Paradigm Shift in Keratoconus Diagnosis and Management

IMPORTANCE OF EARLY KERATOCONUS DETECTION IN STOPPING DISEASE PROGRESSION USING ADVANCED SCREENING TOOLS AND TREATMENT OPTIONS

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VISIONIX

Keratoconus is a bilateral, asymmetric, noninflammatory disease characterized by progressive corneal thinning resulting in corneal protrusion and irregular astigmatism. It affects both sexes and all ethnicities and results in distorted and decreased vision.[1,2] Onset often occurs at puberty and stabilizes at midlife, and although early and late-stage cases can occur, they are uncommon.[2]

The incidence of keratoconus in the general population was reported to be 54.5 per 100,000 in 1986, 1 per 2,000 in 1998, and 1 per 375 in 2017.[3-5] This tremendous increase in reported prevalence may be the result of advanced diagnostic tools being used for early detection throughout the past two decades.

Historically, the diagnosis of keratoconus was based on subjective symptoms and clinically significant objective findings that were able to be observed on physical examination. Although keratoconus does have well-described clinical signs, early forms of the disease often go undetected,[3] with mean age at diagnosis reported as 28 years.[4]

The classical management for keratoconus has long been based on improving visual acuity with contact lenses, specifically rigid gas permeable lenses, and monitoring the disease. However, nothing could be done to stop the progression of the disease.[6] Over time, approximately 10% to 20% of patients with keratoconus needed a penetrating keratoplasty due to factors, such as corneal scarring, steeper corneal curvature, worse visual acuity, contact lens discomfort, and poorer vision-related quality of life.[6,7]

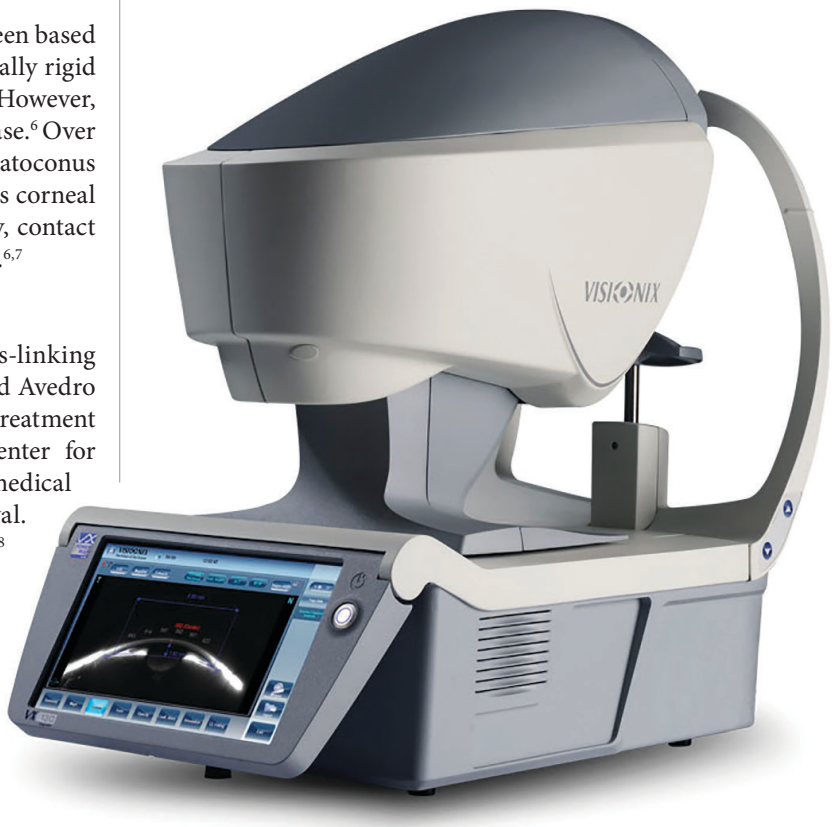
SLOWING DISEASE PROGRESSION

In 2016, the FDA approved a corneal collagen cross-linking (CXL) system, Avedro KXL UV illumination device and Avedro Photexra and Photexra Viscous riboflavin, for the treatment of progressive keratoconus. Our clinic, the CLEI center for Keratoconus, and specifically Dr. Peter Hersh, was the medical monitor for the clinical trial leading to the approval. CXL can stop keratoconus progression in patients.[8] Outside the U.S., CXL systems were approved and commonly used for more than a decade as the standard of care. They have been shown to be effective in treating progressive keratoconus and achieving long-term stabilization with an excellent safety profile.[9]

With the approval of this system for the treatment of progressive keratoconus, CXL has effectively shifted the priorities of managing keratoconus and has placed the timing of intervention to early in the disease process, with the goal of stopping disease progression as soon as possible.[10] However, the availability of an effective earlier intervention, such as CXL, imposes diagnostic challenges associated with early detection versus the commonplace identification of moderate-to-advanced keratoconus.[10]

UPDATING KERATOCONUS CLASSIFICATION

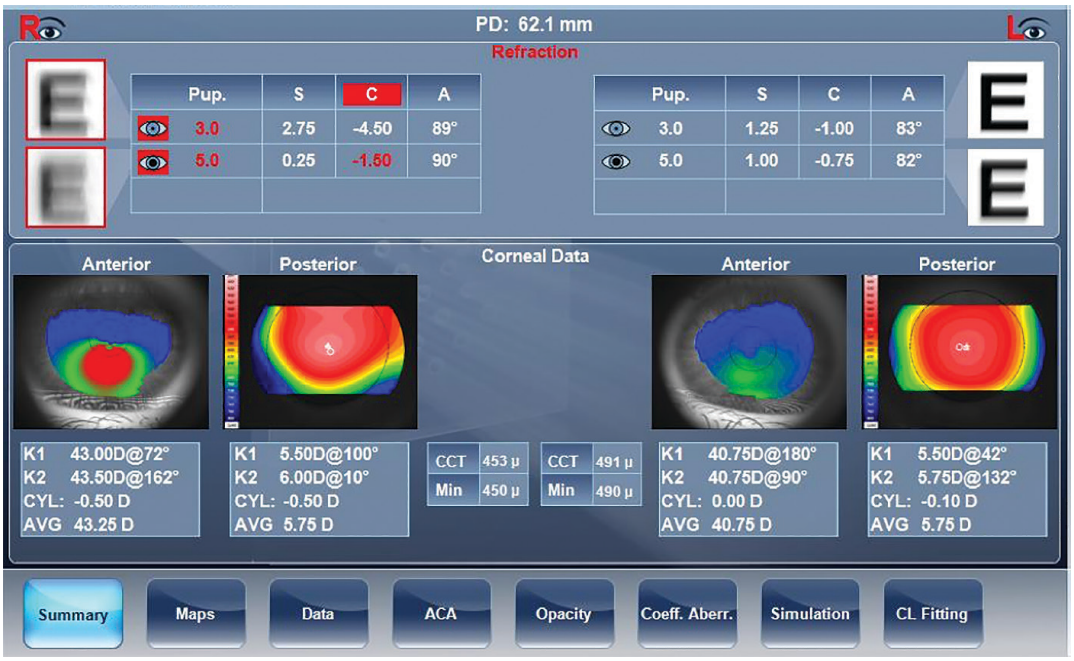
The classic diagnosis of keratoconus was based on a combination of subjective and objective findings, including corneal steepening, visual distortion, apical corneal thinning, and central corneal scarring.[11] The Amsler-Krumeich Keratoconus Grading Scale is among the oldest yet still most widely used classification system for keratoconus, grading severity from stage 1 to 4 using central keratometry, spectacle refraction, presence or absence of scarring, central corneal thickness, and subjective patient vision.[11] Unfortunately, the Amsler-Krumeich scale is outdated and doesn't make use of technological advances in corneal imaging or



The VX130 is a multifunctional diagnostic tool.

take into account the need for earlier diagnosis due to new treatment modalities.

In 2015, an article titled "Global consensus on keratoconus and ectatic diseases" was published in the journal *Cornea*. In this paper, corneal societies from around the world — including the Asia Cornea Society, Cornea Society, EuCornea, and PanCornea — formed a panel to discuss the current grading of keratoconus. The authors concluded that the current definition by Amsler-Krumeich is not up to date because it does not take into account abnormal posterior ectasia, abnormal corneal thickness distribution, clinical noninflammatory corneal thinning, current information, and technological advances.[11] The expert panel agreed that steepening of the anterior corneal surface, steepening of the posterior corneal surface, and thinning and/or an increase in the rate of corneal thickness change from periphery to the thinnest point are mandatory findings to diagnose keratoconus, and that a change in two of the three constitute progression with the exact values varying.[11] The panel felt that it was beyond the scope of the discussion to create a new keratoconus classification system, but agreed that one was needed.[11]



The VX130 summary page shows an overview of findings, note differences in mesopic and scotopic refraction OD, inferior steeping anterior on anterior curvature maps despite normal sim k's OU, and abnormal corneal pachymetry. More in-depth data can be accessed via the VX130 software.

DEVELOPING NEW DEVICES FOR CORNEAL IMAGING

The development of sensitive algorithms and classifications for the early diagnosis of keratoconus is important due to the approval of CXL to slow or stop disease progression.[12] Fortunately, the need for early detection has been met with great improvements in corneal imaging.[10]

New devices can collect data from multiple points and track point of measurement for ease of comparison and peripheral corneal data collected to provide central and global cornea data, including anterior and posterior cornea surface data, as well as thickness data.

Devices, such as manual keratometers and auto keratometers, which are still frequently used in clinical practice, measure only anterior corneal metrics in a 3-mm central zone. With the advent of placido ring corneal topography, the measured area of the anterior cornea has expanded greatly, covering the majority of the corneal surface. This is an improvement because when only the central 3 mm are evaluated, keratoconus can be missed. Here at the CLEI center for Keratoconus, we investigated steepest keratometric curvature location and CXL effect and found 42.4% of cones are located within the central 3 mm, 32.3% are located from 3 mm to 5 mm, and 25.3% are located >5 mm.[13] Clearly, not all cones are located in the central 3 mm where manual and auto keratometers measure.

In recent years, tomography has been gaining attention in early detection, with slit-scanning and Scheimpflug imaging techniques being used.[10,14] These devices are sensitive and measure anterior, posterior and pachymetry corneal metrics.

Other instruments have been found to be useful in differentiating normal eyes from those with keratoconus. Subtle changes in the earliest of keratoconus eyes, such as posterior corneal elevation, epithelial thickness, corneal hysteresis, cornea resistant factor, and higher-order aberrations, can be detected by tomography, biomechanics, and wavefront sensor, but none of these metrics have enough sensitivity or specificity to be used alone for the earliest diagnosis of keratoconus.[14] A multiple-factor system combining diagnostic variables, such as curvature measurements, elevation measurements, pachymetry, biomechanics, and wavefront, could diagnose the earliest stage of keratoconus.[14,15]

USING A COMBINED DATA APPROACH

Using a combined data approach with different diagnostic technologies could provide the earliest diagnosis possible by differentiating normal from early disease, while also monitoring for progression and evaluating treatment success, ensuring corneas are stable over time. Improved keratoconus diagnosis

and better monitoring of disease progression with utilization of CXL to stop progression may lead to a delay or even elimination of the need for penetrating keratoplasty.

Evaluating actionable clinical metrics to track changes over time compared with established baselines — including visual acuity, slit lamp findings, anterior curvature, anterior elevation, posterior elevation, posterior curvature, thinnest point, thickness distribution, epithelial thickness, biomechanical strength, and aberrometry — will improve outcomes for patients with keratoconus. Multifunctional devices capable of measuring not only the everyday needs of an optometrist, such as autorefraction and tonometry, but also the ability to efficiently obtain other decision metrics that could aid in the early diagnosis of keratoconus would be beneficial to the profession.

VX130: A MULTIFUNCTIONAL DIAGNOSTIC TOOL

The VX130 is a multifunctional diagnostic tool that can be used in any practice setting. Although it is a small machine, the VX130 combines seven tools that provide improved diagnostic efficiency, increased documentation, automated calculations, and consistent measurements for not just general needs but all relevant in the diagnosis of keratoconus.[16] Due to the multifunctionality, a multitude of test results are provided, including mesopic and photopic refraction, topography, pachymetry, and tonometry.[16] The VX130 provides a complete bilateral analysis in less than 2 minutes, including anterior and posterior keratometry, anterior and posterior topography, mesopic and scotopic refraction, anterior chamber depth, corneal thickness, eccentricity, noncontact and compensated tonometry, corneal asphericity, pupillometry, and ocular aberrations.[16] The VX130 provides a tremendous amount of relevant patient data, is cost effective, time efficient, and can be used on all patients in any clinical office.

CASE STUDY

A 24-year-old male presented with a complaint of difficulty with night driving and expressed an interest in LASIK. Uncorrected visual acuity was 20/50 OD and 20/30 OS. Auto keratometer was 43.00 x 43.50 @072 OD and 41.00 x 41.00 @180 OS with an autorefraction of +2.00-4.00x092 OD and +1.00-1.00x080 OS. Refraction yielded +2.00-1.50x090 $20/20^{-1}$ OD +1.25-0.50x085 20/20 OS. Refractive astigmatism and corneal astigmatism were not equal. Slit lamp and dilated fundus examination were unremarkable. Although the patient initially appeared to have a routine case of hyperopic astigmatism, further evaluation with the VX130 identified abnormal anterior and posterior corneal curvature maps, abnormal pachymetry, differences between mesopic and scotopic refraction and an abnormal aberration profile — all consistent with keratoconus. As a result, he was diagnosed with keratoconus and referred for corneal collagen cross-linking.

EARLY DETECTION IS KEY

Throughout the past 20 years, a revolution has taken place in the knowledge and technology related to the diagnosis and management of keratoconus.[10] Early detection of keratoconus using advanced screening tools is key to stopping disease progression and improving patient outcomes. The new paradigm shift is to diagnose keratoconus as early as possible to stop disease progression using corneal collagen cross-linking, then rehabilitate vision using non-surgical means, such as glasses and specialty contact lenses, while eliminating the need for or keeping penetrating keratoplasty as a last resort. ■

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