Deep Anterior Lamellar Keratoplasty for Keratoconus: Multisurgeon Results

KUNAL A. GADHVI, VITO ROMANO, LUIS FERNÁNDEZ-VEGA CUETO, FRANCESCO AIELLO, ALEXANDER C. DAY, AND BRUCE D. ALLAN

• PURPOSE: To examine clinical outcomes in deep anterior lamellar keratoplasty (DALK) for keratoconus using contemporary techniques in a multisurgeon public healthcare setting.

• DESIGN: Consecutive, retrospective case series.

• METHODS: SETTING: Moorfields Eye Hospital, London, United Kingdom. STUDY POPULATION: Consecutive cases of keratoconus treated with non–laser assisted DALK from September 1, 2012, to September 31, 2016. OBSERVATION PROCEDURE: Data on preoperative status, operative details, intraoperative and postoperative complications, secondary interventions, and visual outcomes were archived for analysis. MAIN OUTCOME MEASURES: Graft failure rate and percentage of patients with corrected distance visual acuity (CDVA) ≥20/40 within 1 year of surgery and at final review after suture removal.

• RESULTS: Three hundred fifty-seven eyes of 338 patients undergoing DALK (91.3% big-bubble technique attempted) were analyzed. A total of 4.2% (95% confidence interval [CI] 2.4%–6.8%) of corneal transplants had failed within the follow-up period (21.8 ± 11.4 months), and 75.9% of eyes had CDVA ≥20/40 within 1 year of surgery, rising to 81% after suture removal. Forty-two primary surgeons (31 trainees) participated. Intraoperative perforation of Descemet membrane occurred in 45.4% of eyes. A total of 24.1% were converted to penetrating keratoplasty (PK) intraoperatively. Conversion to PK increased the risk of transplant rejection ($P = .026$; odds ratio [OR] 1.94; 95% CI 1.1–3.5) and secondary glaucoma ($P = .016$; OR 4.0; 95% CI 1.3–12.4). Transplant rejection increased the risk of graft failure both overall ($P = .017$; OR = 3.9; 95% CI 1.4–11.0) and when cases converted to PK were excluded ($P = .028$; OR = 3.35; 95% CI 1.1–9.9).

• CONCLUSION: DALK for keratoconus achieves early results similar to those published for PK in a multisurgeon setting. Conservative management of intraoperative Descemet membrane perforation, where possible, may be safer than conversion to PK. (Am J Ophthalmol 2019;201:54–62. © 2019 Elsevier Inc. All rights reserved.)

IN A RECENT GLOBAL SURVEY, 27% OF ALL CORNEAL transplants were performed for keratoconus.[1] Penetrating keratoplasty (PK) and deep anterior lamellar keratoplasty (DALK) are the main forms of corneal transplantation used in cases of advanced keratoconus where patients are unsuccessful with contact lenses.[2,3] Both procedures are relatively safe and effective. DALK preserves the host endothelium, eliminating endothelial rejection and dramatically reducing the risk of endothelial failure—the leading cause of graft failure after PK.[4,5] Despite this apparent clear advantage, PK remains the most commonly performed type of keratoplasty for advanced keratoconus worldwide.[1]

Corneal transplant failure is defined by repeat surgery or irreversible loss of transplant clarity.[2] Although endothelial failure is unusual after DALK, primary failure (secondary to a persistent double anterior chamber) and stromal or interface scarring (secondary to transplant rejection) may be relatively common.[2,6,7] Earlier case series and nonrandomized comparisons summarized in a 2011 American Academy of Ophthalmology report,[4] and limited randomized controlled trial evidence,[8] suggest similar graft survival and visual outcomes for PK and DALK in keratoconus. But recent corneal transplant registry reports from Australia[2] and the UK[6] indicate that PK is superior to DALK in terms of corrected distance visual acuity (CDVA) and graft survival. These studies do not review recent data. Jones and associates[6] report results from the UK up to 2005. Coster and associates[2] report on grafts performed in Australia between 1999 and 2012, but include only a relatively low proportion of DALK cases, mostly performed later in the review period. The understanding of DALK techniques, and Descemet membrane–baring DALK techniques in particular, has evolved significantly since then.

Recent reports[5,9] from relatively high-volume single-surgeon series using Descemet membrane–baring DALK techniques suggest lower graft failure rates in DALK for keratoconus (<3%) than indicated by Australian (12%)[2] or UK (8%)[6] registry studies. Here we explore whether these relatively good results using contemporary DALK techniques in advanced keratoconus translate into a busy multisurgeon teaching hospital setting in an analysis of a large consecutive cases series performed between 2012 and 2016.

AJO.com Supplemental Material available at AJO.com.
Accepted for publication Jan 27, 2019.

From the Department of Corneal and External Eye Diseases, Moorfields Eye Hospital, London, United Kingdom.

Inquiries to Bruce D. Allan, Moorfields Eye Hospital, 162 City Rd, London EC1V 2PD, UK; e-mail: bruce.allan@ucl.ac.uk

0002-9394/$36.00
https://doi.org/10.1016/j.ajo.2019.01.022

METHODS

THE STUDY WAS APPROVED AS A CLINICAL AUDIT PROJECT by the Clinical Audit and Effectiveness Committee at Moorfields Eye Hospital. The tenets of the Declaration of Helsinki were followed with informed consent for surgery as part of routine clinical care.

This was a noncomparative interventional case series with retrospective review of case notes and electronic operating theatre records and anonymized archiving of study data.

• **INCLUSION CRITERIA:** The audit period was September 1, 2012 to September 31, 2016. We identified consecutive cases of keratoconus listed for DALK in the audit period from an electronic healthcare record system (Open Eyes v1.18, www.openeyes.org.uk). We excluded cases of femtosecond laser–assisted DALK. We used an "intention to treat" protocol in which cases converted intraoperatively from manual DALK to PK were included for study. The indication for surgery was keratoconus with poor contact lens tolerance and subjectively inadequate spectacle CDVA.

• **SURGICAL PROCEDURE:** We used the big-bubble technique described by Anwar and Teichmann[10] or Melles' air reflection–assisted technique[11] for lamellar dissection. In a small number of cases, we used alternate lamellar dissection techniques, including stromal hydration–assisted and simple layer-by-layer manual lamellar dissection. We categorized these techniques as "big-bubble," "Melles," or "other."

In brief, for the big-bubble technique, surgeons performed a partial-thickness (350–450 μm) trephination of variable diameter, between 7.5 and 9.0 mm, using a suction trephine. The size of trephination was determined according to the size of the cone and the horizontal corneal diameter, aiming to include the entire cone within the area of trephination while leaving a minimum 1 mm boundary of host cornea over 360 degrees. A 27 gauge needle or custom air dissection cannula was introduced into the deep stroma starting at the bottom of the trephination groove and advanced toward the center of the cornea. Air was injected progressively into the stroma, with the aim of achieving the formation of a large air bubble between the pre-Descemet layer and the overlying stroma. A peripheral paracentesis was performed to lower the intraocular pressure. Blunt-tipped scissors were used to divide the anterior stroma into 4 sections, which were then removed, exposing the pre-Descemet layer.

For the Melles technique, surgeons performed a self-sealing side port at the limbus through which the anterior chamber was completely filled with air. Using the air reflection technique to judge the depth of residual stroma in dissection through a 5 mm scleral pocket, a full width, limbus-to-limbus deep lamellar dissection was completed. Air was removed from the anterior chamber, and the posterior lamella was separated from the anterior stromal lamella using an ocular viscosurgical device (OVD) prior to trephination through the anterior lamella to expose the deep stromal bed.

Surgeons secured donor buttons with 10-0 nylon sutures in a continuous or interrupted suture pattern. At the end of surgery, surgeons attempted to minimize astigmatism using intraoperative adjustment of continuous sutures or selective removal and replacement of interrupted sutures. Surgeons injected subconjunctival cefuroxime (125 mg/mL) and betamethasone (4 mg/mL) at termination of surgery.

• **POSTOPERATIVE CARE:** In cases of intraoperative perforation completed as DALK, intensive pupil dilation was followed by an anterior chamber air fill, which was reduced at termination of surgery to approximately 60%. Patients were checked 1 hour after surgery prior to discharge to ensure that there was no pupil block. Patients were then asked to posture face-up to ceiling, when possible, for the 2 days after surgery, and pupil dilation was maintained for 3 days.

Routine postoperative medication for both cases completed as DALK and cases converted intraoperatively to PK included antibiotic (chloramphenicol 0.5%) eye drops 4 times daily for 1 week and a diminishing regimen of topical steroid medication—typically dexamethasone 0.1% 1–2 hourly for 1 week, reducing over 3–6 months after surgery for cases completed as DALK, but continuing for over 1 year in cases converted intraoperatively to PK.

All patients were reviewed in the first week after surgery, with a variable follow-up regimen dictated by clinical progress subsequently.

• **OUTCOME MEASURES:** We archived data retrieved from a retrospective review of case notes and electronic patient records in a customized Excel (Microsoft Corp, Seattle, Washington, USA) spreadsheet with forced choice entry criteria.

Our primary outcome measures were graft survival within the follow-up period and the proportion of patients with CDVA at the driving standard (≥20/40) by 12 months after surgery and at final review after suture removal.

In line with Coster and associates,[2] we defined graft failure as irreversible loss of graft clarity or repeat corneal transplantation. We recorded unaided distance visual acuity (UDVA), CDVA, and manifest refraction data at the last follow-up visit before 12 months postsurgery (early recovery) and at final follow-up, together with the number of glaucoma medications, whether topical steroid medication had been discontinued (yes/no), and whether all sutures had been removed (yes/no).

We recorded preoperative demographic details along with any record in preoperative notes of atopy, hydrops, previous corneal collagen cross-linking, or intracorneal

TABLE 1. Preoperative Status of Patients Undergoing Deep Anterior Lamellar Keratoplasty for Keratoconus in a Multisurgeon Public Healthcare Setting

Variable	Definition	Result
Age	Age at time of surgery (years)	33.5 ± 10.9
Sex	Male/female	230/127
Pachymetry	Minimum corneal pachymetry (μm)	326 ± 68
Disease stage	Keratoconus (Pentacam) Stage II	9 (3.0%)
	Keratoconus (Pentacam) Stage III	60 (20.2%)
	Keratoconus (Pentacam) Stage IV	226 (76.1%)
Co-pathology	Diagnosis other than keratoconus affecting final CDVA	9 (2.6%)
Hydrops	Previous hydrops at preoperative examination	24 (6.8%)
Atopy	Mild = eczema/asthma/hay fever/olopatidine treatment	71 (20.2%)
	Severe = cyclosporine treatment	7 (2.0%)
CXL	Any form of collagen cross-linking before grafting	8 (2.4%)
ICRS	Intracorneal ring segments implanted prior to DALK	4 (1.1%)

CDVA = corrected distance visual acuity; CXL = collagen cross-linking; DALK = deep anterior lamellar keratoplasty; IRCS = intracorneal ring segments.

ring segment implantation. We subcategorized atopy into mild atopy (any history of eczema, asthma, hay fever, or topical treatment with mast cell degranulation inhibitors) and severe atopy (any record of topical treatment with cyclosporine A).

Operative details and events we recorded were as follows: the surgeon career grade (consultant/surgeon in training); donor punch diameter (mm); host trephination diameter (mm); intended lamellar dissection technique (big-bubble/Melles/other); big-bubble result (type I/type II/no bubble/bubble rupture/air injected in anterior chamber/trephination into anterior chamber); perforation into the anterior chamber (yes/no); intraoperative conversion to penetrating keratoplasty (yes/no); suture method (continuous/interrupted); and whether or not donor Descemet membrane had been removed.

Early postoperative events we recorded (yes/no) were as follows: a double anterior chamber (fluid in the lamella interface between donor and host cornea); Urrets Zavalia syndrome (fixed dilated pupil presumed secondary to pupil block glaucoma); and atopic sclerokeratitis (host side inflammation associated with multifocal infiltrates at points of suture entry and suture loosening).

Postoperative interventions we recorded at any time point were as follows: any unscheduled increase in topical steroid medication (transplant rejection); re-suture; air injection into the anterior chamber; the maximum number of glaucoma medications required for intraocular pressure control; glaucoma drainage surgery or cycloablation; cataract surgery; repeat corneal transplantation; and refractive surgery.

• **DATA ANALYSIS:** Continuous data are shown as the mean ± standard deviation. Categorical data are shown as % throughout, where the percentage denominator is the total number of available data points in that category. Accountability data are shown as n (%), where the percentage denominator is the total number of cases studied.

We converted Snellen visual acuities to logMAR values for statistical comparisons. We checked normality in these data using the Shapiro-Wilk test. Two-tailed analyses were used throughout. For continuous data comparisons, we used the *t* test where there were >30 observations in each group or the Mann-Whitney *U* test for smaller group comparisons in skewed (logMAR visual acuity) data. We used Fisher exact test for comparisons of categorical data and the log-rank test for comparison between groups in graft survival data. In exploratory analyses of clinically plausible influences on CDVA, likelihood of big-bubble formation, rejection risk, and secondary glaucoma, we screened independent variables in univariate analyses at a threshold ($P < .15$) for clinically important change in the dependent variable of interest, then checked for covariance before multivariate regression modeling.

We performed statistical tests in Excel (v15.34 for Mac) or using online calculators as follows: Fisher exact test and the Mann-Whitney *U* test (www.socscistatistics.com); logistic regression analysis (www.statpages.info); and Kaplan-Meier survival analysis (www.astata.com) (last accessed August 2, 2018).

RESULTS

AFTER EXCLUSION OF 31 CASES OF FEMTOSECOND LASER–assisted DALK, 357 consecutive cases of 338 patients undergoing DALK with manual trephination were available for study. The overall postoperative follow-up interval was 21.8 ± 11.4 months. Preoperative (Table 1), intraoperative (Table 2), and early (month 1) postoperative data

TABLE 2. Details of Deep Anterior Lamellar Keratoplasty Operations for Keratoconus Performed in a Multisurgeon Public Healthcare Setting

Variable	Result
Surgeon grade, n (%) operations	
Consultant surgeon	115 (32.2%)
Surgeon in training	242 (67.8%)
Graft diameter	
Donor diameter (mm)	8.23 ± 0.27
Host diameter (mm)	8.09 ± 0.29
Donor = host diameter, n (%)	158 (41.3%)
Donor > host diameter, n (%)	203 (58.7%)
Not recorded, n (%)	11 (3.1%)
DALK technique, n (%)	
Big-bubble	326 (91.3%)
Melles	24 (6.7%)
Other	3 (0.8%)
Not recorded	4 (1.1%)
Donor DM, n (%)	
Removed	136 (38.1%)
Not removed	157 (44.0%)
Not recorded	64 (17.9%)
Suture method, n (%)	
Continuous	281 (78.7%)
Interrupted	76 (21.3%)

DALK = deep anterior lamellar keratoplasty; DM = Descemet membrane.

TABLE 3. Intraoperative Complications of Patients Undergoing Deep Anterior Lamellar Keratoplasty for Keratoconus in a Multisurgeon Public Healthcare Setting

Complication	N (%)
Perforation	
Any perforation into A/C	162 (45.4%)
Not recorded	0 (0%)
Conversion to PK	
Total conversion to PK	86 (24.1%)
Elective conversion to PK[a]	12 (3.4%)
Perforation converted to PK	74 (20.7%)
Not recorded	0 (0%)

A/C = anterior chamber; PK = penetrating keratoplasty.
[a]Conversion to PK without perforation (failed big-bubble) owing to pressure on operating theatre time.

(Table 3) were available in all cases, but data capture from free text operation note entries was incomplete for some items (Tables 2 and 3).

Manifest refraction data were available in 162 (45.4%) cases 6–12 months after surgery (early recovery) and in 168 (47.1%) cases at final review after suture removal (25.3 ± 10.2 months after surgery). CDVA was ≥20/40 in 75.9% of cases at early recovery and in 81.0% at final review after suture removal (Figure 1).

Overall, including cases prior to corneal suture removal, manifest refraction data were available in 207 (58%) cases at final review (24.3 ± 10.2 months after surgery). CDVA (0.23 ± 0.32) was ≥20/40 in 77.0% of cases; the manifest refraction spherical equivalent (MRSE) was −3.17 ± 4.37 diopters (D); and the absolute cylinder was 4.11 ± 3.10 D. Within this group, manifest refraction data were available in 144 (40.3%) cases preoperatively. The mean preoperative CDVA was 0.88 ± 0.38 (20/160).

Possible risk factors for worse CDVA at final review identified in univariate analyses were previous hydrops ($P = .013$), DALK surgery with Melles or "other" non-Descemet membrane–baring technique ($P = .015$), and worse preoperative vision (CDVA or UDVA where manifest refraction data were not available) ($P = .133$). But there was clear covariance between each of these factors, suggesting that choice of surgical technique and preoperative vision were both influenced strongly by clinical signs or history of a previous Descemet membrane break (hydrops). Surgeon grade, age, sex, atopy, preoperative thinnest pachymetry, graft diameter, intraoperative conversion to PK, intraoperative removal of donor Descemet membrane, and suture pattern all had no significant influence on final CDVA.

Removal of sutures (ROS) improved CDVA. Seventy-nine (22.1%) cases had manifest refraction data recorded both before and after ROS. After ROS, there was no significant change to the MRSE (−2.63 ± 3.61 before ROS; −3.34 ± 3.63 after ROS; $P = .224$) or the absolute cylinder (4.57 ± 2.96 before ROS; 4.27 ± 2.86 after ROS; $P = .517$); but CDVA was improved approximately 1 Snellen line by suture removal (0.29 ± 0.25 before ROS; 0.18 ± 0.26 after ROS; $P = .013$), from 20/40 to 20/30.

Postoperative complications and interventions are detailed in Tables 4 and 5.

Eighty-eight (54.3%) cases of intraoperative perforation of the posterior lamella were not converted to PK. These cases were managed intraoperatively with intensive pupil dilation and partial anterior chamber air tamponade. Within this group, 38 (43.2%) cases had a double anterior chamber at first postoperative review. The double anterior chamber resolved in 33 cases, either spontaneously (20 cases) or after 1 or more postoperative anterior chamber air injections (13 cases) with pupil dilation to prevent pupil block.[12] Two cases treated conservatively failed to resolve, resulting in graft failure treated with PK. Two cases treated with air injection failed to resolve, resulting in graft failure treated with either PK or, in 1 case in which the donor Descemet membrane had been left in situ, excision of the host Descemet membrane. In this last case, effectively a late conversion to PK, the transplant remained clear at the final review visit.

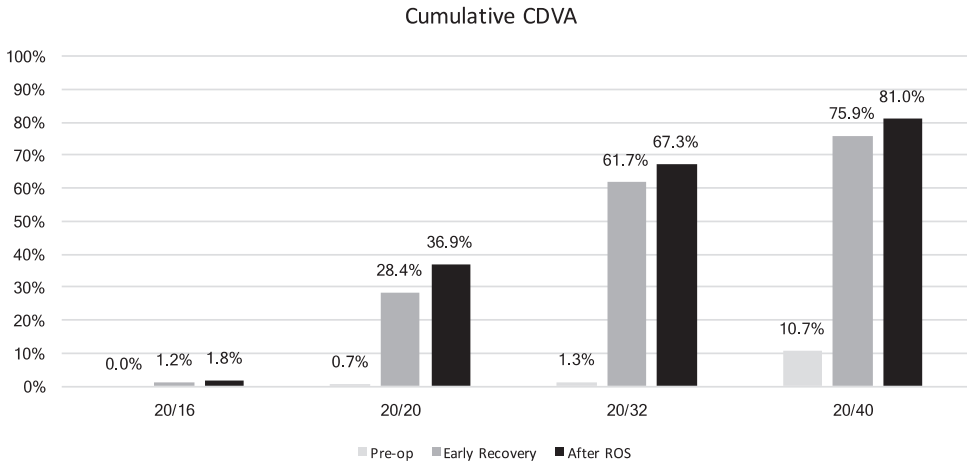

FIGURE 1. Corrected distance visual acuity at baseline, within 1 year (6–12 months after surgery), and at last follow-up after removal of sutures (ROS).

TABLE 4. Postoperative Complications of Patients Undergoing Deep Anterior Lamellar Keratoplasty for Keratoconus in a Multisurgeon Public Healthcare Setting

Complication	Definition	N (%)
Double A/C	Fluid in interface between donor and host cornea at first postoperative review	38 (10.6%)
Urrets-Zavalia syndrome	Fixed dilated pupil from first postoperative review	0
Atopic sclerokeratitis	Host side inflammatory response in early postoperative period (often accompanied by suture loosening) requiring intensive topical steroids or systemic immunosuppression	10 (2.8%)
Raised intraocular pressure	Any medical or surgical intervention for raised intraocular pressure	49 (13.7%)
Infection	Any unscheduled treatment with antibiotic, antiviral, or antifungal drugs	6 (1.7%)
Graft rejection	Any unscheduled increase in topical steroids to treat epithelial rejection line, stromal edema, progressive stromal vascularization, or anterior chamber inflammation	70 (19.6%)
Graft failure	Irreversible loss of graft clarity or repeat corneal transplantation	15 (4.2%)

A/C = anterior chamber.

Within the follow-up period, there was no significant difference in graft survival between cases completed as DALK and cases converted intraoperatively to PK ($P = .84$) (Figure 2). Overall, 15 of 357 transplants (4.2%; 95% confidence interval [CI] 2.4%–6.8%) failed. These comprised 11 (4.1%; 95% CI 2.0%–7.0%) of the 271 completed DALK cases and 4 (4.7%; 95% CI 1.3%–11.5%) of the 86 cases converted to PK after perforation at the original surgery. Causes of corneal transplant failure were as follows: persistent epithelial defect with stromal opacification (4 cases; investigation for infection negative), bacterial infection (3 cases; 2 suture-related, 1 suspected donor infection), persistent double anterior chamber after perforation (3 cases), endothelial failure (2 cases; both secondary to endothelial rejection in cases converted to PK at primary surgery), interface opacification secondary to retained irregular posterior host stroma at primary surgery (2 cases), and interface vascularization and opacity secondary to stromal rejection (1 case). Revision procedures were PK (9 cases), Descemet membrane endothelial keratoplasty (DMEK) with excision of an opacified posterior lamella (1 case), and repeat DALK (4 cases). One case of transplant failure had not been regrafted at the latest review.

Transplant rejection of any kind (epithelial, stromal, or endothelial) was a risk factor for graft failure both overall ($P = .017$; odds ratio [OR] = 3.9; 95% CI 1.4–11.0) and when cases converted to PK after intraoperative perforation had been filtered out ($P = .028$; OR = 3.35; 95% CI 1.1–9.9). Possible risk factors for transplant rejection identified in univariate analyses were intraoperative conversion to PK and female sex. Female sex was not a statistically significant risk ($P = .061$) in multivariate analysis, but the risk of rejection was approximately doubled by intraoperative

TABLE 5. Postoperative Surgical Interventions in Patients Undergoing Deep Anterior Lamellar Keratoplasty for Keratoconus in a Multisurgeon Public Healthcare Setting

Intervention	Definition	N (%)
Air injection	Any postoperative air injection for a double A/C	14 (3.9%)
Wound revision	Any repeat or revision corneal suture placement in the operating room	44 (12.3%)
Glaucoma surgery	Any glaucoma filtration surgery	2 (0.6%)
Cataract surgery	Cataract surgery performed after transplantation	10 (2.8%)
Refractive surgery	Incisional or excimer laser refractive surgery after suture removal	16 (4.5%)
Repeat transplantation	Any revision corneal transplantation procedure with new donor material	15 (4.2%)

A/C = anterior chamber.

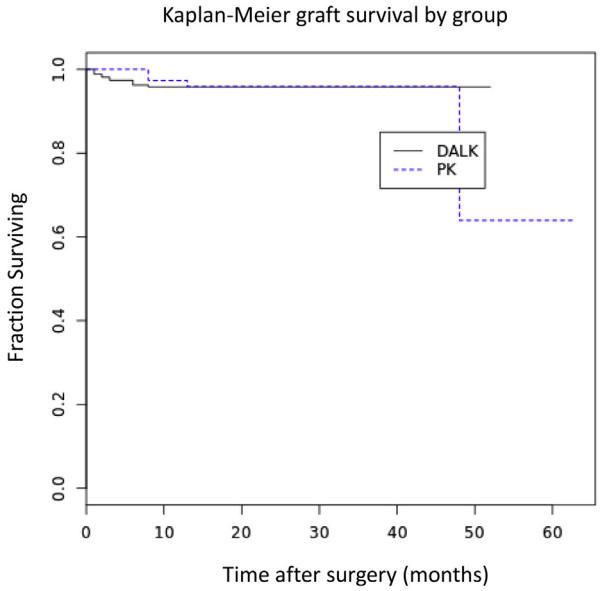

FIGURE 2. Kaplan-Meier plot showing the probability of graft survival over time in consecutive cases (n = 271) completed as deep anterior lamellar keratoplasty (DALK) for keratoconus, and consecutive cases (n = 86) completed as penetrating keratoplasty (PK). All DALK graft failures occurred within a year of surgery. Within the follow-up period, there was no statistically significant difference in graft survival rates between groups (log-rank test: $P = .84$).

conversion to PK ($P = .026$; OR 1.94; 95% CI 1.1–3.5). Age, atopy, graft diameter, perforation at surgery without conversion to PK, and intraoperative removal of donor Descemet membrane had no significant effect on the risk of transplant rejection.

Intraoperative conversion to PK also increased the risk of still requiring glaucoma medication at 12 months after surgery or later ($P = .016$; OR 4.0; 95% CI 1.3–12.4). Both cases requiring glaucoma surgery in the postoperative period were cases converted to PK after intraoperative perforation of the posterior lamella in the original DALK procedure.

There were 42 primary surgeons in total: 11 consultants, and 31 surgeons in training—mostly performing cases under supervision. Intraoperative outcomes in big-bubble DALK were similar for consultants and surgeons in training, mostly operating under supervision (Figure 3). Surgeon grade, patient age, patient sex, preoperative thinnest pachymetry, and graft diameter had no significant influence on the likelihood of big-bubble formation.

DISCUSSION

OUR DATA SUGGEST A RELATIVELY LOW EARLY FAILURE rate (4.2%) in DALK for keratoconus using contemporary manual surgical techniques in a busy, multisurgeon, teaching hospital setting. Over 75% of cases had CDVA at the US driving standard (20/40) or better within a year of surgery (in glasses), rising to 80% after removal of sutures.

This was a retrospective review of case notes and electronic operating theatre records. Although we were able to retrieve data for a large sample (n = 357) of consecutive cases, our study has several weaknesses.

Accurate assessment of preoperative CDVA is not possible in late-stage keratoconus, and accountability for our main postoperative CDVA measures was limited to approximately 50%. Manifest refraction is often delegated to local optometric care in a busy UK public health service setting, and uncomplicated patients are often discharged to referring ophthalmologists relatively early in the postoperative clinical course.

Relatively short follow-up (21.8 ± 11.4 months) may have resulted in an underestimation of later postoperative complications and the graft failure rate in our study; but both our own data and published outcomes for transplantation in keratoconus[6,9,13] suggest that DALK complications are concentrated in the early postoperative period, and most would have been captured here. None of 11 DALK graft failures was recorded at later than 1 year after surgery (Figure 2), double anterior chambers were always evident at the first postoperative review, no infections occurred after suture

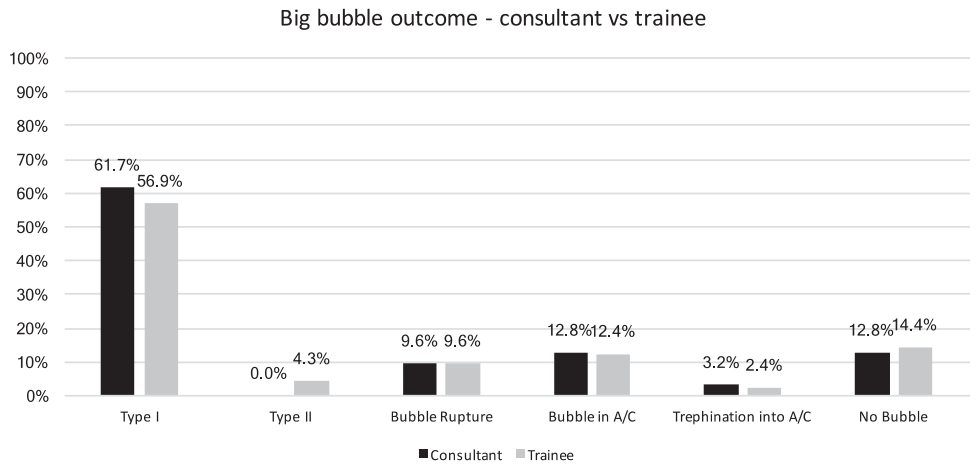

FIGURE 3. Intraoperative outcomes in 326 consecutive cases of deep anterior lamellar keratoplasty surgery using the big-bubble technique by surgeon grade. A/C = anterior chamber; Type I = air cleavage plane anterior to the pre-Descemet layer; Type II = air cleavage plane posterior to the pre-Descemet layer.

TABLE 6. Summary of Studies of Deep Anterior Lamellar Keratoplasty for Keratoconus (N > 100 Cases) Published Since 2009

Study	Type	N	Acct	F/u	CDVA	CDVA >20/40	Failure	Technique	Perforation	Conversion to PK	Rejection
Sarnicola et al 2012[14]	Single-surgeon	236	NR	30	0.1±NR	83%	NR	Various	11%	1.30%	NR
Feizi et al 2010[15]	Single-surgeon	129	NR	21.62±9	0.25±0.2	78%	NR	Big-bubble	4%	2.40%	14.3%
Kubaloglu et al 2011[16]	Single-surgeon	241	72%	51±22.	0.15±0.13	80%	NR	Big-bubble	10%	3%	1.6%
Romano et al 2015[9]	Single-surgeon	158	65%	77±23	0.18±0.8	89%	2%	Big-bubble	10%	0	11.3%
Khattak et al 2018[17]	Two surgeons	108	79%	28±12	0.25±0.22	NR	NR	Big-bubble	NR	NR	3.7%
Jones et al 2009[6]	Registry (UK)	454	51%	24	0.24±0.25	NR	8%	Various	NR	NR	NR
Coster et al 2014[2]	Registry (Australia)	317	80%	NR	NR	61%	12%	Various	NR	14%	NR
Current study	Multisurgeon	357	58%	24.3±10	0.23±0.32	77%	4%	Various	45%	24%	19.6%

Acct = accountability for CDVA data; CDVA = corrected distance vision acuity (logMAR); Conversion to PK = rate of intraoperative conversion to penetrating keratoplasty; F/u = follow-up (months) for CDVA data; Failure = corneal transplant failure rate; N = number of cases; NR = not reported; Perforation = rate of intraoperative perforation of Descemet membrane; Rejection = rate of corneal transplant rejection.

removal, and all rejection episodes were recorded within the first 2 postoperative years.

Other recent studies of DALK for keratoconus[2,6,9,14–17] share similar limitations (Table 6). Follow-up intervals and accountability in relation to summary statistics are variable or not clearly stated, and key outcomes including graft failure are not clearly defined or reported in most single-center studies. In our study, we aimed to work with clearly stated definitions for outcome measures throughout. Our sample size is similar to existing registry study reports[2,6] and, by including recent results from a total of 42 surgeons with varied prior experience of lamellar corneal surgery, we believe our data provide an accurate, contemporary, real-world view of manual DALK outcomes for keratoconus.

The median rate for Descemet membrane perforation in recent high-volume, single-surgeon series is 10% (Table 6). We observed a considerably higher intraoperative perforation rate (43%). Both our own data (Figure 3) and an earlier analysis of UK transplant registry data have failed to demonstrate any benefit for increased surgical experience in DALK for keratoconus. But this does not mean that no benefit exists. Data may be influenced by case mix—senior surgeons tend to operate on the more challenging cases. Also, case volumes for individual corneal surgeons in the UK are relatively low. Over 90% of DALK for keratoconus is performed in a teaching hospital setting.[18] Approximately two thirds of the cases reported here were performed by surgeons in training. Although they may have supervised and partly performed considerably more cases, and would also have performed lamellar corneal surgery for other indications, none of the consultant (nontrainee) surgeons at Moorfields Eye Hospital

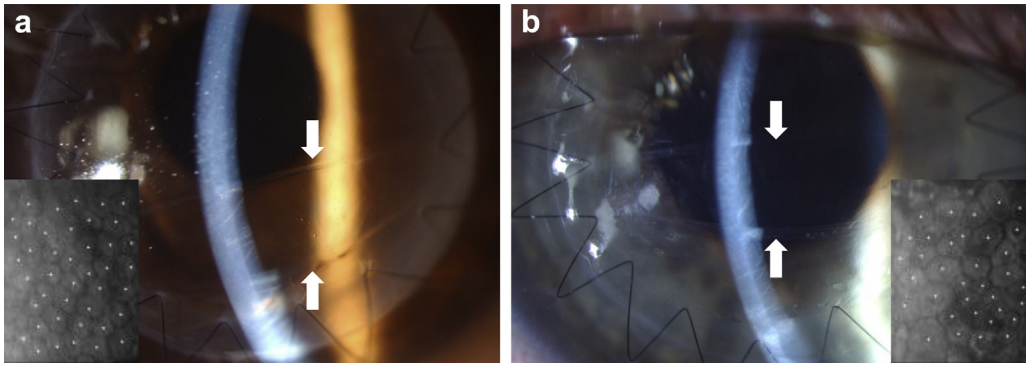

FIGURE 4. Two cases of Descemet membrane rupture during bubble expansion in big-bubble deep anterior lamellar keratoplasty (DALK) treated with air tamponade (a) 12 months and (b) 4 months after surgery. White arrows show the fibrotic edge of the ruptured host Descemet membrane; insets show specular microscopic images of endothelial migration and remodeling within the zone of the rupture. Descemet membrane was removed from the donor cornea in both cases. Four consecutive cases of bubble rupture under the care of the participating surgical team were completed as DALK surgery using intraoperative air tamponade. Two cases required supplementary postoperative air injection.

personally carried out more than 20 cases of DALK for keratoconus in the study period. Similarly, in the 2014 UK transplant registry study of surgeon experience vs outcomes in DALK for keratoconus,[18] only 13 surgeons had performed more than 100 DALK cases for any indication; and, in total, they only performed 51 cases of DALK for keratoconus between 1999 and 2007. Registry studies[2,6,18] monitor graft survival but do not go beyond the rate of intraoperative conversion to PK in capturing data on intraoperative Descemet membrane perforation. The contrast between multisurgeon data presented here and perforation rates for high-volume, single-surgeon case series suggests that experience may be an important determinant of the risk for this intraoperative complication.

We observed a lower graft failure rate (4.2%) than that reported in UK (8%) and Australian (12%) corneal transplant registry studies. Several factors may account for this. Although relatively inexperienced, our trainee surgeons were proctored by consultant surgeons with experience in handling complications in lamellar transplantation, whereas many surgeons contributing to registry study data may have been transitioning to lamellar techniques without supervision. Existing registry reports comprise cases operated on between 1999 and 2012 using a range of DALK techniques. We examined a later time period (2012–2016) in which Descemet membrane–baring techniques,[4] and the big-bubble technique[10] in particular (91% of cases reported here), have become better standardized and more widely disseminated.

Importantly, the management of complications that can lead to DALK failure is now better defined. Conversion to PK in our series significantly increased the risk of transplant rejection and secondary glaucoma, and transplant rejection of any kind significantly increased the risk of graft failure. In addition to suture management and good medical control of preoperative and postoperative inflammation, strategies for avoiding conversion to PK in the event of Descemet membrane perforation are therefore important. Some of these read across directly from DMEK. Shallow, partial Descemet membrane detachments can be expected to resolve in many cases.[19] Intraoperative air tamponade and postoperative posturing can help to avoid the development of a double anterior chamber,[9,14] even where large perforations occur (Figure 4). Postoperative air tamponade, a procedure that can be performed quickly and safely at the slit-lamp microscope, can accelerate resolution of a double anterior chamber; but either strong pupil dilation or a peripheral iridotomy is essential in order to minimize the risk of pupil block glaucoma.[12]

Large-scale collection of data on preoperative status and clinical outcomes, pioneered by the Australian Corneal Graft Registry,[20] has been central to providing reliable, real-world information to inform procedure choice and patient counseling in corneal transplantation over the last 30 years. To build on this, there is a clear need for a standard reporting framework[21] and a shift to automated extracts from electronic healthcare records in place of paper-based double data entry. Steps are being taken in this direction in cataract surgery[22] and other subspecialties[23]; and, acknowledging the conflicting demands of acute care and accurate data collection in a busy public healthcare setting,[24] the Cornea and External Disease Service at Moorfields Eye Hospital, responsible for approximately one sixth of all corneal transplants performed in the UK, has recently set up a dedicated transplant outcomes clinic run by optometrists designed to collect data on key outcome measures, including manifest refraction and endothelial cell density, at 1, 2, and 5 years after surgery.

Our study sits between registry studies and single-surgeon case series in sampling contemporary outcomes in manual DALK for keratoconus. We demonstrate early graft survival and visual results similar to PK for keratoconus in a busy, multisurgeon setting. Longer-term advantages for DALK are already clear.[5] The understanding of DALK techniques and the management of intraoperative complications has evolved since existing registry data on DALK for keratoconus was published.

FUNDING/SUPPORT: THIS RESEARCH HAS RECEIVED A PROPORTION OF ITS FUNDING FROM THE DEPARTMENT OF HEALTH'S NIHR Biomedical Research Centre for Ophthalmology at Moorfields Eye Hospital and UCL Institute of Ophthalmology. The views expressed in the publication are those of the authors and not necessarily those of the Department of Health. Financial Disclosures: The following authors have no financial disclosures: Kunal A. Gadhvi, Vito Romano, Luis Fernández-Vega Cueto, Francesco Aiello, Alexander C. Day, and Bruce D. Allan. All authors attest that they meet the current ICMJE criteria for authorship.

REFERENCES

1. Gain P, Jullienne R, He Z, et al. Global survey of corneal transplantation and eye banking. *JAMA Ophthalmol* 2016;134(2):167–173.
2. Coster DJ, Lowe MT, Keane MC, et al. A comparison of lamellar and penetrating keratoplasty outcomes: a registry study. *Ophthalmology* 2014;121(5):979–987.
3. Keenan TD, Jones MN, Rushton S, et al. Trends in the indications for corneal graft surgery in the United Kingdom: 1999 through 2009. *Arch Ophthalmol* 2012;130(5):621–628.
4. Reinhart WJ, Musch DC, Jacobs DS, et al. Deep anterior lamellar keratoplasty as an alternative to penetrating keratoplasty a report by the american academy of ophthalmology. *Ophthalmology* 2011;118(1):209–218.
5. Borderie VM, Sandali O, Bullet J, et al. Long-term results of deep anterior lamellar versus penetrating keratoplasty. *Ophthalmology* 2012;119(2):249–255.
6. Jones MN, Armitage WJ, Ayliffe W, et al. Penetrating and deep anterior lamellar keratoplasty for keratoconus: a comparison of graft outcomes in the United Kingdom. *Invest Ophthalmol Vis Sci* 2009;50(12):5625–5629.
7. Watson SL, Tuft SJ, Dart JK. Patterns of rejection after deep lamellar keratoplasty. *Ophthalmology* 2006;113(4):556–560.
8. Keane M, Coster D, Ziaei M, Williams K. Deep anterior lamellar keratoplasty versus penetrating keratoplasty for treating keratoconus. *Cochrane Database Syst Rev* 2014;7:CD009700.
9. Romano V, Iovieno A, Parente G, et al. Long-term clinical outcomes of deep anterior lamellar keratoplasty in patients with keratoconus. *Am J Ophthalmol* 2015;159(3):505–511.
10. Anwar M, Teichmann KD. Big-bubble technique to bare Descemet's membrane in anterior lamellar keratoplasty. *J Cataract Refract Surg* 2002;28(3):398–403.
11. Melles GR, Lander F, Rietveld FJ, et al. A new surgical technique for deep stromal, anterior lamellar keratoplasty. *Br J Ophthalmol* 1999;83(3):327–333.
12. Maurino V, Allan BD, Stevens JD, Tuft SJ. Fixed dilated pupil (Urrets-Zavalia syndrome) after air/gas injection after deep lamellar keratoplasty for keratoconus. *Am J Ophthalmol* 2002;133(2):266–268.
13. Feizi S, Javadi MA, Rastegarpour A. Visual acuity and refraction after deep anterior lamellar keratoplasty with and without successful big-bubble formation. *Cornea* 2010;29(11):1252–1255.
14. Sarnicola V, Toro P, Sarnicola C, et al. Long-term graft survival in deep anterior lamellar keratoplasty. *Cornea* 2012;31(6):621–626.
15. Feizi S, Javadi MA, Jamali H, Mirbabaee F. Deep anterior lamellar keratoplasty in patients with keratoconus: big-bubble technique. *Cornea* 2010;29(2):177–182.
16. Kubaloglu A, Sari ES, Unal M, et al. Long-term results of deep anterior lamellar keratoplasty for the treatment of keratoconus. *Am J Ophthalmol* 2011;151(5):760–767.e1.
17. Khattak A, Nakhli FR, Al-Arfaj KM, Cheema AA. Comparison of outcomes and complications of deep anterior lamellar keratoplasty and penetrating keratoplasty performed in a large group of patients with keratoconus. *Int Ophthalmol* 2018;38(3):985–992.
18. Kasbekar SA, Jones MN, Ahmad S, et al. Corneal transplant surgery for keratoconus and the effect of surgeon experience on deep anterior lamellar keratoplasty outcomes. *Am J Ophthalmol* 2014;158(6):1239–1246.
19. Rodriguez-Calvo-de-Mora M, Quilendrino R, Ham L, et al. Clinical outcome of 500 consecutive cases undergoing Descemet's membrane endothelial keratoplasty. *Ophthalmology* 2015;122(3):464–470.
20. Williams KA, Lowe M, Bartlett C, et al. Risk factors for human corneal graft failure within the Australian corneal graft registry. *Transplantation* 2008;86(12):1720–1724.
21. Michelotti M, de Korne DF, Weizer JS, et al. Mapping standard ophthalmic outcome sets to metrics currently reported in eight eye hospitals. *BMC Ophthalmol* 2017;17(1):269.
22. Sparrow JM, Taylor H, Qureshi K, et al. The Cataract National Dataset electronic multi-centre audit of 55,567 operations: risk indicators for monocular visual acuity outcomes. *Eye* 2012;26(6):821–826.
23. Chiang MF, Sommer A, Rich WL, et al. The 2016 American Academy of Ophthalmology IRIS((R)) Registry (Intelligent Research in Sight) database: characteristics and methods. *Ophthalmology* 2018;125(8):1143–1148.
24. Rough K, Thompson JT. When does size matter? Promises, pitfalls, and appropriate interpretation of "big" medical records data. *Ophthalmology* 2018;125(8):1136–1138.