is one of the most important parameters and there have been some previous studies related to this issue.[6-9]

Scheimpflug-based corneal tomography comprises a rotating camera and slit scanning system and provides both the anterior and the posterior corneal surface elevation data.[5] Early and accurate diagnosis of keratoconus is provided by using Scheimpflug-based topographies and elevation maps. The evaluation of the cases is done according to reference mapping methods offered by topography devices. One of the reference surfaces (spherical, aspherical, aspherotorical) is chosen by the clinician for keratoconus diagnosis and classification. Of them, aspherical reference surface is usually preferred by most of the clinicians for keratoconus diagnosis.

There have been few studies about the comparison of the accuracy of the elevation data obtained from the spherical, aspherical and aspherotorical reference surfaces of the anterior and the posterior elevation maps in the diagnosis and classification of keratoconus. This study aimed to compare the sensitivity and specificity of various reference surfaces used in corneal elevation maps to provide a more accurate diagnosis of keratoconus.

MATERIALS and METHODS

This study was conducted at the Ankara Atatürk Training and Research Hospital between June 2011 and August 2011. The study was carried out in accordance with the principles of the Declaration of Helsinki, and approval of the ethics committee was obtained (Ankara Atatürk Education and Research Hospital, 16.06.2011, no:68)

Patients diagnosed with keratoconus and patients candidates for refractive surgery without keratoconus were enrolled in this prospective, methodological study. Control group was consisted of randomly selected age and gender-matched patients who admitted to the eye clinic for refractive surgery and had no ocular surface pathology, and a history of surgery/trauma.

40 eyes of 23 patients with keratoconus and 40 eyes of 25 refractive surgery candidates without keratoconus were included in the study. Subjects over 40 years of age (for both groups) and with history of previous eye surgery or a history of systemic disease were excluded from the study. Patients with any additional eye disease (glaucoma, corneal scar, dry eye, etc) and those with advanced keratoconus were also excluded. Patients who used contact lenses were examined 15 days after removing the lenses.

Comprehensive ocular examination, including best-corrected visual acuity measurement with a Snellen chart, slit lamp examination, topographic measurements using a Scheimpflug camera system were performed in all subjects. Keratoconus was diagnosed with clinical and topographic signs. In addition the topographic data, patients had at least one clinical sign, including Munson sign, scissor reflex during retinoscopy, Fleischer ring, Vogt striae, increased visibility of the corneal nerves, and Rizzuti sign. For topographic measurements, Sirius Scheimpflug analyzer (Phoenix software, CSO-Italy) was used and measurements were obtained by a single experienced examiner. Images were confirmed under a quality-specification window and good-quality scans were included. Flat keratometry (K1), steep keratometry (K2) values (in a central corneal ring, 3 mm in diameter), and apex curvature keratometry (Kmax) values (in 8mm central corneal area) were obtained for both groups using the Scheimpflug camera system. Both anterior and posterior elevation maps were obtained from the spherical, aspherical and aspherotoric reference surfaces by assessing an 8 mm central corneal area.

Topographic data were used to determine a more sensitive and specific corneal elevation mapping method to use in the differentiation of normal and keratoconic corneas.

Statistical Analyses: Statistical analyses were performed using SPSS v. 17.0 software. The corneal elevation values, age, gender, and K values were used as variables. Numerical values were stated as mean ± standard deviation (SD). The parametric distribution of the continuous variables in the keratoconus and control groups was confirmed by the Kolmogorov- Smirnov test. The comparison of the two groups in terms of continuous variables was analyzed using the t-test in the independent groups. The Chi-square test was used for the gender comparison of the two groups. The specificity, sensitivity, cut-off point and area under the curve of height data obtained from all the reference surface maps were calculated using receiver operator characteristics (ROC) curves. A value of $p< 0.05$ was accepted as statistically significant.

RESULTS

There was no statistically significant difference between the keratoconus group and the control group in respect of demographics (age, gender) ($p>0.05$). The Control group included 18 males (78%) and 5 females (22%) with a mean age of 26.9±6.31 years. Keratoconus group was consisted of 16 males (64%) and 9 females (36%) with a mean age of 23.7±8.16 years (Table 1).

Table 1. The main clinical and demographic findings of the keratoconus and control

	Keratoconus		Control	
	Male	**Female**	**Male**	**Female**
Gender, n (%)	16(64)	9(36)	18(78)	5(22)
Age, years (mean±sd)	23.7±8.16		26.9±6.31	
Miyopi, (mean±sd), (D)	5.05±1.85		4.43±1.54	
Astigmatism, (mean±sd), (D)	4.67±2.05		1.68±1.38	
Munson sign (n)	2	1	0	0
Vogt stria (n)	3	1	0	0
Scissors reflex (n)	3	1	0	0
Fleischer ring (n)	2	0	0	0
Rizutti sign (n)	3	1	0	0
Corneal thickness <500 µm, (n)	2	1	1	0

D=Diopter

In the keratoconus group the mean K1, K2 and Kmax values were 50.35±7.6, 54.35±9.3, 58.64±9.32 D respectively. In the control group, the K1, K2, and Kmax values were 41.94±1, 42.61±1.04 and 43.28±1 D respectively. There was a statistically significant difference between the groups in terms of K1, K2 and Kmax values ($p<0.05$, Table 2).

Table 2. The mean and standard deviation keratometry values of the keratoconus and control group

	Keratoconus (n=40)	Control group (n=40)	p values
K1 (D)	50.35±7.60	41.94±1.00	0.001
K2 (D)	54.35±9.30	42.61±1.04	0.001
Kmax (D)	58.64±9.32	43.28±1.00	0.001

K1= flat keratometry, K2= steep keratometry, Kmax= apex keratometry value

The anterior and posterior corneal elevation values of the keratoconus and the control group were assessed according to the spherical, aspherical and aspherotorical reference surface. The differences between the keratoconus group and the control group were found to be statistically significant in terms of the mean anterior and posterior elevation values obtained with all of the three reference surfaces ($p<0.05$) (Table 3).

Table 3. The mean anterior and posterior elevation values obtained from different reference surfaces in the keratoconus and control groups.

	Keratoconus (n=40)	Control (n=40)	p values
PE Spherical (µm)	16.65±30.49	5.15±2.97	0.020
PE Aspherical (µm)	53.07±24.14	6.97±2.30	0.001
PE Aspherotoric (µm)	53.10±24.70	5.80±2.45	0.001
AE Spherical (µm)	11.72±10.56	1.50±1.01	0.001
AE Aspherical (µm)	26.45±14.85	3.05±1.39	0.001
AE Aspherotoric (µm)	25.30±14.17	2.32±1.27	0.001

AE; Anterior elevation, PE; Posterior elevation

The cut-off point, sensitivity and specificity values of each reference surface were analyzed and compared between the groups (Table 4). As shown in Table 4, the highest sensitivity and specificity values were obtained from the aspherical and aspherotorical reference surfaces rather than the spherical reference surface. It was also observed that posterior elevation values were found to be more sensitive and specific than the anterior elevation values.

Table 4. The cut-off point, sensitivity and specificity values of the anterior and posterior elevation maps obtained from different reference surfaces.

	Cut off point (µm)	Sensitivity (%)	Specificity (%)
PE Spherical	7.5	75	80
PE Aspherical	9.5	97.5	90
PE Aspherotoric	7.5	97.5	80
AE Spherical	2.5	85	85
AE Aspherical	4.5	95	82.5
AE Aspherotoric	3.5	95	85

AE; Anterior elevation, PE; Posterior elevation

The predictive accuracy of the anterior and posterior corneal elevation maps was defined as the area under the ROC curves and it was high for the aspherical and aspherotorical reference surfaces in the keratoconus group ($p>0.90$) (Table 5).

Table 5. The estimated accuracy of the anterior and posterior corneal elevation maps was defined as the area under the ROC curves

	Area Under the Curve	Standard Error
PE Spherical	0.819	0.057
PE Aspherical	0.987	0.012
PE Aspherotoric	0.973	0.023
AE Spherical	0.858	0.053
AE Aspherical	0.969	0.022
AE Aspherotoric	0.971	0.021

AE: Anterior elevation, PE: Posterior elevation

Statistical analysis results of both the posterior and anterior elevation map values obtained with three reference surfaces in the keratoconus and control groups were plotted as ROC curves in figures 1 and 2. Also, posterior elevation maps for different reference surfaces of a patient are shown in Figures 3,4 and 5.

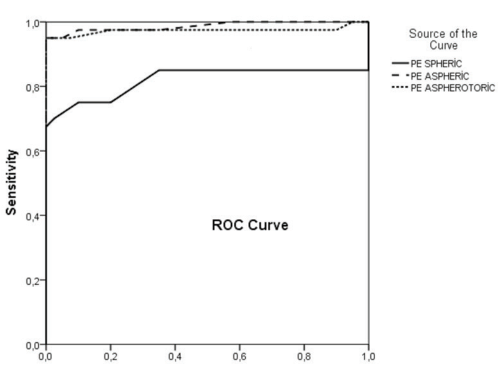

Figure 1:

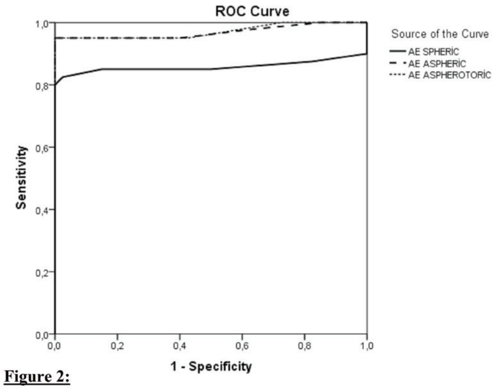

Figure 2:

Figure 1 and 2. The statistical analysis results of both the posterior and anterior elevation map values produced from the three reference surfaces in the keratoconus and control groups

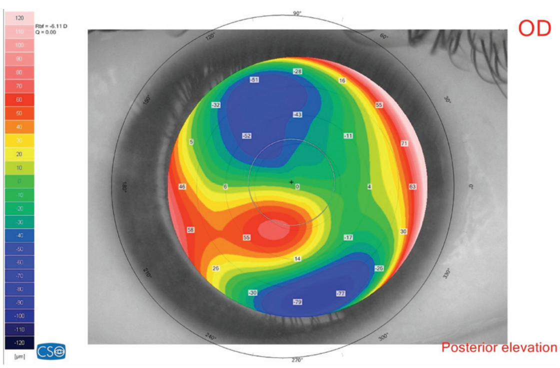

Figure 3

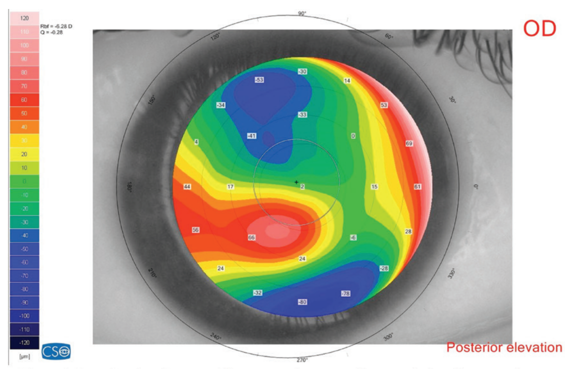

Figure 4

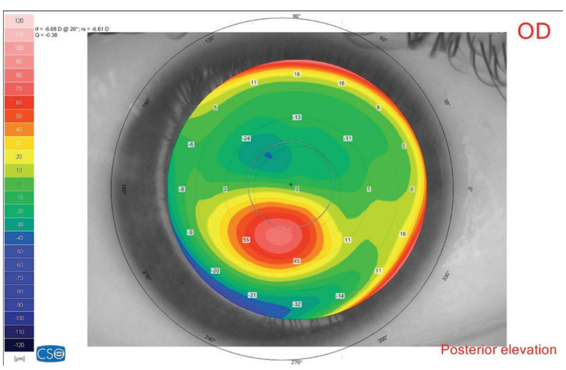

Figure 5

Figure 3, 4, 5. Posterior elevation maps for different reference surfaces of a patient

DISCUSSION

The results of this study demonstrated that the highest sensitivity and specificity values were obtained from the aspherical and asypherotoric reference surfaces rather than the spherical reference surface. Also, our study results showed that posterior elevation values were found to be more sensitive and specific than the anterior elevation values.

Evaluation of the elevation values of the anterior and posterior cornea obtained with Scheimpflug imaging systems in keratoconus diagnosis has gained favor recently. Corneal elevation analyses provide a better assessment of the corneal surface due to the fact that these analyses are independent of the axis, orientation and position.[10-13]

In our study, the difference between the keratoconus and control group was found to be statistically significant in terms of both anterior and posterior elevation values according to all three reference surfaces. In a study, anterior and posterior corneal power, elevation and thickness values were analyzed with the Scheimpflug imaging system and a significant difference was found between ectatic and normal corneas in these parameters.[14] Jafarinasab et al. demonstrated that anterior and posterior elevation maps measured with Galilei analyzer in the 3-mm zone can effectively discriminate keratoconus from normal corneas.[15] Ishii et al. stated that anterior and posterior corneal surface elevation data obtained with elevation-based tomography provide useful information to improve keratoconus diagnostic accuracy and to grade the severity of keratoconus.[16] The results of the current study are consistent with these studies showing that the elevation data of the anterior and posterior corneal surface are an important criterion in the detection of keratoconus. However, there is no consensus yet on which of the different reference surfaces is better at the determination of keratoconus in elevation mapping. The sensitivity and specificity of the elevation values in the posterior elevation map to spherical, aspherical and aspherotorical reference surfaces were 75%-80%, 97.5%-90%, and 97.5%- 80% respectively. The areas under curve (AUC) values of the spherical, aspherical and aspherotoric maps of the posterior cornea were 0.819, 0.987 and 0.973, respectively. Of the reference surfaces used in the posterior elevation map, the aspherical and aspherotoric reference surface measurements appeared to be more sensitive than those of the spherical reference surface and the most accurate reference surface was the aspherical reference surface. According to the results of this study, posterior elevation values were found to be more sensitive and specific than anterior elevation values on aspherical and aspherotoric reference surfaces. The advantage of the posterior surface measurement is that it is not affected by tear film irregularities. The assessment of the posterior cornea is important in the diagnosis of keratoconus because epithelial compensation may hide the cone formation on the anterior surface.[17] Various studies had shown that posterior corneal elevation data were more accurate than anterior elevation data and also that the aspherical and aspherotoric reference surfaces were superior to the spherical reference surface in keratoconus detection. In a study performed with Galilei dual Scheimpflug analyzer; different reference surfaces were compared. It was reported that the best-fit torical and aspherical reference surface were more effective than the best fit spherical surface in forme fruste and keratoconus diagnosis. They also reported that posterior surface elevation maps relative to best-fit toric and aspherical were more sensitive than the anterior surface maps.[18] In a study by Kovacs et al., posterior corneal elevation was assessed using a Scheimpflug camera, and it was reported that posterior corneal elevation maps could be effectively used in discriminating keratoconic and normal corneas. Furthermore, the toric ellipsoid reference surface was found to be the most sensitive method in identifying keratoconus.19Sideroudi et al. suggested that the toric ellipsoid reference surface, with a diameter of 8 mm and an eccentricity of 0.4, should be used in the diagnosis and follow-up of keratoconus cases.[20]

Assessing an aspherotoric normal cornea in relation to an aspherotoric reference surface is expected to reveal less topographic differences compared to spherical reference surfaces. In other words, the best-fit contact lenses for a normal cornea would be contact lenses with an aspherotoric surface. Asphericity and toricity induce a rigid pattern seen in elevation maps compared to the spherical reference surface, therefore affect the precise assessment of the elevation data.[17] This aspherotoricity becomes more prominent in keratoconic cornea. Therefore, evaluation of the aspherotoric reference surface minimizes the influence of the corneal aspherotoricity which could result in miscalculation of the elevation data, and it also helps to detect subtle differences on a normal aspherotoric corneal surface.

This study contained some limitations. Firstly there was a limited number of patients and the patients were at different stages of keratoconus which could affect the analysis results. It is possible to obtain clearer results by carrying out further studies involving a greater number of patients of a similar stage and a larger control group.

In conclusion, the selection of an appropriate reference surface is very important in the diagnosis and classification of keratoconus in Scheimpflug systems. According to the current study results, a topographic assessment of the posterior cornea based on the aspherical and aspherotoric reference surfaces appears to be more effective in determining keratoconus.

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