Deep Anterior Lamellar Keratoplasty
Using the Big-bubble Technique
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Javad Amoozadeh, MD1 • Hassan Hashemi, MD3,4

Abstract

Purpose: To review the visual outcome and complications of deep anterior lamellar keratoplasty (DALK) using the big-bubble technique in patients with corneal ectasia

Methods: Eighteen consecutive patients with keratoconus or post-LASIK ectasia with poor spectacle-corrected visual acuity and/or contact lens intolerance were enrolled in this study between October 2005 and September 2006. DALK big-bubble technique was carried out in 17 eyes. In one eye, intraoperative conversion to penetrating keratoplasty (PKP) followed large Descemet's membrane perforation. Visual and refractive outcomes and intraoperative and postoperative complications were assessed.

Results: Seventeen procedures (94%) were completed as DALK. The mean follow-up time was 9.5 months. At the last follow-up visit, mean best corrected visual acuity (BCVA) was 20/32 (0.20±0.14 LogMAR) and BCVA of 20/40 or better was achieved in 82% of the eyes. The mean postoperative topographic cylinder was 4.4±1.6 diopter (D), and the mean spherical equivalent was -3.3±6 D. Main postoperative complications included graft rejection (2/17, 12%), graft infection (1/17, 6%) and double anterior chamber (2/17, 12%).

Conclusion: DALK is a valuable and successful alternative to PKP in patients with keratoconus. Graft rejection is a rare complication but is associated with good recovery because the endothelium is not involved.

Keywords: Deep Anterior Lamellar Keratoplasty, Keratoconus, Descemet's Membrane, Penetrating Keratoplasty

Introduction

Penetrating keratoplasty (PKP) has been regarded as the preferred surgical technique for keratoconus for many years.1,2 In recent years deep anterior lamellar keratoplasty (DALK) techniques have been improved markedly allowing surgeons to completely excise corneal stroma as far as Descemet's membrane (DM) at least along the visual axis, which leads to improved postoperative visual acuity.

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Compared with a PKP, a lamellar technique has a number of advantages. It is mainly an extracocular procedure, so it lacks most postoperative intraocular complications and there is less risk of graft rejection and other long-term complications.

Endothelial rejection is the most common type of rejection which occurs in 20-30% of cases undergoing PKP. DALK is a technique that can avoid the risk of endothelial rejection in eyes in which endothelial cell function has been preserved. However, DALK is still not the first choice of surgery for many surgeons due to technical difficulties, longer surgery time, and a steep learning curve compared with PKP.

DALK was first described by Anwar in 1974 and later by Archila in 1985. The first extensive study on the results of DALK was reported by Sugita and Kondo in 1997. They showed that restoration of postoperative visual acuity was quite adequate with no episodes of endothelial rejection in 120 eyes undergoing DALK surgery.

Several techniques have been used to facilitate lamellar dissection. These include delamination combined with injection of air, saline, or viscoelastic materials. In 2002 Anwar and Teichmann proposed a technique, which they called the big-bubble technique, where air is injected in such a way that a large bubble is created between stroma and DM. This technique largely facilitates the operation and reduces intraoperative complications.

In this study we report the clinical outcomes of the DALK big-bubble technique in unselected consecutive patients with keratoconus or post-LASIK ectasia.

Methods

Between October 2005 and September 2006, a total of 18 unselected consecutive patients (18 eyes) with moderate to advanced keratoconus or post-LASIK ectasia referring to Farabi Eye Hospital were included in a prospective interventional case series study to evaluate the clinical outcomes of DALK using the big-bubble technique.

Inclusion criteria were diagnosis of keratoconus or post-LASIK ectasia, poor spectacle-corrected visual acuity (≤20/100) in the more affected eye, and/or contact lens intolerance. Exclusion criteria were any coexisting ocular disease other than corneal ectasia and high myopia, that could affect visual acuity and history of hydrops. Diagnosis of keratoconus was made on the basis of clinical slit-lamp findings (such as stromal thinning, Fleischer ring, and Vogt striae), keratometry and characteristic topographic findings.

Preoperative and postoperative eye examinations including Snellen uncorrected and best spectacle-corrected visual acuity (BSCVA), slit-lamp examination, tonometry, fundus examination, manifest refraction (if possible), keratometry, corneal topography and orbscan pachymetry were carried out by one investigator (AA). Central corneal thickness was assessed by ultrasound pachymetry as well. Visual acuity, refraction and topography were checked at one, three, six and 12 months after surgery. Ultrasound pachymetry was done at 6 and 12 months follow-up. Intraoperative and postoperative complications were recorded.

All surgeries were carried out by one surgeon (HH) experienced in DALK surgery. The big-bubble technique described by Anwar was used. In brief, between 70-80% of stromal thickness was trephined by means of Hessburg-Barron trephine (mean: 8 mm, range: 7.75-8.5 mm according to vertical corneal diameter). A 27 gauge needle attached to a 5 ml air-filled syringe was bent up 60° at about 5 mm from its tip with the bevel facing down. The tip was inserted into the corneal stroma deep in the trephination groove and advanced toward a paracentral position for approximately 3-4 mm from the entry point. Air was injected into the stroma until an effect was noted. The aim was the formation of a large air bubble between the DM and stroma which usually appeared in the form of a whitish semiopaque disc, and was indicated by the sudden easing of resistance of the plunger of the syringe. Paracentesis was performed at a site peripheral to the edge of the bubble. A partial thickness keratotomy was performed with a crescent knife. A 15° stab knife held tangentially to the cornea was used to make a small nick, just off center, through the remaining stromal layers. A blunt spatula was inserted through the opening and delamination was carried out, the deepest stromal layers then were incised by rubbing over the spatula with a stab-knife, in four
radial directions and then were removed by cutting each quadrant at the edge of the trephination by Vannas scissors, exposing the DM.

We used fresh donor sclerocorneal button preserved by Optisol. Its deep surface was dried with cellulose sponge and the endothelium was removed with cellulose sponges. The cornea was then punched out from the endothelial side with the Hessburg-Barron punch (same size in cases with axial myopia or 0.25 oversize in others) and transferred to the host bed and sutured in place either by using 16 interrupted sutures, or 8 interrupted sutures combined with a single continuous 10-0 nylon sutures. All knots were buried. All eyes received subconjunctival injection of gentamicin and betamethasone.

If a small perforation occurred during the deep lamellar dissection (2 cases), the dissection was continued in a new plane slightly superficial to the perforation. If the perforation was large the operation was converted to PKP (1 case).

Postoperatively, all patients received chloramphenicol drops until complete epithelialization and betamethasone drops for 3 months in a tapering manner followed by flurometholone for 2 months. The eyes were examined at days 1, 3, 7, then weekly for the first month, then monthly for 6 months and every 2 months thereafter.

All the patients were closely monitored for signs of inflammation, graft rejection, infection, suture related problems, raised intraocular pressure and refractive outcome. Selective suture removal for the reduction of astigmatism started 3 months after surgery. Otherwise sutures were left in place as long as they were not excessively tight, loose, exposed, or attracting blood vessels.

Data were analyzed using SPSS software version 11.5.

**Results**

DALK surgery was attempted in 18 eyes of 18 patients and was completed in 17 eyes of 17 patients. In one eye, intraoperative conversion to PKP followed large DM perforation. The patients' characteristics and descriptive results are listed in table 1. 15 patients were male (88%) and 2 were female (12%). The mean age of the patients at the time of surgery was 25±6.6 years (range 16-38 years), and the average follow-up period was 9.5±3.7 months (range 6-18 months) from the date of surgery.

<table>
<thead>
<tr>
<th>Table 1. Patients characteristics, and preoperative data of eyes undergoing DALK surgery</th>
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</thead>
<tbody>
<tr>
<td>Age (mean±SD) years</td>
</tr>
<tr>
<td>Follow-up (meansSD) months</td>
</tr>
<tr>
<td>Male/Female</td>
</tr>
<tr>
<td>Diagnosis</td>
</tr>
<tr>
<td>Keratoconus</td>
</tr>
<tr>
<td>Post-LASIK ectasia</td>
</tr>
<tr>
<td>Corneal scar</td>
</tr>
<tr>
<td>Superficial or no scar</td>
</tr>
<tr>
<td>Deep scar</td>
</tr>
</tbody>
</table>

In 15 patients (88%) keratoconus was the indication of surgery and 2 patients (12%) had post-LASIK ectasia. 14 eyes (82%) had superficial or no scar, and 3 eyes (18%) had deep corneal scar not extending to the DM.

Baring of DM during DALK was achieved in all eyes at least in visual axis. More than one air injection was required in 3 cases. Mean preoperative pachymetry, measured at the cone apex was 397.23±50 μm (range: 298-480) and increased to 512.75±38.6 μm (range: 459-577) postoperatively. The mean keratometric value preoperatively was 60.1±7.3 D (range: 49-78.5) and changed to 44.86±2.4 D (range: 39.5-48.25) postoperatively. Table 2 compares central corneal pachymetry, keratometry and topographic astigmatism before surgery and at last visit which shows statistically significant difference (paired T-test).

**Visual outcome**

Preoperatively mean uncorrected visual acuity (UCVA) was 20/400 (1.30±0.17 LogMAR) and BSCVA was 20/320 (1.19±0.23 LogMAR), only 6% of all eyes were able to achieve a corrected visual acuity of 20/100.

At the last visit, mean UCVA was 20/50 (0.43±0.16 LogMAR), mean BSCVA was 20/32 (0.20±0.14 LogMAR) and 82% of all eyes were able to achieve a corrected visual acuity of 20/40 or better. BSCVA<20/25 was observed in 47% of patients. The mean topographic astigmatism was 8.26±4.5 D (range: 4-19) preoperatively and 4.4±1.6 D (range: 1-7) at the last postoperative visit. A topographic
cylinder of 5 D was measured in 59% of patients. At the last examination, mean spherical equivalent was -3.3±6 D.

Table 2 and figure 1 show improvement in BSCVA at different postoperative examination times (1, 3 and 6 months) (repeated measures ANOVA, P< 0.0001).

Table 2. Comparison of preoperative and postoperative central pachymetry, keratometry and topographic astigmatism of DALK big-bubble technique

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Preoperative</th>
<th>Last visit</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central pachymetry (μm)</td>
<td>397.23±50</td>
<td>512.75±38.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Keratometry (Diopters)</td>
<td>60.1±7.3</td>
<td>44.86±2.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Topographic astigmatism (Diopters)</td>
<td>8.26±4.5</td>
<td>4.4±1.6</td>
<td>&lt;0.0005</td>
</tr>
</tbody>
</table>

DALK: Deep Anterior Lamellar Keratoplasty
Values are expressed as mean±SD (Standard Deviation)

Table 3. Comparison of preoperative and postoperative LogMAR visual acuity of DALK big-bubble technique

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>1 month</th>
<th>3 month</th>
<th>6 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patient</td>
<td>17</td>
<td>17</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Mean BSCVA</td>
<td>1.19</td>
<td>0.66</td>
<td>0.37</td>
<td>0.22</td>
</tr>
<tr>
<td>SD (Standard Deviation)</td>
<td>0.23</td>
<td>0.27</td>
<td>0.21</td>
<td>0.16</td>
</tr>
<tr>
<td>P-value*</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td></td>
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</tbody>
</table>

BSCVA: Best Spectacle Corrected Visual Acuity
DALK: Deep Anterior Lamellar Keratoplasty
* : Repeated measures ANOVA

Figure 1. Mean best spectacle-corrected visual acuity (BSCVA) before and after deep anterior lamellar keratoplasty (DALK) big-bubble technique
Complications
The complications are listed in Table 4. Intraoperative perforation of DM occurred in 3 cases (16.6%). In 1 patient (5.5%) perforations were too large to complete the lamellar dissection and required conversion to PKP during surgery. In 2 cases there were microperforations in the DM and it was possible to complete the surgery by conservatively removing most of the corneal stroma, trying to expose the DM in the central 4 mm optical zone, and then suturing a donor button in place. A double anterior chamber occurred in one of them two weeks after surgery. In one eye Descemet’s splits occurred at the Schwalb line with direct penetration of air into the anterior chamber during intrastral air injection. The dissection was completed after injection of air and at the end of surgery an anchoring suture was used to directly suture the unrolled DM to the donor and recipient stroma.

Table 4. Complications of DALK big-bubble technique (No. of patients=17)

<table>
<thead>
<tr>
<th>Complications</th>
<th>Rate</th>
</tr>
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<tbody>
<tr>
<td>Descemet’s perforation</td>
<td>3 (16.6%)</td>
</tr>
<tr>
<td>Conversion to PKP</td>
<td>1 (5.5%)</td>
</tr>
<tr>
<td>Double anterior chamber</td>
<td>2 (12%)</td>
</tr>
<tr>
<td>Rejection episodes</td>
<td>2 (12%)</td>
</tr>
<tr>
<td>Persistent epithelial defect</td>
<td>2 (12%)</td>
</tr>
<tr>
<td>Loose suture</td>
<td>4 (23.5%)</td>
</tr>
<tr>
<td>Graft infection</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>Regraft</td>
<td>1 (6%)</td>
</tr>
</tbody>
</table>

A double anterior chamber was noted in 2 patients (12%). One occurred in immediate postoperative period, supposedly due to inadvertent air injection into donor-recipient interface at the end of surgery and responded to interface air drainage. The other one which was secondary to intraoperative DM microperforation, occurred 2 weeks after surgery and did not resolve with conservative management over a period of 2 weeks, but was managed successfully with a single injection of air into the anterior chamber from the limbus. Immunological graft rejection episodes occurred in 2 eyes (12%). In one eye, epithelial rejection episode was diagnosed 4 months after operation in the presence of decreased vision, with subepithelial infiltrates and without stromal edema. In the other eye with a history of delayed reepithelialization, stromal graft rejection was diagnosed 6 months after surgery with sudden decrease in vision, stromal haze and edema. Both responded well to intensive topical corticosteroids (betamethasone) and the graft cleared after 1-2 weeks of treatment.

Loose sutures were noted in 4 cases (23.5%) over the follow-up period. However, only 2 cases required surgical intervention (resuturing). There was one case of traumatic wound dehiscence 5 months after surgery that required resuturing. Delayed reepithelialization (beyond two weeks after surgery) occurred in 2 patients (12%) and was successfully managed with temporary tarsorrhaphy.

Graft–host interface haze and/or vascularization were not seen in our patients. Graft infection occurred in 1 (6%) eye one month after surgery and streptococcus pneumonia organism was isolated. The ulcer did not respond to fortified antibiotics and regraft was necessary. The recipient bed was not involved and only the corneal button was replaced.

Discussion
Lamellar keratoplasty (LKP) which has been performed to treat a range of corneal pathologies without endothelial involvement "was first suggested by von Walther in 1830 and improved on by von Hippel in the 1880s and Filatov in the 1930s". An LKP has several advantages over PKP. The ocular tissues in the keratoconus eye are often very unstable during PKP, with bulging of the iris and lens diaphragm, but LKP is an extraocular procedure with greater intraoperative globe stability and less chance of postoperative intraocular complications such as glaucoma, cataract and cystoid macular edema.

There is no endothelial rejection reaction and the occurrence of late graft failure is reduced which is particularly beneficial in patients with poor access to ophthalmic care.
or a history of poor compliance, the mentally handicapped, and those with risk factors for rejection. "This is in contrast to PKP where endothelial graft rejection occurs in 20-30% of grafted patients" and "around 10% of grafts have failed at 10 years mainly because of endothelial rejection".

Since the endothelial cell integrity is not important in LKP, more donor corneas can be used. A further advantage of LKP is the earlier discontinuation of topical steroids which may decrease the risk of infection, glaucoma and cataract. However, until recently LKP did not gain popularity because of poorer visual results mainly due to interface scarring and irregularities, and being technically more difficult to perform than PKP. Interest in LKP was renewed by studies that demonstrated the possibility of deeper corneal dissection down to DM, allowing optimal graft–host interface clarity and smoothness with improved visual acuity to be obtained.

DALK combines the advantages of lamellar keratoplasty with those of PKP while avoiding the disadvantages of both operations. In contrast to continuous loss of endothelial cells noted in PKP, corneal endothelial density stabilizes after 6 months in DALK. "This endothelial cell loss is 11% within the first 6 postoperative months and then approaches a more physiologic rate of cell loss in the order of 1-2% after 6 months".

Several lamellar keratoplasty techniques have been described. The most recent development in this field is the method of the big-bubble proposed by Anwar, based on a particular way of injecting air to facilitate separation of DM from the corneal stroma before excising the stroma.

In this prospective study carried out on unselected consecutive patients with corneal ectasia, we investigated the clinical outcomes of the DALK big-bubble technique.

DM perforation is a well-described complication of DALK surgery. In this study, DM perforation occurred in 3 (16.6%) of the 18 eyes. This compares well with rates from other studies, which reported between 9% and 40%. This wide range may be due to different corneal pathologies, grade of keratoconus, and different surgical techniques. Small perforations can be managed by injection of air, tissue glue, or direct suturing of DM at the area of perforation, and perforations did not appear to have a negative impact on the final visual acuity in cases which DALK surgery could be completed successfully. In our study DALK surgery was completed in 2 of the 3 eyes with DM perforation.

If the perforation is large, conversion to PKP may be required, which occurred in 1 eye (5.5%) in our study. Other studies have reported 0% to 14% conversion rate. In our study, mean postoperative UCVA and BSCVA were (0.43±0.16 LogMAR) and (0.20±0.14 LogMAR) respectively, and 82% of all eyes were able to achieve a corrected visual acuity of 20/40 or better at the last follow-up visit. In these studies between 80% and 100% of patients with keratoconus undergoing DALK have achieved a vision of 20/40 or better. Watson et al reported "88% of patients with keratoconus achieved vision of 6/12 or better after at least 8 months' follow-up". In Noble et al's study, 84.9% of the eyes with different corneal pathologies had a final best visual acuity of 6/12 or better and the results for patients with keratoconus alone was 92.7%. This result is slightly inferior to the results of international studies on PKP, which reported 86% to 95% of eyes reached 20/40 or better at the final follow-up.

Average topographic astigmatism in our study was 4.4 D (range: 1-7). This is nearly similar to astigmatism previously reported for PKP and DALK. Since the follow-up period was less than one year in most of our patients and the reported data are suture-on, the mean astigmatism level may change by further follow-up through suture removal and incisional techniques and a better judgment on the final astigmatism can then be made.

The mean spherical equivalent (SEQ) in this study was -3.3±6 D (range: -21.75 to +4.25 D), which equates well with other studies, with reported values between -1.62 and -4.13 D. The SEQ values after PKP have varied between -1.63 and -4.16 D. The SEQ of -21.75 was seen in a patient with preexisting high myopia and an axial length of 30.63 mm.

In our study a same size donor graft was used in 9 eyes (53%) with mean SEQ of
-3.72±3.62 D (-8.5 to +2.0 D) and a 0.25 mm undersize donor graft in 8 eyes (47%) with mean SEQ of -3.09±8.27 D (-21.75 to +4.25 D).

Same size donor grafts have been used with the purpose of reducing the postoperative myopia in PKP. Since in DALK the anterior chamber is closed and there is no risk of wound leak, even an undersize donor graft can be used safely, bearing in mind that it may induce DM folds in some patients with severe ectasia which is usually reversible after suture removal.21

Immunologic graft rejection is an infrequent complication of DALK, occurring in 0%10,31 to 9.6%15 of patients with keratoconus. In our study 2 eyes (12%) developed immune mediated graft rejection and both cases responded completely to short courses of topical steroids therapy. However, immune-mediated stromal rejection can be sight-threatening and "Soong and Saini reported irreversible loss of vision after LKP due to presumed stromal graft rejection in 1 (1.9%) of 52 eyes, and 2 (1.4%) of 138 eyes respectively".19 It is not still known whether the presence of risk factors such as corneal vascularization,32 recent PKP in the fellow eye, and atopic keratoconjunctivitis21 are associated with a higher rejection rate after DALK as is the case with PKP.

Infectious keratitis after DALK in eyes with keratoconus is very rare,19 similar to PKP.2,8 It occurred in 1 eye (6%) in our study. This patient came to the clinic late following 2 loose sutures and subsequent melting of the graft with bacterial superinfection. Regraft was necessary in this patient.

The sample size of this study is small and the follow-up period is less than one year in most cases. Nevertheless our results are in line with other DALK published series and confirm the efficacy and safety of this procedure which seems to offer comparable visual results to PKP, with less graft failures and fewer major postoperative complications.

**Conclusion**

In conclusion, the DALK big-bubble technique is a valuable and successful alternative to PKP in patients with keratoconus and seems to offer advantages over PKP. Although it still remains a challenging procedure, surgeons trained in the technique can offer DALK as a surgical treatment of choice for patients with keratoconus, specially for high risk cases such as eyes with corneal vascularization. Larger randomized series of patients with keratoconus with longer follow-up are needed to continue assessment of the results of DALK compared with PKP.

**References**