Subclinical Keratoconus: Detection at Its Earliest Stage

An objective scoring system can quantify the status of the cornea with a single value.

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Identifying patients at risk for subclinical keratoconus and distinguishing a normal from a pathologic case at its earliest stage have been elusive goals for refractive surgeons. As the main risk factor for postoperative corneal ectasia,1-3 undetected subclinical keratoconus is a contraindication for refractive surgery. Unfortunately, slit-lamp examination and corneal topography may not accurately detect subclinical keratoconus at its earliest stages.4-7

In an effort to improve on current methods for identifying subclinical keratoconus, we have undertaken a series of investigations. We first explored the efficacy of combining indices from corneal topographic and tomographic devices in a discriminant function to detect mildly ectatic corneas.4 Subsequently, we validated an objective method of detecting subclinical keratoconus in eyes susceptible to ectasia based on this type of analysis.5 These investigations demonstrated that an automated system based on a combination of Placido-disc–based topography and corneal tomography parameters can be used to create a sensitive and specific screening method for mild manifestations of keratoconus.

BACKGROUND

Corneal ectasia is characterized by progressive topographic steepening associated with irregular astigmatism and loss of visual acuity. Risk factors include patient age less than 25 years, myopia greater than 8.00 D, residual stromal bed thickness less than 250 µm, keratometry (K) greater than 47.00 D, and central pachymetry less than 500 µm.5 Some ectasia risk scores weigh these factors to identify at-risk corneas; however, as Binder observed in an analysis of more than 9,000 eyes with at least one of these risk factors,4 postoperative ectasia does not always develop in these cases.

Eyes with keratoconus experience noninflammatory, progressive, and localized corneal thinning and protrusion. Although keratoconus can be easily recognized in its advanced stages, there is no exact definition of, nor are there widely accepted criteria for, subclinical keratoconus—also referred to as keratoconus suspect or forme fruste keratoconus.

With that said, localized steepening on corneal topography and slight bowing of the posterior corneal surface on tomography are the most significant independent risk factors for post-LASIK ectasia.9-16 Our research has demonstrated4,17 that study of the topographic and tomographic characteristics of the more normal eye of a patient with asymmetric keratoconus can be used to create criteria for identifying corneas at risk for subclinical keratoconus. These data can be used to develop a scoring system, the implementation of which can hopefully lower the incidence of post-LASIK ectasia by giving surgeons a more concrete way to determine if an eye is susceptible to an ectatic outcome.

LINEAR DISCRIMINANT ANALYSIS

We performed a linear discriminant analysis to distinguish a population of healthy corneas from those with subclinical keratoconus using data from the Orbscan IIz (Bausch + Lomb Technolas). Analysis performed by the Corneal Navigator for the OPD-Scan II (Nidek Co., Ltd.) classified 143 eyes into three populations: normal, subclinical keratoconus, and keratoconus.

The normal population consisted of 72 eyes that had undergone LASIK without an ectatic outcome at 2-year
follow-up. There was no focal or inferior corneal steepening and no eye had a central K greater than 47.00 D—two topographic patterns suggestive of subclinical keratoconus. The subclinical keratoconus group included 40 contralateral eyes of patients with unilateral keratoconus, and the keratoconus group included 31 eyes, with keratoconus diagnosed by an experienced corneal specialist on the basis of clinical and topographic signs. In the subclinical group, all eyes were negative for keratoconus suspicion based on examination with the Corneal Navigator, which uses 21 indices derived from a computerized analysis of anterior Placido maps.

Between the normal and subclinical keratoconus eyes, there were no differences in anterior or posterior best-fit sphere and maximum and minimum simulated K (sim-K). However, the subclinical keratoconus group had significantly higher corneal irregularity, thinner central pachymetry, thinner and more decentered thinnest pachymetry, and a larger difference between the central and thinnest pachymetries than the normal eyes.

Between the normal and keratoconus groups, the level of corneal irregularities and the central and thinnest pachymetries were significantly different. Additionally, in the keratoconus group, there was a significantly larger difference between the central and thinnest pachymetries; the thinnest pachymetry was more inferotemporally located; and maximum anterior corneal elevation, maximum posterior corneal elevation, and anterior and posterior elevation of the thinnest pachymetry were all significantly greater.

**CORNEAL CURVATURE, THICKNESS**

Comparing anterior corneal curvature between the normal and keratoconus groups, the mean curvature was significantly different for any distance from the thinnest pachymetry, except at 8 and 9 mm, between the normal and keratoconus groups. This difference was not seen between the normal and subclinical keratoconus groups. In the subclinical keratoconus group, corneal flattening at 5, 6, and 7 mm from the thinnest pachymetry was significantly faster than in the normal group.

With regard to posterior corneal curvature, corneal flattening was significantly faster between 3 and 9 mm from the thinnest pachymetry in the keratoconus group than it was in the normal group. Additionally, from 1 to 6 mm away from the cornea’s thinnest point, the mean posterior curvature was significantly lower in the keratoconus group.

Across all corneal zones, the mean thickness was significantly lower in the subclinical keratoconus and keratoconus groups than it was in the normal group, and these two groups also experienced faster thickening of the cornea in all zones compared with the normal group.

This study confirmed that the differences between normal and keratoconic eyes are easily noted. Key observations of this study include the following:

- Combination of the anterior surface irregularity indices alone can be used with great accuracy only to detect frank keratoconus, as it is insufficient to provide acceptable accuracy for the detection of early subclinical keratoconus;
- Only the combination of all the studied indices in a discriminant function provided good accuracy (92% specificity and 92.5% sensitivity) in differentiating normal corneas from those with subclinical keratoconus. The same combination of indices also provided 100% specificity and 97% sensitivity for differentiating between normal and keratoconic corneas;
- Spatial thickness profile indices and maximum posterior corneal elevation were the most important contributors to the discriminant function;
- Indices generated from corneal thickness and curvature over the entire cornea and the calculations of percentage of thickness increase and anterior and posterior curvature variation from the thinnest point to the periphery were able to identify even very mild forms of keratoconus undetected by topography, and
- Because of overlap in parameters between normal and pathologic corneas, no single parameter can sufficiently distinguish a normal from a suspect cornea.

**ELEVATION AND TOMOGRAPHY COMBINED**

These results confirmed that the combination of elevation and tomography data is a more sensitive and specific detector of early subclinical keratoconus compared with either Placido-disc topography or elevation data alone. Including elevation and tomography data with other measurements such as corneal biomechanics or wavefront sensing could further increase the specificity and sensitivity of these tests for early subclinical keratoconus detection. Although it is unclear whether eyes would show changes in either posterior elevation or pachymetry without showing changes in anterior curvature, we believe it is safer to define any eye with abnormal thinning and posterior elevation as suspicious of subclinical keratoconus, as this characteristic is reflective of the physiopathogeny of keratoconus. Our investigations suggest that alterations to anterior curvature suggestive of keratoconus should be considered as subclinical keratoconus when accompanied by tomography and/or posterior elevation changes.

We subsequently validated the results of these investigations in a retrospective evaluation of 183 consecutive corneal elevation and Placido-disc–based topographies of patients not included in the previous analysis. One surgeon classified each eye as normal or as at risk for post-LASIK ectasia. An objective scoring system based on (Continued on page 60)
Combination of topography and tomography data was also used to classify the corneas. The surgeon classified 159 eyes as normal and 24 as at risk for post-LASIK ectasia. The scoring system correctly classified 153 eyes as normal and 22 eyes as at risk. The system generated six false positives (normal eyes classified as at risk) and two false negatives (at risk eyes classified as normal). The sensitivity of the automated system was therefore 92%, and the specificity 96%.

Conclusion

Identifying subclinical keratoconus remains a challenge for refractive surgeons. Our investigations suggest that an automated system based on a combination of elevation and tomography data may allow more sensitive recognition of subclinical keratoconus that is undetectable with Placido-disc-based topography alone. A system based on the type of analysis described in this article (the Score system; Bausch + Lomb Technolas) has been designed by the authors and is awaiting regulatory approval in the European Union.

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