Outcome of Descemet stripping automated endothelial keratoplasty in eyes with an Ahmed glaucoma valve

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Abstract

Purpose The purpose was to investigate the survival of Descemet stripping automated endothelial keratoplasty (DSAEK) in eyes with an Ahmed glaucoma valve (AGV).

Methods The study had a retrospective case-series of patients with an AGV in the anterior chamber undergoing a DSAEK. Included in the analysis were graft size, number of previous operations, post-operative glaucoma medications, post-operative intraocular pressure (IOP) control, graft size and donor factors (age, endothelial cell density, and post-mortem time). A generalised linear model with binary logistic regression was used to test for an effect on graft survival at 1 year and 1.5 years.

Results Fourteen eyes from 13 patients were included. The survival rate of the first DSAEK at 6, 12, 18, 24 and 30-months was 85%, 71%, 50%, 36% and 30%, respectively. The mean duration to graft failure was 12.9 ± 6.2 months. Five of the seven failed first grafts went on to have a repeat DSAEK. The mean follow-up in this subgroup was 30.7 ± 18.4 months. The survival rate of second DSAEK at 6, 12, 18 and 24 months was 100% (5/5), 100% (5/5), 75% (3/4) and 67% (2/3). Only one second DSAEK failed in the duration of the study and went on to receive a third DSAEK which failed at 18-months. The mean IOP within the first year was significantly lower for grafts that survived at 1 and 1.5 years (17.4 mmHg, 16.9 mmHg) than for grafts that failed (19.4 mmHg, 19.4 mmHg) (p = 0.04, p = 0.009).

Conclusion DSAEK is a viable alternative to PK to restore visual function in eyes with an AGV sited in the anterior chamber. IOP is an important risk factor for graft failure.

Keywords Descemet stripping automated endothelial keratoplasty · DSAEK · Endothelial keratoplasty · Ahmed glaucoma valve · AGV · Glaucoma drainage device · Graft survival

Introduction

Graft survival following a penetrating keratoplasty (PK) in the presence of an Ahmed glaucoma valve (AGV) is significantly reduced [1–4]. The reported incidence of graft failure at 1-year varies between 8 and 42% [1–4]. Tube-related corneal endothelial failure is well-recognised and numerous reasons for graft failure have been proposed including the mechanical trauma of the surgery, tube endothelial contact [5, 6], intermittent or persistently high intraocular pressure (IOP) [7], and anterior chamber inflammation after implantation of the drainage device [8, 9].

Over the last decade, Descemet stripping automated endothelial keratoplasty (DSAEK) has surpassed PK as the most widely performed endothelial keratoplasty for endothelial disease [10, 11]. This trend is likely attributed to the significant advantages of DSAEK over PK which includes a lower refractive error, quicker visual recovery and less suture related problems [12]. Performing DSAEK in the presence of an AGV, however, poses new challenges. A drainage tube in the anterior chamber may damage the donor endothelium...
during manipulation, interfere with graft placement and tamponade [13] and increase the risk of graft detachment [14]. Intra-operative and early post-operative complications associated with AGV have been reported [7, 13, 15, 16]; however, data on graft survival is limited. To date, there have only been two published case series reporting on graft survival following previous AGV implantation. The larger series reported nine out of 18 graft failures with a mean graft survival time of 9.3 months [15]. The second series reported two graft failures in 11 eyes with a mean follow-up of 20.2 ± 10.7 months (range 3-37) [16]. The aim of this study is to investigate DSAEK survival in eyes with AGV(s) in situ and determine potential risk factors influencing graft survival.

Methods

Patients

The clinical notes of patients who had at least one AGV (Model S2 or FP7, New World Medical, California, USA) tube implant placed in the anterior chamber prior to DSAEK for corneal endothelial failure were reviewed. All operations were performed by senior surgeons at St. Paul’s Eye Unit, Royal Liverpool University Hospital, Liverpool, United Kingdom, between October 2005 and April 2013. Patients undergoing glaucoma surgery with an Ahmed Glaucoma Valve (New World Medical) had the primed valve plate secured in the superonasal or superotemporal quadrant as access to the interior would allow. The plate was secured at least 8 mm from the limbus. The tube was cut with an upward bevel to a length so that approximately 3 mm was in the anterior chamber, and the external tube was covered with a double-layered human pericardial patch, Tutoplast (Innovative Ophthalmic Products, Inc., Costa Mesa, CA, USA) before closing the conjunctiva. The data collected included ocular comorbidities, pre- and post-operative best-corrected visual acuities (BCVA), IOP, intra- and post-operative complications; post-operative course, medications and status of corneal graft. All IOP values represent Goldmann applanation tonometry readings, and the measurements used were those recorded preoperatively and 1 week, 1 month, 3 months, 6 months and 12 months post-operatively.

The donor cornea was prepared on an artificial anterior chamber with a 350 μm head Moria microkeratome (Moria, Antony, France) then cut on a Barron donor corneal punch (Katena Products, Inc., Denville, USA) with a graft diameter determined by the surgeon’s preference [17]. For grafts ≥ 9 mm in diameter, a peripheral dissection of the remaining donor cornea prior to trephination was undertaken to thin the graft as previously described [18]. An anterior chamber maintainer was inserted into the recipient’s eye, a 5.0 mm limbal incision made, and the Descemet membrane striped manually from the posterior stroma. Venting incisions were performed in some cases. The donor graft was transferred to a Busin glide and pulled through the main section using a pair of Grieshaber® DSP 20G forceps (Alcon, Fort Worth, USA). The main section and paracentesis were sutured with 10-0 nylon prior to inflating the anterior chamber with air using a 30G needle. Patients were advised to remain supine for 50 min of each hour for the first 24 hours postoperatively. Topical prednisolone 1% hourly during the waking hours and chloramphenicol 0.5% four times daily were prescribed for the first week before tapering. Topical prednisolone was continued for at least 2 years.

Corneal graft failure was defined as irreversible corneal oedema with loss of optical clarity as determined by slit-lamp biomicroscopy. Corneal graft rejection was defined as the presence of inflammation in the anterior chamber (aqueous humour cells, flare, keratic precipitates) and/or on the graft (inflammatory infiltrates, rejection lines, peripheral full thickness hazy associated with limbal injection which was previously clear); and/or circumcorneal injection. The tenets of the Declaration of Helsinki were adhered to and the ethics committee board approval was not required for this audit (reference TA000127).

Analysis

The visual acuities were converted from Snellen to logarithm of the minimal angle of resolution (logMAR) for analysis. The Wilcoxon signed rank and Mann-Whitney tests were performed on non-parametric data. A generalised linear model with binary logistic regression was used to test for an effect of the number of AGV and previous glaucoma surgery, post-operative glaucoma medications and post-operative IOP control on graft survival at 1 year and 1.5 years. A p < 0.05 was considered statistically significant. Graft survival was evaluated by the Kaplan-Meier estimate. All statistical analysis was performed using IBM® SPSS® Statistics version 22.

Results

Fourteen consecutive eyes of 13 patients had AGV prior to DSAEK. The mean age of the recipients at the time of the first DSAEK was 58 ± 17 years (range 28–88), and there were four male and ten female patients. The mean follow-up period for DSAEK was 30.2 ± 11.8 months (range 18.0-60.2), and the indications for AGV are provided in Table 1. Eight eyes (57%) had one AGV, five eyes (36%) had two AGV’s and one eye (7%) had three AGV’s. Of these, eight eyes (57%) had had failed trabeculectomy (six augmented with mitomycin-C and two with 5-fluorouracil) and three (21%) failed deep sclerectomy prior to AGV. No patient developed a
<table>
<thead>
<tr>
<th>Eye</th>
<th>Indication for AGV</th>
<th>Previous procedure</th>
<th>No. of AGV</th>
<th>Anti-glaucoma treatment</th>
<th>Baseline cup:disc</th>
<th>First DSAEK status</th>
<th>Follow-up (months)</th>
<th>Additional treatment post-DSAEK</th>
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<td>1</td>
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<tr>
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<tr>
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<td>10</td>
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<td>11</td>
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<td>3</td>
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<td>0.9</td>
<td>Survived</td>
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<td></td>
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</tbody>
</table>

Abbreviations: POAG – primary opened angle glaucoma, FHC – Fuch's heterochromic cyclitis, ASD – anterior segment dysgenesis, CACG – chronic angle closure glaucoma, TR- trabeculectomy, DS – deep sclerectomy, ACZ – acetazolamide SR, m - month
postoperative graft detachment or pupillary block. There was no documented tube and corneal endothelial touch.

**Graft survival**

A Kaplan-Meier survival curve is included in Fig. 1. The number of surviving grafts at 6, 12, 18, 24 and 30 months were 12/14 (85%), 10/14 (71%), 6/12 (50%), 4/11 (36%) and 3/10 (30%), respectively. All grafts failed from endothelial failure, of which only one was secondary to two separate episodes of rejection (anterior chamber inflammation). The mean duration from DSAEK procedure to the first documented graft failure was 12.9 ± 6.2 months with a median of 12.0 months (range 5-22 months). The mean donor ECD and age were 2828 ± 251/mm² (range 2400-3150) and 64.2 ± 12.7 years (range 40.6–79.3). The mean time from death to processing in the eye bank was 25.4 ± 7.9 hours (range 15-46) (Table 2). There was no significant effect of donor age (p = 0.32), ECD (p = 0.32) and post mortem time (p = 0.14) on graft survival at 1.5 years within the range of donor variables.

Five of the seven eyes with failed grafts underwent a repeat DSAEK. The mean follow-up in this subgroup was 30.7 ± 18.4 months (range 15-49 months). The number of surviving DSAEK following repeat grafts followed-up at 6, 12, 18 and 24-month was 100% (5/5), 100% (5/5), 75% (3/4) and 67% (2/3). The Kaplan-Meier survival curve for the second DSAEK is included in Fig. 1. Only one second DSAEK failed in the duration of the study and went on to receive a third DSAEK, which eventually failed after 18 months (eye 9 in Table 1).

**Intraocular pressure and graft survival**

The median IOP before DSAEK was 16 mmHg (range 12-20 mmHg). Four eyes were on topical anti-glaucoma monotherapy, one on dual therapy and four on triple therapy or more (Table 1). Postoperatively, three patients required additional anti-glaucoma medication to control their IOP. One patient had an additional AGV inserted 2 months after DSAEK surgery to control an IOP of 32 mmHg. The IOP remained high and diode laser cyclophotocoagulation was performed. Despite improved IOP, control was achieved, the graft failed at 11 months post-DSAEK.

There were no apparent effects of the number of previous AGV (p = 0.9), glaucoma surgery prior to AGV (p = 0.48) or the use of post-DSAEK glaucoma medications (p = 0.60) on graft survival at 1 year (Table 1). In the only eye with three AGVs, the graft remained clear at 35.2 months.

An IOP cut-off of ≤ 21 mmHg or > 21 mmHg within the first year was not associated with graft survival at either 1 year (p = 0.28) or 1.5 years (p = 0.34). The mean IOP within the first year, however, was significantly lower for grafts that survived at 1.0 and 1.5 years (17.40 mmHg, SD 4.55 and 16.86 mmHg, SD 4.14) than for grafts which failed (19.35 mmHg, SD 3.62 and 19.43 mmHg, SD 4.29) (p = 0.04, p = 0.009).

**Visual acuity**

Median preoperative BCVA was 1.0 logMAR (20/200) with range 0.8-2.0 (20/120-HM). Six-month post-DSAEK, the median BCVA (including failed grafts) was 0.6 logMAR (20/80), range 0.3-1.0 (20/40-20/200) (p = 0.008) and at 1 year post-
DSAEK, 0.8 logMAR (20/120), range 0.3-1.7 (p = 0.03). The median BCVA for the surviving first DSAEK at the close of study, with a median follow-up of 24.8 months (range 15.0-35.2) was 0.6 logMAR (20/80), range 0.3-1.2. This was significantly better than their preoperative BCVA (p = 0.018). The median BCVA for the four surviving second DSAEK at the close of study, with a median follow-up of 26.7 months (range 15.3-48.9) was 0.5 logMAR (20/60), range 0.3-0.8. There was, however, no significant difference between their pre- and post-operative BCVA (p = 0.068).

Discussion

The results of this study show that DSAEK is a viable procedure to restore visual function from endothelial failure in eyes with an AGV sited in the anterior chamber. There is limited published outcome data on this patient group [15, 16, 18] compared to other corneal graft populations. Direct comparison to these studies is also difficult due to the different underlying ocular comorbidities, length of follow-up, time point of BCVA assessment and surgical technique. Both our study and two of the three previous studies showed a significant improvement in BCVA following DSAEK [15, 16]. The average time from graft to documented failure in our series was 12.9 months (range 5-22) compared to 9.3 months (range 1-20) in Schoenberg et al. [15]. Although this data was not provided by Kim et al. [16], the authors noted that only two out of 11 DSAEKs failed during a mean follow-up of 20.2 ± 10.7 months (range 3-37). In the third study, 33% of the DSAEKs with previous aqueous shunt and trabeculectomy failed within a mean follow-up of 6.5 months (SD 6.9 months) [18]. The presence of one or more AGVs in the anterior chamber can make surgery challenging.

None of our patients had post-operative graft detachment or re-bubbling compared to the other series which reported rates between 26 and 39% [15, 16, 18]. Our surgical technique (described in Romano et al.) [19] evolved over the study period [17]. Almost 75% of our group had a graft of at least 9.0 mm diameter compared to 6.5-8.0 mm (Schoenberg et al.) [15], 8.0-8.5 mm (Kim et al.) [16] and 8.0 ± 0.6 mm (Decroos et al.) [18]. The absence of graft detachment may be related to the larger graft sizes and technique used to thin the graft prior to insertion [19].

The reported incidence of graft survival following PK in eyes with an AGV is better than endothelial keratoplasty (EK), with survival rates between 68 and 92% at 1 year, and 43 and 77% at 2 years [1–4]. This may, however, reflect the significantly better survival of PK compared to EK for both Fuchs endothelial dystrophy (FED) and pseudophakic bullous keratopathy (PBK) in the UK [20]. The reported survival rate for the same time period for EK in the UK undertaken for PBK is 70% (95% confidence interval (CI), 66% to 74%) [20].

The presence of glaucoma (defined as the use of glaucoma medications and/or glaucoma surgery) significantly increases the hazard of EK failure for FED by 2.1 times and PBK by 1.7 times [20]. Previous glaucoma intervention was associated with nine times greater risk of EK failure for one prior glaucoma surgery, which increased to 27 times for two or more surgeries. Although less pronounced, the presence of glaucoma (medically and surgically controlled) also carries a relative risk of 1.5 times for topical and 2.0 times for oral anti-glaucoma treatment, compared to those without glaucoma.

We believe that the increased failure rate associated with increased numbers of glaucoma surgeries is the result of an altered anterior chamber environment. Although no correlation has been shown between central or peripheral corneal

<table>
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<tr>
<th>Eye</th>
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</table>
endothelial cell loss and the distance between the tube and the cornea and the iris or the intracameral length of the tube [6], alterations in aqueous humour proteomics in eyes with a pre-existing glaucoma drainage device may precipitate oxidation, apoptosis and inflammation, potentially causing corneal endothelial damage [22].

In the literature there is a trend toward using an IOP threshold of 24-25 mmHg in the exploring concomitant EK and glaucoma [23–25]. None of these reports, however, were able to identify whether the pressure of 25 mmHg was useful to discriminate the risk of graft failure. The probability of an IOP ≥ 25 mmHg in the 12 months after EK is more likely in medically controlled versus surgically controlled glaucoma [23–25]. The majority of our cases did not have raised IOP, and we attribute this to the high rates of previous glaucoma surgery (trabeculectomy, deep sclerectomy, or AGV) which is supported by previous findings [23–25]. We note that two of our cases that resulted in graft failure did have IOP greater than 25 mmHg, but the majority of cases did not. We acknowledge that not all cases of graft failure can be attributed to raised IOP, but in our study, grafts that survived following DSAEK, had a significantly lower IOP within the first year than grafts which failed. Although there are likely to be many factors involved in graft survival, this would suggest that a lower target IOP may be associated with improved EK graft survival outcomes.

In our cohort, a few patients underwent more than one DSAEK in the same eye. To our knowledge, this is the first paper looking at the graft survival of subsequent DSAEK in eyes with a glaucoma drainage device. Of the first DSAEK grafts that failed, five went on to have a second DSAEK. All of second DSAEK grafts survived for a minimum of 12 months. One patient had a third DSAEK after the second graft failed at 18 months. The third graft also failed at 18 months. This observation differs from the outcome of penetrating keratoplasty [27] and further study is needed to investigate the survival rate of repeated DSAEK. Schoenberg et al. [15] concluded that DSAEK surgery in the setting of previous AGV implantation presented success rates of 50% comparable with penetrating keratoplasty [27] and further study is needed to investigate the survival rate of repeated DSAEK.

There are a few limitations to our study. We draw attention to the fact that this data was collected in a retrospective fashion, but given the somewhat ‘rare’ nature of the group; a prospective study would be difficult. Our cohort heterogeneity means there may be other factors influencing the graft survival that is not apparent in the analysis such as size of graft and number of AGVs. Unfortunately, the ECD was not performed consistently or at all in some patients in the post-operative period, which would have added valuable information.

Despite these limitations, the results of this study show that DSAEK is a viable procedure to restore visual function from endothelial failure in eyes with an AGV sited in the anterior chamber. It is of note that repeat DSAEK appeared to perform no worse than the failed first graft, which is in contrast with the reduced survival for repeat PK. In light of this, and given the comparatively rapid visual rehabilitation in patients undergoing EK versus PK, it is arguable that repeat EK in eyes with a previously sited AGV could prove a positive step forward in restoring and maintaining vision in these uncommon, but complicated cases.

Compliance with ethical standards

Funding No funding was received for this research.

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers’ bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

For this type of study formal consent is not required.

Informed consent Informed consent was obtained from all individual participants included in the study.

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