REVIEW/UPDATE

New perspectives on the detection and progression of keratoconus

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Laser refractive surgery has increased markedly in recent years, making the detection of corneal abnormalities extremely relevant. For this reason, an accurate diagnosis of clinical or subclinical keratoconus is critical. Corneal topography is the primary diagnostic tool for keratoconus detection, and pachymetry data and corneal aberrations are also commonly used. Recently, tomographic measurements using optical coherence tomography and corneal biomechanical indices have been used. In incipient and subclinical keratoconus, the use of a single parameter as a diagnostic factor is not sufficiently accurate. In these cases, the use of algorithms and predictive models is necessary. In addition, determining whether the disease will progress is crucial to selecting the most appropriate treatment. Some factors, such as age, keratometric indices, corneal elevation data, and corneal thickness, seem to be useful in predicting keratoconus progression.

J Cataract Refract Surg 2017; 43:1213–1227 © 2017 ASCRS and ESCRS

Keratoconus is an ectatic corneal disorder characterized by progressive corneal thinning that generates a corneal protrusion, irregular astigmatism, and decreased vision.[1,2] The corneal protrusion, which has a conical shape, is generated by stromal tissue degeneration, leading to a mechanical weakening of the corneal structure.[2,3] Keratoconus typically affects both eyes. Although the etiology is not fully understood, keratoconus has traditionally been considered a noninflammatory disease.[1] However, recent evidence suggests that proinflammatory factors are involved in keratoconus pathogenesis, presenting some controversy about this issue.[4–6]

Keratoconus usually begins to develop at puberty and progresses until the third or fourth decade.[7] The incidence varies depending on factors such as the ethnic group of the sample evaluated or the criteria used to establish the diagnosis. An incidence between 50 cases and 230 cases per 100 000 has been estimated in the general population,[1] higher in the Asian population than the white population.[8] The risk factors for keratoconus development include constant eye rubbing, the presence of some systemic diseases, floppy-eyelid syndrome, allergies, as well as a family history that predisposes to the development of the pathology.[1,2]

At present, the main tool used to diagnose keratoconus is corneal topography, which enables the clinician to detect the conical protrusion and the inferior–superior (I–S) asymmetry, which are typical signs of keratoconus (Figure 1).[2,9,10] This tool is usually combined with biomicroscopic examination; in moderate and advanced stages, this shows the corneal protuberance, stromal thinning, the Fleischer ring, and even the Vogt striae.[1] Therefore, the detection of advanced keratoconus is not difficult. However, in incipient or preclinical stage cases, the diagnosis becomes complicated. The term *subclinical keratoconus* refers to an incipient stage of keratoconus that can be undetected in routine clinical practice (Figure 2). The standard diagnostic criteria are shown in Figure 3.[2] Subclinical keratoconus is usually asymptomatic and is considered the most significant risk factor for the development of ectasia after laser refractive surgery.[11]

Because laser refractive surgery has increased markedly in recent years, the diagnosis of subclinical keratoconus has become extremely relevant because an accurate diagnosis is mandatory to avoid ectasia after refractive surgery.

This review attempts to define and compile the diagnostic systems and indicators for keratoconus and subclinical keratoconus, including the latest commercially released corneal topography systems, the analysis of anatomic structures of the eye with the latest optical coherence tomography (OCT) technology, the analysis of corneal biomechanics, and the use of new predictive models.

Submitted: April 10, 2017 | Final revision submitted: June 3, 2017 | Accepted: July 7, 2017

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0886-3350/$ - see frontmatter
http://dx.doi.org/10.1016/j.jcrs.2017.07.021

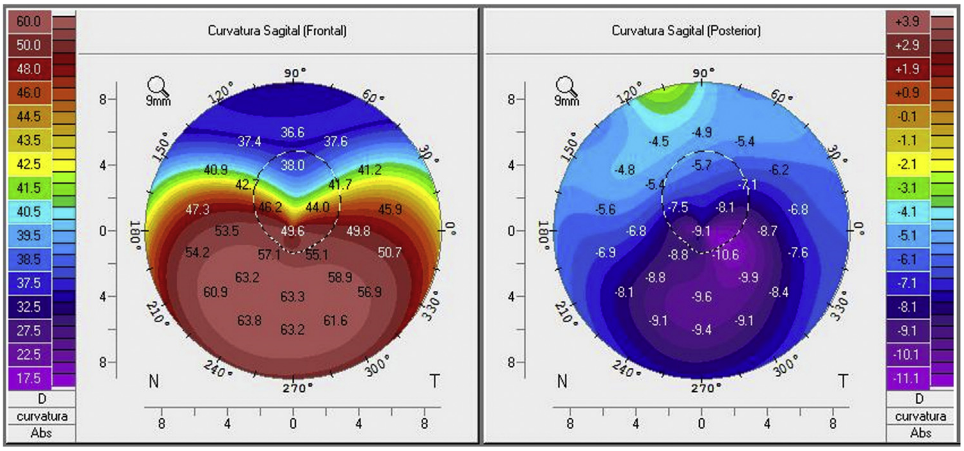

Figure 1. Anterior (*left*) and posterior (*right*) sagittal topographic map of keratoconus, in which the presence of a marked corneal protrusion and high I–S asymmetry is present (N = nasal; T = temporal).

DETECTION OF KERATOCONUS

Topographic Indices

The importance of corneal topography in the detection of keratoconus is well-known.[2,9] Initially, keratometric data were used to differentiate healthy eyes from keratoconic eyes; the curvature of the cornea was significantly higher in the latter.[1] Recent studies analyzing the diagnostic ability of mean keratometry (K) in keratoconus have shown an acceptable accuracy (sensitivities >80% and specificities >70% for cutoff points between 45.2 diopters [D] and 45.7 D). However, this parameter is poor for the detection of subclinical keratoconus, with no ability to differentiate significantly between subclinical keratoconic eyes and healthy eyes.[12–14]

Astigmatism, both anterior (3.93 D ± 2.74 [SD]) and posterior values (0.93 ± 0.64 D), has been shown to be significantly higher in keratoconus.[15] With a topographic astigmatism of 2.5 D as a cutoff point, the ability to detect keratoconus is acceptable (sensitivity and specificity >75%)[13] but the specificity decreases considerably in the case of subclinical keratoconus (<65%), indicating that it is not a good diagnostic parameter.

In recent years, the most studied topographic parameter as a predictor of keratoconus has been corneal elevation, especially posterior elevation, which has good diagnostic ability; sensitivities and specificities >90% have been obtained in most samples.[12,14,16–18] In the detection of subclinical keratoconus, there is significant variability in the elevation data between studies. De Sanctis et al.[19] obtained sensitivity of 73.3% and specificity of 86.5% for posterior elevation, but others obtained a more limited diagnostic accuracy.[14,18,20]

New vector indices such as ocular residual astigmatism (ORA) and topography disparity have also been used to detect keratoconus and subclinical keratoconus; prediction accuracy for keratoconus was better with ORA (cutoff 1.255 D, sensitivity 82%, specificity 92%) and for subclinical keratoconus, with topography disparity (cutoff 0.710 D, sensitivity 73.7%, specificity 68.0%).[21]

Indices based on digital analysis of the Placido disk image were defined by Ramos-López et al.[22]; for example, PI1 (maximum distance between centers of mires), PI2 (drift of the centers of consecutive mires), and SL (alignment of the centers of mires). The ability of the indices to detect keratoconus was good for an area under the receiver operating characteristic curve of more than 0.90. The indices also have potential for detecting subclinical keratoconus.

Corneal Pachymetry

Corneal pachymetry is an important tool in the diagnosis and progression of corneal ectasias, such as keratoconus and subclinical keratoconus. The stromal thinning produced in keratoconus can be quantified by current imaging

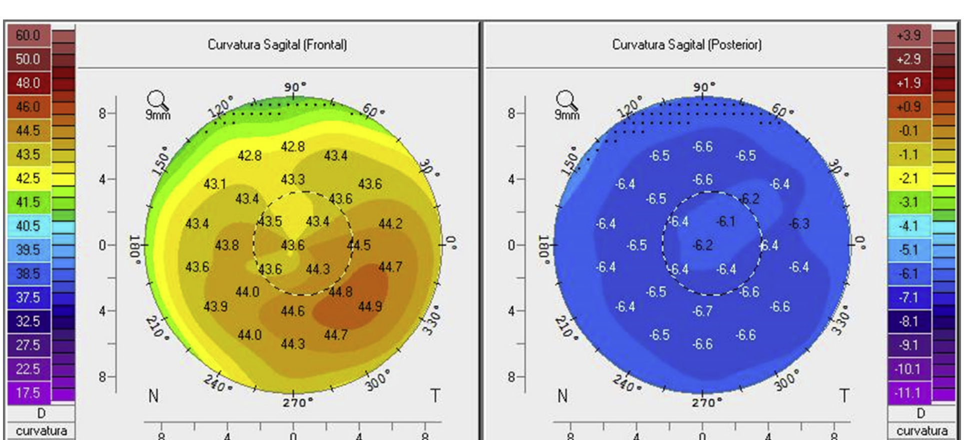

Figure 2. Anterior (*left*) and posterior (*right*) sagittal topographic map of subclinical keratoconus, in which a minimal corneal protrusion is present and the I–S asymmetry is limited (N = nasal; T = temporal).

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