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Five-Year Graft Survival Comparing Descemet Stripping Automated Endothelial Keratoplasty and Penetrating Keratoplasty

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Purpose: To compare 5-year graft survival after Descemet stripping automated endothelial keratoplasty (DSAEK) and penetrating keratoplasty (PK) in Asian eyes.

Design: Prospective, nested, cohort study.

Participants: Consecutive patients who underwent DSAEK (423 eyes) or PK (405 eyes) for Fuchs' endothelial dystrophy (FED) or bullous keratopathy (BK).

Methods: Clinical data and donor and recipient characteristics were recorded from our prospective cohort from the Singapore Corneal Transplant Registry. All surgeries were performed by the corneal surgeons at our center, which included cases performed or partially performed by corneal fellows in training under direct supervision.

Main Outcome Measures: Five-year cumulative graft survival.

Results: Overall mean age was 67.8 ± 9.8 years, and 50.1% of patients were men. There were no significant differences in age ($P = 0.261$) or gender ($P = 0.78$) between PK and DSAEK groups in our predominantly Chinese (76.6%) Asian cohort, with more BK compared with FED (68.1% vs. 31.9%; $P < 0.001$). Overall 5-year graft survival was superior for DSAEK compared with PK (79.4% vs. 66.5%; $P < 0.001$, log-rank test). Median 5-year percent endothelial cell density loss was significantly greater in PK compared with DSAEK (60.9% vs. 48.7%; $P = 0.007$). Cox regression analysis revealed that BK was a significant factor associated with graft failure (hazard ratio [HR], 3.30; 95% confidence interval [CI], 2.05–5.33; $P < 0.001$), and PK was more likely to fail compared with endothelial keratoplasty (HR, 1.61; 95% CI, 1.08–2.41; $P = 0.02$) adjusting for confounders such as recipient age, gender, and donor factors. Five-year cumulative incidence of complications such as graft rejection ($P < 0.001$), epitheliopathy ($P < 0.001$), suture-related corneal infections ($P < 0.001$), and wound dehiscence ($P = 0.002$) were greater in the PK group compared with the DSAEK group.

Conclusions: In Asian eyes from the same study cohort with standardized surgical and postoperative regimes, 5-year graft survival was superior for DSAEK compared with PK in eyes with FED and BK. *Ophthalmology 2016;■:1–7 © 2016 by the American Academy of Ophthalmology.*

Over the past decade, endothelial keratoplasty (EK) gradually has overtaken penetrating keratoplasty (PK) as the corneal transplantation of choice for endothelial disease.[1] In the United States, Descemet stripping automated endothelial keratoplasty (DSAEK) became the most common keratoplasty procedure (50% of all grafts performed) in 2014; the most common indications were Fuchs' endothelial dystrophy (FED; 22%), followed by bullous keratopathy (BK) or corneal edema after surgery (12%).[2] A similar change in surgical indications and the trend toward EK also is reflected in reports from Singapore,[3] Australia, the United Kingdom, and parts of Europe.[4] It is now recognized that although PK offers patients a similar visual improvement in the long term, its potential disadvantages, including a prolonged visual recovery, surgically induced astigmatism, suture-related problems, graft rejection, and potential wound dehiscence, all are reduced significantly with DSAEK.[1]

However, recent publications from Australia and the United Kingdom suggest that graft survival of EK may be significantly poorer compared with PK for the same indications, contrary to reports from single-center studies in the United States and Singapore.[5–7] The suggested explanations for this observation include the effect of using registry data from multiple centers with varying surgical techniques and surgeon experience and the consequence of comparing a relatively newer EK procedure with an established PK technique, with differences in survival follow-up times between techniques,[6] all of which are compounded by potential differences in donor age and endothelial cell density (ECD), which were not well described.[8] Nonetheless, although the discussion continues regarding which surgical technique is best with respect to graft survival for treating cornea endothelial disease, most agree that more long-term studies directly comparing EK and PK outcomes are required.[9]

Analyzing registry data reduces selection bias by including a large number of cases performed by multiple surgeons and may be more representative of the so-called average overall outcome.[6] However, although a randomized controlled trial is not always feasible when comparing a surgical technique against an established method, evaluating a relatively newer procedure should be performed under standardized conditions to reveal specific differences in the outcomes of interest.[9] The Singapore Cornea Transplant Registry provides a unique opportunity to balance the advantages (and disadvantages) of using registry data with a long follow-up in a large cohort of patients, combined with a controlled setting of multiple surgeons with varying degrees of surgical experience, and various standardized techniques and postoperative regimens, where outcomes are monitored, audited, and presented annually.[10] Therefore, we conducted a 5-year review of outcomes between PK and DSAEK procedures from the same cohort of subjects with either FED or BK and used cumulative graft survival as our primary outcome measure because this was the main area of contention in the published literature.[9]

Methods

We analyzed data from the ongoing prospective cohort from the Singapore Corneal Transplant Study, which tracks and records all preoperative clinical data, surgical outcomes, and complications in an annual audit.[10] Our inclusion and exclusion criteria have been described previously[7]: in brief, inclusion of consecutive patients with either FED or postsurgical BK who underwent either a primary DSAEK or PK for purely optical reasons with a minimum of 5 years of follow-up, excluding regrafts and patients with high risk of failure requiring systemic immunosuppresion.[11] The 8 corneal surgeons from the Singapore National Eye Center performed all surgeries over the same period (1991–2011), which included cases performed or partially performed by 26 local or international corneal fellows in training under direct supervision. Our main outcome measure from this audit was graft survival, where graft failure was defined as irreversible loss of optical clarity sufficient to compromise vision for a minimum of 3 consecutive months.[12] Our study followed the principles of the Declaration of Helsinki, with ethics approval obtained from our local institutional review board (SingHealth Centralized Institutional Review Board, R847/42/2011).

Surgical Technique

Surgical techniques for all PK and DSAEK surgeries have been described previously.[7] Essentially, PK surgeries were performed using a standard technique with a Hanna vacuum trephine system (Moria SA, Antony, France). Briefly, the recipient cornea first was excised using the Hanna trephine system. A 0.25- to 0.50-mm oversized donor cornea then was punched out endothelial side up and sutured on to the recipient with 10-0 nylon, using either an 8-bite, 10-0 nylon double continuous running suture or a combination of a single 8-bite 10-0 nylon continuous and 8 interrupted sutures. All DSAEK surgeries were performed using pull-through techniques as described previously.[13] Donors (approximately 150-μm thickness) were prepared by the surgeon or eye bank technician using an automated lamellar therapeutic keratoplasty system (ALTK; Moria SA). Essentially, after recipient Descemet's membrane stripping and insertion of anterior chamber maintainer and preplaced venting incisions, a DSAEK forceps (ASICO, Westmont, IL) was used to pull the donor cornea through the

scleral incision using a sheets glide (Beaver-Visitec International, Waltham, MA)[13] or a donor inserter device (Endoglide, Network Medical Products, North Yorkshire, United Kingdom).[14] An inferior peripheral iridectomy was performed through a limbal stab incision. Wounds were secured with 10-0 nylon interrupted sutures, and a full air tamponade under slight compression was achieved with a large bubble in the anterior chamber for varying periods, ranging from 2 to 8 minutes, while removing interface fluid from the venting incisions. For both PK and DSAEK surgeries, a bandage contact lens was placed at the end, and dexamethasone 0.1% (Merck & Co., Inc., Rahway, NJ), 14 mg/ml gentamicin (Schering AG, Berlin-Wedding, Germany), and 50 mg/ml cefazolin (GlaxoSmithKline, Durham, NC) was injected subconjunctivally after all surgeries. All PK and DSAEK patients received a standard postoperative steroid regimen during the study period as part of our Singapore Corneal Transplant Study protocol: topical prednisolone acetate 1% every 3 hours for 1 month, 4 times daily for 2 months, which was tapered by 1 drop every 3 months to 1 drop daily by 1 year, and thereafter continued indefinitely.

Statistical Analysis

All statistical analysis was performed by a biostatistician (H.M.H.) using the Statistical Package for the Social Sciences version 22.0 (SPSS, Inc., Chicago, IL), including descriptive statistics, where the mean and standard deviation were calculated for the continuous variables, whereas frequency distribution and percentages were used for categorical variables. All clinical data were collected in a prospective manner as part of our Singapore Corneal Transplant Study audit, which included graft survival, predetermined parameters, and complications such as primary graft failure, graft rejection, and graft-related infections, as previously defined.[15] Endothelial cell density evaluation was performed by certified ophthalmic technicians using a noncontact specular microscope (Konan Medical Corp., Hyogo, Japan) as described previously.[16] Comparisons between categorical variables were conducted using the Fisher exact test, whereas the 1-way analysis of variance was used for means. Kaplan-Meier survival analysis was conducted to determine 5-year survival probabilities of PK and DSAEK groups. Cox regression was performed to estimate the factors associated with graft failure represented using hazard ratios (HRs) and relative 95% confidence intervals (CIs). A *P* value of less than 0.05 was considered statistically significant.

Results

During the study period, a total of 828 consecutive patients who underwent either DSAEK (423 eyes) or PK (405 eyes) met our inclusion criteria. Overall mean age was 67.8±9.8 years, and 50.1% of patients were men. There were no significant differences in age (*P* = 0.261) or gender (*P* = 0.78) between the PK and DSAEK groups in our predominantly Chinese (76.6%) Asian cohort. Similar to most parts of Asia,[4] we had a overall higher proportion of patients with BK compared with FED (68.1% vs. 31.9%; *P* < 0.001); however, there were no significant differences in demographics or characteristics of patients with BK or FED between the groups. The main outcome measure of our study, which was 5-year cumulative graft survival, was superior for DSAEK compared with PK (79.4% vs. 66.5%) because the cumulative survival consistently was better for DSAEK compared with PK (survival probabilities at 1 to 4 years: 95.5% vs. 91.4%, 90.7% vs. 82.2%, 86.9% vs. 76.3%, and 82.9% vs. 71.5%, respectively; *P* < 0.001, log-rank test; Fig 1).