Corneal Collagen Crosslinking for Ectasia after Refractive Surgery
Anders Behndig, MD, PhD - Umeå, Sweden

The development of corneal ectasia has been recognized as a complication after LASIK since the first case report from Seiler and Quirke1 in the late 1990s. The clinical picture of iatrogenic corneal ectasia resembles that of progressive keratoconus with reduced corneal biomechanical strength, increasing central corneal steepness, irregular refractive errors, and decreasing visual acuity. Since the first reports, the phenomenon has gained substantial scientific interest, and more than 500 articles have been published on the subject. Ways to reduce the risk for this complication include avoiding cases with too high myopia2 and forme fruste/manifest keratoconus,1,3,4 and leaving sufficient residual stroma after the LASIK treatment.5,6 Despite taking these and other safety measures, however, iatrogenic ectasia keeps occurring also in cases with lower myopia,5,6 cases without any obvious preoperative signs of keratoconus,4,7 and even after photorefractive kerectomy.8

An early 2000 review from Sugar et al9 concluded that treating low-grade myopia with LASIK is predictable and safe, and that the overall risk for corneal ectasia is low. With the development of improved lasers, algorithms, and preoperative evaluations, this is even more valid today. Still, we have to accept that we will not be able to identify and steer free of every single case with a potential risk for corneal ectasia. Therefore, as with all serious surgical complications, we need the backup of a safe and effective treatment in the rare cases in which the complication occurs.

Corneal collagen crosslinking (CXL) has been suggested as a treatment for post-LASIK ectasia over the past decade,10 and the safety and efficacy of the treatment have been demonstrated in smaller studies.11-13 As with keratoconus, CXL appears to have a chiefly stabilizing effect on the disease course, but some degree of regression of the ectatic changes and some improvement in visual acuity also have been reported.11-13 In attempts to improve the refractive outcomes further, concurrent intracorneal ring segments14 and topography-guided photorefractive keratectomy15 have been advocated. Yet another option might be to customize the CXL treatment on the basis of the topographic findings.16 Internationally, CXL has had profound effects on the way we handle both keratoconus and ectasia today. The treatment has been shown to be cost-effective from a healthcare payer’s perspective,17 and it has recently been suggested that it significantly reduces the number of keratoplasties performed for keratoconus.18

In this issue of Ophthalmology (available at www.aaojournal.org/article/S0161-6420(17)31019-9/fulltext), an important study from Hersh et al19 is presented. The study data are derived from the clinical trials carried out for the Food and Drug Administration premarket approval of CXL as a treatment for corneal ectasia after refractive surgery. In 2 pooled multicenter randomized clinical trials involving a total of 179 subjects from 11 centers, standard CXL is compared with sham treatment. As expected, the majority of cases had developed ectasia after LASIK, but the study also includes 4 subjects with post–photorefractive keratectomy ectasia. The authors convincingly show that CXL has a stabilizing effect in progressive ectasia with some degree of improvement, whereas the controls continue to progress over the observation period. The best results were reached in cases with steep corneas. In accordance with previously published studies,11,12,14 some degree of worsening can be observed up to 1 month post-CXL, after which an improvement phase occurs between 1 and 6 months, and the values stabilize after that. From a safety perspective, the rate of significant adverse events was low, as was the rate of corneal endothelial cell loss.

The interpretation of the study results—supported by previous studies and a decade of worldwide clinical experience—should be that CXL is a safe and effective treatment for halting progressive ectasia after corneal refractive surgery. Some degree of improvement can be expected, but with the CXL regimens currently used likely not to the degree that it is noticed by the individual patient. The results also are a bit less consistent in CXL after ectasia than in primary keratoconus. Although the present study is important and generally well conducted, some weak points in the study design should be mentioned. First, using pooled data from 2 studies with slightly different design may not be optimal. Furthermore, the controls showing progression were treated with CXL after 3 months, and the 3-month data from these controls were carried forward to 12 months using a last observation carried forward method. In actual fact, this means the study is not a true randomization between CXL and no treatment with a full 12-months follow-up. Still, on the basis of the safety and efficacy outcomes of the present study, CXL was approved by the United States Food and Drug Administration for the treatment of corneal ectasia after refractive surgery in July of 2016.
In many aspects, ectasia after corneal refractive surgery is as elusive as its “idiopathic sibling” keratoconus. The starting point and course of ectasia after a corneal refractive procedure are highly variable, and it is not always possible to identify obvious risk factors for its development. Similar to keratoconus, a recipe for successful management of ectasia after refractive surgery includes early detection, careful monitoring, and prompt CXL treatment in progressive cases, particularly in cases with steep corneas and preferably before the symptoms become too pronounced.

References


Footnotes and Financial Disclosures

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Correspondence: Professor Anders Behndig, MD, PhD, Clinical Sciences/Ophthalmology, Department of Clinical Sciences/Ophthalmology, Umeå University, Umeå, Sweden 90185. E-mail: anders.behndig@umu.se.