

Keratoconus: Pediatric Prevalence and a New Treatment Option



As a recent study reveals a high prevalence of keratoconus in a pediatric population, a new form of lamellar keratoplasty, CTAK, is expanding the treatment options for affected patients.

BY JOHN D. GELLES, OD, FAAO, FIAOMC, FCLSA, FSLs, FBCLA, AND STEVEN A. GREENSTEIN, MD

Keratoconus was commonly thought to affect individuals beginning in their teenage years, with a prevalence of 50 to 230 subjects per 100,000.¹ A recent study by Harthan et al discussed the prevalence of keratoconus in an urban pediatric population at the Princeton Vision Clinic, part of Illinois College of Optometry in Chicago.² The study was a collaboration between the Illinois College of Optometry and the International Keratoconus Academy. Its outcomes suggest that the prevalence of keratoconus in the pediatric population is higher than previously thought.

PEDIATRIC KERATOCONUS STUDY

This prospective, observational study was performed on children aged 3 to 18 years (n=2007). Every patient who presented for a comprehensive examination received a Scheimpflug tomography scan on the Pentacam® HR (OCULUS Optikgerate GmbH). The Pentacam®'s Belin/Ambrósio Enhanced Ectasia Display (BAD3; Figure 1) was analyzed to screen for keratoconus.

Previous studies have only reported the final D value of the BAD analysis as a proxy for keratoconus diagnosis. In contrast, this study increased specificity for keratoconus by combining the Final D value with Back Elevation data at the Thinnest Point (BETP). This combination can filter for keratoconus within a group of abnormal corneas.³

Assessing these measurements, we found a higher prevalence of keratoconus than in previous studies, and specifically in the pediatric population, which has seldom been analyzed separately. Six patients were keratoconic (prevalence of 1:334),

three patients were keratoconus suspects (prevalence of 1:669), and the total prevalence of the two combined was 1:223. In comparison, in a meta-analysis of data from 15 countries, Hashemi et al (2020) estimated the prevalence of keratoconus at 1 out of 725 individuals.⁴

CONSIDERING CHANGES TO OPTOMETRIC SCREENING CRITERIA

To our knowledge, this was the first prospective study of keratoconus prevalence conducted in a US-based pediatric population. However, it was a single site in an urban location, with predominantly Black and Latinx pediatric patients. Its findings should not be extrapolated to wider populations. Yet, it raises the alarm about the general prevalence of keratoconus and justifies the need for similar multicenter studies. This study also debunks a popular misconception that

children under a certain age are unable to sit still for corneal testing.

Furthermore, the results of this study confirmed our preference for using tomography for keratoconus screenings, especially in the pediatric population, to diagnose this disease early, ideally at its onset. Without sensitive diagnostic equipment, subclinical keratoconus cannot be found—it is not detectable at the slit lamp or with other clinical testing. Further clouding a diagnosis is the fact that many of these patients still correct to 20/20, especially if the affected cornea is not located directly over their visual axis to produce a visual effect.

REFERRAL CRITERIA FOR CROSS-LINKING

Once diagnosed, the first step in managing keratoconus is to stop it from progressing. Corneal cross-linking (CXL) is the only treatment to halt keratoconus'

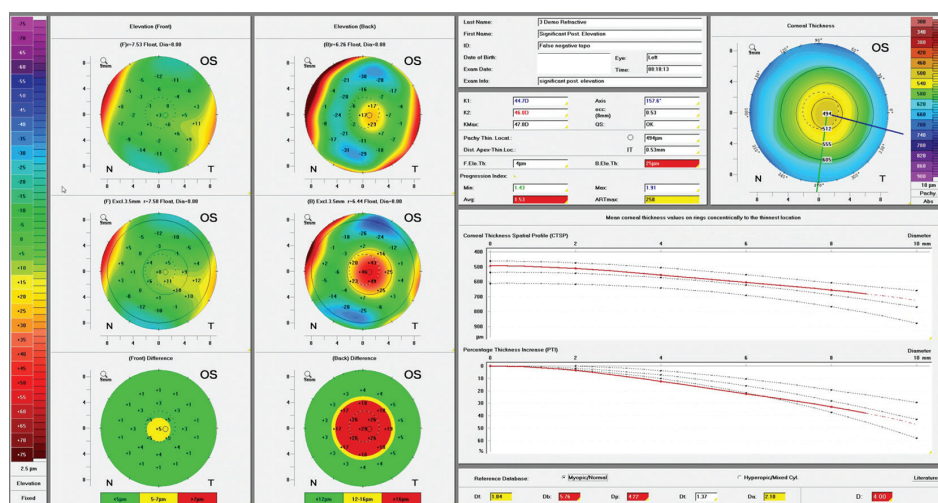


Figure 1. The Belin/Ambrósio Enhanced Ectasia Display, as shown on the OCULUS Pentacam®.

"The results of this study confirmed our preference for using tomography for keratoconus screenings, especially in the pediatric population, to diagnose this disease early, ideally at its onset."

progression. Changes in the cornea's thickness and posterior curvature are among the two most important factors when evaluating whether to refer a patient for CXL. The Pentacam® has specialized software called the Belin ABCD Progression Display (OCULUS GmbH), which can show parameters relevant to keratoconus progression detection (Figure 2). The software measures the front and back radius of curvature within a 3- to 4-mm diameter surrounding the thinnest point, along with the cornea's thinnest point, to assess the severity and track the progression of keratoconus. It also allows the physician to monitor the patient's visual acuity and changes in those metrics over time.

Separately, this software can analyze disease progression in patients who have already been treated with CXL and might require a repeat treatment or other surgical intervention. Tracking keratoconus progression on this software is straightforward, with simple bar graphs and confidence interval markers for the user's ease. In practices without this progression monitoring software, it is prudent to use the criteria set forth by the US FDA clinical trial,^{5,6} which include one or more of the following changes over a period of

24 months: a 1.00-D or more increase in maximum keratometry (Kmax), a 1.00-D or more increase in manifest cylinder, or an increase of 0.50 D or more in manifest refraction spherical equivalent. The authors recommend referring any pediatric patient with a confirmed diagnosis of keratoconus for CXL.

CTAK: A NEW SURGICAL OPTION FOR KERATOCONUS

Corneal procedures for keratoconus can broadly be categorized as additive, subtractive, or replacement. All types can be successful, and each one has its limitations and challenges. Classically, corneal transplants have been used for eyes with severe keratoconus with visually significant scarring or contact lens failure. These cases come with various challenges intraoperatively, postoperatively, and in the long term.

Corneal tissue addition keratoplasty (CTAK [CorneaGen]) is a new, tissue-additive option for treating keratoconus. We developed this form of lamellar keratoplasty in our clinic along with our co-creator, Peter Hersh, MD, who performed the first procedure in an IRB clinical trial in early 2016.

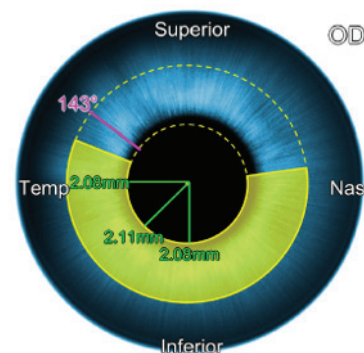


Figure 3. An example of a CTAK surgical plan.

CTAK started as lenticules of preserved corneal tissue. The lenticular shape was achieved by using both excimer and femtosecond lasers. The lenticules were implanted into the cornea through an intrastromal pocket, which was also created with a femtosecond laser. Although this initial approach greatly improved tomography, the visual outcomes did not correspond, due to irregularity overlying the visual axis. The procedure quickly changed to spare the visual axis, and the excimer laser was abandoned. Since then, CTAK has evolved to include proprietary planning algorithms for tissue size and placement as well as its own instrument set (the CTAK Instrument Set [Corza Medical]), enhancing the procedure's precision and efficiency.

CTAK is currently available to all ophthalmologists in the United States. For each case, CorneaGen receives Pentacam® data that are evaluated to assist in planning the customized tissue specifications. These specifications are then provided to the surgeon for review. Once the surgeon confirms the desired tissue parameters, CorneaGen prepares the tissue and shapes it using a femtosecond laser (FEMTO LDV Z8 [Ziemer Group]). The tissue then undergoes a gamma-radiation process that eliminates host antigens and preserves it for a shelf life of up to 2 years at room temperature. The tissue is sourced from the stromal cap of endothelial keratoplasty tissue preparations, which would otherwise become waste. This extends the gift of donation to multiple recipients.

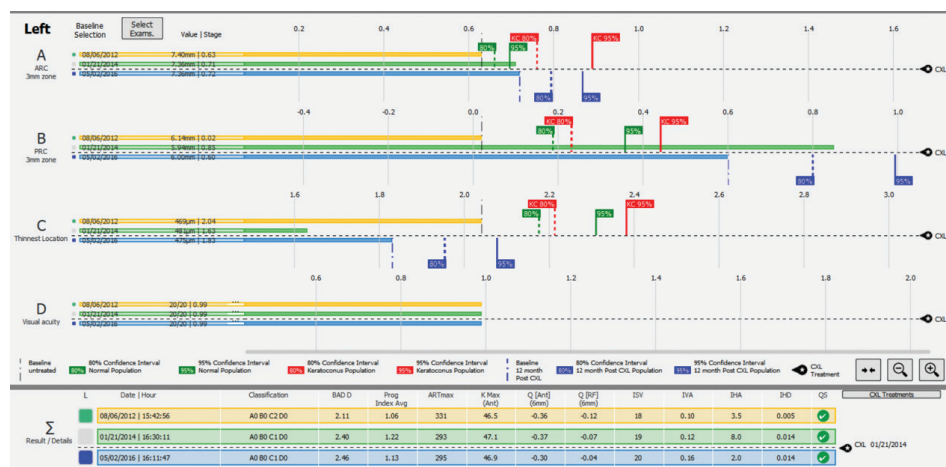


Figure 2. Belin ABCD Progression Display.

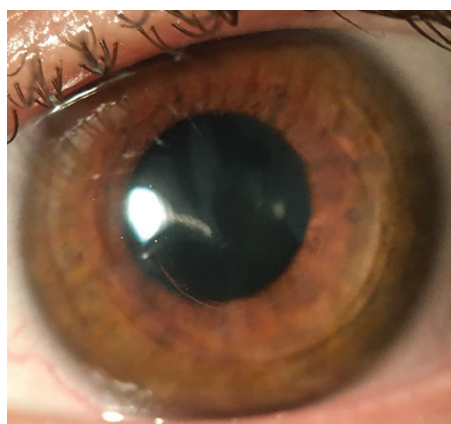


Figure 4. The CTAK tissue in place.

The surgeon receives the custom-shaped tissue and recommended surgical plan (Figure 3). Using the CTAK instruments and a femtosecond laser with channel cutting options, the surgeon creates a corneal stromal channel, places the tissue into the channel, and smooths it into its final position (Figure 4). The critical elements are (1) centering the femto cuts according to the corneal marks, (2) a full channel dissection free of adhesions, (3) the use of countertraction, (4) a hand-over-hand technique to stabilize the tissue during initial insertion, and (5) ensuring the tissue has been pushed around the channel mid-point prior to directional smoothing.

KEY FINDINGS FROM THE CTAK CLINICAL TRIAL

The clinical trial for CTAK was a prospective, open-label trial performed at a single center on 21 eyes of 18 patients. The study evaluated changes to Kmax, maximum keratometry flattening (Kmaxflat), mean keratometry (Kmean), uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), and manifest refraction spherical equivalent (MRSE). The 6-month results were impressive:

- An average gain of 5 lines of UDVA, or from an average of 20/327 to 20/82 (from 1.21 ± 0.35 logMAR lines [LL] to 0.61 ± 0.25 LL) ($P < .001$).
- The average corrected distance visual acuity (CDVA) improved from 20/82 to 20/43 (0.62 ± 0.33 LL (20/82) to 0.34 ± 0.21 LL ($P = .002$).
- MRSE changed from -6.25 ± 5.45 D to -1.61 ± 3.33 D ($P = .002$).
- The Kmean flattened by -8.44 D ($P = .002$); Kmax flattened by -6.91 D ($P = .096$); and Kmaxflat (the point of maximum keratometry flattening) was -16.03 D.

No eyes in the study lost lines of UDVA. Individually, 20 eyes (95.2%) gained greater than 2 lines of UDVA, whereas 10 eyes (47.6%) gained more than 6 lines. With CDVA, 12 eyes (57.1%) gained at least 2 lines, and 1 eye worsened by more than 2 lines. These are impactful outcomes (Figure 5) that contribute to meaningful improvements in recipients' quality of life and their ability to perform tasks of daily living.

PATIENT SELECTION AND POSTOPERATIVE MANAGEMENT

Whether a cornea needs 4.00 D or 20.00 D of flattening, the customization capabilities of CTAK make it possible to treat a wide range of patients. The ideal eye for CTAK is one with a cone located in the central 6 mm without visually significant central scarring. Visual improvement with the CTAK procedure is immediately noticeable for many patients on day 1. The procedure is well tolerated, and patients report minimal discomfort during or immediately after the procedure. Swelling of the tissue diminishes rapidly over the first postoperative week. The postoperative topical medications are typically an

antibiotic QID for 1 week and a steroid QID on taper over 4 weeks.

CONSIDERATIONS

Reviewing the comprehensive visual needs of patients diagnosed with keratoconus is prudent. Many patients with keratoconus report that specialty contact lenses provide adequate vision, but may not express their complete dependence on them to function. CTAK can change this, improving UCVA and BCVA in a meaningful way. Additionally, the recontouring of the cornea by CTAK provides more options for patients, including expanded contact lens and surgical options. Last, the impact on keratometry can improve calculation accuracy for phakic and pseudophakic IOLs, yielding improved refractive outcomes. ■

1. Ortiz-Toquero S, Fuente C, Auladell C, et al. Influence of keratoconus severity on detecting true progression with Scheimpflug imaging and anterior segment optical coherence tomography. *Life (Basel)*. 2023;13(7):1474.
2. Harthan JS, Gelles JD, Block SS, et al. Prevalence of keratoconus based on Scheimpflug corneal tomography metrics in a pediatric population from a Chicago-based school age vision clinic. *Eye Contact Lens*. 2024;50(3):121-125.
3. Zhuang X, Harthan JS, Block SS, Tullio W, Barry Eiden S. Analysis of corneal tomography in select Black and LatinX children. *Cont Lens Anterior Eye*. 2022;45(6):101717.
4. Hashemi H, Heydari S, Hooshmand E, et al. The prevalence and risk factors for keratoconus: a systematic review and meta-analysis. *Cornea*. 2020;39(2):263-270.
5. Greenstein SA, Hersh PS. Corneal crosslinking for progressive keratoconus and corneal ectasia: summary of US multicenter and subgroup clinical trials. *Transl Vis Sci Technol*. 2021;10(5):13.
6. Hersh PS, Stulting RD, Muller D, et al. United States Crosslinking Study Group. United States multicenter clinical trial of corneal collagen crosslinking for keratoconus treatment. *Ophthalmology*. 2017;124(9):1259-1270. Erratum in: *Ophthalmology*. 2017;124(12):1878.

JOHN D. GELLES, OD, FFAO, FIAOMC, FCLSA, FSLs, FBCLA

- Director, Specialty Contact Lens, Cornea and Laser Eye Institute - CLEI Center for Keratoconus, Teaneck, NJ
- Clinical assistant professor at Rutgers New Jersey Medical School
- johngellesod@gmail.com
- Financial disclosures (relevant): Consultant (CorneaGen, Corza, Oculus)

STEVEN A. GREENSTEIN, MD

- Medical Director and Director, Refractive Surgery, Cornea and Laser Eye Institute - CLEI Center for Keratoconus, Teaneck, NJ
- Clinical assistant professor at Rutgers New Jersey Medical School
- sgreenstein@vision-institute.com
- Financial disclosures (relevant): Consultant (CorneaGen, Corza, Oculus, Ziemer)

24 y/o Female

UCVA 20/70
BSCVA 20/30

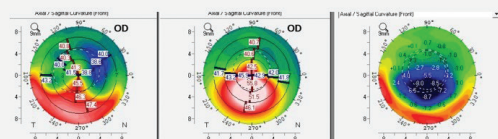


Figure 5. Topographic change from the CTAK procedure.