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Improvements Needed in Keratoconus Diagnosis Criteria

The refinement and augmentation of early diagnostic indications may enable more timely and cost-effective intervention.

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Because corneal collagen crosslinking (CXL) is intended to be applied to eyes developing progressive ectasia, it is of paramount importance to establish early and sensitive criteria to diagnose keratoconus and substantiate progression.

Various keratoconus diagnosis, staging, and progression criteria are in clinical use. Criteria can include data from clinical evaluation and topography- and topometry-derived indicators. Clinical data include distance UCVA and BCVA and manifest refractive spherical equivalent (MRSE). Quantitative and qualitative topographic and topometric measurements include keratometry (K), anterior and posterior corneal elevation, curvature asymmetry, and corneal pachymetry. These parameters can be incorporated in various decisiontree schemes and/or staging keratoconus classification systems, such as the Rabinowitz,[1] Klyce,[2] and Amsler- Krumeich criteria.[3]

Clinical experience with keratoconus screening and management, however, suggests that corneal pachymetry and visual acuity measurements may not always be reliable indicators of ectasia or keratoconus progression.[4-6] Reduced visual acuity, for example, may not correlate with severity of keratoconus and may manifest only in advanced stages of the disease. The assessment of keratoconus severity and visual function has yielded poor results in keratoconic eyes when compared with several anterior-surface–derived topographic parameters, including K, pachymetry, and surface-asymmetry indices (Figure 1).[7] Other published reports also indicate the limitations in specificity and sensitivity of traditionally employed keratoconus criteria.[4,8,9]

Despite the use of several topographic and topometric diagnostic criteria, ophthalmologists in everyday

practice often face cases that cannot fully fit into either the keratoconus or normal cornea group. These suspect cases present diagnostic and management challenges for the clinician, emphasizing the need to explore potential improvements in keratoconus diagnosis.[3,10] Thus, the refinement and augmentation of early diagnostic criteria for keratoconus is of clinical significance because it may enable more timely intervention.

CURRENT METHODS OF DIAGNOSIS

Keratoconus diagnosis employs criteria based either on clinical or topographic and topometric measurement (Figure 2). Among these criteria is K, obtained with a manual keratometer, or, in the past 20 years, topography- and/or topometry-based computer-derived measurements. Topography systems provide anterior curvature data based on Placido-disc, slit-scan, or Scheimpflug tomography measurement. Pachymetry measurements, obtained by ultrasound, slit-scan tomography, or Scheimpflug imaging, are also used, as are subjective visual acuity and MRSE.

Limitations on these criteria do exist: For example, the curvature measurement accuracy of Placido–discbased topographers[11] may be compromised by tear film insufficiency or corneal warpage in rigid contact lens wearers, and pachymetry measurements by Scheimpflug imaging[12] may be subject to error if corneal clarity is compromised.

Established criteria for detecting keratoconus progression in comparison with baseline measurements in contemporary clinical evaluation include the following:

- Kmax (steepest K): ≥1.00 D increase;
- Kmax – Kmin (flattest K): ≥1.00 D increase;
- Kmean (average of Kmax and Kmin): ≥0.75 D increase;
- Pachymetry: ≥2% decrease in central corneal thickness;
- Corneal apex power (measured with cone location and magnitude index): ≥1.00 D increase; and
- MRSE change: ≥0.50 D.[13-15]

Several established decision trees exist based on combinations of the above criteria, such as the Klyce indices of surface asymmetry and surface regularity and the keratoconus percentage index.[16]

TREATMENT OPTIONS

Traditionally, keratoconus progression was observed and visual rehabilitation was managed with spectacle correction and/or soft contact lenses until irregular astigmatism necessitated application of rigid gas permeable (RGP) contact lenses. In cases in which this was not possible or patients were RGP intolerant (up to 21% of cases[17]), penetrating keratoplasty (PKP) was generally employed.[18] This procedure, however, is associated with significant morbidity,[19-21] as usually it takes about 1 week for the patient to return to everyday life and months, if not years, before the eye can be adequately visually rehabilitated. Despite use of this drastic procedure, visual rehabilitation may still necessitate additional repair or refractive procedures[22] to reduce the irregular astigmatism[23,24] and high postoperative anisometropia commonly associated with PKP.[25]

Even in cases in which PKP achieves generally acceptable visual outcomes, long-term graft survival in keratoconic eyes declines rapidly after the second decade, as the donor's endothelial cells tend to be slowly rejected by the host. Primary graft survival rates have been reported to be 50% at 20 years,[25,26] falling even further with repeat grafts.

An alternative to PKP is deep anterior lamellar keratoplasty (DALK), which does not have the disadvantage of short lifespan and associated complications.[27] With DALK, the risk of graft rejection

may be lower, as the endothelial cell layer of the host is preserved. A median graft survival of 49 years for DALK versus 17 years for PKP has been reported.[28] However, DALK techniques are technically challenging.

Other treatment options for keratoconus are the insertion of intrastromal corneal ring segments (ICRSs) and CXL. ICRSs appear to shift the shape of the cornea and may provide significant visual rehabilitation; however, there is no consensus regarding their stability and safety.[29,30] CXL has been shown to effectively arrest the progression of keratoconus and corneal ectasia.[11-30] The standard epithelium-off Dresden protocol,[31,37] as well as other methods,[38-52] have been effective in halting keratoconus progression. Still, clinicians have reported a range of complications associated with CXL.[53-60]

In addition to standard CXL, protocol variations include alternative levels and amounts of energy, pulsing, oxygen supplementation, riboflavin solution concentration, and route of administration of the riboflavin solution within the cornea. The underlying premise of these alternatives is that delivering a similar effect over a shorter period will not compromise safety in comparison with the standard protocol.

SUMMARY

Problems, treatment gaps, and shortcomings in the current treatments for keratoconus include the following:

- Currently used keratoconus diagnosis and progression criteria have potential limitations;
- Progression documentation for keratoconus (ie, to indicate the need for CXL application) is also not well defined or universally accepted; and
- Recently introduced CXL protocols have not been evaluated and correlated as extensively, either clinically or ex vivo, as the original CXL protocol parameters.

We consider the development of a potentially more sensitive system for early diagnosis of keratoconus to hold great value for clinicians, patients, and health care systems. Criteria that can detect this progressive disease at early stages when it can be addressed with treatments that are more cost-effective and involve less morbidity for patients could be beneficial for all parties. On the other hand, lack of comparative data on CXL techniques is a noteworthy shortcoming.

Our experience suggests a significantly higher incidence incidence of keratoconus in the southern European countries, specifically the Eastern Mediterranean region. The incidence in Greece may be especially high, at almost one in every 40. We have also noted clinically that there may be a much higher genetic correlation of the disease, as we have observed signs of keratoconus using topography and/or tomography in the range of more than 80% in immediate family members of keratoconus patients in our population. Evidently, additional research to explore potential improvements in keratoconus diagnosis and subsequent refinement and augmentation of early diagnostic criteria is truly of clinical significance.

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