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REVIEW ARTICLE

Deep Anterior Lamellar Keratoplasty for Ectatic Disease

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ABSTRACT

Recently, deep anterior lamellar keratoplasty (DALK) has received attention for patients with ectatic diseases not affecting the endothelium. However, it was not always so. For years, DALK was overlooked due to the difficulty in achieving good visual results, which were considered weak in comparison with the results of penetrating keratoplasty (PK). DALK was proposed to retain a patient's healthy endothelium; thereby avoiding some possible complications of PK. Preservation of the endothelium contributes to prolonged survival of the button and thus overcomes a major cause of failure after PK. DALK is now accepted as a viable alternative to PK. With advances in surgical techniques, instruments, and imaging technologies, visual results obtained with lamellar keratoplasty are equivalent to visual outcomes with PK, in addition to providing a transplant cost benefit owing to a better transplantation survival rate.

Keywords: Keratoplasty, Keratoconus, Ectasia, Big bubble, Deep anterior lamellar keratoplasty, Low vision.

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INTRODUCTION

Lamellar surgery was the first process to succeed in corneal transplants. It was first achieved by the pioneering Arthur Von Hippel in 1877, following earlier work by Von Walther and Mulhabauer in the years 1830 to 1840.[1,2] The first successful partial transplant was performed in Zirm in 1950.[3] Since then, various surgical techniques have been described, as well as several suggestions for their further use.[4-6] Deep anterior lamellar keratoplasty (DALK) was long considered safer than penetrating keratoplasty (PK), although its use was restricted to tectonic transplants because visual results were not as good as those with PK. In the 1970s, only 3 to 8% of transplants were performed by lamellar surgery.[7,8]

PK transplantation remains the most common method, with a wide lead over lamellar surgery. In fact, 2009 data show that in the USA, only 2% of the transplants were lamellar; in the UK, the number was 12%.[9,10] However lamellar surgery is beginning to change the game. In 2012, 59% of transplants performed at the University of Toronto were lamellar.[11]

This resurrection of DALK has been associated with the development of modern surgical techniques and instruments specific for the transplant technique.[12] Many centres are now demonstrating a clear shift to lamellar procedures because of their enhanced graft survival, improved visual outcomes compared with previous techniques, and reduced endothelial cell loss compared with PK.[13,14] Several centres have adopted this technique, but not in patients with stromal pathologies affecting the corneal endothelium; in such cases, the recipient's corneal stroma is totally replaced, leaving intact the recipient's Descemet membrane and endothelium.[15-21] The lack of corneal endothelial cells with the potential for immune rejection and the expected retention of recipient corneal endothelial cells in most DALK surgeries, compared with the rapid decrease in donor corneal endothelial cell density after PK surgery, is at least a theoretical advantage of DALK over PK.

The objective of this review was to document the evolution of lamellar keratoplasty techniques and results, providing comparisons with PK for ectatic disease, and to evaluate the cost-benefit relationship of the procedure in corneal transplants.

TECHNIQUES

Techniques for Preparing Donor Tissue

Filatov demonstrated that corneal tissue could be collected postmortem and used for transplants. In 1935, he developed a manual trephine with a protective insert that allowed him to obtain cadaveric corneas immediately after enucleation of the eye.[22] In 1942, Arruga developed a manual trephine, with which it was possible to control the incision depth.[23]

Later, Castroviejo performed a lamellar transplant instead of PK and developed a burr with a depth regulator.[24] He treated cases of advanced keratoconus, performing what he called a total lamellar transplant. The donated button was prepared in two stages. First, Castroviejo used a burr to reach the desired depth. Second, he performed a lamellar keratoplasty dissection using a blunt-scissors keratectomy.[25] The technique was further improved by using the Castroviejo electrokeratome.[26]

Barraquer developed a microkeratome for donated corneas.[27] Hallerman, in 1959, proposed the use of a full-thickness donor graft with intact endothelium in lamellar keratoplasty.[28] The development of these tools and techniques was fundamental to the modern era of lamellar transplantation.[29]

Techniques for Tissue Dissection in the Recipient

In DALK, the recipient bed should ideally consist of only Descemet's membrane and endothelium. According to Barraquer, the recipient bed should be made as deep as possible to reduce problems of opacity at the interface, and it should be uniform in thickness, rather than aligned with the donated button, to obtain uniform traction sutures.[27]

Until 1965, only the Barraquer microkeratome was available for cutting a recipient bed, and it was difficult to achieve a depth greater than 300 microns.[29] Without sufficient bed depth, DALK can cause problems with opacity at the interface and decreased visual acuity. To achieve maximum depth in a recipient bed, Malbran suggested the technique of 'peeling-off'.[30,31] Archila described a technique of injecting of 0.1 cc of air to dissect the stroma, as did Price and Chau, in the late 1980s/early 1990s.[32-34]

Several authors then began to report techniques for the removal of the stroma.[35,41] Morris described using viscoelastic material and a paracentesis.[42] Tsubota used the 'divide-and-conquer' principle of cataract surgery.[43] The technique of Melles et al used a limbal approach to visualize the depth of the lamellar dissection in DALK. This technique involved exchanging the air with an aqueous solution and creating an optical endothelium-air interface, which acts as a convex mirror to reflect back the depth of an instrument in the deep stroma.[44,45]

Malbran proposed a two-step procedure as a useful alternative when there is a high risk for corneal perforation (e.g. in advanced keratoconus). In this surgery, trephinations were performed at two different diameters (7.75 and 9.5 mm), allowing the option of changing from DALK to PK in case of a perforation. Then, using a 30-gauge needle with the bevel side up, 1 cc of air was injected into the deep stroma. Using a limbal paracentesis to prevent bulging of the Descemet membrane during late resection of posterior fibers, Malbran then began peeling off the stroma at the 12 o'clock side of the smaller trephination, using the blunt side of a razor blade. He then the periphery was dissected until reaching the 9.5 mm trephination, and the keratectomy was completed using right and left scissors.[46]

Anwar and Teichmann subsequently reported a technique referred to as the 'big bubble,' in which a large bubble of air was used to facilitate the separation of the Descemet membrane from the corneal stroma.[47] They used a 27/30 gauge needle attached to an air-filled syringe. The needle was inserted into the corneal stroma, bevel down and advanced 2 to 4 mm posteriorly toward the Descemet membrane. Air was forcefully injected into the deep stroma, reaching the plane and causing the separation of the Descemet membrane from the overlying stroma. Many surgeons have adopted the big-bubble DALK technique, and several published studies have confirmed excellent visual outcomes with this technique.[17-21,48,49] Indeed, big-bubble DALK is one of the most popular techniques for DALK with full stromal removal.[29]

Tan and Mehta described a modification of the original technique. To allow for more consistent needle placement into the posterior stroma, they first performed a manual dissection of the anterior stroma to a depth of 50 to 60% of the stromal thickness, exposing the posterior half of the stroma. Then, a 27-gauge needle was introduced into the posterior stroma, bevel down, and advanced 3 to 4 mm at an angle almost parallel to the cornea. Owing to the parallel plane of the needle (at almost 90° to the shaft), this method allowed safer placement of the needle tip at a depth close to the Descemet membrane. The risk for inadvertent perforation is reduced when the needle is angled more than in the originally described technique. Confirmation of bubble formation was made by injecting a small air bubble into the anterior chamber. Peripheral localization of this bubble at the highest point of the anterior chamber confirmed the presence of a big bubble between the Descemet membrane and the posterior stroma. With this method, a big bubble was achieved in more than 93% of cases and with a low perforation rate of only 7%.[14]

Innovations continued with the introduction of the femtosecond laser, which presents the possibility of transplants with edges modelled to increase the contact surface, reduce the healing time, and enable earlier spot removal, thus allowing quicker recovery.[50-52] Femtosecond laser corneal cutting may offer greater safety, reproducibility, predictability and flexibility. Moreover, the risks for irregular cutting and microperforation are reduced.[53]

Buzzonetti et al reported a variation of the big-bubble DALK technique, referred to as the IntraBubble, using an IntraLase femtosecond laser.[54] Farid and Steinert[55-58] and Price et al[59,60] also described the use of an IntraLase femtosecond laser combined with a big-bubble DALK to create zigzag side cuts in the recipient and donor corneas (so-called IntraLase-enabled keratoplasty, IEK), thus improving the accuracy of the air-needle placement and the matching of the graft-host junction.

Disadvantages and Complications of DALK *vs* PK

DALK is technically more difficult, requires more time for learning, and involves the use of various tools.[29] Problems related to the interface, including irregularities and scarring,

can result in poor visual results. Nevertheless, modern techniques, when performed without complications, have significantly reduced these issues,[29] although there can still be problems related to postoperative superficial epithelialization.[13] When a significant amount of pre-Descemet stroma is left in the recipient bed, visual acuity in DALK eyes may be compromised.[61-64] There is a definite learning curve for both PK and DALK procedures, but most corneal surgeons already possess the skills needed for PK surgery. The operative time for DALK is usually longer than that for PK, and both procedures require more operative time than endothelial keratoplasty because of the extensive suturing of the DALK or PK donor graft.

The most common complication involves puncturing the Descemet membrane, with either a microperforation (0.1 mm or less) or a macroperforation. This usually leads to converting the operation to a PK.

Advantages of DALK over PK

The main causes of failure in PK are endothelial rejection and delayed failure.[65] In DALK, the recipient's own healthy endothelium is retained, eliminating the risk for endothelial rejection. The risk for late endothelial failure is also reduced in DALK.[21]

PK can, even with the least trauma, rupture incisions and have dramatic consequences. In DALK, the structure of the Descemet membrane remains intact, which decreases the risk for corneal trauma,[66-68] and there may also be higher resistance to rupture after blunt trauma.[69] As DALK is a minimally invasive surgery, the incidence of intraocular surgical complications such as suprachoroidal hemorrhage, retinal detachment, macular edema and endophthalmitis is reduced.[70-74]

Less immunosuppression is required in DALK. Because there is no risk for endothelial rejection, exposure to topical corticosteroids is lower, which decreases the incidence of intraocular pressure changes and cataract formation.[75,76] In addition, the potential pool of donor corneas is larger for DALK than for PK because corneas that are acceptable for PK due to low endothelial counts are viable for DALK.[77] Given the safety of the procedure, DALK is the procedure of choice for grafting in intellectually disabled patients.[78,79]

DALK also allows the use of large diameter grafts (9-11 mm), making it possible to treat whole corneal ectasia without the increased risk for graft rejection associated with a penetrating graft. Also, with a larger button, the induction of postoperative astigmatism is lower.

In summary, the most obvious advantage of DALK is that the host corneal endothelium is not subject to immune rejection. The major long-term advantage of DALK over PK relates to the long-term preservation of host corneal endothelial cells, as measured by specular microscopy and reported as endothelial cell density. Complications such as positive pressure, iris prolapse, and choroidal effusion/hemorrhage are reduced greatly with DALK, and because topical corticosteroids can usually be discontinued 3 to 4 months after DALK, there is a lower incidence of corticosteroid-associated intraocular pressure elevation. Traumatic rupture of PK wounds months to decades after surgery is a potential complication of PK.[80] However, DALK wounds have a theoretical advantage over PK wounds, and clinical evidence of traumatic dehiscence of DALK wounds suggests that the injuries are less severe than those seen in PK eyes.[81]

Outcomes of DALK compared with PK

To compare the results of DALK and PK, it would be ideal to split lamellar keratoplasty procedures into two major groups: Pre-Descemetic techniques (Malbran's peeling-off, air, and lamellar dissection; Melles technique) and Descemetic techniques (big-bubble DALK technique and Tan). However, in most reports, the techniques are not distinguished, and this can influence the reported DALK results and comparisons with PK.

A. Visual Acuity

In most studies, PK outcomes are better in terms of best spectacle-corrected visual acuity (BSCVA) only in the immediate postoperative period, after which DALK and PK outcomes are similar.[29] In a study of patients with keratoconus, Sarnicola found a mean BSCVA of 20/25, with 20/30 in 85% of cases, at 30.4 months postoperatively.[82] Also, they found no difference between pre-Descemetic and Descemetic techniques in the group having a faster visual recovery.[82] Soong et al reported that 79% of patients referred for optical transplantation required 1 year after lamellar keratoplasty to achieve 20/40, and there was progressive improvement in visual acuity with time. They noted that problems at the interface limited the results and suggested maximum stroma removal to achieve the best possible visual acuity.[83]

Han et al studied only patients with keratoconus who underwent the modified Anwar Tan DALK or PK procedure and found that 1 year later, 64.3% of the DALK patients and 67% of the PK patients achieved a BSCVA of 20/20. This study included one pre-Descemetic technique, but superior results were obtained with Descemetic techniques.[62] Jones et al compared visual outcomes at 2 years in 243 keratoconus patients who underwent unspecified DALK techniques and 1,136 patients who

underwent PK from 1999 to 2005; the mean BSCVA in both groups was 20/30.[13] Cohen et al, without specifying the DALK technique, reported similar BSCVA at 22 months postoperatively in 11 eyes that underwent DALK and 30 that underwent PK in patients with keratoconus.[84] Feizi et al compared the visual outcomes of the Anwar technique when a big bubble was used *vs* a manual dissection in patients with keratoconus.[85] After 12 months, the group in which the big bubble was used showed better results; however, at 22 months of follow-up there was no statistically significant difference between the groups. It was concluded that there may be a delay in visual recovery with the manual technical.[85]

Most reports have shown faster visual rehabilitation after PK, but the results are similar between DALK and PK after a year of follow-up.[29] The development of DALK techniques and the improved quality of the donor button preparation have resulted in significantly better visual acuity outcomes.[15,16,20,62,85-88]

B. Endothelial Cell Loss

Van Dorren et al showed that cell loss in DALK with the Melles technique was low within the first 6 months after transplant and occurred at a physiological rate after that time.[89] Kubaloglu et al reported changes in endothelial cell density after DALK (Descemetic, big-bubble technique) in 166 keratoconus cases.[90] The average losses were 8.1 ± 4.6% at 1 year and 10.5 ± 5.7% at 2 years. They concluded that the rate of cell loss was less in DALK than in PK. The same authors reached the same conclusion after a 4-year follow-up in another study of patients with keratoconus.[91]

Salouti et al found a slight increase in endothelial cell density after DALK (Melles technique) in keratoconus cases in which there were no complications.[92] In addition, the mean cell area had decreased compared with preoperative measurements. This finding, along with a later decrease in the standard deviation of mean cell area, suggested that notable postoperative changes in corneal biomechanical forces may affect endothelial cell profile measurements.[92] In a recent study, Bordiere et al reported 22% cell loss after DALK and 50% after PK at a 5-year follow-up.[93] Acar et al studied the effects of phacoemulsification on endothelial cell density in patients with PK or DALK and in patients with no previous surgery. Cell loss was similar between the DALK group and patients with no previous surgery, whereas cell loss was significantly higher in the PK group.[94] In a review article, Reinhart et al reported higher cell counts after DALK than after PK in the studies surveyed.[69] It is expected that cell loss in DALK would be similar to physiological rates in a normal adult.[89,95,96]

C. Intraoperative Complications

Even with the development of new techniques and instruments, it is difficult to remove all of the stroma without discontinuities or holes.[97-99] When a perforation occurs, the surgeon can choose to convert to PK, or can make adjustments using intracameral air injection or patches to complete the stromal lamellar dissection without converting to PK.[29]

The complication rate of microdrilling can be high, reaching 39%, even for experienced surgeons.[15,43,44,62,63] Perforations smaller than 0.1 mm can occur with the big-bubble technique as in other forms of dissection. On average, these microapertures occur in 11.7% of cases, but intraoperative conversion to PK occurs in only 2.0% of cases. One of the main consequences of microperforations is the formation of a double anterior chamber, although this can also occur in the absence of perforations.[100]

D. Postoperative Complications

Graft failure: In a comparative study between PK and DALK, considering Descemetic *vs* pre-Descemetic techniques, we obtained 100% transplant survival after 3 years in the DALK and PK groups with Descemetic techniques and 73% transplant survival in the preDescemetic DALK group (manual lamellar keratoplasty).[62] In another study, after 2 years, survival was 90% for PK, 98% for manual DALK, and 100% for big-bubble DALK.[101] Cheng showed no significant difference in cell loss between DALK and PK after 1 year of monitoring.[96] Borderie studied survival of the button, reporting 97.2 ± 2.0% survival after DALK and 73.0 ± 2.0% survival after PK.[102]

A single retrospective study conducted in the UK showed different results compared with the other reports in the literature: The risk for failure in DALK was three times the risk in PK.[13] In the opinion of other authors; this result was related to the technical difficulties of lamellar keratoplasty and complications related to surgeon experience.[29]

Graft rejection: In a retrospective study of 500 DALK surgeries performed between 1980 and 2008, Malbran reported only four cases (0.8%) of rejection. All stromal-related rejection occurred between 5 and 13 months postoperatively.[29] Watson et al studied the pattern of rejection in seven DALK cases between 1997 and 2001; one case involved epithelial rejection, three involved stromal rejection, and three cases involved epithelial and stromal rejection.[103] Han et al described rejection rates of 15% after PK and 0% after DALK.[62] Similarly, Cohen reported 13.3% rejection after PK and no rejection after DALK.[84] Cheng found 3.57% epithelial rejection in the DALK group and 10.71% endothelial rejection in the PK group.[96] It is clear

that DALK has an advantage over PK in this regard. While endothelial rejection is responsible for failure in PK, the stromal and epithelial rejections in DALK are more readily resolved without jeopardizing the donated button.

Cataracts and glaucoma post-transplant and corneal biomechanics: Han et al reported glaucoma rates of 10% in DALK and 15% in PK.[62] Leccisotti evaluated phacoemulsification and IOL implantation after DALK procedures and suggested safety and predictability in visual rehabilitation.[104] Biomechanical studies have shown that eye corneas are weak after PK when compared with eyes after big-bubble DALK, but these results show corneal hysteresis similar to that in non-operated eyes.[105,106] Recent research has shown that pre-Descemetic and Descemetic DALK techniques differ with regard to biomechanical data, with higher values in eyes that underwent pre-Descemetic DALK procedures.[107]

Cost-Benefit Analysis

Cost-benefit analysis helps governments evaluate health policies. The economic feasibility or cost effectiveness of a technique can influence its adoption. To increase the number of surgeons using a particular technique, it is important that complications are reduced and outcomes are improved with increased experience.

In a study of the treatment of keratoconus between January 1991 and January 2009, both PK and DALK had good cost-benefit characteristics, but DALK was superior to PK at the end of 20 years.[108] In the Netherlands, another study reached the same conclusion; DALK offered the best value owing to its lower failure rate compared with PK.[97] Thus, the cost-effectiveness of DALK is greater over time because the transplant survival rate is higher.

CONCLUSION

With advances in surgical techniques, instruments and imaging technologies, the results of DALK have improved greatly. Today, DALK has visual results similar to those of PK with the benefit of low endothelial cell density loss. Improvements in the DALK technique have made it more popular, and its better cost-benefit properties, attributable to a higher survival rate, may make it preferable as a matter of public policy. The results are compelling, and DALK should be the technique of choice for cases of ectatic disease where there is impairment of the endothelium.

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