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Biomechanical properties of early keratoconus: Suppressed deformation signal wave

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ABSTRACT

Purpose: To examine the diagnostic validity of different corneal biomechanical parameters for the detection of early keratoconus
Methods: Sixty-one eyes with a diagnosis of early keratoconus and 61 topographically normal eyes were enrolled in the study. All participants underwent testing with the Ocular Response Analyzer (ORA), and 40 indices from each cornea were included in the analysis.
Results: The mean (standard deviation: SD) of keratometry and central corneal thickness in keratoconic corneas was 46.9 (2.5) diopter (D) and 473 (31) μm, respectively. Of the 40 evaluated indices, 32 showed a significant difference between the two groups using *t*-test ($p < 0.05$). According to the results of logistic regression, the indices of height from the lowest to the highest point in peak 2 ($H2^1$) and corneal resistance factor (CRF) with $R^2 = 0.79$ were the best predictors of early keratoconus ($p < 0.001$). $H2^1 \leq 190$ with a sensitivity and specificity of 87% and 91.8%, respectively, and CRF ≤ 8.6 with sensitivity and specificity of 87% and 85.3%, respectively, yielded an overall diagnostic accuracy of 97.3%.
Conclusion: This study results point to the important role of novel waveform-derived indices measured by ORA, along with conventional biomechanical indices, for the early diagnosis of keratoconus. The best predictors of keratoconus in its early stages are $H2^1$ and CRF which showed very high sensitivity and specificity for the detection of early keratoconus.

1. Introduction

Corneal biomechanical examinations consist of the two components of viscosity and elasticity, and they characterize certain corneal properties that are influenced by the structure of the corneal collagen in the stroma [1]. Since about 90% of the corneal thickness is composed of stroma, a strong association between elasticity and corneal thickness is quite expected [2]. However, there are still unknown facts, especially in regard to cases of post-surgical ectasia who had a residual stromal bed (RSB) >250 μm after keratorefractive procedures [3,4]. On the other hand, there have also been cases with RSB less than 250 μm who did not develop any post-operative complications [5,6]. Current protocols for the preoperative evaluation of surgical candidates includes special attention to their corneal topography and thickness. In particular, care is taken to make sure that RSB estimates are accurate when photoablative techniques are used. However, it seems that all these measures cannot guarantee that postoperative ectasia does not develop. Biomechanical properties of the cornea could resolve this ambiguity, and their evaluation, along with corneal topographic and thickness data, may improve surgical safety.

Keratoconus, as an ectatic disorder of the cornea, is of particular interest in studies of corneal biomechanics. In keratoconus, the diameter of collagen fibrils is decreased, and fibril layers, especially in the central cornea, lose their normal orientation. These changes, which can cause corneal deformation, result in the loss of corneal rigidity [7–9]. Common biomechanical indices, namely the CRF and corneal hysteresis (CH), have not shown agreeable levels of sensitivity and specificity for the diagnosis of ectasia. [10–12] However, recent versions of the Ocular Response Analyzer (ORA, Reichert Ophthalmic Instruments, Buffalo, NY) software provide data on changes in the corneal shape during applanation in the

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form of 34 indexes which are recommended for the diagnosis of keratoconus eyes and keratoconus suspects.

A number of studies have compared these indices between keratoconus and normal eyes, and some have found that these new waveform-derived biomechanical parameters are more useful than CRF and CH in predicting and detecting early keratoconus [10–12]. This is while some other recent studies suggest that conventional indices, i.e. CRF and CH, are better predictors and perform better in the early diagnosis of keratoconus [13]. They also suggest that even combining these novel indices with conventional factors does not improve their diagnostic ability [13].

In light of the inconsistencies in the literature in this regard, it seemed necessary to conduct further studies. The present study was designed to perform a complete assessment of the diagnostic ability of new waveform-derived and conventional ORA indices for the early and accurate detection of early keratoconus.

2. Materials and methods

In this cross-sectional study, subjects were selected from patients examined at the Cornea Clinic of Noor Eye Hospital (Tehran, Iran) enrolled using a database of patients with normal corneas who were candidates for refractive surgery and a database of cases diagnosed with early keratoconus.

The two groups were similar in terms of age and gender. All participants had complete eye examinations including visual acuity, refraction, retinoscopy, and slit-lamp examination. They also had corneal topography (Pentacam HR, Oculus, Germany), and the diagnosis of early keratoconus was based on the ophthalmologist's interpretation of the four topography and pachymetry maps and the Belin/Ambrósio display along with keratoconus indices based on McMahon criteria.

The inclusion criteria of this study were:

1. A definite diagnosis of keratoconus by an ophthalmologist based on topographic maps and Pentacam numerical data
2. Compatibility with McMahon criteria of mild keratoconus
3. No history of ocular surgery

The inclusion criteria for the control group were:

1. No sign of corneal disease on slit lamp examination
2. No suspicion of keratoconus in corneal topographic maps
3. No history of ocular surgery
4. Match a keratoconus patient in terms of age (±5 years) and gender

The study was approved by the Institutional Review Board of Noor Ophthalmology Research Center. All cases and controls signed informed consents before participation in the study.

All participants were tested twice with the ORA (software version 3.01), and the one with a better waveform score (WS) was recorded.

The ORA applies a dynamic bi-directional applanation process for the assessment of corneal biomechanical properties. A rapid air puff causes the cornea to move backward, past applanation, and into concavity. After the initial applanation, as the air force reduces, the cornea returns from concavity to its normal configuration and passes through a second applanation. Viscous damping in the cornea results in an offset between the backward and forward pressure values. The difference between these motion applanation pressures is the CH which indicates viscous damping in the cornea. CRF is a measure of both the viscous and elastic resistance of the corneal surface [12,14,15].

The new version of the ORA device provides 34 new indices in addition to CRF and CH, which are derived from waveform data.

Table 1 presents the descriptions of the indexes evaluated in this study. Fig. 1 illustrates these indices in the deformation profile of a healthy cornea. In the control group, one eye was randomly selected in each participant. In keratoconus patients, the data of the eye with a diagnosis of mild keratoconus was used for analysis. Independent-samples *t*-test was used to compare the mean values of the indexes between the two groups. To identify the best predictors of early keratoconus, 40 biomechanical indices were evaluated in a stepwise logistic regression model (P removal = 0.05).

3. Results

Sixty one keratoconic patients with a mean (SD) age of 23.9 [4] years and 61 controls with a mean age of 22.1 [7] years were

Table 1
Characterization of corneal deformation signal indices.

Parameter	Description
CRF	Corneal resistance factor
CH	Corneal hysteresis
p1area,p2area	Upper 75% area of peak
p1 area1,p2area1	Upper 50% area of peak
Aspect1, Aspect 2	Aspect ratio of peak height/width
Uslope1, Uslope 2	Rate of increase from 25% point to peak
Uslope11,Uslope21	Rate of increase from 50% point to peak
Dslope1,Dslope2	Rate of increase from peak to 25% point
Dslope11,Dslope21	Rate of increase from peak to 50% point
H1, H2	Height from lowest to highest point in peak
H11, H21	Height from 50% point to highest point in peak
Dive1, Dive2	Backside of down slope of peak (absolute value of peak until the first break)
Mslew1,Mslew2	Maximum single increase in the rise of peak (longest continuous line without a break)
Slew1,Slew2	Aspect ratio of dive1 where dive is divided by width
aplhf	High frequency noise in regions between peaks normalized by product of average of heights*width of region
Bindex	Number of breaks in the peak2
Aindex	Number of breaks in the peak1
TFI	Tear film index
Aspect11, Aspect21	Aspect ratio of peak height/width from 50% point
Path1, Path2	Absolute value of path length around peak
Path11, Path21	Upper 50% of absolute value of path length around peak
W11, W21	Width of peak 1/2 at point of 50% of the base region
w1,w2	Width of peak 1/2 at point of 25% of the base region