Toward Safer Treatment Options for Advanced Keratoconus

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Abstract

Keratoconus is a bilateral and progressive corneal disease characterized by a significant increase in irregular astigmatism and corneal thinning. Numerous treatments—including penetrating keratoplasty (PK), deep anterior lamellar keratoplasty (DALK), ultraviolet-crosslinking (UV-CXL), and intracorneal ring segments—are available for halting progression and/or obtaining (partial) visual rehabilitation. Recently, midstromal Bowman layer transplantation has been introduced as a new treatment option for advanced keratoconus. This technique has shown significant promise in halting disease progression and postponing riskier procedures such as PK or DALK.

Keywords

Advanced keratoconus, penetrating keratoplasty, deep anterior lamellar keratoplasty, Bowman layer transplantation, review

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Endothelial keratoplasty was borne of the recognition that full thickness corneal transplantation may be an inherently flawed operation because, by compromising the ocular surface, a litany of serious complications could ensue. Nevertheless, still today penetrating keratoplasty (PK) and its cousin deep anterior lamellar keratoplasty (DALK) remain the standard of care for eyes with advanced keratoconus (KC) once visual acuity becomes unacceptable and/or contact lens intolerance develops.[1,2] And while the outcomes of these operations are often described as "good," this may only be true in a relative sense, i.e. in comparison to the commonly disappointing results following transplantation for other indications, such as perforated ulcer or herpetic keratitis.[3,4]

In fact, many patients with advanced KC seem to be poor candidates for both PK and DALK. Nearly all are young, in some cases extremely so, making the surgeries themselves more technically challenging and the postoperative care more difficult, especially if there is some coexisting cognitive or behavioral limitation (which is not altogether uncommon).[5–8] Young eyes also tend to be phakic: in the first few years after transplantation, many develop cataracts. As a result, lens extraction may be necessary, potentially risking the graft's health in the process.[9,10] Children already suffer poorer graft survival than adults,[11] but even if the statistics were identical, still it is very likely that young patients will "outlive" their first transplant and therefore require re-operation(s). And because the outcomes of second and third transplants tend to be far inferior to the first, many patients who seem—initially—to "do well" with both surgeries may, ultimately, be destined for problems.[12] This is especially true given that advanced KC is found in patients with severe ocular surface disorders, many of which are exacerbated by PK/DALK and their large incisions, sutures, and the neurotrophic corneas they produce.[13,14] Beneath the ocular surface, the wound healing problems continue, since the stroma at the junction between the graft and the recipient probably never securely "heals," predisposing these eyes to inadvertent traumatic rupture and ongoing ectasia at the tissue interface (and thereby "recurrence" of their disease).[15]

All of these difficulties are fundamental problems intrinsic to DALK and PK themselves and therefore not likely to be cured by refinements to operative technique or instrumentation. The solution may instead require an entirely new surgical approach, possibly one that abandons the idea of exchanging or replacing the recipient cornea with donor tissue. To this end, recently there has been a strong push to intervene early against eyes with mild KC in the hopes of arresting progression before PK or DALK (and all their attendant complications) become necessary. Both ultraviolet-crosslinking (UV-CXL) and intracorneal ring segments (ICRS) have been evaluated for this purpose, each with demonstrated success. Nevertheless, many eyes are not candidates for either operation. Those with corneas steeper than 58 diopters (D) or thinner than 400 µm, for example, are ineligible for both procedures at the moment. In the US, ICRS

are not approved in patients younger than 18 years old, and UV-CXL is not licensed yet.

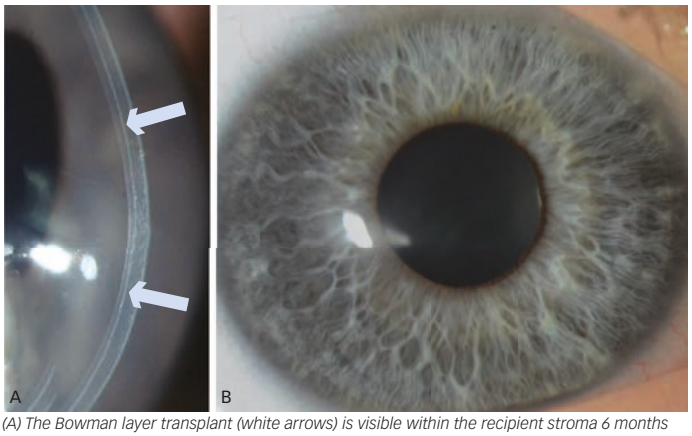
Other exclusions also apply: corneas with prior herpetic disease are disqualified from UV-CXL, and a history of recurrent erosions rules out ICRS placement. Overall, it may be fair to say that, for various reasons, many patients with "active" or "ongoing" KC are ineligible for these disease-halting therapies, and are therefore allowed to continue to progress.[16,17] Eventually, contact lens intolerance might develop. Many patients then receive either PK or DALK and subsequently suffer a lifetime of consequences.

What has been badly needed is an operation to arrest keratoconic progression in eyes poorly suited for UV-CXL or ICRS, before PK or DALK become necessary. For this reason, in 2014, we published our first results with a new operation known as Bowman layer transplantation (see *Figure 1*).[18] One of the most sensitive and specific manifestations of KC is the fragmentation of the Bowman layer, an insult that critically destabilizes the surrounding cornea, predisposing it to ongoing ectasia. As a result, we reasoned that an isolated Bowman layer transplant might flatten the cornea into a more normal architecture and bolster it against further deformation.

For our first surgeries, we chose only patients with extremely advanced KC, all with maximum keratometry values ≥70 D. The operation itself was performed by manually dissecting a midstromal pocket, limbus-to-limbus, 360° within the recipient cornea, then sliding in an isolated Bowman layer graft. All surgeries were uneventful with no complications. Postoperatively, average best spectacle vision dramatically increased (from approximately 20/400 to 20/125), whereas best contact lens vision remained unchanged. Most importantly, however, corneas were flattened by an average of 8–9 D, and in all cases, disease progression was arrested and comfortable contact lens wear was preserved or restored.[18]

Since our original study, we have operated on a growing number of additional patients with the same technique. Overall, the surgery seems

Figure 1: Slit-lamp Images of an Eye after Bowman Layer Transplantation



(A) The Bowman layer transplant (white arrows) is visible within the recipient stroma 6 months postoperatively. (B) However, the cornea is clear, without any interface haze or stromal reaction.

effective in >90 % of eyes at halting ongoing ectasia. In addition, no known postoperative complications have been observed. Specifically, no ocular surface matters have arisen (likely because the technique employs no surface incisions and no sutures), nor have there been any occurrences of either cataract formation or allograft reaction.[19] In fact, because the Bowman layer transplant is acellular, graft rejection may be a highly improbable event. Therefore, much fewer (and possibly no) steroids may be required postoperatively, eliminating a major source of postoperative risk.

So far, our experience with Bowman layer transplantation has led us to believe that the operation may be a promising way to arrest keratoconic progression, even in those eyes ineligible for other procedures. Further study will be necessary, but it is possible that with continued effort, we may continue in the tradition of endothelial keratoplasty by abandoning the idea of full thickness cornea transplantation and, instead, choose a more limited and specific corrective intervention. ■

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