Increasing the Storage Time from Pre-Cutting of Donors to the Date of Transplantation Does Not Affect Dislocation Rates, Graft Failure Rates, or Endothelial Cell Loss

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ABSTRACT

Purpose: To determine if the time from pre-cutting tissue with a microkeratome in the Eye Bank to transplantation affects post-operative complications or donor endothelial cell density (ECD) loss.

Methods: We identified 797 Descemet stripping automated endothelial keratoplasty (DSAEK) surgeries performed at two sites between 2008 and 2014. The time from microkeratome cutting to transplantation, and complications were recorded. Six month correlation analysis was performed on 620 grafts that had ECD counts preoperatively and at 6 months. Preparation to transplant intervals of < 1 day (n=53), 1 day (n=444), 2 days (n=113) and > 2 days (n=10) were compared for dislocation rates, iatrogenic graft failure rates, late graft failure rates, and post-op % ECD loss.

Results: There was a weak but statistically significant relationship between ECD loss and time between pre-cutting and transplantation (p=.02). The mean % ECD loss was 24%, 20%, 18% and 29% for tissues stored <1 day, 1 day, 2 days and >2 days. There were 0 dislocations in the <1 day group (0%), 12 in the 1 day group (3%), 5 in the 2 day group (3%) and 1 in the greater than 2 day group (10%) respectively. There were 3 iatrogenic graft failures, and no late graft failures.

Conclusion: Dislocation rates, graft failure rates, and ECD loss at 6 months after DSAEK is similar whether the tissue is cut immediately before use or stored for 2 days. Surgeons can feel comfortable accepting tissue which is cut at least 2 days before use.

Key Words: DSAEK, pre-cut, eye bank

INTRODUCTION

Treatment for endothelial dysfunction in the United States has evolved through several iterations, taking advantage of continuously refined graft preparation techniques.[1] Historically, patients with endothelial dysfunction received full thickness corneal replacements, penetrating keratoplasties (PKP). Ever evolving techniques and tools by both surgeons and eye banks however, have allowed the PKP procedure to give way to the less invasive endothelial keratoplasty (EK).[2]

Descemet stripping automated endothelial keratoplasty (DSAEK) is currently the standard EK surgery for the treatment of Fuchs Endothelial Dystrophy in the United States and in many developed countries.[3] Over the last five years, DSAEK has been to shown to provide excellent clinical and visual outcomes for patients. In 2014 there were 23,100 DSAEK surgeries reported in the United States, replacing PKP as the most common method of corneal transplant in 2012.[4]

From the eye banking perspective, preparing donor tissue for a DSAEK procedure is a technically more challenging task than preparing a PKP graft. DSAEK requires an additional pre-cutting procedure to isolate Descemet membrane and its posterior stromal carrier. As a result, Eye Banks have taken on increasing tissue preparation responsibilities and have worked alongside surgeons to provide quality DSAEK tissue, in a timely manner that maximizes the available donor pool.[5-8]

Corneal tissue is a precious and limited resource and thus, needs to be managed well by eye banks while maintaining excellent clinical outcomes for patients. Overseeing the logistics of pre-cutting tissue is part of the management of this public gift. As DSAEK has matured over the years, there is ample anecdotal evidence that the cut to use interval of at least one day has no deleterious effects on the tissue.[9] However, there is no specific large scale study we are aware of comparing cut intervals to clinical outcomes.

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Our primary goal in this study was to evaluate the window period from when DSAEK tissue is pre-cut to when it is surgically implanted and any potential impacts on clinical outcomes. In order to answer this question, we measured rates of graft dislocations, graft failure, and post-operative cell loss at 6 months. By identifying a minimally safe timeline that DSAEK pre-cutting can occur to when grafts are implanted there is the potential to increase the availability of tissue and extend the time frame that pre-cut tissue can be shipped both nationally and internationally.

In an effort to better understand if the DSAEK surgery complication rates are influenced by pre-cut-to-surgery times, we combined data from two clinical sites both supplied tissue by the same eye bank (Lions VisionGift, Portland, OR). Using these data we analyzed iatrogenic graft failure rates, late graft failures, graft dislocation rates, and endothelial cell loss at 6 months post-surgery.

METHODS

We retrospectively combined and analyzed DSAEK cases completed at two different surgical sites, Devers Eye Institute (DEI) and SightLine Ophthalmic Associates (SOA) between April 2008 and March 2014. Every patient in this report is part of an ongoing Institutional Review Board (IRB) approved, HIPAA compliant study of endothelial keratoplasty and has signed an IRB approved, HIPAA compliant clinical research consent form. IRB approval and consent was obtained at the patients' surgical center. This research adhered to the tenets of the Declaration of Helsinki. All DSAEK cases were reviewed to identify primary graft failures rates, dislocation rates, and endothelial cell loss at 6 months.

Surgical Procedure

DSAEK surgeries were performed as previously described by Chen et al.[10] and Terry et al.[11] All tissue was processed by Lions VisionGift (LVG, Portland, OR). The study included patients with corneal endothelial dysfunction due to Fuchs dystrophy or pseudophakic bullous keratopathy.

Tissue Preparation

All tissue was prepared by LVG in a standardized technique which closely mirrors the protocol outlined by Woodward et al.[12] Some minor variations occurred over time such as the use of ocular coherence tomography for pachymetry in lieu of ultrasonic measurements. All tissue was stored and shipped in Optisol GS (Bausch & Lomb, Irvine, CA). All DSAEK baseline ECD measurement were obtain by averaging 2-4 specular image ECD counts taken prior to preparation using a Konan Kerato analyzer EKA-10 (Konan Medical, Inc. Hyogo Japan). Six month endothelial cell densities were obtained by taking specular images at either DEI using a Konan Noncontact Specular SP-9000 (Konan Medical Inc., Hyogo, Japan) or at SOA using a Tomey EM-3000 Specular microscope (Temey, Nagoya, Japan) during standard protocol visits. Graft cut-to-use times were determined by the time and date of graft preparation to the time and date of tissue use.

Statistical Analysis

In this study we tested for statistically significant differences in rates of iatrogenic graft failures, late graft failures, dislocations, and endothelial cell loss at 6 months at different time intervals from pre-cutting tissue to transplant. In order to control for site bias, we compared clinical outcomes between DEI and SOA by matching cut-to-use days. Statistical evaluation was performed using an alpha level of 0.05 to determine statistical significance. Endothelial cell loss is presented as mean percent values. For normally distributed data, groups were compared by analysis of variance (ANOVA). When comparing occurrences of complications, a chi squared test was performed between groups. We evaluated the relationship between 6 month endothelial cell loss and cut-to-use times with multiple regression analysis. Statistical analysis was performed using SPSS software version 12.0 (SPSS Inc., Chicago, IL) and Microsoft Office Excel 2010 (Microsoft, Redmond, WA).

RESULTS

A total of 620 eyes were able to be analyzed. Data were placed into four categories based on the number of days between tissue resection and transplantation. We identified 53 grafts that were pre-cut and transplanted on the same day, 444 grafts that were transplanted one day after pre-cutting, 113 grafts that were transplanted 2 days after precutting, and 10 grafts that were transplanted more than 2 days after precutting. The average cut to use time was 1.15 days. SOA had a slightly longer average cut to use time (1.29 ± .47 days) compared to DEI (1.13 ± .83 days). Of the non-failed grafts, 174 eyes did not have 6 month endothelial cell counts and thus could not be included in the final analysis.

Iatrogenic Graft Failure, and Late Graft Failure Rates

We identified 3 iatrogenic graft failures post DSAEK surgery. One graft failure occurred when the tissue was prepared and used within less than 1 day, the second graft

failed at 1 day, and the third graft failed at 2 days. There were no late graft failures occurring between 8 weeks and 6 months post-surgery.

Dislocation Rates

The number of dislocation rates post-surgery were 0 (0%), 12 (3%), 5 (2%) and 1 (10%) for pre-cut and transplanted DSAEK grafts less than 1 day, at 1 day, at 2 days and greater than 2 days respectively. We found no statistically significant difference in dislocation rates for DSAEK grafts pre-cut and transplanted at different time intervals (p=0.33).

6 Month Endothelial Cell Loss

The mean percent endothelial cell loss at 6 months post-surgery was 24%, 20%, 18% and 29% for pre-cut and transplanted DSAEK grafts less than 1 day, at 1 day, at 2 days and greater than 2 days (range; 3-11 days) respectively. We did find a statistically significant difference in rates of 6 month endothelial cell loss with grafts transplanted more than 2 days showing elevated levels of endothelial cell loss (p=0.02) when performing a chi squared analysis comparing groups by days.

However, we did not find a statistically significant trend in endothelial cell loss when comparing preparation to transplant times when using a Pearsons correlation coefficient (r= -0.0567, p= 0.158), as shown in Figure 1.

Additionally, we did find a statistically significant difference overall in endothelial cell loss between DEI (n=508) and SOA (n=112). DEI had an average of 22% ECL at six months and SOA had an average of 14% ECL at six months (p<.001).

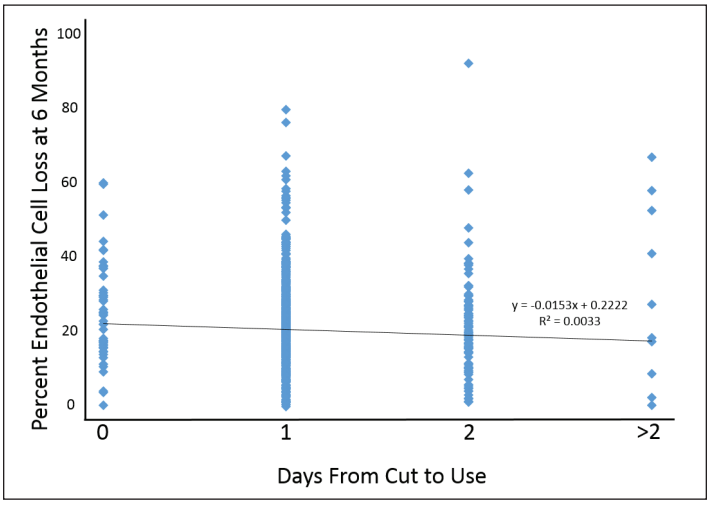

***Figure 1**. DSAEK microkeratome cut to transplantation intervals and the 6 month percent endothelial cell loss.*

DISCUSSION

This is the first publication comparing outcomes of DSAEK cut-to-use times in the literature in a large combined series. DSAEK currently occupies the middle ground between the more invasive PKP and the evolving Descemet membrane endothelial keratoplasty procedure (DMEK). While DMEK can provide superior outcomes compared to DSAEK, many surgeons have been slow to adopt DMEK because it is a technically a more difficult procedure and because of the interest in ultra-thin DSAEK.[13-15] In addition, DSAEK will not likely be falling out of practice as it is the preferred EK technique for complex cases which may be unsuitable for DMEK.[16]

Eye bank prepared pre-cut tissue has been shown to be 'just as effective' as surgeon prepared tissue and provides several benefits.[14] The use of pre-cut tissue provided by eye banks enhances the surgeon's knowledge about the quality of the tissue in use, and decreases the likelihood of tissue damage in the operating theater. Using eye bank prepared tissue decreases the amount of time surgeons need to dedicate to each surgery, eliminates the need for expensive equipment, and decreases the number of new skills a surgeon needs to learn when adopting the procedure.

Donor cornea tissue is a precious and limited resource. From the eye bank's perspective, surgeon acceptance of longer time frames between pre-cutting DSAEK tissue allows for the development of a larger pool of tissue which can safely be used. Surgeon acceptance of pre-cut tissue that is not prepared the same day or one day prior will ease the burden on eye banks for processing demands and the logistics of distribution. Additionally, corneas processed for surgical cases that are cancelled can more easily be re-allocated to a new case without any concern for increasing the risk of dislocation, graft failure, or higher cell loss. We feel strongly that surgeons should feel comfortable accepting tissue pre-cut 2 days or less before surgery. In this study we found that DSAEK tissue pre-cut at 2 days before transplant showed no increased rates of graft failures, dislocations, or cell loss at 6 months. We did not find an upper limit in pre-cut to surgery times or an association with increased rates of complications.

At 6 months post-surgery, we did find a statistically significant difference in percent endothelial cell loss when comparing days from pre-cutting tissue to transplantation, with slightly higher endothelial cell loss occurring at greater than 2 days from preparation to use. However this may be because we had relatively few transplants falling into this group and the range for preparation to use times was wide and resulted in only 29% endothelial cell loss at 6 months.

Interestingly, we did find a statistically significant slightly negative trend for cell loss with increased time from cut-to-transplantation times (Figure 1). This may suggest that longer cut-to-use times results in better 6 month outcomes.

It should also be noted that graft failure rates, dislocation rates, and endothelial cell losses are low in this report compared to previously reported outcomes. This may suggest that the time from pre-cutting to transplant times are less important than other factors that can affect clinical outcomes, such as utilizing the same standard DSAEK forceps inserter technique.[13,17]

While this study utilized a large dataset, a weakness is that we were unable to identify the extent to which tissue can safely be used after cutting with the bulk of the DSAEK grafts being transplanted 0-2 days after pre-cutting. Extended cases of DSAEK cut-to-use times have been reported overseas with comparable clinical outcomes.[18,19] Additionally, we did find slight differences in the amount of endothelial cell loss at 6 months when comparing between sites. This may be because DEI is a training site with a new fellow being trained each year. It should be noted that SightLine cell loss is superior to DEI in spite of a longer average cut to use interval.

In summary, the iatrogenic graft failure rate, late graft failure rate, dislocation rate, and the endothelial cell loss at 6 months after DSAEK surgery is similar whether the tissue is cut immediately before use or stored after cutting for at least 2 days. Eye banks should feel comfortable providing tissue which is pre-cut within 2 days of transplantation. The upper limit of the cut to transplant time interval is not known; however unpublished data from tissue shipped internationally suggests that two days is a minimum interval of comfort and much longer intervals should pose no problems for excellent surgical outcomes.

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