IDENTIFYING KERATOCONUS RISK WITH GENETIC TESTING

With the debut of the AvaGen™, The Genetic Eye Test (Avellino), it's never been easier to identify the presence or risk of keratoconus and other corneal genetic disorders. AvaGen uses next-generation DNA sequencing to provide objective keratoconus risk scores and definitive transforming growth factor-beta induced (TGFBI) diagnosis to confirm five corneal dystrophies. In a series of articles, Melissa Barnett, OD, FAAO, FSLS, FBCLA; Mitchell Jackson, MD; William B. Trattler, MD; and more discussed the prevalence of keratoconus, the importance of genetic testing for early diagnosis, AvaGen's role in personalizing keratoconus management, and more.

USE IN PRE-REFRACTIVE SURGERY EVALUATIONS

One of the biggest concerns that refractive surgeons face, according to Mitchell Jackson, MD, is corneal ectasia in the postoperative period. Another potential complication of laser vision correction is the development of granular corneal dystrophy (GCD) type 1 or type 2. GCD is an autosomal-dominant condition caused by genetic mutations on the TGFBI gene that are associated with the wound-healing process of the cornea.

- "Knowing my patient's genetic risk for keratoconus or a corneal dystrophy that does not manifest until after refractive surgery has done wonders for easing my mind when I'm developing a treatment plan for a patient," said Dr. Jackson. "We incorporate AvaGen into nearly all of our refractive surgery evaluations."
- Every additional piece of information physicians can get is worthwhile if it can prevent adverse events.
- Genetic testing will detect genetic variants much earlier than a clinical exam will, and the earlier you can diagnose keratoconus (or a high risk for developing it), the easier it is to treat.

So where to begin? Even if you're not a corneal refractive surgeon, everyone sees keratoconus, or patients you may suspect to have keratoconus. It's not unusual to see normal diagnostic tests (corneal topography/tomography/epithelial mapping), but if there is a family history of keratoconus and/or the corneal diagnostic tests are borderline, those are the patients who benefit most from undergoing a genetic test. If the test comes back with a low risk score, physicians can be more comfortable moving ahead with refractive surgery. If it's a moderate or high risk score for keratoconus, you may recommend corneal cross-linking (CXL) first to stabilize the cornea and reduce the risk of postoperative complications.

TESTING FAMILY MEMBERS

For patients already diagnosed with keratoconus, Avellino can offer genetic testing to help identify family members (siblings, children, etc.) who may be at risk for developing keratoconus in the future. AvaGen can help quantify the risk for patients. In some cases, the test may support that that patient has irregular against-the-rule astigmatism with a low risk of developing keratoconus in the future. In other cases, the risk of developing keratoconus may be high enough that the patient would benefit early from CXL.

- For candidates who are at high risk for keratoconus, or who have a family history of keratoconus, genetic testing may be helpful in further assessing their risk and optimizing their vision needs management.
- If there is a family history of keratoconus–including siblings–even slight irregularities in corneal shape could prompt the eye care provider to consider genetic testing to assess the overall risk.
- Melissa Barnett, OD, FAAO, FSLS, FBCLA, is using the availability of the genetic test as a starting point for conversations about keratoconus in patients who have a family member with the disease, even if they don't have any suspicious clinical signs. "I find that my patients are excited about the AvaGen test's ability to provide early information that will be helpful for management over their lifetime," she said.
- Other applications for the test in clinical practice include any patient who is interested in refractive surgery and who has a family history of the disease or suspicious clinical signs during the surgery evaluation. "That happens in about 5 to 10% of patients," said William B. Trattler, MD.
- After getting AvaGen results, someone may find out they have one or more TGFBI variants that lead to a particular corneal dystrophy. A genetic counselor can explain the need to have other family members tested. This kind of advice is received by anyone who has been found to have a predisposition to a genetic disorder.

ASSESSMENT OF EARLY KERATOCONUS & PROGRESSIVE MYOPIA

The ability to differentiate early progressive myopia from early progressive keratoconus is critical. Why make the comparison between progressive myopia and emerging keratoconus?

- The presentation of progressive myopia can be very similar to a patient with developing keratoconus.
- Both conditions have subjective complaints that vision is getting progressively worse.
- The age of onset is similar.
- On a slit-lamp exam, both progressive myopia and early keratoconus would display clinically normal corneas, as the classic keratoconus slit-lamp findings are not present in early disease.
- What this means: Due to this similar clinical presentation, subclinical keratoconus can go undetected until the disease has advanced to a stage where CXL treatment is no longer effective.
- CXL is most effective in halting keratoconus progression if done in early stages. It is important for practitioners to make the diagnosis early and get those individuals treated with CXL as soon as possible to stabilize their vision. Therefore, diagnosing keratoconus risk early is critical.

All authors are paid consultants of Avellino.