Management Modalities for Keratoconus

An overview of noninterventional and interventional treatments.

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Management of keratoconus has advanced during the past few years, and surgeons can now choose among numerous traditional and modern treatments. Traditional modalities such as spectacle correction, contact lenses, penetrating keratoplasty (PKP), and conductive keratoplasty (CK) are still effective; however, demand for the last two has decreased with the advent of modern alternatives, specifically intrastromal corneal ring segments (ICRSs) and corneal collagen crosslinking (CXL). Caution should be used when considering these newer treatment modalities, and surgeons should be aware of their indications, contraindications, conditions, and complications before proceeding with treatment.

Keratoconus treatments can be divided into two categories, interventional and noninterventional. In this article, particular attention is given to ICRSs and CXL, as they are the most popular emerging interventional management modalities for keratoconus.

NONINTERVENTIONAL MANAGEMENT

Spectacle correction. In early stages of keratoconus, spectacles can suffice to correct regular astigmatism and minimal irregular astigmatism. In moderate stages, when the refraction is stable and quality and quantity of vision are reasonable, spectacles are likely the best choice.

Contact lenses. As the condition progresses and the cylindrical power increases beyond 4.00 D, visual intolerance may warrant correction with contact lenses. The type of contact lens traditionally used for keratoconus management is rigid gas-permeable (RGP) for two reasons. First, hydrophilic lenses tend to conform to the shape of the cone and therefore have a diminished effect. Second, hybrid lenses that are hard in the center and soft on the periphery are also available, but these are not always effective for managing keratoconus. Another alternative is a piggyback contact lens strategy, in which an RGP lens is worn over a soft lens.

Advances in lens designs and materials have increased the proportion of keratoconus patients who can be fitted with contact lenses. Among the types of contact lenses currently available are standard, large diameter (9.7 mm) RGP lenses; spherical lenses for moderate nipple cones; small, steep lenses for moderate-to-severe nipple cones; lenses for steep oval and globus cones when standard spherical lenses have failed; and gas-permeable, preformed scleral lenses, which can be tried for extremely distorted corneas or in the presence of corneal contact lens intolerance.

INTERVENTIONAL MANAGEMENT

CK. Today, CK is not commonly used to treat keratoconus or other ocular disorders. However, it has been applied on the flat axis, either symmetrically or asymmetrically, to decrease astigmatism. CK is generally a temporary measure, as resteepling can occur.

PKP. Approximately 10% to 25% of eyes with keratoconus progress beyond the point of visual rehabilitation.12 This is especially common in patients who present at a young age (younger than 20 years), in those with keratom-
Keratoconus is one of the most frequent indications for PKP, accounting for 15% to 25% of such surgeries.3-5 Following surgery, visual recovery can take weeks or months, with full stabilization often occurring 3 to 6 months after suture removal. Recently, PKP has been indicated in patients with advanced progressive disease and significant corneal scarring.

PKP is a relatively low-risk procedure; however, complications including allograft rejection, iatrogenic astigmatism, and significant endothelial cell loss have been reported after corneal transplantation.6-8 Side effects caused by long-term use of topical corticosteroids (eg, secondary glaucoma and cataract) and recurrence of keratoconus on the graft itself are also possible.9-12 Clear grafts are obtained in more than 95% of cases,10,13,14 but optical outcomes may be unsatisfactory if iatrogenic astigmatism and anisometropia are present. Between 30% and 50% of grafted eyes require contact lens correction or further keratorefractive surgical procedures.12,14,15

Figure 1. ICRSs are made of biocompatible PMMA.

Figure 2. The Barraquer thickness law states that when a material is added to the periphery of the cornea or an equal amount of material is removed from the central area, a flattening effect is achieved. In contrast, when a material is added to the center or removed from the corneal periphery, the surface curvature is steepened.

Figure 3. Principle of action of ICRSs: The corrective result varies according to the thickness and the diameter of the segment. The greater the thickness, the greater the correction (Barraquer principle). The smaller the diameter, the greater the correction (Blavatskaya principle).

Figure 4. Mechanism of action of ICRSs. The flattening effect occurs on the virtual line (C-D) connecting the two tips of the segment.

Figure 5. The steepening effect on the flat axis is achieved by the skew action of the segment. (A) The position of the segment when implanted; (B) the final position of the segment after the skew (a = tangent angle).
Lamellar keratoplasty/deep anterior lamellar keratoplasty (DALK). The corneal endothelium of keratoconic eyes is generally intact and healthy, even after many occurrences of acute hydrops. Therefore, the trend in recent years is to perform partial-thickness (lamellar) rather than full-thickness (penetrating) techniques. These procedures replace the diseased stromal part of the keratoconic cornea and leave the healthy endothelial cells relatively intact, negate the risk of endothelial rejection, and theoretically improve the postoperative mechanical stability of the cornea. There is also less chance of wound dehiscence and possibly less induction of iatrogenic astigmatism with lamellar keratoplasty.

Indications for DALK in keratoconus include presence of anterior corneal scars; advanced disease with stress lines (Vogt striae) and clear cornea; K reading greater than or equal to 65.00 D; corneal thickness less than 350 µm at the thinnest point; or very high refractive error (ie, sphere greater than -6.00 D and/or cylinder greater than 6.00 D; this is a relative indication).

ICRSs. Implanting ring segments (Figure 1) can regularize the corneal surface and achieve some refractive correction without affecting the central visual axis. ICRSs can delay the need for corneal grafting procedures in keratoconus patients; however, long-term stability remains a concern.

In general, ICRSs flatten the center of the cornea (Figure 2) and can provide some biomechanical support for the thin ectatic cornea. In contrast, when material is added to the center or removed from the periphery, the corneal curvature steepens according to the thickness and the diameter of the segment (Figure 3). Every segment creates a flattening effect along the virtual line connecting the two ends of the segment and a steepening effect on the flat axis perpendicular to the virtual line (Figures 4 and 5). Thus, ICRSs are implanted on the steep axis. The flattening action of the arc is greater when the arc is longer, but the perpendicular steepening action is greater when the arc is smaller. On the other hand, the overall flattening of the central cornea is greater with thicker segments.

The closer the ICRS is to the center of the cornea, the stronger the astigmatic correction will be, and the further the segment from the center of the cornea, the better the flattening effect (myopic correction). Therefore, segments implanted on a 5-mm optical zone, such as the Ferrara Ring (Ferrara Ophthalmics) and Keraring (Mediphacos), have a better effect on astigmatism, and those implanted on a 7-mm optical zone, such as Intacs (Addition Technology, Inc.), have better effect on myopia. Newer designs, namely the Kera6 and Intacs SK, are implanted on a 6-mm optical zone, which may help prevent glare. Most of the effect of ICRS implantation is noticed on the anterior surface of the cornea (Figures 6 and 7).
A mechanical tunnel creation technique for intrastromal corneal ring segment (ICRS) implantation can lead to the following complications:

- Epithelial defects at the keratotomy site;
- Anterior and posterior perforations due to inaccurate measurements of corneal thickness or inadequate intraocular pressure;
- Extension of the incision toward the central visual axis or the limbus;
- Shallow and/or uneven placement of the ICRS;
- Infectious keratitis;
- Persistent incision gaping;
- Decentration;
- Stromal thinning;
- Corneal stromal edema around the incision and tunnel;
- Segment migration and extrusion;
- Corneal melting;
- Tunnel neovascularization or deposits;
- Subconjunctival hemorrhage;
- Superficial corneal incision opacification; and
- Late dislocation of the ICRS into the anterior chamber.

Using a femtosecond laser to create the tunnels for ICRS implantation carries less risk of complications. The main complication is posterior perforation, occurring when the corneal thickness along the proposed tunnel site is too thin.

**CASE STUDY**

Figure 1 shows corneal topography of an eye with keratoconus. ICRS implantation was planned on the 140º axis (Figure 2). During tunnel creation with a femtosecond laser, a posterior perforation occurred in the superior tunnel. Upon review of the topographic maps, a thin area was noted on the passage of the superior tunnel (Figure 3).

This case demonstrates the importance of corneal thickness throughout the entire route through which passage of an ICRS will occur. The tunnel should be made at 80% of the depth in the thinnest area rather than 80% of the depth at the incision site.
Guidelines for use of ICRSs are listed in this paragraph; however, expert surgeons may go beyond these limits in selected cases: corneal thickness greater than 350 µm at the thinnest point; maximal K reading (K-max) less than 60.00 D; refractive error (spherical equivalent [SE]) less than -6.00 D; and clear cornea with no central scars or stress lines.

Poor visual outcomes can result if preoperative K is greater than 55.00 D, preoperative pachymetry is 350 to 400 µm at the thinnest point, or paracentral opacities are present.

Contraindications include high visual expectations; uncontrolled autoimmune, collagen vascular, or immunodeficiency disease; pregnancy or nursing; a habit of continual eye rubbing; corneal thickness less than 350 µm at the thinnest point; K-max reading greater than 65.00 D; and corneal scarring.

In patients with large (greater than 4 mm), dense scars that obstruct the pupillary area, ICRSs are unlikely to be effective. Reticular scarring (Figure 8) does not preclude ICRS use but may be responsible for poor visual outcomes. Hydrops should be resolved before considering ICRSs, as the corneal shape will change once the edema is resolved and the degree of corneal scarring emerges. After hydrops, however, the cornea will most likely need DALK.

For information on the complications and practical considerations for ICRS use, refer to the sidebar included with the online version of this article.

CXL. The use of riboflavin and ultraviolet-A (UV-A) light to induce CXL has become extremely popular in the past few years. The procedure increases mechanical and biochemical stability of the stromal tissue (Figures 9 through 11), slows or arrests keratoconus progression, and can delay or avoid recourse to keratoplasty. To describe the procedure briefly, after topical anesthesia is applied and the epithelium removed, the cornea is rinsed with riboflavin 0.1% solution and exposed to UV-A light.

Progression of keratoconus should be confirmed before treating with CXL, for which parameters include at least one of the following during 1 year of follow-up: change of K-max by more than 1.00 D; thinning of the cornea by more than 30 µm; increase of topographic astigmatism by more than 1.00 D; patient age less than 20 years; and pellucid marginal degeneration, forme fruste keratoconus before PRK, corneal ectasia after refractive surgery, or corneal deformation after

Complications of corneal collagen crosslinking (CXL) can include:

- Activation of herpetic keratitis with iritis;
- Diffuse lamellar keratitis (Note: use of topical steroids should precede CXL in eyes with iatrogenic keratectasia);
- Loss of BCVA of 2 or more Snellen lines after 6 months to 1 year postoperative;
- Haze, which usually decreases during the first postoperative year;
- Corneal melting; and
- Microbial keratitis caused by Acanthamoeba or Pseudomonas (very rare).

Figure 9. The aim of CXL is to increase corneal stiffness and achieve corneal stability.

Figure 10. In keratoconus, there is a deficiency in intercellular collagen fiber bonding.

Figure 11. CXL can be used to increase the number of bonds.
radial keratotomy.

Contraindications include corneal thickness less than 400 µm at the thinnest point (Figure 12), K-max greater than 60.00 D, high visual expectations, corneal epithelial healing disorders or corneal melting disorders; previous herpes keratitis, pregnancy, continuous eye rubbing habit, and corneal scarring.

As a result of CXL, collagen fibers bond and shrink and the cone is displaced toward the center of the cornea, leading to an increase in K and in the negative spherical component of the refractive error by 2.00 to 2.50 D. These changes can last for 3 to 4 months and then diminish gradually. This may be followed by a reduction of K-max. CXL also causes a temporary reduction of central corneal thickness by 30 to 50 µm; the cornea usually recovers its preoperative thickness within 1 year.

Changes in the cornea after CXL mainly occur on the anterior two-thirds of the corneal surface (Figures 13 through 15). Typical clinical outcomes provide a reduction of K-max by 1.00 to 2.00 D, statistically significant improvement in stability for up to 48 months, and 1- to 2-line gain in BCVA. However, CXL may also be associated with low to moderate haze noticeable up to 6 months after surgery. For information on complications associated with CXL, refer to sidebar included with the online version of this article.

**Phakic IOLs.** These IOLs can be implanted as a stand-alone or additive treatment in keratoconus patients. The following are suggestions for use of phakic IOLs as stand-alone versus additive procedures:

- When the case is stable, there is high refractive error (greater than -6.00 D SE), and BCVA is reasonable, it can be a standalone procedure.
- When the case is stable, there is high refractive error, and BCVA is unreasonable because of high corneal irregularities, it can be an additive procedure in combination with ICRSs.

- When the case is unstable, there is high refractive error, and BCVA is reasonable, it can be an additive procedure in combination with CXL.
- When the case is unstable, there is high refractive error, and BCVA is unreasonable, it can be an additive procedure in combination with ICRSs and CXL.

In addition to a stable refraction, the patient must have an anterior chamber depth (ACD) of at least 2.8 mm. Contraindications include ACD less than 2.8 mm, myopia other than axial, evidence of nuclear sclerosis or developing cataract, history of uveitis, anterior or posterior synechiae, corneal dystrophy, glaucoma or intraocular pressure higher than 20 mm Hg, any other pathology in the anterior segment, personal or family history of retinal detachment, and diabetes mellitus.

**Combined treatment modalities.** It is not unusual that an eye with keratoconus can—or in some cases must—be treated with more than one treatment modality. For exam-
ple, progressive cases with high refractive errors and good BCVAs can be treated with CXL to stabilize the cornea and phakic IOLs to correct the high refractive error. In eyes with progressive moderate keratoconus with moderate refractive errors, CXL can be combined with contact lenses, spectacles, or ICRSs. In stable, moderate keratoconus with very high refractive error but good BCVA, ICRSs can be combined with phakic IOLs in a secondary procedure.

**MANAGEMENT PARAMETERS**

To fully evaluate the keratoconic patient, use of RGP contact lenses must be stopped for at least 2 weeks before evaluation to achieve correct measurement of the corneal shape. Furthermore, do not use anecdotaly reported refractive changes as a basis for decision-making; however, measurements previously performed in other clinics can give an idea of the progression of the disease. Progression of ectasia should be determined only by follow-up visits.

Making the right management decision is not a simple process. The patient’s age, sex, and environment should be considered, and disease progression must be documented. Corneal thickness at the thinnest point, K-max, corneal transparency, the existence of stress lines (Vogt striae), refractive error, and UCVA and BCVA with and without pinhole test are also important factors affecting the decision.

My systematic approach to managing keratoconus (Figures 16 through 22) depends on determining factors in the following order:
1. Corneal transparency and stress lines (Vogt striae);
2. Age;
3. Progression;
4. Contact lens tolerance;
5. Refractive error;
6. UCVA and BCVA with and without pinhole test,
7. BSCVA.

**Figure 16.** If the patient is contact-lens tolerant, contacts are one management option.

**Figure 17.** If the patient is younger than 20 years of age, the disease should be considered progressive and should be stabilized; if the patient is older than 30 years, the disease can be considered not progressive and can be treated; if patient age is between 20 and 30 years, the disease should be monitored.

**Figure 18.** A BCVA of 6/10 is the cutoff point for DALK.

- with evaluation of BCVA over a gas permeable contact lens when possible;
- K-max;
- Corneal thickness; and
- Sex.

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