“Will I be a candidate for laser vision correction after my crosslinking procedure?”

The scenario is common. A patient comes to your office with high hopes of scheduling a surgery that can offer spectacle or contact lens independence and then is told for the first time that they have keratoconus. This news comes unexpectedly and has multiple layers of impact for the unsuspecting patient, who hears in rapid succession the following bits of information: (1) you are not a candidate for laser refractive surgery, (2) in addition to that disappointing news, you have a progressive corneal disease that could lead to loss of vision even with spectacles or contact lenses, and (3) finally, some good news: a treatment is available, corneal crosslinking (CXL), and it offers a high likelihood of stabilizing (but not necessarily improving) this condition.

At this point in the visit, the patient likely has not suddenly forfeited their desire to reduce their dependence on spectacles or contact lenses. In fact, many keratoconic patients who are diagnosed during a refractive surgery screening examination originally schedule their consultations because they are aware that their visual quality is suboptimal in spectacles or contact lenses and they hope that laser refractive surgery might be able to rectify their vision. The question of whether corneal refractive surgery can be performed after CXL therefore flows naturally from the patient’s underlying motivations and is a logical extension of our explanation of how CXL works. If CXL increases the biomechanical strength of a pathologically weakened cornea, then why would not laser refractive surgery become an option? Given that keratoconus has significant adverse effects not only on vision but also on quality of life, we share the patient’s goal of trying to improve vision, not merely stabilize it, and we are sympathetic to the question.1

However, the conscientious refractive surgeon instinctively recoils at the idea of performing ablative corneal surgery in the setting of ectatic disease. The primary risk factor for postrefractive surgery ectasia is topographic evidence of keratoconus, and the prospect of performing any procedure that involves tissue incision or removal carries a risk of further destabilization.2,3 Even if we could assume that CXL fully restores the normal biomechanical state of the keratoconic cornea, the prospect of performing a subsequent ablative procedure is troubling because it would involve removing tissue that was specifically stiffened to achieve corneal shape stability. Would not this directly undermine the purpose of CXL in such patients?

In an attempt to balance the goal of visual rehabilitation with the concern of destabilization, several studies have explored sequential, same-day excimer laser treatment followed immediately by CXL. There is an inherent advantage in combining the time-tested stiffening efficacy of an epithelium-off CXL procedure with a rehabilitative procedure such as transepithelial phototherapeutic keratectomy (PTK) or photorefractive keratectomy (PRK) that also requires removal of the epithelium. This approach nullifies the need to debride the epithelium again for PRK at a later date and avoids any potential related complications of a second epithelial defect. And, as noted earlier, there is a strong rationale for performing CXL as the final step in the procedure to avoid ablation of the crosslinked stroma. The variety of approaches has taken many forms, including but not limited to the following, which have been published with at least 12 months of follow-up data:

1. Topography-guided (TG)-PRK and accelerated CXL (Athens protocol)4
2. TG-PRK and standard CXL5
3. Transepithelial PTK and accelerated CXL (Cretan protocol)6
4. Transepithelial PTK, conventional PRK, and accelerated CXL (Cretan protocol plus)7
5. Transepithelial PRK and accelerated CXL (Tel-Aviv protocol), similar to a transepithelial ocular wavefront-guided PRK + accelerated CXL approach described by Gore et al.8,9

These methods all combine a tissue-sparing ablation for regularizing the corneal surface and/or reducing myopia and astigmatism with a stabilizing CXL treatment. Despite wide-ranging differences in the ablation and CXL parameters, each approach has been shown to be capable of significantly improving visual acuity and topographic metrics, albeit with a limited follow-up in most reports. The aforementioned report from Gore et al. extended follow-up to 24 months and reported no postoperative instability, and a recent landmark report on 10-year outcomes of 144 eyes treated with the Athens protocol showed significant improvements in uncorrected distance visual acuity, corrected...
distance visual acuity (CDVA), and corneal curvature metrics at 1 year, with 94.4% of eyes exhibiting stability between 1 and 10 years.\(^9,10\) Of the remaining 5% of eyes, most demonstrated progressive topographic flattening with hyperopic shift rather than disease progression, and only 3 of 144 eyes showed mild topographic evidence of keratoconus progression. Less than 5% of eyes demonstrated any loss of CDVA.

With such favorable results for simultaneous PRK and CXL, is there still a viable case for delayed, sequential CXL and PRK? We have discussed some key concerns, so what are the arguments in favor of the approach? One is the opportunity to establish preoperative refractive and topographic stability to enhance the refractive precision of the subsequent outcome. A CXL-first approach provides an opportunity for topographic stabilization and a period of observation to assess whether disease progression is ongoing despite CXL. In some cases, dramatic flattening can occur after CXL, and a period of observation allows the surgeon to take individual variations in the response to CXL into account.\(^11,12\) However, stability remains the chief concern because crosslinked tissue is ablated with this approach, and such data are sparse. In this issue of the JCRS, Nattis et al. (page 507) help fill this gap. The authors report 6-month and 12-month post–TG-PRK outcomes in 62 eyes treated first with a modified epithelium-on (mechanical irradiation) accelerated 5-minute ultraviolet irradiation protocol. TG-PRK was performed no sooner than 3 months (and on average, 30 months) after CXL because of a stabilization criterion for moving forward with PRK. Compared with the post-CXL baseline, significant and ongoing improvements in uncorrected distance visual acuity, CDVA, corneal astigmatism, maximum kermometry, and corneal higher-order aberrations were observed at the 6-month and 12-month intervals. Although the results of this study are very encouraging, a concerted effort to expand follow-up to 5 years or more is important for addressing long-term stability.

Finally, a major gap in our ability to assess the relative risk of sequential vs simultaneous PRK and CXL is our current inability to determine how deeply a given CXL effect extends in the stroma. Measurements of depth-resolved biomechanical properties will be important for characterizing the effects of different CXL protocols because they produce widely varying estimated magnitudes and depths of stiffening. Such measurements could be crucial for answering the question posed at the beginning of this editorial. If a particular accelerated epi-on CXL protocol results in a zone of stiffening that extends only 50 μm into the stroma, a subsequent PRK with a maximal stromal ablation depth of 50 or 60 μm would be a far less desirable option than a same-day PRK with CXL. However, if the depth of stiffening extends to 300 μm and this can be confirmed in the patient’s eye after CXL, the advantages of a customized PRK treatment after a period of stabilization could lead to a more favorable refractive outcome. I am excited about recent advances in this area and look forward to more long-term data on the safety and effectiveness of refractive surgical options in epithelial patients.

REFERENCES


Disclosures: Dr. Dupps is a consultant for Glaukos Corp., Alcon Laboratories, Inc., Carl Zeiss Meditec AG, and CorneaGen; has equity holdings with Glaukos Corp.; and has patents held by Cleveland Clinic in the areas of computational modeling and optical elastography.