

A 5-year analysis of endothelial vs penetrating keratoplasty graft survival in Chinese patients

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Abstract

• **AIM:** To determine if there is any difference in long term graft survival between Descemet's stripping endothelial keratoplasty (DSEK) and penetrating keratoplasty (PK).

• **METHODS:** A retrospective 5-year cases analysis of bullous keratopathy secondary to Fuchs' endothelial dystrophy or pseudophakic bullous keratopathy, receiving either DSEK or PK. A total of 42 DSEK cases and 25 PK cases were included in the analysis.

• **RESULTS:** In the 5-year analysis, graft survival rates were very similar in the two groups (DSEK 77.1% vs PK 76.0%, $P=0.918$, 95%CI: -6.3 to 33.4). Sub-analyses at 1y (DSEK 81% vs PK 95%, $P=0.085$, 95%CI: -29 to 3.6) and 2y (DSEK 81% vs PK 88%, $P=0.381$, 95%CI: -25.9 to 11.8) show a trend towards lower survival rates of DSEK vs PK, but the results were not statistically significant.

• **CONCLUSION:** Long term 5-year graft survival is similar between the DSEK and PK methods of corneal transplant in Chinese patients with bullous keratopathy.

• **KEYWORDS:** cornea; endothelial keratoplasty; corneal graft

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INTRODUCTION

In the past fifty years, penetrating keratoplasty (PK) with full thickness corneal transplantation was the gold standard for treatment for visual rehabilitation in cases of

Fuchs' endothelial dystrophy (FED) and pseudophakic bullous keratopathy (PBK). In the past decade however, endothelial keratoplasty (EK) techniques [in particular deep lamellar endothelial keratoplasty (DLEK) and Descemet stripping automated endothelial keratoplasty (DSAEK)] emerged and surpassed PK in popularity for many countries^[1-4]. Findings of superiority in EK compared with PK such as earlier postoperative visual recovery, reduced wound and suture related complications, less astigmatism and graft rejection have most likely led to this change^[5-6].

Despite this, the current literature does not have conclusive evidence on the long-term survival rates of EK versus PK grafts especially in the local Chinese population. Thus, whilst there are some clear advantages of EK compared to PK, the evidence regarding which surgical procedure has a better long-term survival is still not fully established. In light of the above, we attempt to evaluate the long-term graft survival and visual outcomes comparing PK and EK in our centre. The focus will be mainly on the long-term graft survival. In this tertiary centre in Hong Kong, EK was initially introduced in 2005 starting with DLEK. Later on, Descemet's stripping endothelial keratoplasty (DSEK) became the main EK procedure performed in Prince of Wales Hospital since 2006.

SUBJECTS AND METHODS

Ethical Approval The study was conducted in full conformance with principles of the Declaration of Helsinki, Good Clinical Practice, and within the laws and regulations of Hong Kong Special Administrative Region. Approval was granted by the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee Cref No: 2015.371.

Methods This is a retrospective cohort study, on the majority of DSEK and PK procedures performed in the Prince of Wales Hospital from 2006 to 2013. Patients who received primary DSEK or PK for FED or PBK in the New Territories East Cluster of Hong Kong within this time frame were recruited for the study. We excluded patients who received DLEK, and patients aged <18 years old due to ethical reasons. We measured graft survival rates and compared the two groups at 1, 2, and 5y respectively. The definition of graft failure in our study was based on the definition used in the collaborative

corneal transplantation studies. We defined a graft failure by: second graft or in its absence, a cloudy cornea with loss of central graft clarity sufficient to compromise vision for a minimum of 3 consecutive months^[7].

Statistical Analysis Cumulative probabilities of graft survival were calculated using the Kaplan-Meier method and analysed with log rank test. Missing/lost follow up data or patients who died during the study were censored from the analysis appropriately. Primary failure rates were compared with Chi-squared test. Cox regression was used to assess the association of baseline recipient factors with survival in univariate and multivariate analyses. A *P*-value of less than 0.05 was considered statistically significant. All statistical analyses were conducted using IMB SPSS® Ver 22. Software.

RESULTS

Forty-two DSEK cases and twenty-five PK operations done on Chinese patients in the same centre in Hong Kong were included in the analyses. There were no significant differences in mean age between the DSEK and PK groups (73.14±9.2y vs 72.64±11.2y, *P*=0.84). In the DSEK group, the primary diagnosis was FED (as opposed to PBK) in 64.3% vs 28% of PK cases (*P*=0.004).

The primary failure rate in DSEK was 14.3% vs 0 in PK (*P*=0.048). Graft survival at 1y for DSEK was 81% vs 95% in PK (*P*=0.085), 95%CI: -29 to 3.6]. At 2y, the percentage of grafts survival between the two groups were 81% vs 88%, respectively (*P*=0.381, 95%CI: -25.9 to 11.8 log-rank test). For 5-year survival analysis, there was also no demonstrable difference in percentage survival for DSEK compared with PK (DSEK 77.1% vs PK 76.0%, *P*=0.918, 95%CI: -6.3 to 33.4, log-rank test). Cox regression analysis revealed that primary diagnosis (PBK vs FED), age, and laterality of surgery showed no significant effects on the survival rates (Figures 1-3).

DISCUSSION

The main aim in this study was to compare the long-term survival rates in DSEK vs PK performed in the local Chinese population. From the analyses on our relatively small cohort, we found that the 5y survival rates between DSEK and PK in our centre were reasonably good, with a combined rate of >76% survival at 5y. This correlates to the current published literature that there is no definite evidence to suggest an advantage in the long term survival with the EK procedure compared to PK.

Our long-term survival figures are comparable to a similar study in Singapore (DSAEK 79.4% vs PK 66.5%), although our 5y survival rates were much more similar between the two groups (EK 77.1% vs PK 76%). Their large cohort consisted of mainly Chinese patients with FED or PBK. Their figures for 5-year graft survival was significantly better for DSEK compared with PK (79.4% vs 66.5% survival). These surgeries

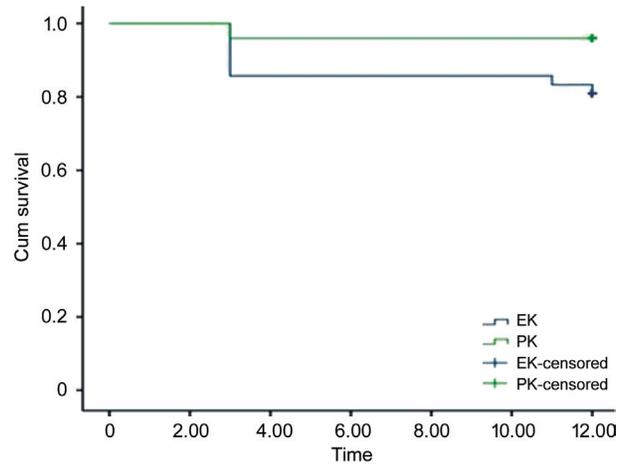


Figure 1 1y survival analysis.

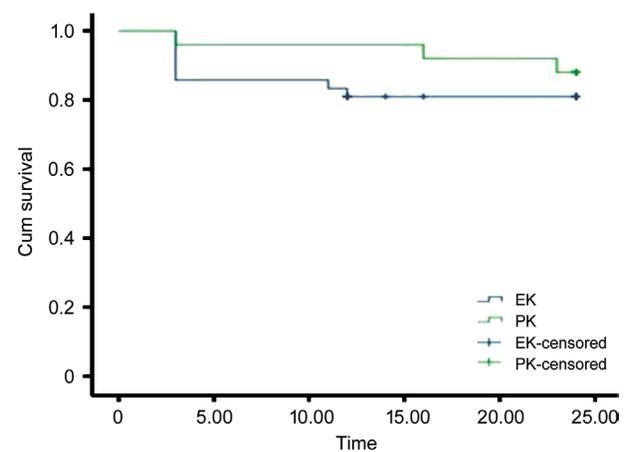


Figure 2 2y survival analysis.

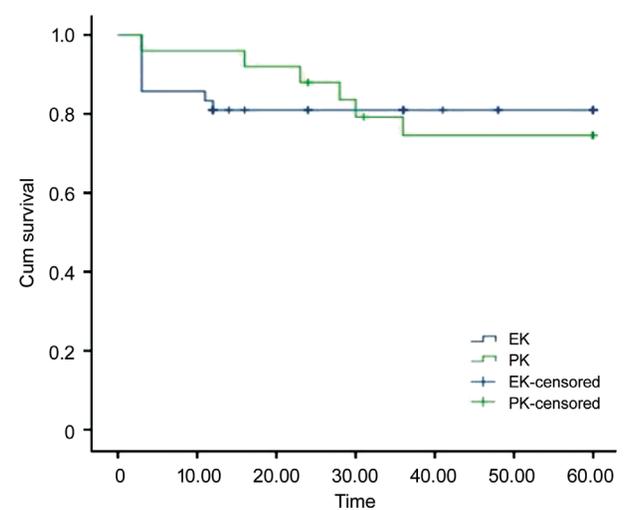


Figure 3 5y survival analysis.

included those performed by senior surgeons as well as supervised corneal fellows in training^[8].

Correspondingly, in a Cochrane Review in 2014 comparing the randomized controlled trials of EK and PK in FED, it found no strong evidence of any difference in the final outcome between EK and PK for patients with FED^[9]. In a more recent study by Dickman *et al*^[10] 2016 in the Netherlands, it was found that both EK and PK have similar survival rates in the long

term, although the short-term survival for EK is lower. Two-year survival rates were significantly better in the PK patients compared to EK patients, however at 5y the survival rates were comparable^[10].

Although our main aim was to look at long term survival, the short-term survival data is interesting to note. In terms of short-term survival, sub-analyses were done at 1 and 2y respectively. On analysis of survival at year 1 and year 2, (although overall statistical significance was not reached) there was a trend towards poorer survival at the earlier stages in EK cases. At year 1, 95% of the PK grafts had survived but only 81% of the EK grafts had survived—this was due to a significantly higher rate of primary failure (14.3% in EK vs 0 in PK, $P=0.048$) in EK procedures. This is comparable to other studies which reflected higher rates of failure at an early stage. For example, Coster *et al*^[11] in 2014 reported survival of EK to be worse than the survival of PK grafts performed for the same indications over the same time frame, with many EK failing at an early stage. Similarly, a study on patients with EK done on Chinese patients revealed primary failure to occur in 18.2% of cases^[12]. This may reflect the high learning curve of EK procedures, however, in our study the cases were recruited within an extended time period from 2006 to 2013 and the same group of experienced surgeons performed the EK/PK for all of those years. The very early cases where there would be an expected learning curve were not included in this study. There may be other reasons for high primary failure rates, possibly due to increased risk of early postoperative complications such as graft dislocation, intraocular pressure spikes, and endothelial cell injury in EK procedures as reported by other studies^[13-17]. These complications can make the early postoperative period more complicated than the traditional PK.

By year 2, however, there were more similar rates of survival in the EK and PK cases, suggesting that the EK graft survival is improved and stable after overcoming the high primary failure rate. Likewise, no significant difference was found between the survival in the two groups at 2y. This is also similar to the study by Dickman *et al*^[10] who also reported that the survival became more similar in the long term.

One factor which may have affected the results is that patients receiving EK were more likely to have FED in our study as opposed to PBK compared to those receiving PK. Those receiving PK were more likely to have a primary diagnosis of PBK as opposed to FED (64.3% had FED in EK group vs 28% in the PK group). This may be due to the extent of the disease as to which procedure to choose for each case. Those with PBK may more likely to have had full thickness corneal involvement requiring PK. These factors were adjusted for during the analyses and no significant effects were found on the results of long-term graft survival. There is an obvious

limitation in this study in the relatively small sample size, although it does show a specific cohort of Chinese patients. Whilst we did adjust for age of patient, primary diagnosis, and laterality of surgery, there are still other factors which we could not account for. We could not adjust for the donor age and endothelial cell densities which are suggested by other authors to contribute to confounding results^[18].

In summary, we have found that both techniques gave similar long-term survival rates within our centre on Chinese patients with FED and PBK. The PK technique is not proven to be inferior to EK with regards to long-term or short-term survival in our centre. It is clear that the current evidence on corneal graft survival is still lacking, and with fast changing techniques such as emergence of Descemet membrane endothelial keratoplasty (DMEK) and Descemet membrane endothelial transfer (DMET), further research is needed to achieve the best practice for our patients^[19-20].

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