

News in Review

COMMENTARY AND PERSPECTIVES

CXL Eyes Stable After 10 Years

Ophthalmologists at University Hospital in Dresden, Germany, have reported long-lasting effectiveness of corneal collagen cross-linking (CXL) in halting progression of keratoconus.¹

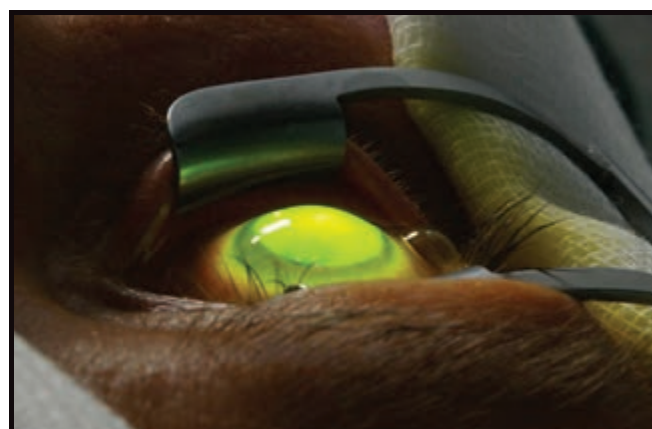
Treatment benefits. CXL significantly reduced the maximum and minimum corneal curvatures, as well as the curvature at the apex, in eyes with progressive keratoconus. These benefits endured in most eyes after 10 years. “Until now, nobody knew how long the positive effect of the CXL procedure would last,” said lead author Frederik Raiskup, MD, PhD, FEBO.

Although keratoplasty remains the definitive treatment for advanced keratoconus, this study adds to a body of literature suggesting that CXL is a promising, less invasive therapeutic

alternative to more costly and complex corneal transplantation. (At time of press, CXL was not approved in the United States, but an FDA ruling on one system was expected in March.)

In CXL, the corneal stroma is exposed to riboflavin (vitamin B₂) and ultraviolet light, and the ensuing photochemical reaction strengthens and stabilizes corneal stromal collagen fibers.

Indications and cautions. CXL is indicated for keratoconus patients who have visual acuity “that allows good functioning in daily life” and also have solid



ENDURING EFFECT. Researchers in Germany found that the treatment effect of CXL in eyes with keratoconus persisted for at least 10 years.

evidence of disease progression, Dr. Raiskup said.

Additionally, to prevent damage to the corneal endothelium, central corneal thickness should be at least 400 μm after removal of the epithelium during the treatment. In this study, in which mean corneal thickness was 488 μm , no clinical signs of endothelial decompensation were apparent, and endothelial cell counts remained constant.

Significant study findings. The retrospective interventional case series involved 24 progressive

keratoconus patients (34 eyes), with a mean age of 28.4 years. Preoperatively, five eyes (14.7 percent) were in an advanced stage of keratoconus, showing corneal scarring; nevertheless, all eyes still had good corrected distance visual acuity (CDVA).

Among the statistically significant results at 10 years compared with baseline:

- The mean apical keratometry value decreased from 61.5 D to 55.3 D.
- Mean astigmatism was reduced from 5.7 D to 4.0 D.
- Mean CDVA improved

from 0.40 to 0.26 logMAR; this outcome was attributed to a reduction in astigmatism and corneal distortion and to a better fit of hard contact lenses.

Retreatment is possible. If progression of ectasia resumes, CXL can be repeated, as long as CDVA is still good, said Dr. Raiskup. In this study, two eyes needed retreatment—one after five years, the other after 10—due to increases in the K value following a period of long-term stability. At

baseline, these two eyes had maximum K values higher than 58 D and thinner corneas, which the authors believe predisposed them to further progression. In both cases, retreatment stabilized progression and did not create additional side effects compared with the initial treatment.

Complications. No serious complications occurred, although one eye developed a permanent stromal corneal scar that limited visual acuity following treatment.

The anterior stroma in 13 eyes showed a persistent haze at 10 years, but it did not affect the CDVA.

The benefit of aging. The enduring effect of CXL was something of a surprise, Dr. Raiskup said. It may be attributable, in part, to the natural stiffening of the cornea that occurs over time. “There is an ongoing ‘cross-linking’ process in all of the tissues in our body,” he said. “With age, collagen in the ectatic cornea will become naturally stiffer.”

Given this natural stiffening process, in combination with effective CXL therapy that “overlaps” the very active stage of corneal ectasia, the probability is high that the majority of suitable candidates will remain stable after the first treatment, Dr. Raiskup said.

—Miriam Karmel

1 Raiskup F et al. *J Cataract Refract Surg.* 2015;41(1):41-46.

Dr. Raiskup reports no related financial interest.

Surgical News

Cataract Wound Leaks: Sealant vs. Sutures

A prospective randomized study of 500 eyes at 24 sites has found that a hydrogel sealant (ReSure) was significantly better than sutures in stopping leakage following clear corneal incision (CCI) cataract surgery.¹ Patients who were found to have wound leaks, either spontaneous or with application of calibrated pressure, after uneventful surgery were randomized to receive either sealant or sutures. At follow-up visits, leakage occurred with pressure provocation in 12 of 295 eyes of the sealant group (4.1 percent) versus 60 of 176 sutured eyes (34.1 percent).

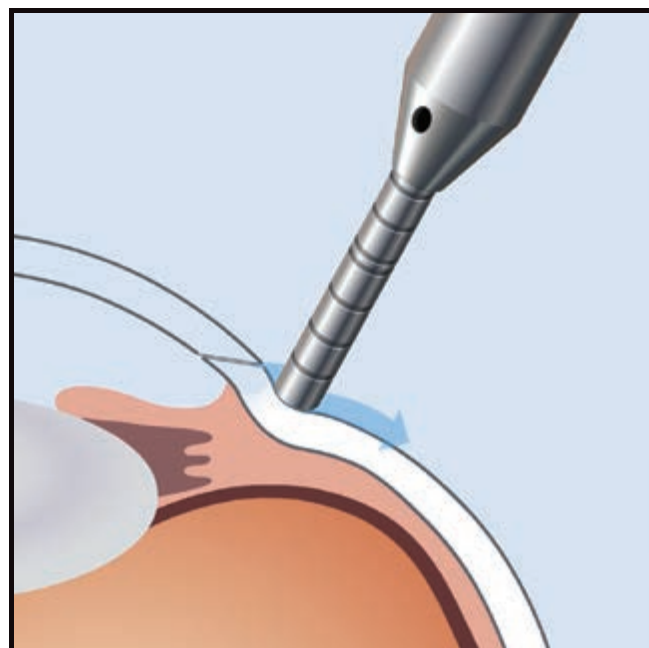
A role for both. But cataract surgeons should not abandon their needles. “Sealant and sutures each play a different role,” said author Samuel Masket, MD,

a cataract surgeon in Los Angeles. The type of wound construction will determine the surgical course.

He noted that previous investigations revealed that a paracentesis-type incision without a groove is most likely to leak. That common type of wound construction—single-plane CCI of 3.5 mm or less—was used for all eyes in this study.

The sealant’s value is in covering and hermetically sealing the incision in the postoperative period while the epithelium is healing, Dr. Masket said. “While sealant cannot make up for poor incision construction, in this investigational model it proved to be more effective than sutures.”

A high incidence of leakage. Though the researchers anticipated leakage, they were surprised by the



UNDER PRESSURE. Drawing shows egress of fluid from corneal incision on pressure from the calibrated force gauge.

large proportion of incisions—488 of the overall 500, or 97.6 percent—that initially leaked, either spontaneously or with provocation equivalent to forced blinking or eye touching. “This is a sobering piece of information that surgeons should heed,” Dr. Masket said.

Key takeaways. “Incision construction definitely matters, and leaking wounds

are a concern,” he said. “Surgeons should take the opportunity to carefully test the incision. And don’t leave the table with a leaking wound.” —Miriam Karmel

1 Masket S et al. *J Cataract Refract Surg.* 2014;40(12):2057-2066.

Dr. Masket is a consultant to, shareholder of, and medical monitor for Ocular Therapeutix.

Glaucoma Risk Factors

Meta-analysis Confirms Diabetes-Glaucoma Link

Although diabetes has long been proposed as a risk factor for glaucoma, epidemiologic studies have yielded inconsistent results, making the association controversial. Over the past decade, there has been no systematic review of the literature on the correlation between diabetes and glaucoma or between glaucoma risk and other metabolic abnormalities.

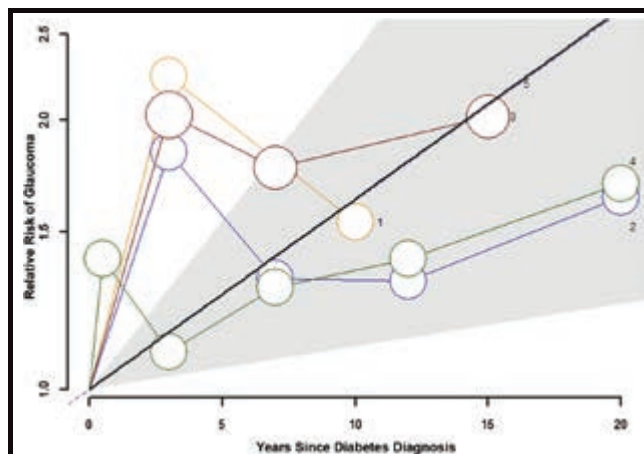
This gap has recently been filled by Myung Hun Kim, MD, at Saevit Eye Hospital in Goyang, Korea, and his colleagues, who conducted an updated systematic review and meta-analysis. They found that diabetes, duration of diabetes, and fasting glucose levels were associated with a significantly higher risk of primary open-angle glaucoma and that diabetes and fasting glucose levels were associated with slightly increased levels of intraocular pressure (IOP).¹

Proposed mechanisms. The mechanisms relating diabetes to glaucoma are not clear. Various studies have suggested that diabetes causes microvascular damage and vascular dysregulation of the retina and the optic disc, increasing the susceptibility of the optic nerve head to glaucomatous damage. Diabetes also may disrupt the trabecular meshwork function, thereby elevating IOP.²

Most robust association. Longer duration of diabetes was consistently associated with higher risk of glaucoma across cross-sectional, case-control, and longitudinal studies and was independent of age, race, gender, and other confounders controlled in the original studies. Patients with longer duration of diabetes particularly need to be aware of the importance of glaucoma screening and management, according to the authors.

Authors' perspective. "We were not surprised to find an association between diabetes and the risk of glaucoma," said Dr. Kim, "but we were somewhat surprised by the degree of heterogeneity of the associations and the variability between studies. We were reassured that even longitudinal studies, which are less prone to bias than cross-sectional or case-control studies, found positive associations. "However, since patients with diabetes are more likely to be in contact with eye care providers, diagnostic bias is still an issue that will require additional research. That said, the associations seen in our study were from population-based prevalence studies, which should remove this bias."

Strengths and weaknesses. A notable strength of this meta-analysis is the large sample size: 47 studies that included 2,981,342 in-



RISK OVER TIME. Graph shows the relative risk for glaucoma with increasing duration of diabetes in a dose-response meta-analysis. Circle areas are inversely proportional to the variance of the log relative risks. The pooled linear risk trend (thick solid line) and its 95 percent confidence band (shaded region) were obtained using a random-effects dose-response meta-analysis.

dividuals from 16 countries. Other strengths include the evaluation of multiple diabetes-related exposures and glaucoma-related outcomes, as well as the inclusion of prospective studies. Dr. Kim noted that prospective studies are important in providing estimates of incidence and temporal trends and helping to establish the temporal sequence required for causal inference.

The main weakness of the meta-analysis was the substantial variation in the methods and quality of the original studies. "This likely contributed to the high degree of heterogeneity in the results," Dr. Kim said.

Clinical implications. The results support the recommendation that patients with diabetes be referred to ophthalmologists to check for glaucoma. "In addition to diabetic retinopathy, patients with diabetes should also receive education about glaucoma," said Dr. Kim. He added that the coexistence of diabetic retinopathy and

glaucoma has an important clinical impact.

Areas for future research. Dr. Kim said that additional longitudinal studies are needed. In particular, the authors noted a scarcity of studies on the relationship between glaucoma and glucose biomarkers, prediabetes, and metabolic syndrome and its components. Given the high prevalence of these metabolic abnormalities, the authors recommended that future research evaluate the association between altered glucose metabolism and glaucoma risk.¹

"Once the association is clearly understood, specific guidelines for glaucoma screening and management in patients with diabetes can be developed," said Dr. Kim.

—Gabrielle Weiner

1 Zhao D et al. *Ophthalmology*. 2015;122(1):72-78.

2 Nakamura M et al. *Ophthalmologica*. 2005;219(1):1-10.

Dr. Kim reports no relevant financial interests.

HIV in Children

Early HAART Tx May Spare Youth From Ocular Disease

A recent study reports some good news for young patients with perinatally acquired HIV: Those who receive highly active antiretroviral therapy (HAART) and survive into adolescence may avoid the ocular diseases typically found in adults with chronic HIV.¹ In the United States, most children affected by perinatal HIV receive HAART; this has been the care standard since 1999.

Eye findings in young HIV patients. The study by Tina Rutar, MD, and col-

leagues found that when HAART treatment results in long-term survival in these patients, most are likely to avoid cytomegalovirus (CMV) retinitis, HIV retinopathy, and keratoconjunctivitis sicca into their teen years and possibly beyond. Dr. Rutar is a pediatric ophthalmologist with the Cataract and Laser Institute, Medford, Ore.; at the time of the study, she was associate professor of ophthalmology and pediatrics at the University of California, San Francisco (UCSF), where



the study was performed.

The researchers examined 22 patients, treated at the UCSF pediatric HIV clinic, who had survived to age 12 years or older (range, 12-23 years) to determine whether they had ophthalmic manifestations of HIV. All but one of the patients had a CD4 count of at least 200 cells/ μ L, and five had an AIDS-defining illness. Surprisingly, the researchers found no CMV retinitis or HIV retinopathy, little vision-threatening disease, and generally good visual

acuity (mean best-corrected visual acuity, 20/22).

Unanswered questions.

In an unexpected result, "We did find that 18 percent of these patients had strabismus, which is higher than the general U.S. prevalence," said Dr. Rutar. "Also, we noted that, worldwide, the visual health of millions of children with perinatally acquired HIV is likely to be impacted by whether they receive early, intensive treatment that enables long-term survival. Both questions warrant further study."

—Mary Wade

1 Rutar T et al. *Br J Ophthalmol*. 2014 Nov. 21. [Epub ahead of print.] doi:10.1136/bjophthalmol-2014-305557.

Dr. Rutar reports no related financial interests.

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