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CLINICAL STUDY

Comparative cohort study of the outcomes of deep lamellar keratoplasty and penetrating keratoplasty for keratoconus

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Abstract

Aim **To compare the outcomes and complications of deep lamellar keratoplasty (DLK) and penetrating keratoplasty (PK) for keratoconus.**

Methods **A cohort of 20 consecutive PKs, for keratoconus, was compared with 20 consecutive DLKs, for keratoconus. The PKs were performed between June 2000 and July 2001, the DLKs between October 2001 and October 2002. Surgery was performed by one surgeon. Best-corrected visual acuities (BCVA), refraction and complications were recorded at the time of surgery, 6 and 12 months postoperatively. χ^2-tests were used to compare visual acuity outcomes and independent *t*-tests in the analysis of astigmatism.**

Results **Groups were comparable for age, sex, and ethnicity. All PKs were uncomplicated. Two of the DLK group had microperforations of Descemet's membrane. There was no significant difference in the proportion of patients achieving 6/9 or better between the PK and DLK groups (85 *vs* 78%, $P = 0.54$). PK patients were, however, more likely than the DLKs to achieve 6/6 at 1 year; 70% (14/20) of PKs compared to 22% of (4/18) DLKs ($P = 0.04$). Astigmatism was significantly higher in the PKs compared to the DLKs ($P = 0.022$). There were two cases of graft rejection in the PK group, while none in the DLKs.**

Conclusions **This study confirms good visual results from both PK and DLK in keratoconus with similarly high percentages reaching 6/9 BCVA. DLK appears to cause less astigmatism and also has the advantage of no endothelial graft rejection. The apparent cost, however, is a reduction in the likelihood of achieving 6/6 BCVA.**

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Introduction

Penetrating keratoplasty (PK) is a highly successful operation with good visual outcomes.[1] Unfortunately however, graft failure remains a problem with 18% of primary grafts failing within 10 years.[2] The commonest reasons for graft failure are endothelial rejection and chronic endothelial cell loss.[2,3] Anterior lamellar keratoplasty reduces rejection rates by preserving the patient's own endothelial cells. Unfortunately, visual results have been disappointing due to interface scarring.[4] Deep lamellar keratoplasty (DLK) is a relatively new technique in which deep stromal dissection down to Descemet's membrane (90–95% corneal depth) is performed to create a smooth interface between the graft and recipient, therefore reducing scarring.

Several different surgical techniques have been described to enable deep lamellar dissection. These include layer-by-layer surgical dissection assisted by the expansion of stromal lamellae with air or balanced salt solution, blunt surgical dissection, or direct separation of

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Descemet's membrane from the overlying stroma with the injection of air or viscoelastic.[4–9] Initial techniques had high endothelial perforation rates (9–25% reported); however, the use of anterior chamber air to allow visualisation of the endothelium has reduced this.[5–7]

Keratoconus is the commonest condition requiring corneal graft surgery. These patients are usually young and free from ocular comorbidity, thus making them a good group in which to study graft surgery. This is the first study to compare DLK using entirely Melles' technique and PK in keratoconus.

Materials and methods

A cohort of 20 consecutive PKs, by one surgeon (BAN), for keratoconus was compared retrospectively with 20 consecutive DLKs, for keratoconus by the same surgeon. The PKs were performed between June 2000 and July 2001 and the DALKs between October 2001 and October 2002. The patients had either become intolerant of contact lens or had best-corrected visual acuity with contact lens of 6/12 or worse.

Penetrating keratoplasty was performed using donor and host trephines of the same size. Hessburg–Barron trephines (Katena Products) of between 7.5 and 8.5 mm (median 7.5 mm) were used. The trephination was centred on the cornea, as measured at the time of surgery, rather than decentred over the cone apex. Suturing was typically with eight interrupted and a single continuous 10-0 nylon suture.

DLK was performed using the Melles' technique. The surgeon had already mastered this technique prior to the start of the study. He had 3 years of experience in various DLK techniques and found Melles' technique to be the most reliable. The anterior chamber was filled with air via a paracentesis. A limbal scleral flap was created and a keratome was inserted through this incision into the cornea, down to 90–95% corneal thickness, with the aid of specular reflection to gauge the depth of dissection. DORC (Zuidlands, Netherland) blades were used to continue the lamellar dissection across the cornea. Once the dissection was completed, Healon was injected to displace the deep layer posteriorly and a Hessburg–Barron trephine (median 7.5 mm, range 7–8.5 mm) was used to trephine through the anterior corneal lamellae. The interface was irrigated with copious quantities of balanced salt solution. An identical size donor button was trephined after removal of the endothelium using vision blue staining and cellulose sponges (Surgi swabs John Weiss). The button was sutured with either eight interrupted and a single continuous or double continuous 10-0 nylon. If small Descemet's tears occurred during the deep lamellar dissection, surgery continued in the normal manner with extra care taken to remove all Healon in the deep lamellar interface. The anterior chamber was filled with air at the end of surgery to act as a tamponade.

Postoperatively, all patients received prednisolone acetate and chloramphenicol drops. Patients were monitored closely in the postoperative period for signs of inflammation, graft rejection, infection, suture related problems, glaucoma, and refractive outcome. The chloramphenicol was discontinued after 2 weeks, the topical steroids gradually reduced and sutures removed as clinically indicated.

Best (spectacle)-corrected visual acuities (BCVA) (or unaided visual acuity when not available), refraction, postoperative management, and complications were compared at the time of surgery, 6 and 12 months postoperatively. Patients with co-pathology affecting visual outcomes were not included in visual acuity results. Statistical analysis was performed using χ^2-test (Yate's correction) for visual acuity and duration of steroid usage. Independent *t*-tests were used for astigmatism and Mann–Whitney *U*-test for spherical equivalence (as these data were not normally distributed).

Results

The PK and DALK groups were comparable for age, sex and ethnicity (Table 1). Follow-up data were complete for all patients except two cases in the PK group, which were not refracted at their 12-month appointments. Two cases in the DLK group were amblyopic and therefore were excluded from the visual acuity results, but included in the refractive outcomes. Preoperative visual acuities were comparable in both groups; median BCVA was counting fingers. Visual acuities improved in all patients. The median BCVA at 6 months was 6/9 in both the groups and at 12 months, 6/6 and 6/9 in the PK and DLK groups respectively (Table 2). Figure 1 shows the best-corrected acuities reached by 12 months. The

Table 1 Patient demographics

	PK	*DALK*	P-*values*
Number of eyes	20	20	
Age (years) (SD)	32 (11)	28 (8.5)	0.13
Sex	6 female 14 male	9 female 11 male	0.51
Race	13 Caucasian 7 Asian	17 Caucasian 3 Asian	0.45
Coexisting pathology: amblyopia	0	2	
Preoperative BCVA: median (range)	CF (6/18-HM)	CF (6/18-HM)	

Table 2 Patient outcomes

	PK	*DALK*	P-*values*
6 months BCVA: median (range)	6/9 (6/5–6/36)	6/9 (6/9–6/24)	
12 months BCVA: median (range)	6/6 (6/5–6/60)	6/9 (6/5–6/24)	
Topical steroids discontinued by 6 months	0% 0/20	40% 8/20	0.003
Topical steroids discontinued by 12 months	25% 5/20	85% 17/20	0.000

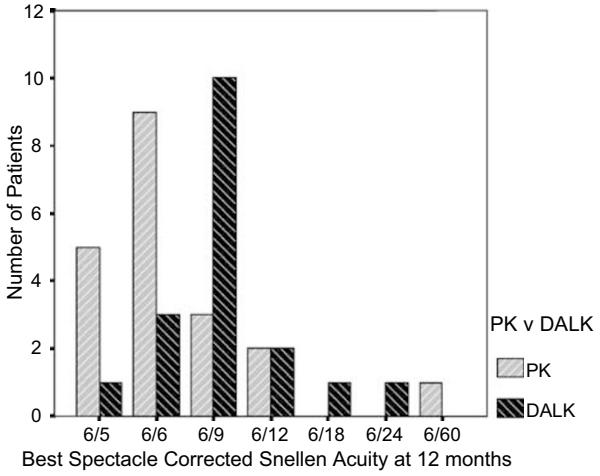

Figure 1 BCVA 12 months following PK *vs* DALK.

Table 3 BCVA: numbers of patients achieving 6/9 or 6/6 visual acuity

Snellen Visual Acuity	*PK*	*DALK*	P-*values*
6/9 or better at 6 months	65%, 13/20	55%, 10/18	0.74
6/6 or better at 6 months	30%, 6/20	5.6%, 1/18	0.093
6/9 or better at 12 months	85%, 17/20	78%, 14/18	0.54
6/6 or better at 12 months	70%, 14/20	22%, 4/18	0.04

percentage of patients achieving 6/9 or better BCVA in both the PK and DLK groups at 6 and 12 months was similar; 85% (17/20) of the PKs and 78% (14/18) of the DLKs achieved 6/9 at 12 months ($P = 0.54$). PK patients were, however, significantly more likely than the DLKs to achieve 6/6 at 1 year; 70% (14/20) PKs compared to 22% (4/18) DLKs ($P = 0.04$) (Table 3).

Astigmatism was significantly higher in the PKs compared to the DLKs at both 6 and 12 months (Table 4). The mean cylindrical error in the PK at 6 months was 5.7 dioptres (standard deviation (SD) 2.5; range 0.0–10.0 dioptres) *vs* 3.4 dioptres (SD 2.0; range 0.0–7.0 dioptres) in the DLKs. ($P = 0.03$) At 12 months, mean astigmatism was 5.0 dioptres (standard deviation (SD) 3.5; range 0.75–14.0 dioptres) in the PK group and 3.1 dioptres (SD 1.7; range 0–6.0 dioptres) in the DLK group ($P = 0.022$) (Figure 2). A similar number of patients in both groups underwent surgery to correct astigmatism. A trend towards more myopia in the DLK group was also found; −3.0 dioptres (range −15.5 to 0.63) compared to −1.0 dioptres (range −9.5 to 9.0) at 6 months in the PKs (Table 4).

The suturing technique used in the PKs was eight interrupted and one continuous suture in all but two

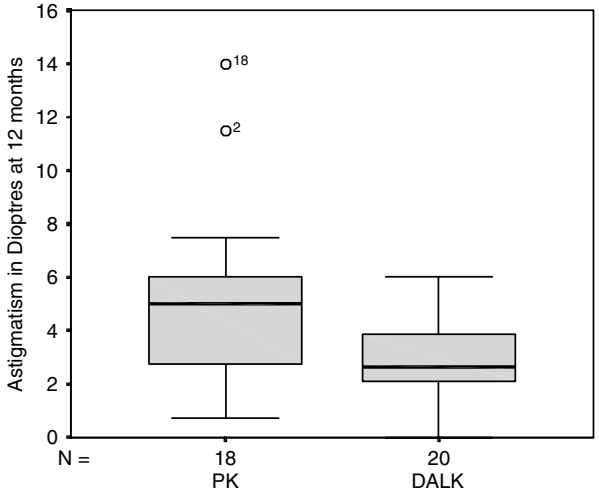

Figure 2 Astigmatism 12 months following PK *vs* DALK.

Table 4 Refractive outcomes following graft surgery

	PK	*DALK*	P-*value*
Median spherical equivalent at 6 months (range)	−1.0 (−9.5 to 9.0)	−3.0 (−15.5 to 0.63)	0.13
Median spherical equivalent at 12 months (range)	−2.1 (−15 to 2)	−3.5 (−13 to 2.8)	0.48
Mean dioptres of cylinder at 6 months (standard deviation, 95% confidence intervals)	5.7 (2.5, 4.6 to 6.8)	3.4 (2.0, 1.9 to 4.9)	0.03
Mean dioptres of cylinder at 12 months (standard deviation, 95% confidence intervals)	5.0 (3.5, 3.4 to 6.6)	2.9 (1.7, 1.6 to 4.2)	0.022

cases where an intraoperative decision was made to use 16 interrupted and one continuous suture to improve the graft lie. Of the DLKs, 14 were sutured with eight interrupted and one continuous suture. Later cases were sutured with four subsequently removed cardinal sutures and a double continuous suture. This change in technique was due to the evolution of techniques during the study. Five of the DLKs required resuturing, one at a week, two at 2 months, and the other at 4 months. Five of the PKs also required resuturing with two requiring this at 5 months and one at 8 months. There was no significant difference or apparent trend in refractive outcomes between the different suturing techniques in either group. Sutures were removed earlier in the DLK group with 8/20 (40%) having all sutures removed before 1 year compared to none of the PK group.

Patients in the DLK group required a shorter period of topical steroid treatment following surgery. Of the DLK patients 40% (eight) had discontinued topical steroids at 6 months increasing to 85% (17) at 12 months. The length of treatment ranged from 3 to over 12 months. This compared to the PK group who were all on topical steroid treatment at 6 months (8 months was the shortest duration of treatment) with only 25% (five) having discontinued the drops at 12 months. This difference was highly significant ($P = 0.000$ and 0.003 respectively) (Table 2).

There were no intraoperative complications in the PK group. Three of the DLKs were complicated by small perforations of Descemet's membrane. Of these patients, one had no postoperative problems and achieved BCVA of 6/6 at 12 months, the second had an elevated IOP on day 1, continued on treatment for glaucoma and achieved 6/24 at 12 months, and the third required lamellar repositioning after the cornea decompensated due to retained Healon in the interface. The graft then settled and a BCVA of 6/9 was achieved at 12 months. Specific postoperative interventions were required in 13 cases in the PK group and nine cases in the DLK group ($P = 0.20$). Three cases in the PK group had rejection episodes, one graft failed due to infective keratitis and required regrafting 9 months after the initial surgery. This case had only 6/60 vision at the 12-month follow-up as refraction had not yet been performed following the regraft. Two eyes developed high intraocular pressures requiring topical treatment, five underwent resuturing, and three had arcuate keratotomies. In the DALK group, there were no cases of graft failure and only one case of mild stromal rejection that settled quickly on topical medication. Four cases required topical treatment for raised intraocular pressure, five were resutured and one had arcuate keratotomy performed (Table 5).

Table 5 Surgical complications and postoperative management

	PK	*DALK*
Intra-op. complications	0/20	3/20 (Descemet's perfs)
Post-op. interventions	13/20	9/20
Graft failure	1 (infective keratitis regrafted 9 months)	0
Graft rejection	3	1 (Mild stromal rejection)
Graft resutured	5	5
Arcuate keratotomies	3	1
Tension sutures	1	0
High IOP requiring topical treatment	2	4

Discussion

This is the first study to compare the outcomes of DLK using entirely Melles' technique, with PK in keratoconus. DLK potentially has advantages compared to PK in terms of the preservation of endothelial cells, absence of endothelial-mediated rejection, stronger graft host junction, and therefore reduced likelihood of dehiscence during accidental trauma. With these potential advantages, it is not surprising that many corneal surgeons have changed their practices to performing DLK where possible. There is, however, little research comparing the outcomes of the two forms of surgery.

This study supports both PK and DLK as successful surgical options for patients with keratoconus. All patients had improved BCVA following surgery and a similarly high percentage of patients achieved 6/9 or better following both forms of surgery; 85% of PKs and 78% of the DLK group at 12 months. These results compare well with the published literature. BCVA of 6/9 or better was reported by Coombes *et al*[6] in 64% of patients 1 year or more after DLK. Buzard *et al*[10] achieved 6/9 BCVA 3 months following PK for keratoconus in 88%. Anwar *et al*[7] reported that 27% of patients with keratoconus achieved 6/9 or better and 89% 6/12 or better following DLK.[7] Watson *et al*[11] reported 95% of PKs and 87.5% of DLKs achieving 6/12 or better in keratoconus. The percentages of patients achieving 6/9 were not reported. Lim *et al*[12] reported 87% of keratoconic eyes obtained 6/12 or better following PK, with a mean follow up of 56.5 months. Benson *et al*[13] performed lamellar keratoplasty using a cryolathe to dissect the donor cornea and achieved 6/9 acuity in 74% of patients at 1 year.

Debate remains as to whether PK and DLK provide the level of visual acuity. In this study, BCVA of 6/6 was significantly more likely to be achieved in the PKs than

the DLKs at 12 months; 70% of PKs *vs* 22% of DLKs ($P=0.04$). Watson *et al*[11] reported that 64% of PKs compared to 32% of DLKs achieved 6/6. This difference was not statistically different. Sugita *et al*[14] commented on poorer than expected postoperative acuities following DLK but did not directly compare to PK. Shimazaki *et al*,[15] however, randomised patients to PK or DLK and found no difference in BCVA, although a trend for poorer contrast acuity was noted in the DLK group. Panda *et al*[8] reported significantly more eyes achieved 6/18 acuity following DLK compared to PK at 6 months. There was, however, no significant difference at 12 months.

The slightly reduced BCVA following DLK is thought to be due to interface haze or scarring as well as scarring as a consequence of hydrops where this has occurred.[13] The study by Watson *et al*[11] excluded any patients who had previously had hydrops and this may be the reason for their slightly higher percentage in achieving 6/6 acuity (32% compared to 22%). In the future, pharmacological modulation of wound healing may well allow us to prevent this haze developing. Femtosecond laser has been used to cut posterior lamellar flaps for endothelial keratoplasty in both enucleated porcine and donor human eyes.[16] The use of this technology may enable the formation of a clear interface in DLK.

In this study, corneal astigmatism was found to be significantly less in the DLKs compared to the PKs. The mean astigmatism was 3.1 dioptres (SD 1.7) in the DLKs compared to 5.0 dioptres (SD 3.5) in the PKs at 1 year ($P=0.022$). Panda *et al*[8] also reported similar findings, with 83% (20/24) of DLKs compared to 33% (8/24) of PKs having astigmatism less than 3 dioptres. In contrast, Watson *et al*[11] reported astigmatism to be similar in both the groups, 4.00 dioptres in the DLKs and 3.25 in the PKs. Shimazaki *et al*[15] had a similar finding, although there was a trend for higher astigmatism in the DLKs. Coombes *et al*[6] and Anwar *et al*[7] had comparable degrees of astigmatism in their DLKs to this study, 3.85 and 3.25 dioptres respectively. Astigmatism following PK was reported by Lim *et al*[12] as 5 dioptres improving to 4 dioptres postrefractive surgery. Buzard *et al*[10] also reported a mean of 4 dioptres following refractive enhancement where required. The layer of residual stroma and Descemet's membrane provides a bed on which to rest the donor button in DLK. This may allow for more accurate alignment and stability of the graft–host junction and may be the cause for the reduced astigmatism found in this study.

The trend in this study towards more myopia in the DLK compared to the PK group, median −3.00 dioptres (range −15.5 to 0.63) compared to −1.00 dioptres (range −9.5 to 9.0), was similar to the outcomes of Watson *et al*.[11] Watson *et al*[6] reported a median −4.13 dioptres (interquartile range −5.00 to −2.00) in the DLKs compared to −1.63 dioptres (interquartile range −4.00 to −2.25) in the PKs. Coombes *et al*,[6] however, reported only, an average of −1.65 dioptres of spherical equivalent refractive error (range −10.25 to +7.00). Further studies are required to determine the true effect of DLK on the spherical equivalent.

No relationship between the suture technique and refractive outcomes was found. It is of interest to consider the impact the pre-existing corneal shape on refractive outcomes. Despite well-established data from PKs on both spherical outcomes and astigmatism, it is still not possible to predict the refractive outcomes from corneal graft surgery.

In the early postoperative period, there were cases in both the PK and DLK groups that required resuturing; however no DLKs over 5 months old required resuturing compared to three PKs. The sutures were also removed sooner in the DLKs, 40% had all sutures removed by one year compared with none of the PKs. It appears that the healing process is faster following DLK. This rapid healing is likely to be due to a combination of the healing that occurs at the deep lamellar interface as well as the reduced requirement for topical steroids following DLK.

Topical steroid treatment in the DLK group was shorter than in the PK group with 85% having stopped them by 1 year. The reduced duration of steroid treatment should also reduce the likelihood of steroid-induced ocular hypertension. In this study, however, the number of patients with raised postoperative pressures was similar in both groups.

DLKs are reported to have fewer postoperative complications and this study supported those finding.[4,8,9] There were three cases of rejection in the PK group whereas in the DLK group there was only one case of mild stromal rejection. Watson *et al*[11] found reported 11 rejection episodes in the 22 PK patients (mainly endothelial rejection) compared to one stromal and one epithelial rejection in the DLKs. Trimarchi *et al*[4] found a rejection rate of 4% in PKs compared with 0% of DLKS. Shimazaki *et al*[15] had one patient with a stromal haze post-DLK. This settled on topical steroids and was thought to be due to stromal rejection. Stromal rejection is usually mild and settles quickly. There are no reported cases of severe graft rejection in patients following DLK. Endothelial counts have been found to be significantly higher in DLKs compared to PKs at 2 years.[15] This preservation of endothelial cells is thought to be likely translated into prolonged graft survival.

DLK has been proposed as the treatment of choice in corneal conditions not affecting the endothelium.[4,10,14,15] The advantage of a greatly reduced likelihood of rejection makes DLK particularly attractive in high-risk grafts such as in those with profound vernal keratoconjunctivitis. This study confirms good visual

results from both PK and DLK in keratoconus, although patients who underwent DLK were significantly less likely to reach 6/6 BCVA. Further studies are required to see if this is a clinically important difference. Assessments of visual functioning using contrast and glare sensitivity as well as quality of life assessments are required. The evidence provided by this study is limited by its retrospective and nonrandomised design. When this study was planned, limited evidence concerning the speed of visual recovery following DLK was available. It was therefore decided to perform repeat hypothesis testing of outcomes at both 6 and 12 months. *P*-values were not formally adjusted due to the exploratory nature of the study. A prospective randomised trial of PK *vs* DLK is planned to further investigate these findings.

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