Screening for Ectasia Risk: What Are We Screening For and How Should We Screen For It?

Renato Ambrósio, Jr., MD, PhD; J. Bradley Randleman, MD

How should we screen our patients for postoperative ectasia risk prior to excimer laser corneal refractive surgery, or laser vision correction, in 2013? This has been debated in the literature\textsuperscript{1-4} and remains a “hot topic” at most meeting venues. The challenge we face as refractive surgeons in daily practice is to most accurately identify individuals who have increased susceptibility for developing biomechanical failure (progressive ectasia), without excluding candidates who may safely benefit from laser vision correction procedures.

In screening, sensitivity (the ability to detect disease) and specificity (the ability to confirm absence of disease) are the most basic aspects to evaluate the efficacy of diagnostic tests. In studies that aim to evaluate screening ability of a test, it is critical to use the appropriate study populations; this may include individuals who have developed a specific complication (ectasia after LASIK) or patients who are at known high risk to develop the complication. The first population is easy to identify but difficult to find when studying rare complications; the second population is difficult to find because, by definition, suboptimal strategies for identifying those individuals exist. A reasonable substitute for the “at-risk” group is a population with subclinical or very mild disease, because these are closest to the individuals we want to identify. Patients with disease that is easily identified by other testing are only helpful to establish a basic “proof of concept” that a new test might be able to identify the target population.

Among eyes known to be susceptible for ectasia progression are those with relatively normal corneal topography from patients with clinical keratoconus detected in their fellow eyes. Such cases have been designated as “forme fruste keratoconus” (FFKC) by Klyce\textsuperscript{6} and others. Other reasonable alternatives are cases with progressive ectasia after laser vision correction with no identifiable agreed-upon risk factors.\textsuperscript{6}

The role of Placido-disk based corneal topography and central corneal thickness in screening have been well recognized,\textsuperscript{7} but shortcomings exist, necessitating that we move beyond, but not discount, the data topography provide as an isolated screening evaluation. A variety of Placido and tomography units and automated screening systems are available and have been proposed to facilitate this screening.\textsuperscript{8-11} Yet, peer reviewed data, which should provide the critical basis for these technology comparisons, have lagged behind anecdotal information and suppositions.

So, what should we do to appropriately screen our patients? Should the primary testing modality be topography, tomography, some combination, or something else? Two articles in this issue of the Journal of Refractive Surgery highlight some benefits and possible shortcomings of each approach, when viewed within the context of what is and is not currently known.

**USING CORNEAL TOPOGRAPHY FOR SCREENING**

As corneal topography came into use for refractive surgery, authors began describing abnormal patterns that were associated with “subclinical” keratoconus, and termed those cases as FFKC. In 1989, Rabinowitz and McDonnell described and validated a straightforward method for detecting FFKC based on keratometric values, asymmetry within the superior and inferior halves of the cornea, and asymmetry between eyes.\textsuperscript{12} Not surprisingly, the first published reports of ectasia after LASIK in 1998 occurred in patients with FFKC.\textsuperscript{13,14} This finding was repeated in multiple small case series, and summarized with in-depth statistical analysis in 2003.\textsuperscript{15} In 2005, members of a joint committee from the...
Scheimpflug imaging with the Pentacam (Oculus Optikgeräte GmbH, Wetzlar, Germany) have been proposed by the Rio de Janeiro Corneal Tomography and Biomechanics Study Group. Through a three-dimensional reconstruction of the cornea, corneal tomography enables calculation of elevation maps of the front and back surfaces along with pachymetric mapping. Validated criteria for diagnostic interpretation and proper understanding of the generated data are critical for the clinician to take full advantage of the information generated by new technology. Tomographic thickness characterization was shown to be effective for discriminating between normal and keratoconic cornea, and the validity of these metrics for detecting very mild (susceptible) cases has been proposed. However, this is still a topic that remains to be better elucidated in the literature.

**PEARLS AND PITFALLS IN SCREENING FROM NEW REPORTS**

In this issue, Smadja et al. provide information for the interpretation of elevation tomography using the dual-Scheimpflug GALILEI system (Ziemer, Port, Switzerland) for detecting ectasia-susceptible eyes. This study included patients from a valuable study group, namely patients with FFKC (defined as fellow eyes with relatively normal topography from patients with very asymmetric keratoconus) in addition to normal patients and patients with clinical keratoconus. Two different reference surfaces for the computations of front and back elevation were tested: best-fit toric and aspheric and best-fit sphere. Maximum posterior elevation using a best-fit toric and aspheric reference was the most accurate parameter, with 99% sensitivity and 99% specificity for detecting keratoconus (cut-off = 16 μm) and 82% sensitivity and 80% specificity for distinguishing between FFKC and normal corneas (cut-off = 13 μm).

Different cut-off values and different sensitivity and specificity are expected when detecting disease (keratoconus) as compared to preclinical conditions (FFKC). Although 82% sensitivity for detecting FFKC may seem unacceptably low as a single diagnostic parameter, it is important to remember that these cases had a relatively normal front surface topography, so the 82% identified could represent an improvement over topography alone and could be applied additively with other screening parameters to create a more efficient combined diagnostic test. The integration of various parameters has been effective, as demonstrated in the ERSS and other screening tools that consider tomographic and topometric data. Another integrated system, the Belin/Ambrósio Enhanced Ectasia Display, combines data from maximal keratometry, tomographic thickness distribution, and enhanced elevation to facilitate the detection of keratoconus, and may also prove to be effective for the detection of mild ectasia, although more data are needed to confirm this.

In contrast, the report by Guilbert et al. in this issue demonstrates the continued utility of Placido-based metrics for screening. In their case, a patient who developed ectasia after LASIK was found to have an abnormal topographic pattern, with an abnormal preoperative KISA index, whereas no abnormal tomographic features were detected on the Orbscan (Bausch & Lomb, Rochester, NY) Quad Map. Unfortunately, advanced tomographic analysis, as described by Saad and Gatinel, was not possible in this case. It is possible that the remarkable tomographic features provided a false sense of security for the surgeon in this case when the Placido map clearly indicated increased risk.

**ADDITIONAL SCREENING TOOLS**

Additional metrics, especially epithelial thickness mapping with very high frequency ultrasound or high-resolution optical coherence tomography, can differentiate keratoconic and normal eyes and seem promising for detecting early corneal ectatic processes. Other hopeful but as yet unvalidated techniques include biomechanical characterization using the Ocular Response Analyzer (Reichert, Buffalo, NY), which, although theoretically promising, has demonstrated limited ability in screening for ectatic diseases and the recently FDA-approved Oculus Corvis ST.
SUMMARY: SCREENING TODAY

So, what should we be using to screen our patients in 2013? Well-established Placido-based criteria remain an integral part of screening until this is definitively surpassed by other technology. Central corneal thickness remains important; however, mounting evidence suggests that regional and relational corneal thickness metrics, available through the variety of aforementioned technologies, likely provide more useful information than central thickness alone. Measuring posterior surface changes remains an exciting and potentially useful metric, but more actual data are needed. Finally, using these data in combination with established clinical parameters, especially patient age, should provide the best and safest screening approach we can have today. More data are needed to support or refute the validity of other metrics, including specific posterior elevation values, optimal best-fit reference shapes, automated screening systems, and the newer technologies discussed. With this information, we will be able to modify these recommendations and our screening approaches. We remain excited to see what the future will bring!

REFERENCES