

Identifying predictive variables

CXL analyses guide treatment

Devising algorithm for clinical care helps determine appropriate approach for patients

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Reviewed by Peter S. Hersh, MD

Chicago—Now that outcomes data have established corneal collagen crosslinking (CXL) as an effective procedure both for ameliorating the progression of keratoconus and cor-



Dr. Hersh

neal ectasia and improving visual function parameters in some patients, one of the next questions in need of answering is whom should be treated, said Peter S. Hersh, MD, at the annual meeting of the American Society of Refractive Surgery.

Cataract and Refractive Surgery.

To address this issue, Dr. Hersh and colleagues have begun to analyze data from their cohort of patients who underwent CXL as part of an FDA clinical trial, with the aim of iden-

Take-Home Message

With the aim of devising a treatment algorithm for corneal collagen crosslinking, one investigator has begun to analyze his data to identify variables that independently predict anatomic and functional outcomes.

tifying predictive variables to use in devising a CXL treatment algorithm.

"As we learn more, we can devise an appropriate algorithm for clinical care," said Dr. Hersh, clinical professor of ophthalmology, University of Medicine and Dentistry, New Jersey-New Jersey Medical School, Newark. "Then, when patients come into the office, we can decide whether to treat now or wait while continuing with close follow-up."

Dr. Hersh enrolled 85 eyes at his center, Cornea and Laser Eye Institute–Hersh Vision Group, Teaneck, NJ, as part of the CXL clinical trial that randomly assigned eyes to CXL or sham control. His cohort comprised 56 eyes with progressive keratoconus and 29 eyes with postLASIK ectasia.

CXL was performed using the traditional Dresden protocol with a 9-mm zone of epithelium removal, 30 minutes of treatment with riboflavin 0.1% drops to saturate the cornea, and then 30 minutes of exposure to 365-nm ultraviolet A light at 3 mW/cm².

With data pooled for the keratoconus and postLASIK ectasia eyes, maximum K (Kmax) measured by topography with a Scheimpflug imaging device (Pentacam, Oculus) showed slight worsening at 1 month post-CXL, but progressive improvement thereafter. Mean change from baseline to 1 year was -1.6 D, which was clinically and statistically significant.

Other 1-year outcome analyses showed CXL treatment was associated with statistically significant improvements in three of six keratoconus indices analyzed by the Scheimpflug imaging device and in both total higher-order aberrations and coma measured by wavefront aberrometry (LADARWave, Alcon Laboratories). CXL-treated eyes also benefited with a statistically significant, 1-line improvement at 1 year in both uncorrected visual acuity (UCVA) (20/137 to 20/111) and best spectacle-corrected visual acuity (BSCVA) (20/45 to 20/34).

In addition, responses on a subjective visual function questionnaire showed the CXL treatment was associated with statistically significant improvements in night driving, glare, halo, starburst, difficulty reading, and foreign body sensation.

"These data show CXL results not only in quantitative improvement, but also that the treated patients are noting qualitative improvement in visual function," Dr. Hersh said.

Dissecting the data

To begin to develop a treatment algorithm, Dr. Hersh and colleagues performed a multivariate analysis to identify incoming characteristics that might influence outcomes. Factors considered were gender, age, diagnosis, cone location, Kmax, UCVA, BSCVA, and pachymetry at the thinnest point. They were analyzed as potential independent predictors for improvements in Kmax and BSCVA.

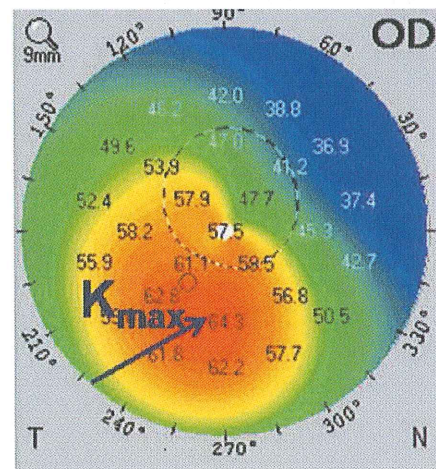


Figure 1 Maximum keratometry performed preoperatively may help predict outcomes of corneal collagen crosslinking. (Image courtesy of Peter S. Hersh, MD)

“While the entire population showed a statistically significant improvement in Kmax, it was unchanged in the majority of eyes, improved by 2 D or more in 31%, and worsened in 3.5% of eyes,” Dr. Hersh said. “Similarly, the distribution data for BSCVA change showed that 22% of eyes gained 2 or more lines at 1 year after CXL while 3.5% worsened by 2 lines.”

Results of the multivariate analysis showed that a higher preoperative Kmax value was as-

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sociated with more improvement post-CXL. Specifically, eyes with a Kmax ≥ 55 D were 2.7-fold more likely than those with Kmax < 55 D to have achieved flattening of 2 D or more at 1 year.

"All treated eyes were equally as likely to remain stable or progress, but eyes with worse topography preoperatively tended to improve more," Dr. Hersh said.

Topographic cone location was also found to be associated with change in Kmax. Mean improvements were 2.6 D among eyes with central cones, 1.1 D for eyes with a midperipheral cone, and only 0.5 D for eyes with peripheral cones.

In addition, preoperative BSCVA was independently associated with BSCVA outcome such that eyes entering the study with BSCVA of 20/32 or worse were 4.5 times more likely to have improved by 2 or more lines at 1 year compared with eyes that were 20/25 or bet-

ter. Diagnosis also seemed to matter since eyes with postLASIK ectasia had less robust mean improvements compared with eyes with keratoconus for both mean change in Kmax (1 versus 2 D) and BSCVA (0.5 versus 1.5 lines).

"It's not clear why the latter difference occurred," he said. "It may indicate intrinsic pathophysiologic differences and responses between the two groups. Perhaps, there is a biomechanical difference secondary to the presence or absence of a LASIK flap, or maybe the explanation relates to differences between groups in cone location as the cones in the postLASIK ectasia group tended to be more peripheral."

As more data are accumulated and more is learned about CXL effects, it will be necessary to consider what outcomes represent the best targets for devising a treatment algorithm.

"To make appropriate decisions about clinical

care, we need to determine what our goals should be when treating [patients with] keratoconus and ectasia," he said. "Are we aiming for topographic stability only; or are we trying to obtain topographic improvement, vision stability, or vision improvement; or do we want to minimize the chance of BSCVA loss?"

"We need to assess the likelihood of each of these outcomes based on the characteristics of the individual patient and the clinical outcomes desired," Dr. Hersh concluded. **OT**

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Corneal collagen crosslinking is not FDA approved for the treatment of keratoconus or postLASIK ectasia.