KERATOCONUS AND THE CXL STORY

An overview of the role of the corneal strengthening procedure in managing this ocular disorder.

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Progressive keratoconus is a degenerative eye disease in which there is ongoing thinning and steepening of weakened corneal tissue. It affects approximately one in 2,000 Americans,[1] typically with onset in early adolescence and progression through early adulthood, although older adults may continue to show progression (Figure).

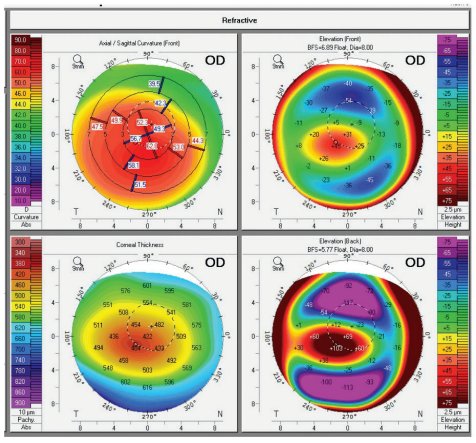
Historically, management of keratoconus has primarily consisted of trying to help patients maintain good vision, moving as needed from toric soft contact lenses to rigid gas permeable lenses, and then to hybrid or scleral lenses.

We have been fortunate in recent years to see an explosion in new contact lens options for keratoconus, along with improvements in lens coatings and fitting procedures that have improved visual outcomes. However, even with good management of vision, the underlying keratoconic disease is unaffected. As many as one in five patients will require a corneal transplant, and more than half of those will need multiple transplants within 20 years.[2,3]

In 2016, the FDA approval of three products for the corneal strengthening procedure known as corneal collagen crosslinking (CXL) changed the paradigm for treatment of progressive keratoconus. The approved products included two formulations of riboflavin—riboflavin 5′-phosphate ophthalmic solution 0.146% (Photrexa, Avedro) and riboflavin 5′-phosphate in 20% dextran ophthalmic solution 0.146% (Photrexa Viscous, Avedro)—and a device, the KXL System (Avedro).

Long-term follow-up has shown that CXL can slow or halt the progression of keratoconus.[4-7] With this CXL system now available in the United States, it is important to identify and refer progressing patients early, even if they still have good vision with contact lenses. Halting progression can preserve these patients' vision correction options. This

A



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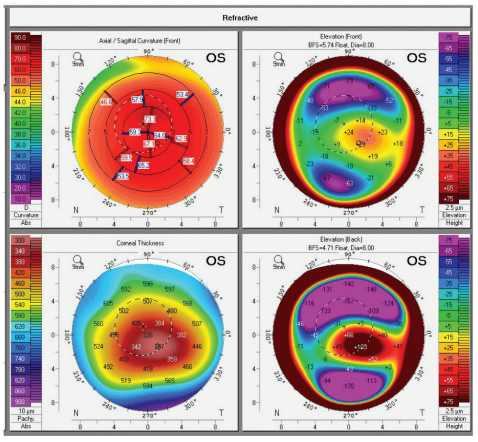

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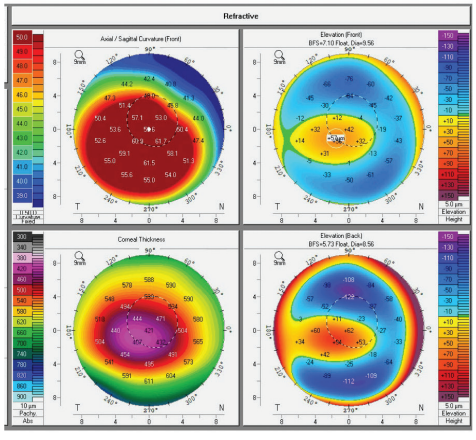

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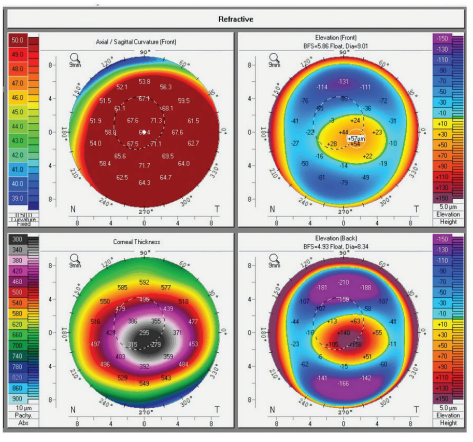

OS, 2019

Figure. This 23-year-old male patient was referred to a cornea specialist for a corneal collagen crosslinking consult based on changes observed in his keratometry from between 2016 (A) and 2019 (B). Although the Pentacam (Oculus) maps show corneal thickness and elevation, it is important to look at the numerical keratometry values, as the color scales are different. There is some ambiguity as to whether this is progressive keratoconus, but the patient is young and already has advanced keratoconus in his left eye, raising the index of suspicion for the fellow eye.

article briefly covers what to look for during the clinical examination, what the CXL procedure entails, and what patients should expect.

EARLY DIAGNOSIS

Optometrists are likely to be the first to notice ectatic disease. Patients typically come in for a comprehensive eye exam because their glasses "just don't work" anymore. The optometrist might already note central corneal striae at the slit lamp. However, rapid change in refraction, high astigmatism, or BCVA worse than 20/20 in a young patient should all be considered red flags for possible keratoconus, even without noticeable signs at the slit lamp.

I recommend a careful manifest refraction in addition to autorefraction. It is important to look at the axis and the amount of cylinder in the prescription in determining the patient's BCVA. I also recommend taking a close look at the mires on manual keratometry because distorted mires hint at an abnormality in the cornea and indicate a need to perform corneal topography or tomography.

Because there is a documented association between eye rubbing and keratoconus,[8] it is also important to ask young patients and their parents about whether they have a tendency to rub their eyes. Patients with this habit should be followed carefully.

If you are suspicious that a patient has keratoconus, it is advised that topography be performed every 6 months because patients with the condition, especially those in their teens and younger, can progress rapidly. If you start to notice an increase in keratometry readings, fluctuating vision, or corneal steepening, refer the patient to a surgeon who performs CXL.

THE REFERRAL RELATIONSHIP

Optometrists might fear that referring a patient for topography or a cornea consultation will lead to loss of that patient, but I encourage my colleagues to be open to working with others to manage patients with this condition. Keratoconus referrals have been a significant differentiator for my practice. Not only do patients appreciate that I am looking out for their best interests, but also the ophthalmology colleagues to whom I refer patients for CXL will often then seek my guidance on specialty contact lenses or other areas.

The surgeon will need to document keratoconus progression for insurance coverage of CXL, so it is helpful to send refractions and VA measurements from the patient's past several visits, keratometry, topography, and any other important diagnostic information you have that will help to demonstrate progression over time.

Once CXL has been performed, the patient should be monitored regularly, by either an OD or a surgeon, and will still need vision correction. The literature has demonstrated a slight flattening effect of the cornea with CXL,

which could change patients' glasses prescriptions (if they are able to wear glasses), and possibly the contact lens design, but it will not eliminate their refractive error.[4,5,9]

Keratoconus management is a great opportunity for optometrists and ophthalmologists to work together to build stronger relationships.

CXL IN A NUTSHELL

The riboflavin solutions and device mentioned above are the only CXL options approved for use in the United States. Other systems are in use internationally and may be performed under an FDA investigational device exemption and clinical trial protocols in this country. The procedure that was evaluated by the FDA requires removal of the epithelium, a 30-minute application of the riboflavin solution, and then 30 minutes of exposure with 365-nm UV-A light at 3.0 mW/cm^2.[9]

Although US surgeons can vary some aspects of this protocol as an off-label practice of medicine, they can't perform CXL with other systems or drugs that haven't been approved in the United States unless they are participating in a clinical trial. Likewise, the approved solutions cannot be used to perform CXL with the epithelium on (epi-on CXL). A phase 3 trial is evaluating the safety and postoperative patient comfort of an epi-on protocol. Until epi-on CXL has gone through the FDA's rigorous evaluation of safety and efficacy, I will continue to recommend only epithelium-off CXL (epi-off CXL).

The standard epi-off procedure is covered by most health insurance plans (95% of those with commercial health insurance), and a J code (J2787) is available for reimbursement of the riboflavin solution. Copays, deductibles, and the provider's network status can all affect the patient's out-of-pocket contribution for the procedure. Non–FDA-approved procedures are not covered by insurance.

SETTING PATIENT EXPECTATIONS

With preoperative preparation time, the need for various checks of corneal thickness, and the half hour required for riboflavin penetration, patients can expect to spend several hours at the clinic or surgery center on the day of the CXL procedure. Typically, only one eye is treated at a time, with perhaps a month or more between the two eyes if both require CXL.

Patients should expect initial discomfort after the CXL procedure and may require management with oral pain medications, bandage contact lenses, or eye drops. In most cases, the patient will be managed by the ophthalmology practice, but some referring optometrists may see the patient early in the recovery process. Patients should be aware that they may not be fully functional visually for a few weeks while the epithelium heals. Eye care practitioners should monitor for infection.

There are no clear guidelines on when patients can or should return to contact lens wear after CXL, but the epithelial defect should be healed beforehand (typically a few weeks to a month), especially in patients who wear soft or rigid gas permeable lenses. Experienced scleral lens wearers might be able to resume wear sooner because these lens designs avoid corneal touch.

I have noticed transient corneal haze and changes in vision in the first few months after CXL, so I wouldn't advise fitting patients in new lenses at 1 month. Ideally, they can continue to use their preoperative vision correction for up to 3 months until their corneas and their vision have stabilized.

It is important that patients realize that they will still need to return for annual eye exams to monitor potential corneal changes and for adjustments in their glasses and contact lenses. Continued progression of keratoconus is possible but not common. Studies have shown a continued rate of progression after CXL ranging from zero to 23%, with the latter seen in a pediatric population with early onset.[10] If necessary, CXL can be repeated, although this is rare.

RECENT AND FUTURE PROGRESS

The future for patients with keratoconus is looking better than ever, and a number of developments are under investigation, including the aforementioned epi-on CXL clinical trials, new riboflavin formulations, and accelerated UV delivery times. Patients and clinicians alike have much to look forward to, as CXL techniques and technologies continue to evolve. ■

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