早期圆锥角膜患者的角膜后表面形态分析

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【摘要】 **目的** 应用Pentacam三维眼前节分析系统分析早期圆锥角膜后表面形态的特点,为完善早期圆锥角膜形态特点的描述提供参考。**方法** 选取亚临床期圆锥角膜患者(43人43眼),可疑圆锥角膜患者(40人40眼)及正常对照(143人143眼)。使用Pentacam三维眼前节分析系统检测角膜,统计分析后表面最大屈光度、后表面最大高度值、分布位置及各指标的组间差异,计算各指标的受试者工作曲线(ROC曲线,反映一项检测指标的敏感度和特异度)下面积。**结果** 亚临床圆锥角膜组、可疑圆锥角膜组和正常组的平均后表面最大屈光度分别为 -6.2 D,$Q=0.5$;-5.6 D,$Q=0.3$;-5.5 D,$Q=0.3$。平均后表面最大高度分别为23 μm,$Q=14$;11 μm,$Q=8.5$;7 μm,$Q=6$。因数据分布为非正态分布,因而采用中位数和四分位间距表示法,Q代表四分位间距。后表面最大屈光度和后表面最大高度在各组之间均存在统计学意义的差别,且在前表面屈光度和高度出现异常前,后表面屈光度和高度已经发生改变。在诊断早期圆锥角膜中,后表面屈光度最大值、后表面高度最大值的ROC曲线下面积最大。**结论** 基于Pentacam三维眼前节分析系统的检测结果,角膜后表面屈光度、后表面高度的变化是早期圆锥角膜形态改变的重要特点。

【关键词】 圆锥角膜; 后表面; Pentacam三维眼前节分析系统
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Posterior surface topography of early keratoconus patients

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【**Abstract**】 **Objective** To investigate the corneal posterior surface topography characteristics of keratoconus at early stages applying the Pentacam anterior segment analysis system. **Methods** The present study included 43 eyes of 43 patients with keratoconus at the subclinical stage (group A), 40 eyes of 40 suspected keratoconus patients (group B), and 143 normal eyes of 143 controls (group C). Based on an examination of the Pentacam anterior segment analysis system of each subject, a series of data, including the posterior surface refractive power, the posterior surface elevation were collected. The differences among the three groups, the correlation among indices, and the area under the receiver operating characteristic (ROC) curves were analyzed. **Results** The mean values of the posterior surface maximum refractive power in 3 groups were -6.2 D, $Q=0.5$; -5.6 D, $Q=0.3$; and -5.5 D, $Q=0.3$, respectively. The mean values of the posterior surface maximum elevation were 23 μm, $Q=14$; 11 μm, $Q=8.5$; and 7 μm, $Q=6$, respectively. The posterior surface maximum refractive power and maximum elevation among three groups were statistically different. The area under ROC (AUR) of posterior maximum refractive power and the AUR of posterior maximum elevation were greater than that of other indices in the diagnosis of early keratoconus. **Conclusions** Based on the results from the Pentacam anterior segment analysis system, the changes of the posterior surface refractive power and elevation are important characteristics of early keratoconus.

【**Key words**】 keratoconus; posterior surface; Pentacam anterior segment analysis system

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Keratoconus is a non-inflammatory, slowly progressive, corneal-thinning disease characterized by central corneal stromal thinning, apical protrusion, and irregular astigmatism. Its etiology is not fully elucidated and may be complicated. Most (90%) of patients present with bilateral involvement[1-3]. Keratoconus often occurs in puberty, and acute cornea hydrops, perforation and scarring may emerge at late stages. It can present either as an independent disease or as a part of several syndromes[1].

The diagnosis devices of keratoconus have experienced several innovations[1]. Computer assisted corneal topography has brought the diagnosis of keratoconus to a new era. However, all of these established diagnosis standards are based on the anterior surface of corneal topography, the posterior surface topography of keratoconus, which do have changes, are not included in those diagnosis standards[4-8].

Several instruments have recently been developed to detect the posterior surface of the cornea, such as Orbscan[4-9] and Pentacam[8] (Measurement and Evaluation System for the Anterior Segment of the Eye, OCULUS, Wetzlar, Germany). Posterior surface changes have been found for early keratoconus using Orbscan Ⅰ and Orbscan Ⅱ in numerous studies, indicating the importance of posterior surface changes in the diagnosis of early keratoconus. However, Orbscan has several shortcomings[10,11] which may be avoided by using Pentacam[12-16]. Thus far, the posterior surface characteristics of keratoconus at the subclinical stage have seldom been described by Pentacam analysis. In the present study, we examined the posterior surface refractive power and elevation in a group of Chinese patients with keratoconus at early stages by Pentacam analysis. The results may be useful in future studies aimed at achieving a complete description of early karatoconus.

SUBJECTS AND METHODS

Subjects and Diagnosis Patients with keratoconus diagnosed in the Department of Ophthalmology, Eye Ear Nose and Throat Hospital of Fudan University, Shanghai, China from September 2005 to January 2007 were enrolled in this study. All the patients were mainly came from southeastern China. Informed consent was obtained from each of the subjects. For each patient, a complete history was taken, followed by a full ophthalmic examination, including visual acuity measurement, slitlamp examination, and funduscopic examination. Patients with any history of other corneal diseases, cornea trauma or surgeries (especially laser *in situ* keratomileusis or laser assisted sub-epithelial keratectomy) or with a family history of glaucoma were excluded from further analysis. Finally, 83 eyes of 83 patients (age range from 8 to 38 years old, 1 eye from each subject) were included in this study; 143 eyes from 143 normal subjects (age range from 9 to 40 years old, 1 eye from each subject) were also included as controls. According to the criteria set by Rabinowitz[17,18] and Fam[4], 83 subjects were divided into two groups. Group A was subclinical stage keratoconus (43 eyes of 43 subjects, mean age = 18 years old, Q = 7, range from 11 to 36 years old), and group B was suspected keratoconus (40 eyes of 40 subjects, mean age = 19 years old, Q = 10, range from 8 to 38 years old). Group C was the control subjects (mean age = 18 years old, Q = 8), and the mean ages among 3 groups were not statistically different (H = 5.452, P = 0.182 3). The diagnosis of subclinical keratoconus was based on the following: the corneal central refractive power was larger than 46.5 D; the refractive power difference between the superior and inferior points of a 3 mm ring was larger than 1.26 D; and the refractive power difference between two eyes was larger than 0.92 D, but without any obvious signs of clinical keratoconus as detected by slitlamp microscopy, including apex protrusion or thinning, Fleischer rings, Vogt striae, and superficial scarring. Suspected keratoconus was defined as the "normal" eye of a patient whose other eye had been diagnosed with clinical keratoconus, according to current diagnostic standards.

Pentacam examination and data analysis All Pentacam (software edition 1.08, OCULUS, Wetzlar, Germany) examinations were performed by the same

qualified and experienced examiner. Each eye was examined 3 times and the best image was taken. The main indices examined included the posterior surface maximum refractive power and maximum elevation, the anterior surface maximum refractive power, and the anterior surface maximum elevation. We recorded the positions of the posterior maximum refractive power point and the maximum elevation point respectively. The correlations between these indices were analyzed, and the distance between the maximum refractive power points and the highest points were also statistically analyzed. For the diagnosis of early keratoconus, several parameters were calculated, such as the area under the ROC curve (AUR) of posterior maximum refractive power, the posterior maximum elevation, the anterior surface maximum refractive power, and the anterior surface maximum elevation.

Statistical analysis were accomplished with a SAS program (software edition 8.2), the Kruskal-Wallis test and ANOVA were used to determine the significance of differences among the study groups. The considered level of statistical significance was $P<0.05$.

RESULTS

The posterior surface maximum refractive power and posterior surface maximum elevation from 3 groups of subjects (subclinical stage keratoconus, suspected keratoconus, and normal controls) are summarized in Table 1. The average posterior surface maximum refractive power and elevation in Group A (subclinical keratoconus) were significantly higher than those of the controls (group C, $P=0.000\ 1$). In the control group, none of the values of the posterior surface maximum refractive power was greater than −6.2 D (98% of them were lower than −6.0 D), and all of the posterior surface maximum elevations were lower than 19 μm, 95% of which were lower than 14 μm. In contrast, the values of the posterior surface maximum refractive power in group A ranged from −5.8 D to −7.8 D, 65% of which were greater than −6.0 D. The posterior surface maximum elevations ranged from 5 μm to 50 μm, 83.7% of which were higher than 14 μm. In group B (suspected keratoconus), the values of the posterior surface maximum refractive power of 9 eyes (22.5%) were greater than −5.8 D, and those of 4 eyes (10%) were greater than −6.0 D. The posterior surface maximum elevations of 14 eyes (35%) were higher than 14 μm.

Tab 1 Average values of the posterior surface maximum refractive power and maximum elevation

Group	Average posterior surface maximum refractive power (*D*)				Average posterior surface maximum elevation (μm)			
	Median	*Q*[1]	Min	Max	Median	*Q*	Min	Max
A	−6.2	0.5	−5.8	−7.8	23	14	5	50
B	−5.6	0.3	−5.2	−6.4	11	8.5	5	33
C	−5.5	0.3	−5.0	−6.2	7	6	−2	19

[1] *Q* stands for quartile range, for the data are not in normal distribution

The average values of the anterior surface maximum refractive power of groups A, B, C were 48.2 D, $Q=1.7$; 44.5 D, $Q=1.25$; and 44.4 D, $Q=2$, respectively. The average anterior surface elevations of the three groups were 13 μm, $Q=7$; 6 μm, $Q=4$; and 7 μm, $Q=4$, respectively. *Q* stands for quartile range, for the data are not in normal distribution. The differences in the two parameters of the anterior surface between Group A and the other two groups were statistically significant, but the differences between groups B and C were not (Kruskal-Wallis test and Bonferroni test, $P>0.05$). As shown in Table 2, there were differences among the values of the average posterior surface maximum refractive power and elevation in the three groups. The differences in the average posterior surface maximum refractive power and elevation between groups were statistically significant (details in Table 2).

Tab 2 Statistical analysis of the differences in the posterior surface maximum refractive power and maximum elevation among different groups

Posterior surface indices	χ^2	P[1]
Posterior surface maximum refractive power	312.402 3	0.000 1
Posterior surface maximum elevation	285.037 5	0.000 1

[1] $P<0.05$ indicates that for each index in the three groups, there is a significant difference between at least two groups. For instance, the posterior surface maximum elevation ($\chi^2=285.037\ 5$, $P=0.000\ 1$) between at least two groups are statistically different.

The distance between the anterior surface and the posterior surface maximum refractive power points, the distance between the posterior surface

maximum refractive power point and maximum elevation point, and the distance between the anterior surface and the posterior surface maximum elevation points are summarized in Table 3. The differences in the RA-RP, RP-EP, and EA-EP (RA-RP: the distance between the anterior surface and the posterior surface maximum refractive power points, RP-EP: the distance between the posterior surface maximum refractive power point and maximum elevation point, EA-EP: the distance between the anterior surface and the posterior surface maximum elevation points) between groups A and C were statistically significant (Kruskal-Wallis test and Bonferroni test, $P = 0.000\ 1$). These results suggest that between the normal and subclinical stages, the maximum points become closer to each other.

The area under the ROC (AUR) of the maximum refractive power of the anterior surface and posterior surface, and the maximum elevation of the anterior surface and posterior surface are shown in Table 4. ROC is a curve reflecting the sensitivity and specificity of a certain index, the larger the AUR is, the higher the sensitivity and specificity of the index are. According to the Pentacam results, the posterior surface maximum refractive power was the most sensitive index (AUR 0.976) to differentiate subclinical keratoconus from normal cornea, while the posterior surface maximum elevation was the most sensitive index to differentiate suspected keratoconus from normal cornea.

Tab 3 The distances between the maximum refractive power points of anterior surface and the posterior surface the posterior surface maximum refractive power point and maximum elevation point, and the maximum elevation points of anterior surface and posterior surface

Group	RA-RP (mm)		RP-EP (mm)		EA-EP (mm)	
	Median	*Q*	Median	*Q*	Median	*Q*
A	1.06	1.25	1.09	0.73	0.49	0.35
B	0.80	1.04	1.52	0.96	0.81	0.85
C	1.22	1.85	1.77	0.92	0.74	0.74

RA-RP: The distance between the maximum refractive power points of anterior surface and posterior surface; RP-EP: The distance between the posterior surface maximum refractive power point and maximum elevation point; EA-EP: The distance between the maximum elevation points of anterior surface and posterior surface.

Tab 4 The AUR of posterior surface maximum refractive power and maximum elevation, and anterior surface maximum refractive power and maximum elevation

Group	Posterior surface maximum refractive power	Posterior surface maximum elevation	Anterior surface maximum refractive power	Anterior surface maximum elevation
A	0.976	0.923	0.975	0.870
B	0.647	0.752	0.482	0.468

A: Differentiation of subclinical keratoconus and normal cornea; B: Differentiation of suspected keratoconus and normal cornea

DISCUSSION

The clinical symptoms and signs of keratoconus are not obvious at the early stage of the disease, which is frequently mistaken for myopia. When late or severe stage disease develops, the treatment outcome of RGP (rigid gas permeable contact lens) is usually unfavorable, and keratoplasty is frequently needed. Therefore, it is important to correctly diagnose keratoconus early in the disease[19-23], especially for patients intending to receive LASIK or LASEK.

There are currently various diagnostic standards for keratoconus, but the posterior surface topography characteristics are not described in them. Since 1995, Orbscan slit lamp topography has been widely used to describe the posterior surface of the cornea. For example, Fam *et al*[4] pointed out that the anterior surface elevation is the best index to distinguish keratoconus from suspected keratoconus. However, the Orbscan method has several disadvantages. Chief among these disadvantages is the fact that it can only take up to 45 pictures in one scan, and all of the resultant images are vertical[10,11].

Pentacam[12-16] is the first cornea scanning instrument to use Scheimpflug theory; it can complete a circumgyrating 360 degree scan and take 50 pictures in 2 seconds, covering the corneal anterior and posterior surfaces at the same time. The data collected by Pentacam have higher resolution than Orbscan data (25 000 data points *vs* 9 600 data points), and its reproducibility and

accuracy are also higher than Orbscan. In addition, a 3-D model reconstruction is available in the Pentacam system. We tried to detect the features of the posterior surfaces of keratoconus applying the Pentacam system, and did have some findings in this study.

Our results indicate that from normal control to suspected keratoconus, and to subclinical keratoconus, the values of the posterior surface maximum refractive power and elevation gradually increase. For 98% of the normal eyes (group C), the values of the posterior maximum refractive power were lower than −6.0 D; only 2 eyes had a value greater than −6.0 D, and their posterior elevation was normal. In the subclinical group, 65% of eyes had posterior surface maximum refractive power values higher than −6.0 D. Thus, we suggest that when the value of the posterior surface maximum refractive power is higher than −6.0 D, and is accompanied by other abnormal signs described by Rabinowitz, early keratoconus should be considered. In addition, the posterior maximum elevation was less than 14 μm in 95% of the eyes of the normal group, and in 83.7% of the eyes of the subclinical stage group, suggesting that, when this value is higher than 14 μm, and is accompanied by other abnormal signs, early keratoconus is indicated. Another important phenomenon was that, from normal group to subclinical groups, the posterior elevation increased faster than the posterior refractive power; in the subclinical group, the posterior surface elevation was higher than that of normal controls, while there was only a modest increase in posterior surface refractive power. These results suggest that the change of the posterior surface elevation is more sensitive than that of the posterior surface refractive power in early keratoconus.

The values of posterior surface maximum refractive power and elevation among the three groups were significantly different, while the differences in the anterior surface maximum refractive power and the anterior surface maximum elevation were not significant. In other words, the values for the posterior surface of suspected keratoconus were significantly different from normal controls, while the values for anterior surface were not. The posterior surface became abnormal while the anterior surface stayed still. In addition, the area under the ROC of the posterior surface maximum refractive power and the area under the ROC of the posterior surface maximum elevation were larger than the others, indicating that these two indices are extremely important diagnostic indicators. It is possible that the posterior surface is the first barrier to sustain the intraocular pressure, so it tends to protrude more easily and at earlier stages in keratoconus.

In summary, although various diagnostic indices have been suggested by researchers around the world, the posterior surface topography of keratoconus have rarely been studied applying the Pentacam system, especially in Chinese populations. The results from the present study may be helpful in the description of early keratoconus. In particular, the posterior surface refractive power and elevation may be the most important indices, the value of the posterior surface indices change earlier than that of anterior surface in keratoconus at early stages. Further studies are needed to follow up the changes in the posterior surface during the development and progression of keratoconus, and to further validate early diagnosis using the proposed indices.

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