Penetrating and Deep Anterior Lamellar Keratoplasty for Keratoconus: A Comparison of Graft Outcomes in the United Kingdom

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Purpose. To compare outcomes after penetrating keratoplasty (PK) and deep anterior lamellar keratoplasty (DALK) for keratoconus in the United Kingdom.

Methods. Patient outcome data were collected at the time of transplantation and at 1, 2, and 5 years after surgery. Data were analyzed by Kaplan-Meier survival curves, Cox regression, and binary logistic regression to determine the influence of surgical procedure on graft survival and visual outcome.

Results. The risk of graft failure for DALK was almost twice that for PK ($P = 0.02$). Nineteen percent of the DALK failures occurred in the first 30 postoperative days compared with only 2% of PK failures. When these early failures were excluded, there was little difference between the 3-year graft survivals for DALK (92%; 95% confidence interval [CI], 85%–95%) and PK (94%; 95% CI, 92%–95%) ($P = 0.8$). Although the mean best corrected visual acuity (BCVA) was similar for the two procedures ($P = 0.7$), 33% of patients who underwent PK achieved a BCVA of 6/6 or better at 2 years compared with only 22% of those who underwent DALK ($P < 0.001$). Those with DALK were also likely to be more myopic (< -3 D) but there was little difference in scalar cylinder.

Conclusions. DALK had a higher overall failure rate than PK. The difference was largely accounted for by early failures, which appeared to be related to the surgeon's experience. DALK recipients were less likely to achieve BCVA of 6/6 than were PK recipients and were more likely to have -3 D or worse myopia. (*Invest Ophthalmol Vis Sci.* 2009;50:5625–5629) DOI:10.1167/iovs.09-3994

Although penetrating keratoplasty (PK) is successful for the treatment of keratoconus,[1–3] deep anterior lamellar keratoplasty (DALK) has become an increasingly common alternative.[4–7] In the United Kingdom, the percentage of transplants for keratoconus in which DALK was used increased from 10% in 1999 to 2000 to 35% in 2007 to 2008. The perceived advantages of DALK are that the recipient's endothelium remains in place and the anterior chamber is not penetrated. There is therefore no apparent risk of graft failure from endothelial rejection and the chronic endothelial cell loss associated with PK should be avoided.[8–10] The complications associated with PK for keratoconus are well known and managed with established procedures. Some of the complications associated with DALK are likely to be different, in particular the risk of intraoperative perforation of Descemet's membrane.[4,7,11,12]

There are conflicting reports concerning the relative outcomes of DALK and PK for keratoconus.[9,13–20] Poorer visual outcomes after DALK have been ascribed to the donor–host interface, and the thickness of the remaining recipient tissue has been proposed to account for the variation in postoperative visual acuity and contrast sensitivity after DALK.[15,16]

In the United Kingdom, approximately 2500 corneal transplants are registered with NHS Blood and Transplant (NHSBT) every year. Postoperative outcome data, including graft function, visual acuity and refraction, rejection episodes, and other complications, are routinely collected. These data provide an opportunity to undertake large-scale, retrospective studies of corneal transplant outcome—in this instance, a comparison of DALK and PK.

Methods

Patients

An analysis was undertaken of all patients registered with NHSBT who had undergone PK or DALK as a first graft for keratoconus between April 1999 and March 2005. Patient data were collected at the time of transplantation and graft outcome data at 1, 2, and 5 years after surgery. The following variables were used as outcome measures for analysis: graft failure, graft rejection, complications (surgical complications, wound leak, suture-related complications, endophthalmitis), best corrected visual acuity (BCVA) and refractive error. Further information on failed DALK grafts was obtained from supplementary questionnaires sent to surgeons to confirm the date of graft failure, reasons for failure, any identified additional preoperative risk factors, and the surgical technique used for the DALK (i.e., big bubble versus Melles technique). Confirmation of graft failure was also established by registration of a repeat corneal transplant. The number of DALKs performed by the surgeon and within the surgeon's hospital before the failed DALK was also included in the analysis as an indication of the surgeon's experience with the technique.

Statistical Methods

χ^2 tests and *t*-tests were used, respectively, to investigate differences in categorical and continuous variables between the DALK and PK groups. Kaplan-Meier survival curves were used to compare univariate differences in graft survival (SAS ver. 9.1; SAS Institute, Cary, NC). A Cox regression model was fitted to investigate the influence of graft type on graft survival while adjusting for other factors. Binary logistic regression was used to investigate differences in spherical equivalent.

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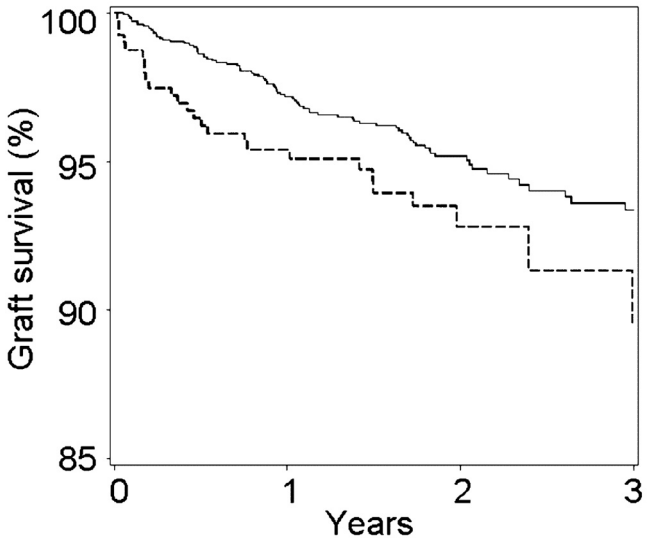

FIGURE 1. Graft survival for PK (*solid line*, $n = 1755$) and DALK (*broken line*, $n = 397$). Three-year graft survival was 93% (95% CI, 92%–95%) for PK and 89% (95% CI, 81%–93%) for DALK ($P = 0.06$).

Snellen visual acuity data were converted into logMAR units for analysis, and refractive data were transformed into Long's matrix formalism[21] and analyzed by the method of Kaye and Harris.[22,23] The refractive error data are presented in spherocylinder form with the magnitude of the cylinder, treated as a scalar value, included in square brackets: for example, sphere/cylinder[cylinder]×axis. The magnitudes of the spherical equivalent and cylinder have been included, to allow comparison with previous reports.

RESULTS

There were 2372 first grafts for keratoconus reported to NHSBT between April 1999 and March 2005, of which 1917 (81%) were PK and 455 (19%) DALK. Follow-up data were available for 2152 (91%) of these transplants.

Graft Survival

Univariate Kaplan-Meier curves (Fig. 1) suggest that graft survival with DALK was lower than that with PK ($P = 0.06$). This difference was confirmed by the Cox regression model (Table 1), which showed that the risk of failure of DALK was two times higher than that of PK (95% confidence interval [CI] 1.2–3.2; $P = 0.006$). There was a higher incidence of reported rejection episodes in the PK group ($P = 0.01$), the difference being largely accounted for by endothelial rejection in the PK group with similar frequencies of epithelial rejection (5.2% and 4.2%, respectively for PK and DALK, $P = 0.4$) and stromal rejection (4.8% and 6.3%, respectively for PK and DALK, $P = 0.2$). Of those grafts that were rejected, 16% of PK and 17% of DALK grafts failed by 3 years. Accordingly, in the Cox model rejection increased the risk of failure 4.6-fold (95% CI, 3.2–6.8; $P < 0.0001$). Other factors that affected graft survival included donor-recipient trephine difference ($P = 0.01$), grafting because of threatened spontaneous perforation ($P = 0.02$), and

TABLE 1. Factors Affecting Graft Survival at 3 Years in the Cox Proportional Hazards Regression Model

Factor	Number at Risk	Relative Risk	95% CI	P*
Type of graft ($P = 0.006$)				
Penetrating	1755	1.0	—	
Deep lamellar	397	2.0	1.2–3.2	0.006
Other surgical procedures ($P = 0.1$)				
No	2037	1.0	—	
Yes	69	2.2	1.0–4.8	0.05
Not reported	46	0.8	0.2–3.7	0.7
Trephine difference ($P = 0.07$)				
0 mm	568	1.0	—	
0.25 mm	1333	0.98	0.6–1.5	0.93
0.5 mm	229	1.9	1.1–3.4	0.03
Not reported	22	1.2	0.1–11.0	0.9
Threatened perforation ($P = 0.03$)				
No	1810	1.0	—	
Yes	36	3.2	1.3–7.9	0.01
Not reported	306	1.4	0.8–2.3	0.2
Rejection episodes ($P < 0.0001$)				
No	1876	1.0	—	
Yes	276	4.6	3.2–6.8	<0.0001
Unit activity levels ($P = 0.3$)				
≤10 per year	600	1.0	—	
>10 per year	1552	1.3	0.8–2.1	0.2
Suturing method ($P = 0.3$)				
Continuous	826	1.0	—	
Interrupted	770	1.3	0.8–2.0	0.3
Mixed	526	0.8	0.5–1.4	0.4
Not reported	30	0.5	0.05–4.3	0.5
Complications at surgery ($P = 0.12$)				
No	2058	1.0	—	
Yes	25	2.7	0.9–7.8	0.08
Not reported	69	2.2	0.6–7.6	0.2
Donor age ($P = 0.13$)				
Continuous	2152	0.99	0.98–1.003	0.14

*Wald test.

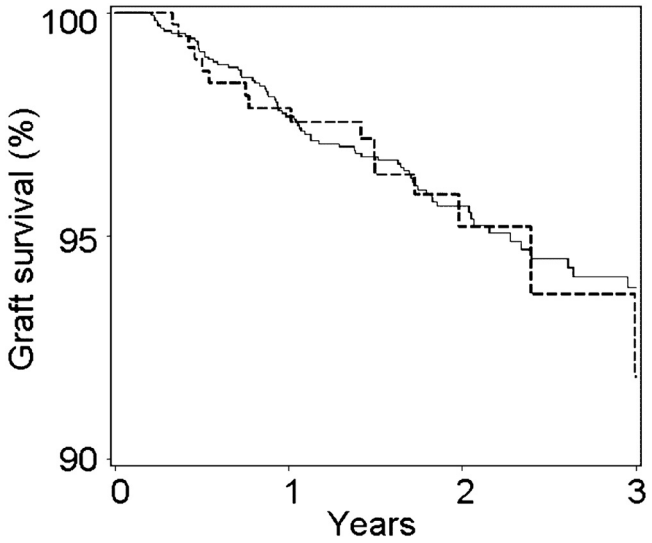

FIGURE 2. Graft survival excluding the early failures for PK (*solid line*, $n = 1749$) and DALK (*dashed line*, $n = 391$). Three-year graft survival was 94% (95% CI, 92%–95%) for PK and 92% (95% CI, 85%–95%) for DALK ($P = 0.8$).

other surgical procedures during the transplant operation ($P = 0.02$). The incidence of surgical complications was higher with DALK than PK (4% vs. 0.5%, $P < 0.0001$) but this did not affect graft survival ($P = 0.12$). Wound leak was a postoperative complication associated with PK (79/1766: 4.5%) rather than DALK (1/410: 0.2%) ($P < 0.0001$). There were no reported occurrences of endophthalmitis or suture-related abscesses. At 18 months, 53% of patients who underwent PK were still on topical steroids compared with just 35% of those with DALK ($P < 0.0001$). Antiglaucoma medication was also more frequently used after PK (12%) than after DALK (7%) ($P = 0.002$). Donor age and suturing method had no influence on survival (Table 1).

Short-Term Failures

A greater proportion of the DALK failures occurred early. By 30 days, 5 (19%) of the 26 DALK failures had occurred compared with just two of the 84 PK failures (2.4%; Fisher's exact test, $P = 0.008$). By 90 days, a further five DALKs had failed, which meant that overall 10 (38%) of the DALK failures had occurred within the first 90 days compared with 14 (17%) of the PK failures (Fisher's exact test, $P = 0.03$). There was a preponderance of big-bubble DALKs in these early failures (7/10), whereas in 13 of the 16 DALKs that failed more than 90 days after surgery, the Melles technique was used.

DALK failure within the first 30 days appeared to be related to the surgeon's experience. In the five early failures, the surgeons had previously performed (SD 3) DALKs compared with 15 (SD 12) previous procedures for the later failures (*t*-test, $P = 0.005$). When these early failures were excluded, there was little difference between the three-year graft survivals for DALK (92%; 95% CI, 85%–95%) and PK (94%; 95% CI, 92%–95%; $P = 0.8$; Fig. 2).

Reasons for Graft Failure

In the patients who underwent DALK, graft and interface opacification were the predominant reasons cited for failure. These were attributed by the respective surgeon to primary opacification (graft never cleared), atopic keratomalacia, graft–interface opacification owing to epithelial ingrowth, interface vascularization, persistent epithelial defects, and stromal rejection. Other causes of DALK failure included persistent double anterior chamber, high irregular astigmatism due to graft and/or host ectasia; in three cases, uncorrectable high irregular astigmatism; and in one case, failure of the host endothelium attributed to a possible tear in Descemet's membrane. By contrast, irreversible rejection was the leading cause of failure for PKs, accounting for 17 of the 50 graft failures in which a reason for failure was reported.

Visual Acuity

There were 1136 PK and 234 DALK surgeries with pre- and postoperative visual acuity data. Preoperative visual acuity tended to be better after DALK, with 47% of patients having a BCVA better than 6/60 compared with only 37% after PK ($P < 0.0001$). Postoperative BCVA was similar with DALK and PK, at 2 years. LogMAR 0.24 (SD 0.4) and 0.24 (SD 0.25), respectively ($P = 0.4$). However, 33% of patients with PK achieved 6/6 or better at 2 years compared with only 22% of patients with DALK ($P = 0.0007$).

Refractive Outcome

The mean refractive error at 2 years was $-3.2/-0.7[3.8]\times18$ for DALK compared with $-2.5/0.2[4.0]\times4$ for PK. Table 2 shows that not only was there a difference in mean spherical equivalent between DALK and PK ($P = 0.001$), but a larger percentage of DALK recipients had myopic spherical equivalents less than -3 D ($P < 0.0001$).

Binary logistic regression was used to determine the extent to which this difference in myopia could be accounted for by differences in donor and recipient trephine sizes. The mean refractive errors for DALK and PK, respectively, for same-size donor and recipient trephines were $-3.1/-1.1[4.1]\times15$ and $-1.7/0.1[3.9]\times27$, and for oversized donor trephines $-3.5/-0.3[3.6]\times31$ and $-2.8/0.2[4.1]\times2$. There was a greater chance of high myopia being less than -3 D at 2 years when the donor trephine was larger than the recipient trephine than when the trephines were the same size (OR, 1.6; 95% CI, 1.1–2.3; $P = 0.01$). Most of the difference in myopia, however,

TABLE 2. Mean Spherical Equivalent and Percentage of Eyes with High Myopia (-3 D) at 2 Years

Graft Type	Donor Trephine	*n*	Spherical Equivalent (D) Mean (SD)	< −3 D (%)
PK	All	566	−2.4 (3.9)	34
	Same size	147	−1.7 (3.8)	24
	Oversize	419	−2.7 (3.9)	38
DALK	All	111	−3.6 (3.7)	56
	Same size	56	−3.7 (3.0)	57
	Oversize	55	−3.7 (4.1)	55

For PK and DALK, the data show the effect of donor trephine size relative to the recipient trephine (same size versus oversize).

was attributable to the type of graft in patients who underwent DALK being more likely to be highly myopic than those who underwent PK (OR, 2.4; 95% CI, 1.6–3.7; $P < 0.0001$).

Discussion

Penetrating keratoplasty for keratoconus, although still susceptible to endothelial allograft rejection, has the highest survival rate of all indications for corneal transplantation. The Australian Corneal Graft Registry reports survivals of 95% and 89% at 5 and 10 years, respectively. The risk of endothelial rejection after DALK should be negligible and, consistent with this result, we found that the higher overall incidence of rejection after PK was accounted for by endothelial rejection. DALKs, however, were still prone to epithelial and stromal rejection and rejection was shown to be an overall risk factor for failure (Table 1) with similar proportions of those with PKs and DALKs that had undergone rejection subsequently failing.

For the period of the study, a patient who had undergone DALK was twice as likely to experience graft failure compared with one who underwent PK. Factors such as the unit activity levels and suturing method did not affect graft survival. Thirty-eight percent of DALK failures occurred within 90 days of the graft, with the main reasons being primary opacification and double anterior chamber. Graft melts occurred mainly between the second and third postoperative months. Based on its reported prevalence in the failed DALKs, atopy appeared to be an important risk factor for failure. The absence of information about atopy for the DALKs that did not fail or for the PKs meant this risk could not be evaluated in the Cox regression model. Of importance, DALK graft survival was similar to PK when early failures were excluded. That the surgeon's inexperience may affect graft survival was borne out by the finding that graft failure within the first month was associated with surgeons who had performed relatively few DALK procedures. Variations of both the Melles and big-bubble DALK procedures had been used for the failed grafts, with an apparent preponderance of the big-bubble technique in the early failures. As the surgical technique was known only for the failed DALKs however, it was not possible to draw further conclusions about whether the specific technique had an influence on either the risk or the timing of failure.

The mean BCVA was similar in the two groups, despite the poorer preoperative visual acuity in patients who had PK. Moreover, the patients who had PK were more likely to achieve a BCVA of 6/6 or better than those who had DALK, with 33% of PK achieving this acuity at 2 years compared with only 22% of patients who underwent DALK. These visual acuity outcomes in a large series of PK and DALK are consistent with previous reports.[7,12–16] Watson et al.[14] reported that, in patients with keratoconus, twice the number in the PK group achieved a BCVA of 6/6 or better compared with those in the DALK group (64% vs. 32%). Therefore, despite the BCVA after DALK approaching that for PK, fewer patients will achieve 6/6 after DALK. It has been proposed that this may be related to the thickness of the residual recipient tissue remaining after lamellar dissection.[15,16]

We found that patients with DALK had significantly more myopia that those with PK, with a larger proportion having spherical equivalents of –3 D or less. Although similar to Watson et al.,[14] who found median spherical equivalents for DALK and PK of, respectively, −4.13 and −1.63 D, this level of myopia is higher than in some other reports.[7,12,24–26] Although the odds of a patient being highly myopic were 1.6-fold greater when the donor trephine was oversized than when it was the same size as the recipient trephine, most of the difference in spherical equivalent was attributable to the type of graft (Table 2).

In terms of the scalar cylinder, we found mean cylinders of 3.8 D for DALK and 4.0 D for PK at 2 years. This result is similar to those in previous reports; for example, Watson et al.[14] reported an average cylindrical correction of −4.00 D after DALK and −3.25 D after PK, whereas Coombes et al.[24] reported −5.56 D after PK and −2.54 D and after DALK for keratoconus. There would therefore appear to be little difference in the amount of scalar cylinder between DALK and PK for the treatment of keratoconus.

Overall, DALK had a higher failure rate than did PK in our analysis, but the difference was accounted for by early failures, which appeared to be related to the surgeon's experience. It is possible, therefore, that this difference in graft survival between DALK and PK in the U.K. data will decrease as surgical experience improves. The trend in graft survival after the two procedures will be investigated in future analyses. The incidence of rejection was lower in DALKs, and suture removal occurred sooner than after PK with, respectively, 61% versus 45% of grafts having all sutures removed by 1 year. This result is consistent with those in reports that advocate suture removal at 6 to 12 months after DALK compared with 18 to 24 months for PK.[14,25] Although mean BCVA and scalar cylinder were similar for the two procedures at 2 years, a greater proportion of PKs achieved 6/6 or better and had less myopia.

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