Deep anterior lamellar keratoplasty for keratoconus: Elements for success

Marco Pellegrini1,2,3, Angeli Christy Yu1,2,3, Massimo Busin1,2,3

Abstract:
Advanced keratoconus may require keratoplasty when the patient can no longer achieve functional vision with glasses and contact lenses. Deep anterior lamellar keratoplasty (DALK) has become the surgical treatment of choice due to its undisputed advantages over penetrating keratoplasty including the reduced risk of intraoperative complications, the absence of endothelial immune rejection, and the longer graft survival. Albeit “big-bubble” DALK still represents the most popular surgical method, several modifications have been developed over the years. This allowed standardization of the technique, with improved success rates and clinical outcomes. This review presents an overview on the literature on DALK surgery for keratoconus. We discuss state-of-the-art surgical techniques, current evidence on the clinical outcomes and complications as well as possible future directions.

Keywords:
DALK; Deep anterior lamellar keratoplasty; Keratoconus

INTRODUCTION
Keratoconus is a progressive ectatic disorder in which the cornea assumes a conical shape due to thinning and protrusion. This leads to irregular astigmatism, myopia, and visual impairment.[1] Keratoplasty is usually required in advanced stages of the disease when the patient can no longer achieve functional vision with glasses and contact lenses.[2]

Penetrating keratoplasty (PK) has been considered the mainstay of surgical treatment for decades.[3] More recently, deep anterior lamellar keratoplasty (DALK) has become an alternative to PK, with the advantages of eliminating the risk of endothelial rejection and avoiding the complications associated with open-sky surgery.[4]

Despite these undisputed advantages, the uptake of DALK among corneal surgeons has been relatively slow, particularly in the U.S.[5] Longer surgical time, steep learning curve, and low patient volume and have been reported as the most important barriers to adoption of DALK.[6] Nevertheless, recent innovations in surgical technique, instrumentation and tissue preparation allowed standardization of DALK, with improved success rates even for inexperienced surgeons.[7]

This review provides an update on lamellar keratoplasty for keratoconus. Three key aspects will be covered: The rapidly changing techniques of modern lamellar surgery; the current evidence on the clinical outcomes and complications; the possible future developments in this evolving specialty.

SURGICAL TECHNIQUE
Different techniques to perform DALK have been proposed, including layer-by-layer manual dissection, pneumatic dissection, and viscoelastic-assisted dissection.[8-10] The method of pneumatic dissection through injection of a “big bubble” described by Anwar[9] represents the most popular surgical method. The technique involves partial-thickness trephination of the stromal stroma followed by forceful injection of air into the deep stroma through a needle or cannula to form a “big bubble” [Figure 1a and b]. After anterior keratectomy, the roof of the bubble is then incised under viscoelastic protection and...
However, although retained viscoelastic in the interface may transiently reduce visual acuity in the 1-month after surgery, the long-term outcomes are comparable to those obtained with pneumo-dissection. In case viscoelastic-assisted dissection also fails, careful layer-by-layer manual dissection may be attempted. This technique is associated with increased risk of perforation but can achieve good visual outcomes if the residual stromal bed is <20 µm.

Performing large 9 mm DALK offers several advantages including providing superior refractive outcomes with more regular astigmatism and maximizing removal of the ectatic with lower risk of late recurrence of ectasia. Following large trephination, removal of the deep stroma may be limited to the central 6 mm optical zone. This reduces the risk of perforation during hand dissection when the bubble does not reach the trephination. Moreover, the crown of deep stroma surrounding the central optical zone protects from inadvertent recipient bed perforation during suturing and confers higher mechanical stability due to the large surface of contact between the host and donor tissue. Figure 2 shows a representative case of a patient with keratoconus treated with 9 mm DALK with clearance of a 6-mm optical zone.

Intraoperative macroperforation of the Descemet’s membrane may require conversion to PK in 15%–35% of cases. Occurrence of a type 2 bubble, manual dissection, presence of scarring and surgeon inexperience have been identified as independent risk factors for the need to conversion of intended DALK to PK. Should conversion to PK be required, rather than a 9-mm PK, a two-piece mushroom keratoplasty may be performed. This technique minimizes the endothelial transplant to the posterior 6 mm lamella while benefitting from the refractive advantages of a large 9 mm anterior lamella with excellent 5-year visual outcomes.

**Clinical Outcomes**

One of the potential concerns of DALK is the presence of a graft-host interface which may cause light scattering and affect vision. Studies comparing the visual outcomes after PK and DALK have been inconsistent. Early reports documented inferior visual outcomes with DALK. However, advancement in surgical techniques have allowed to obtain a thin residual stroma and a smooth interface with improved vision. Three randomized controlled trials comparing big-bubble DALK and PK have demonstrated similar visual outcomes of the two procedures [Table 1].

Although several studies have shown comparable short-term graft survival between DALK and PK, patients with
keratoconus undergoing keratoplasty are usually young, which makes long-term survival necessary. A recent large series demonstrated a significantly higher 10-year survival rate for DALK (94%) compared to PK (72%).[45] Moreover, based on the rate of endothelial cell loss, a statistical model was use to predict a median survival of 49 years for DALK versus 17 years for PK.[46]

Regarding refractive outcomes, most studies reported no significant differences between DALK and PK.[35,39-41] Nevertheless, high astigmatism is common after DALK, representing an important cause of suboptimal vision despite a clear graft.[47-49] Various interventions including photorefractive keratectomy,[50] laser in situ keratomileusis,[51] intrastromal corneal ring segments,[52] and manual[53] or femtosecond laser-assisted[54] relaxing incisions have been used to treat postkeratoplasty astigmatism. Our DALK technique with clearance of the deep stroma limited to the central 6 mm allows deep arcuate blunt relaxing incisions within the stepped graft-host junction with minimal risk of perforation.[53] In the presence of a cataract, phacoemulsification with toric intraocular lens implantation can be performed with good visual and refractive outcomes.[55,56]

One of the advantages of DALK over PK is the excellent safety profile. In particular, the potentially serious complications that can occur during the open sky surgery (e.g., iris prolapse, choroidal effusions, and expulsive hemorrhage) are avoided with DALK.[44] The risk of immune endothelial rejection is also eliminated. Moreover, since topical steroids are usually discontinued earlier after DALK, the incidence of steroid side effects is lower. In agreement with this, a recent meta-analysis demonstrated a reduced risk of cataract and intraocular pressure elevation after DALK compared to PK.[57]

Nevertheless, there are some complications that are unique to DALK such as intraoperative perforation of the Descemet’s membrane which may lead to endothelial decompensation and/or postoperative detachment of the recipient bed with double anterior chamber formation.[58] Our group has previously reported that double anterior chamber formation may also occur without a perforation and is more frequent in scarred corneas and in case of occurrence a type 2 bubble.[20] In most cases, this complication requires rebubbling of the anterior chamber to reattach Descemet’s membrane.

**Key Issues Moving Forward**

Over the past decade, several intraoperative OCT platforms capable of providing the surgeon with extra intraoperative information have become available. Some of the potential applications of intraoperative OCT for DALK are the capacity of assessing the depth reached by the cannula prior to pneumatic dissection,[43] the thickness of the residual stromal bed,[59] as well as confirming that pneumatic dissection has successfully occurred.[60] These information have been shown to be useful in aiding surgical decision-making.[61] However, the utility of intraoperative OCT is still limited by the shadowing produced by metal instruments, the motion artifacts, and the latency

**Table 1: Randomized controlled trials comparing big bubble deep anterior lamellar keratoplasty and penetrating keratoplasty in patients with keratoconus**

| Study                     | Country     | Number eyes | Final BCVA                  | Corneal astigmatism     |
|---------------------------|-------------|-------------|-----------------------------|-------------------------|
| Javadi et al. 2011        | Iran        | 42/35       | 0.18 versus 0.15 logMAR (NS) | 3.89 versus 4.36 D (NS) |
| Cheng et al. 2011         | Netherlands | 28/28       | 0.39 versus 0.31 logMAR (NS) | 3.57 versus 4.16 (NS)   |
| Söğütlü Sari et al. 2012  | Turkey      | 99/75       | 0.18 versus 0.14 logMAR (P=0.09) | 3.16 versus 3.67 (NS)   |

BCVA: Best-corrected visual acuity, NS: Not significant

**Figure 2:** Representative case of a patient with keratoconus treated with deep anterior lamellar keratoplasty. 1 month postoperatively with both running sutures still in place (a); anterior segment optical coherence tomography showing the peripheral stromal shoulder surrounding the 6 mm central optical zone (b); 2 years postoperatively after complete suture removal (c); anterior segment optical coherence tomography showing disappearance of the peripheral shoulder due to stromal thinning and remodeling (d)
between surgeon hand movements and image motion on the screen.

The femtosecond laser is a neodymium glass laser employing ultrashort pulse durations that allows making corneal incisions at the desired depth.[62] Several previous studies have described the use of the femtosecond laser during DALK to create lamellar side cuts[63‑66] and an intrastromal channel for the air injection.[67‑69] To date, the additional costs associated with this technology do not seem justified by the gains in patient outcomes. In fact, a recent comparative study demonstrated similar results of manual and femtosecond laser-assisted DALK in terms of visual recovery and corneal astigmatism.[70] However, a randomized clinical trial comparing manual and femtosecond laser-assisted DALK is currently ongoing (NCT03732599).

Several years after PK for keratoconus, ectasia can re-emerge in the recipient after a period of latency.[71] DALK can be performed in these eyes to selectively replace the diseased stroma while leaving the functional endothelium in place.[72] We have recently developed a technique for DALK by simple peeling of the PK graft without any need for lamellar dissection. The technique involves 9 mm trephination followed by opening of the stromal component of the old PK wound until a natural plane of separation is found. Stromal peeling can then be performed due to the lack of adherence between the stroma of the PK graft and the underlying layers. This technique results in excellent visual outcomes while minimizing endothelial cell loss.[73]

There is an overwhelming imbalance between corneal tissue availability and demand worldwide.[74] Since corneas preserved through hypothermic storage and organ culture remain viable only for 2 and 4 weeks, techniques that can extend storage are of great interest.[75‑77] In the current scenario of COVID‑19 pandemic, long-term preservation of unused corneas due to cancellation of elective surgery may be particularly important to avoid tissue wastage.[78,79] Silica gel dehydation allows preservation of donor corneal stroma with maintenance of thickness, transparency, and biomechanical properties after rehydration.[80] The Veneto Eye Bank Foundation is storing and distributing dehydrated corneas for possible use in DALK. A randomized controlled trial comparing the outcomes of DALK using dehydrated versus standard organ culture stored donor corneas is currently ongoing in our center (NCT04430244).

Alternative solutions to overcome the shortage of donor corneas include the use of biocompatible materials[81] and xenograft tissues.[82] Although in vitro and studies with collagen-based engineered matrices and synthetic polymers have shown promising results,[83] clinical data regarding the use of these materials are still lacking. Decellularized porcine corneas have the potential to provide a scaffold for host keratocyte migration without inducing immune rejection due to the elimination of major immunogenic components.[84] Three clinical trials evaluating DALK using decellularized porcine corneas reported improved corneal transparency and visual acuity in patients with fungal[85,86] and herpetic keratitis.[87] Nevertheless, xenotransplantation is associated with important ethical dilemmas and safety concerns due to the risk of xenogenic rejection and xenozoonosis.[82]
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