Clinical Audit of Glaucoma Drainage Device Insertions for the Treatment of Refractory Glaucoma in the Setting of Corneal Transplant

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Abstract

Purpose: To evaluate clinical outcomes of Glaucoma Drainage Device (GDD) insertions at three anatomical sites; Anterior Chamber (AC), Ciliary Sulcus (CS) and Pars Plana (PP), with respect to various corneal transplantation techniques; Penetrating Keratoplasty (PK), Deep Anterior Lamellar Keratoplasty (DALK), Descemet's Membrane Endothelial Keratoplasty (DMEK) and Descemet's Stripping Endothelial Keratoplasty (DSEK).

Design: Single-centre, nonrandomized retrospective case series.

Participants: Patients aged 18 years or older who had GDD insertion at Sydney Eye Hospital (SEH) between 2006 to 2015, and who also had a corneal transplant at any time period in the same eye.

Methods: Patients in this study either had a Baerveldt 101-350 GDD or a Molteno-R2 GDD placed into one of the anterior chamber (AC), ciliary sulcus (CS) or pars plana (PP) from 2006 to 2015. GDD data was combined with the type of corneal transplant performed, either penetrating keratoplasty (PK) or endothelial keratoplasty (DSEK/DMEK), at any time before or after GDD insertion. Patient data was collected preoperatively for each procedure and postoperatively up to a total of five years where possible. Surgical outcome measures were recorded in the form of intraocular pressure (IOP), visual acuity (VA), number of glaucoma medications and surgical complications at each follow-up visit. The timing between GDD insertion and corneal transplantation along with method of GDD stent occlusion, use of antimetabolites and total follow-up duration was noted as well.

Results: 25 eyes from 25 patient records that met study inclusion criteria were identified. All GDD insertions at the three sites (AC/CS/PP) resulted in a postoperative reduction in IOP. Mean IOP pre-GDD insertion was 25.8 mmHg and mean IOP post-GDD insertion at one year was 13.0 mmHg. The number of glaucoma medications also decreased post-GDD insertion. CS-GDD with keratoplasty had the largest IOP reduction post-GDD insertion on the least number of glaucoma medications. Visual acuity was also best preserved in this group. Overall graft failure rate at six months and one year was 16.7% and 20.8% respectively. Corneal decompensation was highest in AC-GDDs (43%). GDD with endothelial grafts (DSEK/DMEK) had higher graft failure rates in the first year of follow-up compared to PK (37.5% versus 13.3% respectively). Combined qualified GDD and keratoplasty success rate at one year was 82.6%.

Conclusion: GDD insertion is an effective means of IOP control in patients with corneal transplants. CS-GDD insertion with keratoplasty was shown to have the best clinical outcomes in terms of IOP reduction and reduction of number of glaucoma medications. CS-GDD with DSEK graft was associated with best postoperative visual acuity. PP-GDD with PK graft was shown to have the best graft survival rate in the long-term. There was no statistical significance in GDD and corneal graft outcomes by having GDD insertion prior to keratoplasty, no previous glaucoma surgery or by being pseudophakic.

Introduction

Patients with severe corneal disease requiring a corneal transplant are at a higher risk of developing elevated intraocular pressure with subsequent glaucoma [1]. High IOP is itself a risk factor for failure of the corneal transplant [1,2], and management of this can involve medical therapy, laser intervention or surgical intervention [3].

The insertion of a glaucoma drainage device (GDD) is a surgical option for patients with glaucoma not controlled medically, where there is a relatively high risk of failure with trabeculectomy [3]. A GDD acts to lower IOP by diverting aqueous humor from inside the eye towards a surgically created sac in the subconjunctival space [4]. Drainage of the aqueous humor for the treatment of glaucoma was first trailed in 1907 but was not really successful until 1969 [4]. The Molteno device was the first GDD that was introduced commercially more than 40 years ago. Initial GDD insertions were complicated by frequent postoperative hypotony, flat anterior chambers and choroidal effusions [4,5]. Newer GDD devices and insertion techniques have made GDD insertion a viable option to patients with refractory glaucoma who have previously failed or were not suitable for more conventional forms of glaucoma filtration surgery such as trabeculectomy [4,6]. GDDs have become the preferred primary surgical modality in uveitic [7], neovascular [8] and selected pediatric glaucoma presentations [9]. In certain clinical scenarios, GDD insertion has been demonstrated to achieve better IOP reduction, lower incidence of complications and less chance of failure when compared with trabeculectomy [6]. Connors et al. [10] reported that GDD insertions were more cost effective than trabeculectomy surgery in the long term for the management of glaucoma.

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A recent change in practice has seen a reduction in the number of full thickness penetrating keratoplasties (PKs), with a concurrent increase in lamellar transplantation such as Descemet Stripping Endothelial Keratoplasty (DSEK) and Deep Anterior [3] Lamellar Keratoplasty (DALK) [11,12]. These newer techniques have been shown to have lower incidence of graft rejection and post-keratoplasty glaucoma [13,14].

There are different types of GDD available and comparative studies have demonstrated better postoperative IOP control and higher surgical success rate with non-valved GDDs [3,15]. The optimal GDD insertion site (anterior chamber (AC), pars plana (PP) or ciliary sulcus (CS)) and the relative timing of insertion with respect to corneal transplantation remain controversial [15].

Methods

This study protocol was approved by the University of Sydney Medical Faculty, Ophthalmology Department. Ethics approval to conduct this low/negligible risk study was granted by the South-Eastern Sydney Local Health District (Human Research Ethics Committee, Room G71 East Wing, Edmund Blacket Building, Prince of Wales Hospital, Randwick NSW 2031).

Study objectives

(1) The primary objective was to evaluate clinical outcomes of GDD insertions at three anatomical sites (AC/CS/PP) with respect to various corneal transplantation techniques (PK/DALK/DMEK/DSEK).

(2) The secondary objective was to determine the optimal GDD anatomical insertion site with respect to the different corneal graft methods for greatest graft success.

(3) The tertiary objective was to look at pre-operative risk factors of GDD insertion and also the optimal time frame of GDD insertion.

Selection criteria

Inclusion criteria: All patients from Sydney Eye Hospital aged 18 years and over, with insertion of a GDD between 1/1/2006 and 31/12/2015, as well as a corneal transplant in the same eye at any time during or before the study period. Patient medical history and follow-up information from 1/1/2005 through to 31/12/2016 was included if the GDD was inserted in 2006 or 2015. Data from private patient follow-up was only included for patients attending the Save Sight Institute or Sydney Eye Hospital. In the case where two eyes from a patient satisfied the study selection criteria, both eyes were included in the analysis.

Exclusion criteria: Less than one year of follow up or incomplete documentation pre/peri/postoperatively. Private patients who attended follow-up appointments outside of the Save Sight Institute and Sydney Eye Hospital were excluded.

Search strategy

Cases were identified from patient records using the Medicare code for GDD insertion (42752 Insertion of aqueous shunt for glaucoma), and Medicare codes for corneal transplantation (42659 Superficial transplantation of cornea, 42653 Full thickness transplantation of cornea, 90064 other keratoplasty (DSEK)). Any reoperation of the corneal graft was noted as well (42656 Reoperation keratoplasty). As not all patients may have been coded using the appropriate code for GDD insertion, the surgical database was searched using common surgical terms such as "tube", "aqueous shunt" and "glaucoma drainage device".

Outcome measures

Patient data was collected pre-operatively for each procedure (GDD insertion and keratoplasty) and postoperative where available at Day 1, Week 1, Month 1, 2, 3, 6, Year 1, 2, 3, 4 and 5.

Collected data from patient records included basic demographic information, glaucoma subtype, corneal pathology, previous ophthalmic surgeries and postoperative surgical complications. The type of GDD, site of insertion, occlusion methods and administration of antifibrosis agent was recorded. The type of corneal graft, graft clarity, episodes of rejection and graft failure details were noted. For both procedures, IOP, Best-Corrected Visual Acuity (BCVA) (with pinhole) and number of glaucoma medications was noted at each point. Lastly, the dates of surgeries and total follow-up period were recorded. Endothelial Cell Count (ECC) was recorded where available.

Definitions of success/failure

GDD definition of complete success:

- IOP between 5 and 18mmHg inclusive and;

- No use of glaucoma medications and;

- ≥ 30% reduction of IOP from baseline

GDD definition of qualified success:

- IOP between 5 and 21 mmHg inclusive

- With/without glaucoma medications

- No requirement for 30% reduction of IOP from baseline

GDD failure definition

- IOP out of target range (5 and 21 mmHg inclusive) six months post GDD insertion

- Removal of implant or further glaucoma surgery (additional insertion of GDD, Cyclodestructive procedure)

- No light perception in the operated eye

Corneal transplantation success definition

- Clear graft without signs of rejection or failure

Corneal transplantation failure definition

- Persistent corneal stromal oedema lasting more than one month despite maximal steroid therapy

- Graft vascularization/opacification

Episodes of graft rejection were diagnosed at a minimum of one month post corneal transplantation. This required evidence of improvement in graft clarity with steroid therapy.

Combined surgical success was defined using both GDD qualified success and corneal transplantation success criteria. The follow up time points were taken with respect to the most recent procedure performed, either GDD insertion or keratoplasty.

Data collection, analysis and storage

All data collected from patient records was of an electronic nature. Two data sheets were created. The first one contained Medical

Record Numbers (MRN) of study patients against a unique numerical identifier (i.e. patient study number). The second sheet contained the collected data stored with respect to their patient study number. The two data sheets were stored in a non-portable computer at the Sydney Eye Hospital. Computer and file access were password protected. Transportation of data was necessary when recording data from private patients seen during follow-up at Save Sight Institute. Collected data was de-identified and recorded against patient numerical identifier only. An encrypted USB drive key was used to transport data from the two sites where they were entered into the non-portable computer (second sheet) for storage. After this, data from USB was erased securely.

Collected data was collated and statistically analyzed using Microsoft Excel software (2013). Data analysis was centred on GDD surgical success and corneal transplantation failure rates with the different insertion sites and corneal graft types. IOP and number of glaucoma medications were used as primary and secondary markers for glaucoma surgery success. Graft clarity and BCVA were used as primary and secondary markers for graft success respectively. Absolute success rates for GDD insertions and corneal transplantation followed by combined success rates were studied. Grouped analysis involving previous glaucoma surgeries, lens status, glaucoma subtype and corneal pathology was performed. The mean period of follow-up, order of and time between GDD insertion and corneal transplantation, GDD tube method of occlusion and time between graft insertion/rejection/failure. A paired/unpaired Student t test was used to compare two groups where a p value of <0.05 was considered statistically significant.

As part of the ethics approval, data in the non-portable computer will be stored securely for a further five years after study completion and then securely destroyed. The study investigators will be responsible for data safekeeping.

Surgical methods and postoperative care

GDD insertion: The majority of GDDs used in this study were non-valved, Baerveldt implants (BGI, Single Plate Silicone 101-350 mm^2, Pars Plana Silicone 102-350 mm^2). There was only one Molteno implant that was included in the study (MGDD, Double Plate Polypropylene R2/L2 274 mm^2).

AC-BGI: A conjunctival periotomy is performed near the fornix or limbus to create space for insertion of GDD plate. Corneal/scleral stay sutures are placed to improve exposure of the working quadrant. Dissection is performed to identify and isolate the lateral rectus and superior rectus extraocular muscle. The implant tube is irrigated using a 30-gauge cannula with balanced salt solution to ensure patency. Next the BGI is inserted in between and under the two rectus muscles. A ripcord stent consisting of 3/0 nylon is sometimes introduced through the implant lumen. A 6/7/8-0 Vicryl ligature suture is placed to form a watertight seal around the tube (+/- stent). The implant is then secured to the sclera with two 8/9/10-0 nylon sutures. A 23/24/25-gauge needle is used to form the tract into the AC where the tube is then placed with insertion forceps until it overlies the iris without any evidence of corneal touch. Venting slits along the implant tube anterior to the ligature site are sometimes performed using a needle or a knife to facilitate quicker IOP control postoperatively. The implant and tube is covered with either a scleral/corneal patch graft which is then secured with 8-0 nylon or Vicryl sutures. The conjunctiva is closed with 9/10-0 Vicryl and/or nylon sutures in a single layer. At the end of the operation, the implant plate, intraocular tube location and patch graft is checked to see if they are in good position. Conjunctiva is checked for leaks and buttonholes using fluorescein drops.

CS-BGI: Insertion of the implant tube into the ciliary sulcus requires the patient to be pseudophakic prior to tube placement. The surgical steps are essentially the same to insert the BGI into the AC, except that the surgeon enters with the needle more posteriorly through the sclera and aims for the ciliary sulcus. Alternatively an ab-interno approach is used to create the tract: the needle is passed into the inferior cornea, passed across the IOL, into the sulcus and out through the sclera.

PP-BGI: The insertion of the BGI into the PP requires the patient to have a concurrent (or prior) vitrectomy. PP BGIs inserted in this study had undergone concurrent 23-gauge three-port pars plana vitrectomy (TPPV) and used the Hoffman Elbow device (Advanced Medical Optics, Inc. Santa Ana, CA, USA) mounted onto the implant for tube introduction into the posterior chamber.

Mitomycin C (MMC 0.25 mg/ml) is sometimes used prior to BGI insertion. A 6 mm by 4 mm cotton soaked with MMC is placed in the implantation area for 2 to 5 minutes before irrigation of MMC is performed with 200 ml of balanced salt solution. The GDD is then implanted as per the steps outlined in the previous paragraphs.

GDD postoperative care: Subconjunctival cephalothin, dexamethasone and topical chloramphenicol were administered before the eye was padded and a shield applied. All glaucoma medication was ceased perioperatively and restarted as needed postoperatively. Topical dexamethasone and chloramphenicol was administered four times a day. Patients were followed-up according to the schedule mentioned earlier.

Corneal transplantation: The surgical methods for corneal transplantation vary depending on the type of graft transplanted. The first step is the preparation of the donor tissue according to the type of graft required.

PK: Once the donor tissue is prepared, a full thickness trephination of the recipient cornea is performed between 7 to 8.5 mm in diameter. Next, a donor corneal button 0.25 to 0.5 mm larger than the recipient site is inserted with the endothelial side down. This is sutured into position with 10-0 nylon using interrupted and/or running sutures.

DALK: The donor tissue is first prepared by removing Descemet's membrane and endothelium by swabbing the posterior corneal surface of the donor with dry cellulose sponges or by physical removal with forceps. Next, a corneal button is punched out from the prepared donor tissue. Then, a suction trephine is used to cut into two-thirds of the recipient anterior corneal surface. Dissection to Descemet's membrane is performed in conjunction with either intrastromal air injection, hydro-delamination with balanced salt solution or viscoelastic dissection as a means to separate and visualize the stromal-Descemet's membrane interface. The graft is secured with 10-0 nylon and a bandage contact lens applied at the end of the case.

DSEK/DMEK: Anterior lamellar dissection of the donor graft (anterior 80% for DSEK, anterior 95% for DMEK) is performed prior by the Lions NSW Eye Bank (Lions Clubs NSW-ACT Save Sight and Health Care). Donor graft is then trephined. A 5 mm tunneled scleral incision is performed. Air is introduced into the AC and the endothelium and Descemet's membrane stripped using a reverse Sinskey Hook. Donor graft is slightly dehydrated with spears, VisionBlue (DORC, Dutch Ophthalmic, USA) is then applied to ensure endothelium side is facing downwards before graft folded and transplanted. Air bubble is then injected into the AC to facilitate unfolding and provide support to the graft. Main wound is then closed with 10-0 nylon suture.

Corneal transplantation postoperative care: Subconjunctival

cephalothin, dexamethasone and topical chloramphenicol are administered before the eye is padded and a shield applied. Patients are required to lie on their back after surgery for one to two day(s) if DSEK/DMEK graft had been performed. Steroid eye drops are administered every two hours for the first day tapering to four times daily at time of hospital discharge. Chloramphenicol eye drops are also given four times a day for prophylaxis cover.

In the event of graft rejection or complication, additional antibiotics/antifungals, oral/intravenous steroids and anti-inflammatories may have to be given. They may also require hospital admission for intensive eye drops or further surgery such as graft resuturing. Patients are managed accordingly and then followed-up according to the schedule mentioned earlier.

Results

41 eyes were identified using the search criteria outlined earlier. 16 eyes were excluded as they did not meet the selection criteria and/or did not have a minimum of one year follow-up data. 4 patients were private patients, 4 patients had GDD inserted prior to 2006, 3 patients were from overseas and had incomplete follow up, 3 patients only had GDD insertion but no keratoplasty and 2 patients had their initial GDD inserted elsewhere (not Sydney Eye Hospital). A total of 25 eyes from 25 patients were included in the final analysis. Table 1 displays the patient demographic data. The mean age at GDD insertion and keratoplasty

was 60 years and 59 years respectively. Of the 25 eyes, 13 were left eyes and 12 were right eyes. 16 out of the 25 patients were male and nine were female. The most common glaucoma diagnosis was secondary phacomorphic and secondary angle-closure glaucoma. Nine eyes had trabeculectomy with MMC and six eyes had cyclodiode laser therapy prior to GDD insertion. 19 eyes were pseudophakic prior to GDD insertion.

Tables 2-4 show the GDD operative data. Nine eyes had GDD insertion prior to keratoplasty and 16 eyes had GDD insertion after keratoplasty. No one had combined keratoplasty and GDD insertion. The overall mean follow-up period for patients in the study was 5.48 years.

The Baerveldt glaucoma implant (BGI) was inserted in 24 eyes. The remaining one eye had a Molteno glaucoma drainage device (MGDD) inserted. The majority of the GDDs were inserted in the AC (56%) followed by PP (36%) and in the CS (8%). Non-valved GDD occlusion method was performed either with external ligature only (44%) or in combination with an intralumenal stent (56%). Only one eye had perioperative application of MMC.

Table 5 displays the corneal graft data. The most common indication for keratoplasty was Pseudophakic Bullous Keratopathy (PBK) (44%). Of the total number of corneal grafts performed, 15 (60%) were PK, 8 (32%) were DSEK, 1 (4%) DMEK and 1 (4%) DALK.

GDD data is shown in Tables 6-8. Table 6 displays the IOP changes for the three different insertion sites (AC, CS, PP). IOP decreased postoperatively at all three sites with the CS group experiencing the largest IOP drop at six months (63%) when compared to baseline. CS: Pre-Op IOP 32.5 mmHg Post-Op 3 month IOP 15 mmHg, p=0.09, 6 month 12.5 mmHg, P=0.16, 12 month 21.5 mmHg, p=0.40. Although

	N	%
Patient Age Range at Study (mean $\pm$ SD)	27 - 90 (65 $\pm$ 15.6)	
Age range at GDD insertion (mean $\pm$ SD)	24 - 81 (60 $\pm$ 14.9)	
Age range at Corneal Transplant (mean $\pm$ SD)	23 - 82 (59 $\pm$ 15.9)	
Left eye	13	52%
Right eye	12	48%
Sex		
Male	16	64%
Female	9	36%
Glaucoma type (Prior to GDD insertion)		
Primary (Pseudoexfoliative)	3	12%
Primary (Angle-Closure)	3	12%
Primary (Open-Angle)	1	4%
Secondary (Angle-Closure)	4	16%
Secondary (Drug-induced)	3	12%
Secondary (Traumatic)	3	12%
Secondary (Phacomorphic)	4	16%
Secondary (Miscellaneous/Toxic)	1	4%
Secondary (Uveitic)	1	4%
Secondary (Neovascular)	1	4%
Developmental (Congenital Aniridia)	1	4%
Previous Glaucoma Surgery		
Trabeculectomy	9	36%
No trabeculectomy	16	64%
Cataract extraction before GDD		
Yes	19	76%
No	6	24%
Previous laser		
Cyclodiode	6	24%
No laser	19	76%

Table 1: Patient Demographic Data.

First	No. Eyes	%	Time between Procedures
GDD	9	36.0%	2.3 years
Corneal Transplant	16	64.0%	1.9 years

Table 2: Order of GDD and Corneal Transplant.

GDD prior to Transplant	5.0 years
GDD following Transplant	5.8 years
Overall	5.5 years

Table 3: Mean period of follow-up.

	No. Eyes	%
Type of Glaucoma Drainage Device		
Baerveldt + scleral patch	24	96.0%
Molteno + scleral patch	1	4.0%
Anatomical Entry Site		
AC	14	56.0%
CS	2	8.0%
PP	9	36.0%
External ligature only	11	44.0%
Combined intraluminal 3/0 nylon with external ligature	14	56.0%
Perioperative Medications		
Cephalothin/Dexamethasone only	22	88.0%
Vancomycin/Dexamethasone	1	4.0%
Oral Prednisolone/Cephalothin/Dexamethasone	1	4.0%
MMC/Cephalothin/Dexamethasone	1	4.0%

Table 4: Glaucoma Drainage Device Surgical Information.

	No. Eyes	%
Pre-Transplant Corneal Diagnosis		
PBK	11	44.00%
ICE Syndrome	2	8.00%
ABK (Aphakic Bullous Keratopathy)	1	4.00%
Recurrent Epithelial Ingrowth	2	8.00%
Keratoconus	2	8.00%
Failed PK (Corneal Ulcer)	2	8.00%
Crystalline Keratopathy	1	4.00%
Failed DSEK (PBK Fuchs endothelial dystrophy)	1	4.00%
Stromal Scar	1	4.00%
Corneal Blood Stain	1	4.00%
Corneal Ulcer	1	4.00%
Transplant Type		
PK	15	60.00%
DSEK	8	32.00%
DMEK	1	4.00%
DALK	1	4.00%

Table 5: Corneal Transplant Surgical Information.

Anatomical Entry Site	Pre-Op (n=25)	Post-Op Month 3 (n=25)	Post-Op Month 6 (n=24)	Post-Op Year 1 (n=23)	Post-Op Year 2 (n=20)	Post-Op Year 3 (n=15)	Post-Op Year 4 (n=13)	Post-Op Year 5 (n=10)
AC	24.9 (n=14)	14.4* (n=14)	15.5* (n=14)	11.2* (n=13)	14.8 (n=11)	17.4 (n=7)	13.1 (n=7)	10.5 (n=6)
CS	32.5 (n=2)	15.0 (n=2)	12.5 (n=2)	21.5 (n=2)	15.5 (n=2)	11.0* (n=2)	11.0 (n=1)	6.0 (n=1)
PP	25.9 (n=9)	14.6* (n=9)	12.8* (n=8)	13.9* (n=8)	16.4* (n=7)	14.7* (n=6)	12.6* (n=5)	10.0* (n=3)
All	**25.8**	**14.5***	**14.3***	**13.0***	**15.5***	**15.5***	**12.8***	**9.9***

*p<0.05 considered statistically significant relative to baseline.

Table 6: GDD - Mean Intraocular Pressure for each GDD Anatomical Entry Site.

Anatomical Entry Site	Pre-Op (n=25)	Post-Op Month 3 (n=25)	Post-Op Month 6 (n=24)	Post-Op Year 1 (n=23)	Post-Op Year 2 (n=20)	Post-Op Year 3 (n=15)	Post-Op Year 4 (n=13)	Post-Op Year 5 (n=10)
AC	3.6 (n=14)	1.3* (n=14)	0.8* (n=14)	0.6* (n=13)	1.0* (n=11)	1.8* (n=7)	2.3 (n=7)	2.2 (n=6)
CS	4.5 (n=2)	0.0 (n=2)	1.0 (n=2)	0.5* (n=2)	1.5 (n=2)	0.5 (n=2)	0.0 (n=1)	0.0 (n=1)
PP	3.9 (n=9)	0.9* (n=9)	1.4* (n=8)	1.3* (n=8)	1.0* (n=7)	0.7* (n=6)	0.0* (n=5)	0.3* (n=3)
All	**3.8**	**1.0***	**1.0***	**0.8***	**1.1***	**1.1***	**1.2***	**1.4***

*p<0.05 considered statistically significant relative to baseline.

Table 7: GDD - Mean No. of Glaucoma Medications for each GDD Anatomical Entry Site.

Anatomical Entry Site	Pre-Op (n=25)	Post-Op Month 3 (n=25)	Post-Op Month 6 (n=24)	Post-Op Year 1 (n=23)	Post-Op Year 2 (n=20)	Post-Op Year 3 (n=15)	Post-Op Year 4 (n=13)	Post-Op Year 5 (n=10)
AC	1.11 (n=14)	1.49 (n=14)	1.11 (n=14)	1.37 (n=13)	1.92 (n=11)	1.64 (n=7)	2.53* (n=7)	1.66 (n=6)
CS	0.50 (n=2)	0.47 (n=2)	0.60 (n=2)	0.65 (n=2)	0.65 (n=2)	1.02 (n=2)	2.00 (n=1)	1.18 (n=1)
PP	1.45 (n=9)	1.50 (n=9)	1.48 (n=8)	2.05* (n=8)	2.25* (n=7)	2.55* (n=6)	2.21* (n=5)	1.87* (n=3)
All	**1.19**	**1.41**	**1.19**	**1.55**	**1.91**	**1.92***	**2.37***	**1.67***

*p<0.05 considered statistically significant relative to baseline.

Table 8: GDD - Mean LogMAR for each GDD Anatomical Entry Site.

the CS-GDD results were not statistically significant, there was a relatively large decrease in IOP and it is most likely explained by the very small number of cases (n=2). IOP reduction at three, six and 12 month follow-up was statistically significant in the AC and PP groups only. AC: Pre-Op IOP 24.9 mmHg Post-Op 3 month IOP 14.4 mmHg, P=0.03, 6 month 15.5 mmHg, p=0.001, 12 month 11.2 mmHg, p=0.0003. PP: Pre-Op IOP 25.9 mmHg Post-Op 3 month IOP 14.6 mmHg, P=0.02, 6 month 12.8 mmHg, p=0.02, 12 month 13.9 mmHg, p=0.003. There was no statistical significance when comparing the percentage of IOP reduction between the three insertion sites at six months and 1 year. AC/PP: IOP reduction from baseline Post-Op 6 month p=0.81, 12 month p=0.43. AC/CS: IOP reduction from baseline Post-Op 6 month p=0.29, 12 month p=0.56. PP/CS: IOP reduction from baseline Post-Op 6 month p=0.37, 12 month p=0.75. Overall mean IOP preoperatively was 25.8 mmHg. At six months and 12 months postoperatively, overall IOP was 14.3 mmHg and 13.0 mmHg respectively.

Table 7 shows the mean number of glaucoma medications for each GDD insertion site. The overall mean number of preoperative glaucoma medications was 3.8. There was a decrease in glaucoma medication requirements at all GDD insertion sites at six months and 12 months of follow-up. AC: pre-Op number of medications=3.6; Post-Op 6 month number of medications=0.8, p=0.000001; 12 month=0.6, p=0.000002. PP: Pre-Op number of medications=3.9; Post-Op 6 month number of medications=1.4, p=0.03; 12 month=1.3, p=0.004. CS: Pre-Op number of medications=4.5; Post-Op 6 month number of medications=1.0, p=0.26; 12 month=0, p=0.0008. The AC group then experienced an increase in the number of glaucoma medications at two, three and four years but remained below preoperative values.

Table 8 shows the visual acuity with the different GDD insertion sites. VA deteriorated with all three insertion sites (p=0.06) with the PP group resulting in the worst decrease in visual acuity at 12 months (P=0.02). The CS group had the least decrease in visual acuity at 12 months postoperatively (p=0.50). AC group showed a decrease in VA at 12 months postoperatively as well but this was not statistically significant (P=0.48).

Figures 1-3 are graphical representations of mean GDD IOP, mean number of medications and mean VA over the five year follow-up period.

Tables 9 and 10 show the corneal transplant data.

Table 9 shows the mean IOP values for each graft type. There was no significant difference in the preoperative and postoperative IOP between corneal graft types. PK: Pre-Op IOP=17.9 mmHg; Post-Op 6 month IOP=18.4 mmHg, p=0.95; 12 month=16 mmHg, p=0.43. DSEK: Pre-Op IOP=19 mmHg; Post-Op 6 month IOP=16.7 mmHg, p=0.39; 12 month=21.1 mmHg, p=0.62.

Table 10 shows the pre-and post-keratoplasty visual acuity. Visual acuity at three months postoperatively was most improved in the DMEK group (n=1) followed by the DSEK group (n=8). However this was not statistically significant (DSEK: Pre-Op LogMAR=1.88; Post-Op 3 month=1.54, p=0.63. No statistically significant improvement was seen in VA at 12 months post-keratoplasty for DSEK (p=0.77). Visual acuity for PK group was better than baseline and plateaued with follow-up. VA improvement for PK was shown to be statistically significant at six months postoperatively (p=0.04). The overall improvement of visual acuity for all graft types was not statistically significant at three, six and 12 months post-keratoplasty (p= 0.08, 0.05, 0.08 respectively).

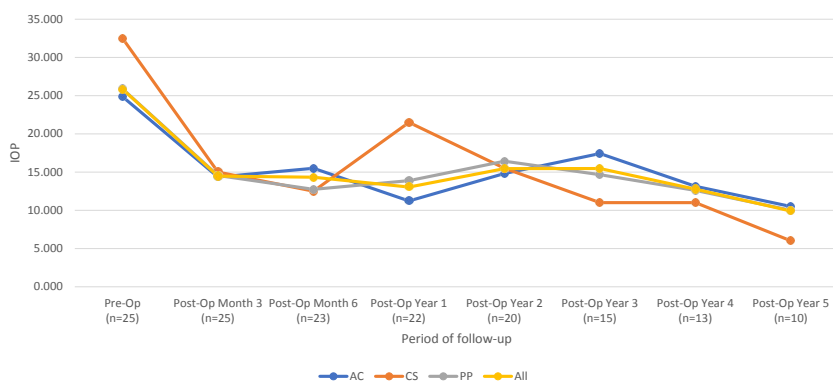Figures 4 and 5 are graphs displaying mean IOP and mean VA with

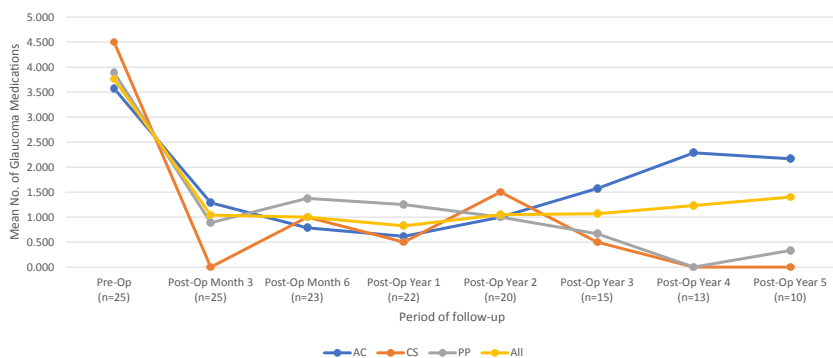**Figure 1:** GDD - Mean IOP for each GDD Anatomical Entry Site.

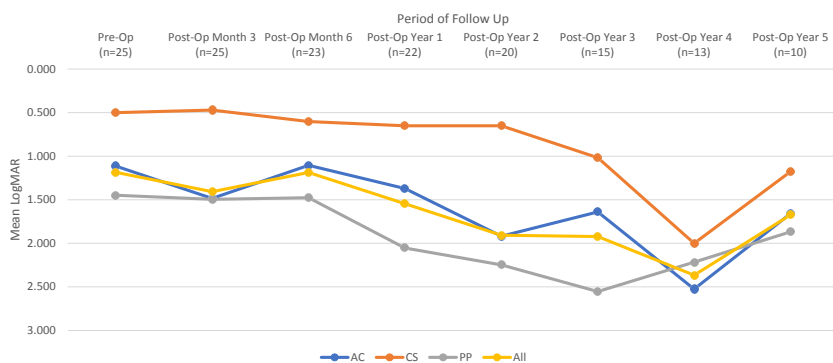**Figure 2:** GDD - Mean No. of Glaucoma Medications for each GDD Anatomical Entry Site.

Figure 3: GDD - Mean LogMAR for each GDD Anatomical Entry Site.

respect to the various corneal grafts over the five year follow-up period.

Tables 11 and 12 show the complete and qualified success rates post GDD insertion. Complete success rate for GDD insertion was 29.2% and 25% at six months and 12 months respectively. There were no complete GDD successes by the third year of follow-up. 95.8% of GDD insertions were qualified success at six months and 79.2%, 71.3%, 71.3% were qualified success at one year, three years and five years respectively.

Figure 6 shows Kaplan-Meier survival plots of qualified and complete GDD success rate.

The corneal graft success rate is shown in Table 13. Corneal graft success rate was 83.3%, 79.2%, 44.5% and 26.7% at six months, one year, three years and five years respectively.

Figure 7 shows the Kaplan-Meier survival plots for corneal transplantation success rate.

Table 14 shows the combined surgical success rate of qualified GDD insertion with corneal transplant. Combined success rate for both procedures was 91.3% and 82.6% at six months and 12 months postoperatively. Success rate fell to 60.1% by year three and remained unchanged till the fifth year of follow-up.

Figure 8 is the Kaplan-Meier survival plot for combined surgical success rate for GDD insertion (qualified success) and corneal transplantation.

The individual combined surgical success rates for GDD insertion and corneal transplantation are shown in Table 15. At six months and 12

months postoperatively, the AC-DALK group was observed to be most successful but this was only based on one eye. CS-DSEK combination also had high surgical success rates but this was based on two eyes only.

Transplant Type	Pre-Op (n=25)	Post-Op Month 3 (n=22)	Post-Op Month 6 (n=23)	Post-Op Year 1 (n =24)	Post-Op Year 2 (n=20)	Post-Op Year 3 (n=18)	Post-Op Year 4 (n=15)	Post-Op Year 5 (n=10)
PK	17.9 (n=15)	15.4 (n=14)	18.4 (n=14)	16.0 (n=15)	17.5 (n=15)	14.6 (n=14)	14.4 (n=12)	12.5 (n=8)
DALK	15.0 (n=1)	32.0 (n=1)	19.0 (n=1)	6.0 (n=1)	N/A	N/A	N/A	N/A
DSEK	19.0 (n=8)	15.7 (n=7)	16.7 (n=7)	21.1 (n=7)	12.5 (n=4)	17.0 (n=4)	15.7 (n=3)	10.5 (n=2)
DMEK	13.0 (n=1)	10.0 (n=1)	13.0 (n=1)	9.0 (n=1)	11.0 (n=1)	N/A	N/A	N/A
All	**17.9**	**16.0**	**17.7**	**16.80**	**16.2**	**15.2**	**14.7**	**12.1**

Table 9: Corneal Transplant - Mean Intraocular Pressure for each Transplant Type.

Transplant Type	Pre-Op (n=25)	Post-Op Month 3 (n=22)	Post-Op Month 6 (n=23)	Post-Op Year 1 (n =24)	Post-Op Year 2 (n=21)	Post-Op Year 3 (n=17)	Post-Op Year 4 (n=15)	Post-Op Year 5 (n=10)
PK	2.30 (n=15)	1.64 (n=14)	1.60* (n=14)	1.65 (n=15)	1.80 (n=15)	1.88 (n=14)	1.70 (n=12)	1.41 (n=8)
DALK	2.00 (n=1)	3.00 (n=1)	0.78 (n=1)	3.00 (n=1)	N/A	N/A	N/A	N/A
DSEK	1.88 (n=8)	1.54 (n=7)	1.92 (n=7)	1.60 (n=7)	1.31 (n=4)	1.65 (n=4)	1.29 (n=3)	1.24 (n=2)
DMEK	3.00 (n=1)	0.48 (n=1)	0.60 (n=1)	0.60 (n=1)	0.60 (n=1)	N/A	N/A	N/A
All	**2.19**	**1.62**	**1.62**	**1.65**	**1.64**	**1.83**	**1.62**	**1.37**

*$p<0.05$ considered statistically significant relative to baseline.

Table 10: Corneal Transplant - Mean LogMAR for each Transplant Type.

PP-PK, AC-PK and AC-DSEK combinations were similarly successful at six months and one year postoperatively ($\geq 80\%$). However, after three years postoperatively, PP-PK had better combined success rate than AC GDDs.

Table 16 shows the surgical success rates when GDD insertion was prior to corneal graft. Table 17 shows the surgical success rates when corneal graft was performed prior to GDD insertion. The 12 month surgical success rate of GDD insertion performed prior to corneal transplantation was 78% while GDD insertion post-keratoplasty was 75%. This result was not statistically significant (6 months $p=0.53$, 12 months $p=0.47$).

Table 18 displays the previous ocular procedures prior to GDD insertion. Patient's gender, glaucoma subtype and method of occlusion for the BGI (non-valved) are also shown.

There were more qualified GDD successes in eyes with no prior trabeculectomy surgery and previous cataract surgery prior to GDD insertion. 63% of qualified GDD successes in year one and 78% in year three had no previous trabeculectomy. 74% of qualified GDD success in year one and 89% in year three had previous cataract surgery. In terms of qualified GDD success rate, both of these procedures were not statistically significant (no trabeculectomy 1 year $p=0.23$, 3 years $p=0.35$; cataract surgery 1 year $p=0.39$, 3 years $p=0.43$).

About 89% of eyes with qualified GDD success at six months and 78% at 12 months had no previous cyclodestructive procedures. This result was not statistically significant (6 months $p=0.17$, 12 months $p=0.06$).

Results based on gender and glaucoma subtype pre-GDD insertion were also not statistically significant (1 year $p=0.45$ and $p=0.38$ respectively).

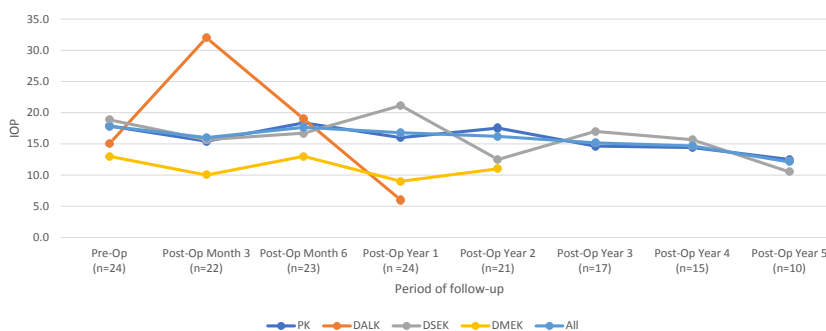Of the 14 eyes who had combined intraluminal stent and external

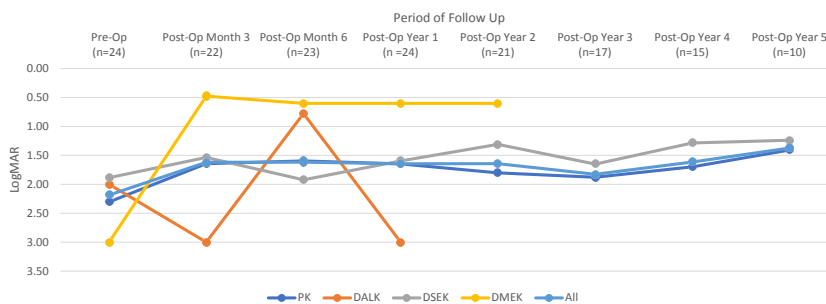**Figure 4:** Corneal Transplant - Mean IOP for each Transplant Type.

Figure 5: Corneal Transplant - Mean LogMAR for each Transplant Type.

	6 months			1 year			3 year			5 year		
	Success (KM%)	Failure	N/A	Success (KM %)	Failure	N/A	Success (KM %)	Failure	N/A	Success (KM %)	Failure	N/A
Total (n=25)	7 (29.2%)	17	1	6 (25%)	18	1	0 (0%)	15	10	0 (0%)	11	14

Table 11: Complete GDD Success Rate.

	6 months			1 year			3 year			5 year		
	Success (KM %)	Failure	N/A	Success (KM %)	Failure	N/A	Success (KM %)	Failure	N/A	Success (KM %)	Failure	N/A
Total (n=25)	23 (95.8%)	1	1	19 (79.2%)	5	1	9 (71.3%)	6	10	7 (71.3%)	4	14

Table 12: Qualified GDD Success Rate.
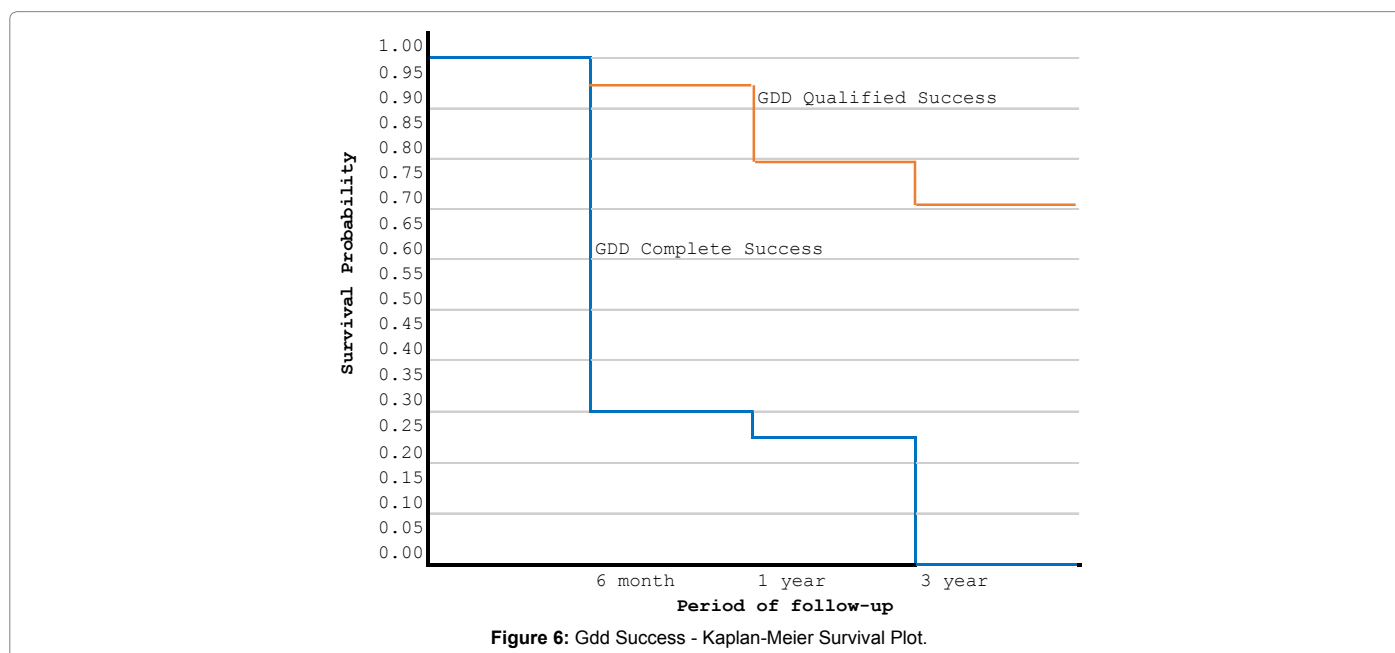
Figure 6: Gdd Success - Kaplan-Meier Survival Plot.

	6 months			1 year			3 year			5 year		
	Success (KM %)	Failure	N/A	Success (KM %)	Failure	N/A	Success (KM %)	Failure	N/A	Success (KM %)	Failure	N/A
Total (n=25)	20 (83.3%)	4	1	19 (79.2%)	5	1	9 (44.5%)	10	6	3 (26.7%)	7	15

Table 13: Corneal Transplant Success Rate.

	6 months			1 year			3 year			5 year		
	Success (KM %)	Failure	N/A	Success (KM %)	Failure	N/A	Success (KM %)	Failure	N/A	Success (KM %)	Failure	N/A
Total (n=25)	21 (91.3%)	2	2	19 (82.6%)	4	2	8 (60.1%)	6	11	4 (60.1%)	3	18

Table 14: Combined Success Rate for GDD and Corneal Transplant.

ligature, 12 (86%) and 11 eyes (79%) were qualified successes at six and 12 months respectively. Of the 11 eyes who only had external ligature as the method of occlusion, 11 (100%) and eight eyes (73%) were qualified successes at six and 12 months respectively. There was no statistical difference between both groups at six and 12 months (p=0.17 and p=0.25 respectively).

The number of qualified successful GDD insertions by anatomical site is shown in Table 19. The overall qualified GDD success rate is 92%

and 76% at six and 12 months respectively (from GDD insertion). PP-GDDs had better qualified GDD success rate overall compared to AC-GDDs. However, only the results from year three postoperatively were statistically significant (1 year p=0.30, 3 years p=0.04). There were only two CS-GDDs inserted.

Corneal graft success was based largely on the appearance of a clear graft during follow-up. Table 20 shows number of successful corneal transplant by graft type. The overall graft success rate was 83.3% and
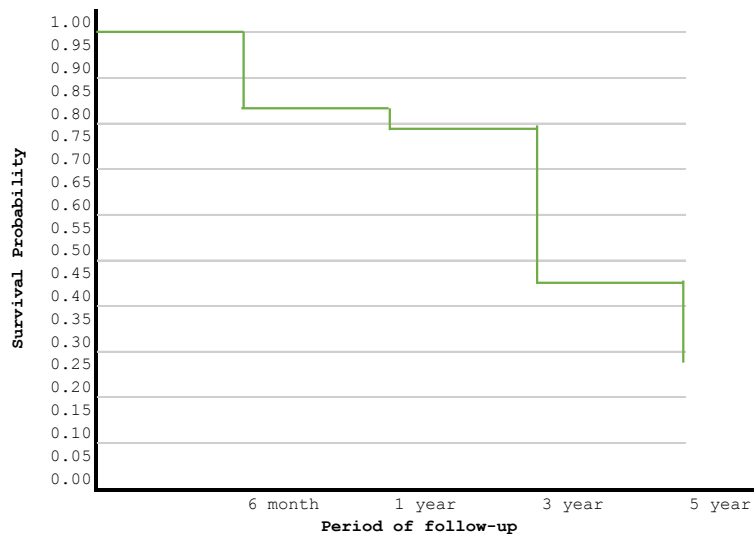
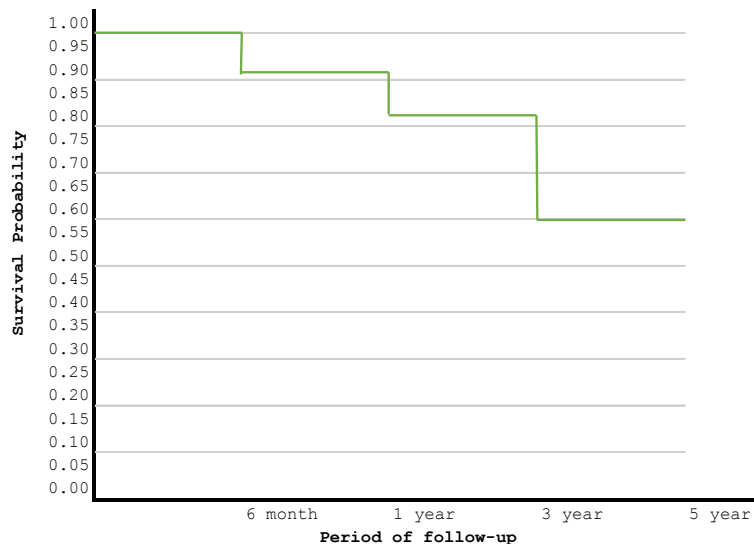**Figure 7:** Corneal Transplant - Kaplan-Meier Survival Plot.

Figure 8: Combined GDD and Corneal Transplant - Kaplan-Meier Survival Plot.

GDD Anatomical entry site	Transplant type	N	6 month combined success	1 year Combined success	3 year Combined success	5 year Combined success
AC	PK	7	86% (6)	86% (6)	14.3% (1)	0% (0)
AC	DALK	1	100% (1)	100% (1)	N/A	N/A
AC	DSEK	5	80% (4)	80% (4)	20% (1)	N/A
AC	DMEK	1	0% (0)	0% (0)	N/A	N/A
CS	DSEK	2	100% (2)	50% (1)	50% (1)	50% (1)
PP	PK	8	100% (8)	88% (7)	37.5% (5)	38% (3)
PP	DSEK	1	N/A	N/A	N/A	N/A
Total		25	21	19	8	4

Table 15: Combined Success Rate for GDD and Corneal Transplant (Insertion Site/Graft Type).

Anatomical Entry Site	Transplant Type	N	Days in between	Pre-Op LogMAR	Pre-Op IOP	6 mth LogMAR	6 mth IOP	Combined Success (n)	12mth logMAR	12 mth IOP	Combined Success (n)
AC	PK	4	760	0.62	18.8	1.33	13.5	100% (4)	1.87	11.3	100% (4)
AC	DSEK	4	785	0.97	29.5	0.95	13.0	75% (3)	0.92	12.8	75% (3)
AC	DMEK	1	1471	0.48	14.0	0.54	14.0	0% (0)	0.0	8.0	0% (0)
All GDD first		**9**	**850**	**0.76**	**23.0**	**1.07**	**13.3**	**78% (7)**	**1.16**	**11.6**	**78% (7)**

Table 16: Combined Success Rate for GDD Insertion First.

Transplant Type	Anatomical Entry Site	N	Days in between	Pre-Op LogMAR	Pre-Op IOP	6 mth LogMAR	6 mth IOP	Combined Success (n)	12mth logMAR	12 mth IOP	Combined Success (n)
PK	AC	3	1010	1.80	15.3	0.78	26.3	67% (2)	0.75	13.0	67% (2)
PK	PP	8	785	1.77	18.9	1.38	16.3	100% (8)	1.69	17.9	88% (7)
DALK	AC	1	10	2.00	15.0	0.78	19.0	100% (1)	3.00	6.0	100% (1)
DSEK	AC	1	370	1.30	42.0	2.00	28.0	100% (1)	2.00	22.0	100% (1)
DSEK	CS	2	530	0.74	18.5	0.29	21.0	100% (2)	0.29	29.5	50% (1)
DSEK	PP	1	583	3.00	12.0	4.00	12.0	N/A	3.00	24.00	N/A
All Graft first		**16**	**709**	**1.71**	**18.9**	**1.22**	**18.2**	**88% (14)**	**1.52**	**18.3**	**75% (12)**

Table 17: Combined Success Rate for Corneal Transplant First.

	6 months	1 year	3 years	5 years
	Qualified Success (%)	Qualified Success (%)	Qualified Success (%)	Qualified Success (%)
Total (n=25)	23	19	9	7
Pre-GDD procedures				
Trabeculectomy (n=9)	8 (88.9%)	7 (77.8%)	2 (22.2%)	2 (22.2%)
No Trabeculectomy (n=16)	15 (93.8%)	12 (75.0%)	7 (43.8%)	5 (31.3%)
Pseudophakic (n=19)	18 (94.7%)	14 (73.7%)	8 (42.1%)	6 (31.6%)
Phakic (n=6)	5 (83.3%)	5 (83.3%)	1 (16.7%)	1 (16.7%)
Cyclodiode (n=6)	5 (83.3%)	2 (33.3%)	2 (33.3%)	1 (16.7%)
No Cyclodiode (n=19)	18 (94.7%)	17 (89.5%)	7 (36.8%)	6 (31.6%)
Gender				
Male (n=16)	15 (93.8%)	12 (75.0%)	5 (31.3%)	5 (31.3%)
Female (n=9)	8 (88.9%)	7 (77.8%)	4 (44.4%)	2 (22.2%)
Glaucoma subtype				
Primary (n=8)	8 (100%)	6 (75.0%)	3 (37.5%)	3 (37.5%)
Secondary (n=17)	15 (88.2%)	13 (76.5%)	6 (33.5%)	4 (23.5%)
Method of Occlusion (Intraluminal: 3/0 Nylon) (Extraluminal or Combined: 6/0 Vicryl, 8, 9, 10/0 Nylon)				
6/0 Vicryl	n=0	N/A	N/A	N/A	N/A
8/0 Nylon	n=2	2 (100%)	1 (50%)	1 (50%)	0 (0%)
9/0 Nylon	n=4	4 (100%)	4 (100%)	2 (50%)	2 (50%)
10/0 Nylon	n=5	5 (100%)	3 (60%)	2 (40%)	2 (40%)

3/0 Nylon + 6/0 Vicryl	n=9	7 (77.8%)	7 (77.8%)	3 (33.3%)	2 (22.2%)
3/0 Nylon + 8/0 Nylon	n=1	1 (100%)	1 (100%)	1 (100%)	1 (100%)
3/0 Nylon + 9/0 Nylon	n=3	3 (100%)	2 (66.7%)	0 (0%)	0 (0%)
3/0 Nylon + 10/0 Nylon	n=1	1 (100%)	1 (100%)	0 (0%)	0 (0%)

Table 18: Pre/Perioperative Factors for GDD Insertion.

	6 months	1 year	3 year	5 year
	Qualified Success (%)	Qualified Success (%)	Qualified Success (%)	Qualified Success (%)
Total (n=25)	23 (92%)	19 (76%)	9 (36%)	7 (28%)
GDD type				
AC (n=14)	13 (92.9%)	11 (78.6%)	3 (21.4%)	3 (21.4%)
PP (n=9)	8 (88.9%)	7 (77.8%)	5 (55.6%)	3 (33.3%)
CS (n=2)	2 (100%)	1 (50%)	1 (50%)	1 (50%)

Table 19: Successful GDD Insertions by Anatomical Site.

	6 months	1 year	3 year	5 year
	Success (%)	Success (%)	Success (%)	Success (%)
Total (n=25)	20 (80%)	19 (76%)	9 (36%)	3 (12%)
Graft type				
PK (n=15)	14 (93.3%)	13 (86.7%)	6 (40%)	3 (20%)
DALK (n=1)	1 (100%)	1 (100%)	0 (0%)	0 (0%)
DSEK (n=8)	5 (62.5%)	5 (62.5%)	3 (37.5%)	0 (0%)
DMEK (n=1)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 20: Successful Corneal Transplant by Graft Type.

79.2% at six and 12 months respectively (from corneal transplantation). Although the DALK graft had the highest success rate at year (n=1), PK grafts had the highest graft success rates at three year postoperatively (p=0.28). Overall graft success rate at three and five years was 44.5% and 26.7% respectively.

The mean, range and standard deviation of the number of days between corneal graft to rejection and failure is shown in Table 21. The mean time period between corneal transplantation to rejection (n=12) was 1.45 years (531 days). The mean time period between graft rejections to eventual graft failure was 0.32 years (116 days). The mean time period between corneal transplantation and graft failure was 2.36 years (862 days).

Tables 22 and 23 shows the incidence of complications associated with GDD insertion and corneal grafting respectively.

Hypotony was associated with 24% of the GDD insertions, more so in the PP group (44%). High IOP post GDD insertion was observed in all groups. One eye in the PP and one eye in the CS group had to undergo cyclodiode procedure post-GDD insertion. Corneal decompensation was highest in the AC group (43%) (p=0.19). The overall incidence of corneal decompensation was 32%.

Overall graft rejection was 52%. 57% of the DSEK grafts and 50% of

the PK grafts experienced rejection. PAS findings were slightly higher in DSEK than PK (13% versus 29%). 25% of all PK grafts had to be resutured and 29% of all DSEK grafts had to be repositioned. Graft infection was more common in the PK grafts (25%). There was only one occurrence of graft-related endophthalmitis. PK grafts had higher incidences of astigmatism (6%) and corneal melt and perforation (13%). Graft redo rates were relatively similar between PK (31%) and DSEK (29%).

Discussion

Based on our results, GDD insertion was shown to be an effective method of IOP control in corneal transplant patients. CS-GDDs demonstrated the best clinical outcomes in terms of IOP control, decreased number of glaucoma medications and preservation of visual acuity; however this result was derived from only two cases in this cohort. IOP lowering was similar between the PP-GDD and the AC-GDD group, however AC-GDDs required more medications

	Time from transplant to rejection (days)	Time from rejection to failure (days)	Time from transplant to failure (days)
Range	4 – 1685	7 – 490	11 – 2883
Mean	531	116	862
Standard deviation	±466	±140	±779

Table 21: Time Period between Graft Rejection and Graft Failure.

	AC	CS	PP	TOTAL
	n=14	n=2	n=9	n=25
Hypotony	2 (14%)	0 (0%)	4 (44%)	6 (24%)
Choroidal effusion	1 (7%)	0 (0%)	1 (11%)	2 (8%)
Elevated IOP	2 (14%)	2 (100%)	2 (22%)	6 (24%)
Tube extrusion	1 (7%)	0 (0%)	2 (22%)	3 (12%)
Tube reposition	4 (29%)	0 (0%)	1 (11%)	5 (20%)
Rubeosis	0 (0%)	0 (0%)	1 (11%)	1 (4%)
Lens subluxation	1 (7%)	0 (0%)	0 (0%)	1 (4%)
Posterior capsule opacity	0 (0%)	0 (0%)	1 (11%)	1 (4%)
Diplopia	0 (0%)	0 (0%)	1 (11%)	1 (4%)
Retinal detachment	0 (0%)	0 (0%)	1 (11%)	1 (4%)
Corneal decompensation (Pre-Keratoplasty)	6 (43%)	0 (0%)	2 (22%)	8 (32%)

Table 22: Postoperative GDD Complications.

	PK n=16	DALK n=1	DSEK n=7	DMEK n=1	TOTAL n=25
Graft rejection	8 (50%)	0 (0%)	4 (57%)	1 (100%)	13 (52%)
PAS	2 (13%)	0 (0%)	2 (29%)	1 (100%)	5 (20%)
Graft resuture	4 (25%)	0 (0%)	0 (0%)	0 (0%)	4 (16%)
Graft reposition	0 (0%)	0 (0%)	2 (29%)	0 (0%)	2 (8%)
Wound dehiscence	2 (13%)	0 (0%)	1 (14%)	0 (0%)	3 (12%)
Endophthalmitis	0 (0%)	0 (0%)	1 (14%)	0 (0%)	1 (4%)
Astigmatism	1 (6%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
Corneal epithelial growth	4 (25%)	0 (0%)	0 (0%)	0 (0%)	4 (16%)
Graft infection	4 (25%)	0 (0%)	0 (0%)	0 (0%)	4 (16%)
Corneal melt / perforation	2 (13%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)
Redo graft	5 (31%)	0 (0%)	2 (29%)	0 (0%)	7 (28%)

Table 23: Postoperative Corneal Transplant Complications.

postoperatively compared to the PP-GDD group. PP-GDD insertions were associated with the highest rate of tube complications including hypotony.

Differences in complete versus qualified success

The overall qualified success rate for GDD insertion (with/without keratoplasty) was 95.8% and 79.2% at six and 12 months respectively. AC-GDD and PP-GDD insertions had similar rates of qualified success (93% and 89%) at six months postoperatively. Qualified success for PP-GDDs at three years was higher and statistically significant when compared to AC-GDDs (p=0.04). Qualified success rates may be influenced in part by the IOP-lowering effect of glaucoma medications used postoperatively. The number of medications used post-GDD insertion fell sharply but remained relatively unchanged between three, six and 12 months follow-up, similar to postoperative IOP measurements from that period. This indicated that insertion of GDD had a short-term IOP-lowering effect independent of the effects of glaucoma medication. Our results show 29.2% and 25% complete GDD success rate at six and 12 months follow-up but zero percent success rate after three years postoperatively suggesting that IOP control is possible but may diminish with time. In patients with corneal transplants, it is highly likely that over time maintenance of IOP control requires glaucoma medications as adjunct therapy. This is likely due to multiple factors such as change in aqueous composition with GDD insertion [16] and corneal decompensation [4,17,18].

Visual acuity differences between tube position

Visual acuity decreased postoperatively at all three insertion sites. Visual acuity was best preserved in CS-GDD (n=2) but this could be due to selection bias as the CS-GDD had the best VA preoperatively compared to AC-GDD and PP-GDD. These findings regarding acuity difference are likely largely due to different indications for GDD insertion at the different sites. In this series, PP-GDD insertion was more common in eyes with posterior complications such as retinal detachment and choroidal neovascularization where visual acuity was poorer than that of the CS-GDD and AC-GDD group. 22% of PP-GDDs had pathology of the retina compared to 7% of AC-GDDs. Only

results from PP-GDD insertion were statistically significant for reduced visual acuity (p=0.02).

Differences in complication rates between different tube insertion sites

Corneal decompensation was recorded in 43% of the AC-GDDs (p=0.19 relative to other graft types). AC-GDDs were also shown to have the highest rate of tube repositioning (29%). In our study, corneal decompensation and/or inadequate IOP control despite removal of the intraluminal stent prompted all AC-GDDs to be repositioned to the PP. Corneal decompensation was less common in PP-GDDs (22%) suggesting that there is a background rate of corneal decompensation that occurs with GDD insertion. There was no documented occurrence of corneal decompensation in the two CS-GDD cases. Hypotony was observed most commonly with PP-GDDs (44%). Tube extrusion occurred most commonly in PP-GDDs, which may be due to the design of the Hoffman Elbow device. The device facilitates GDD insertion into the posterior chamber and maintains the tube position so it lies radial and perpendicular with respect to the overlying sclera. Elevated IOP measurements at follow-up visits were noted with all three GDD insertion sites. Depending on insertion site, this could be due to IOP spikes from intermittent tube block from iris/lens touch and vitreous material occluding tube. Both cases of CS-GDD insertions experienced elevated IOP at 12 months postoperatively.

Corneal graft survival with GDD insertion

In this series, AC-GDD with DALK graft (n=1), CS-GDD with DSEK graft (n=2) and PP-GDD with PK graft (n=8) had 100% qualified GDD and corneal graft success rates at six months follow-up. At three years follow-up, PP-GDD with PK graft was shown to be most successful in terms of IOP control and graft survival.

IOP remained largely stable post-keratoplasty. Three month postoperative IOP increase in the DALK graft was due to documented AC-GDD tube blockage. Based on this study, corneal transplantation did not seem to have an impact on IOP. The impact of prophylactic corticosteroid therapy was also found to have not contributed significantly to elevations in IOP. However, this could be due to the prior or subsequent insertion of GDDs and administration of glaucoma medications. GDD insertion prior to corneal transplantation may lead to a blunted steroid response.

Visual acuity was most improved in the CS-GDD with DSEK graft (61%) and AC-GDD with DALK graft (61%) compared to baseline. Overall visual acuity improvement post-keratoplasty was 24.7% and 23.3% at six and 12 months respectively. Graft selection was likely influenced by preoperative visual acuity and pre-transplant corneal diagnosis. Eyes with better visual acuity and eyes with endothelial dystrophy or failure preferentially had endothelial grafts transplanted. Although short-term elevation in IOP has been shown to decrease endothelial cell count [19], the resultant decrease in visual acuity may not manifest until later. The AC-GDD with DMEK graft experienced best visual acuity at three months postoperatively, when IOP was observed to be highest despite medical glaucoma therapy. Based on the limited number of CS-GDD insertions in our study, they experienced better visual acuity outcomes even when in combination with endothelial grafts.

From our results, there was no statistically significant difference in corneal graft success between AC-GDDs (86%, n=14), PP-GDDs (89%, n=9) and CS-GDDs (100%, n=2). AC-GDDs have been hypothesized to result in lower graft survival rates compared to PP-GDDs due to the

potential for development of endothelial cell failure, which has been described in a previous study as the most common cause of corneal graft failure [20]. However, PP-GDD insertion has not been shown to increase graft survival compared to AC-GDD as yet [21]. From our results, endothelial graft survival decreased after the first year postoperatively compared to PK irrespective of GDD insertion site. This finding could be related to late-stage endothelial cell failure and/or long-term effects of GDD insertion on the cornea graft.

The most common GDD insertion site associated with increased graft rejection was in the AC. PP-GDD with DSEK graft was associated with the lowest incidence of graft rejection. From our study, incidence of rejection for DSEK graft was higher than PK graft (57% versus 50%), but this was not statistically significant (p=0.44). Finding of PAS in DSEK grafts also outnumbered that in PK grafts (20% versus 13%). These results are likely distorted by the small sample size as current literature has shown less rejection episodes and astigmatism with endothelial keratoplasty [22,23]. AC-GDD with PK grafts experienced the highest likelihood of needing repeat grafting (31%). Unlike PK repeat grafts where PBK was the most common indication, repeat grafts for DSEK were largely due to graft dislocation. The incidence of DSEK graft dislocation was also highest with AC-GDDs highlighting the potential effects of AC-GDD insertion on the corneal endothelium.

Pre-operative risk factors of GDD insertion

GDD was inserted prior to corneal graft in nine out of the 25 eyes (36%). Corneal graft was performed prior to GDD insertion in 16 out of the 25 eyes (64%). The average time period between GDD insertion to corneal transplantation was 2.3 years. The average time period between corneal transplantation to GDD insertion was 1.9 years. 12 months combined qualified GDD success rates and corneal graft success rates were similar for both GDD-first and graft-first (78% and 75% respectively). As a single group looking at combined success rates, results from AC-GDD insertions were not statistically significant as well when corneal transplant was performed prior to GDD-insertion at 12 months (p=0.38). Previous studies have reported that GDD insertion prior to corneal grafting had led to decreased medication postoperatively and better graft survival [24]. This study was unable to elicit a significant difference between the two groups which may relate to the relatively small sample size.

All GDD insertions prior to keratoplasty were AC-GDDs. In phakic patients without pre-existing corneal pathology, AC-GDDs are still currently regarded as the default GDD insertion site as it requires less time and is a familiar procedure to most surgeons. Furthermore, there is no need for the patient to be pseudophakic (CS) or have a prior or concurrent vitrectomy (PP).

Although there were also more men (n=16) than women (n=9) in this study, it isn't clear why this was the case.

Pseudophakia was not associated with increased GDD qualified success rate (compared to no previous cataract surgery) (73.7% versus 83.3% at 12 months, p=0.39).

Results from no previous trabeculectomy (compared to trabeculectomy) (75% versus 77.8% at 12 months) were not statistically significant (p=0.23) in terms of qualified GDD success. However, postoperative mean IOP was lower in the eyes with previous trabeculectomy than eyes with no prior trabeculectomy (p=0.005 at 12 months). The decreased mean IOP in eyes with prior trabeculectomy may represent some of these eyes having partially functioning trabeculectomies.

Qualified success rates based on no cyclodestructive procedures prior to GDD insertion (compared to cyclodestructive procedure) (89.5% versus 33.3% at 12 months, p=0.06) were not statistically significant.

GDD qualified success rates at 12 months for external ligature only versus combined intraluminal stent/external ligature were 73% and 79% respectively. There was no statistical significance at 12 months (p=0.25) between the two methods. However, when comparing both methods in terms of postoperative mean IOP, there was a statistically significant result at six months (p=0.03). The external ligature only method had a lower mean IOP compared to the combined intraluminal/external ligature method (11.2mmHg versus 17mmHg respectively at six months). This was most likely due to the more rapid IOP control with the external ligature only method. With the combined intraluminal stent/external ligature method, there would be less aqueous flow through the tube in the early postoperative period when the intraluminal stent would be still *in situ*. However, there was no evidence for increased requirements for glaucoma medications postoperatively between the two methods.

Study limitations

This retrospective chart review was done to evaluate multiple outcomes of combined GDD insertion and corneal transplantation. Given the nature of this retrospective study type, the results would have been affected by selection and information bias. No patient had both eyes included in the study even though the study inclusion criteria allowed for this. Pre-existing corneal or glaucomatous pathology would have likely resulted in selection bias within the study. Patients with known corneal pathology who then require GDD insertion would have been less likely to receive AC tubes where there would be increased rates of adverse outcomes to the cornea. In patients who had GDD insertion prior to corneal transplantation, only AC-GDDs were inserted due to the absence of pre-existing corneal pathology and current guidelines favouring AC-GDD insertions. Data collected for this study was dependent on accurate and complete record-keeping of patient records and on the correct ICD-10 classification by hospital coding staff.

The combination of GDD insertion and corneal graft surgery in the same eye is relatively uncommon. Sample size (i.e. study power) was insufficient to accurately assess outcomes of CS-GDD insertions, DALK and DMEK corneal grafts. The effect of GDD insertion on corneal endothelial cell count was also unable to be evaluated as there were limited endothelial cell counts performed postoperatively. Study sample size was also not large enough to make recommendations on optimal GDD location and corneal graft type for the different glaucoma types and corneal pathology respectively. There is however, evidence of procedure selection as demonstrated in this study where most endothelial corneal pathology underwent endothelial keratoplasty (DSEK/DMEK) and PP-GDD insertions.

Another limitation of retrospective studies is that the method of IOP and VA measurements could not be standardised. The development of cataracts (if aphakic) post-GDD insertion and refractive errors post-keratoplasty would negatively impact on VA measurements as well. Further, surgeon technique and preferences, along with varying threshold of GDD insertion and corneal transplantation between patients would have had an impact on clinical outcomes. Treatment escalation guidelines for elevated IOP post-GDD insertion were also not established.

There was also no standardised abstraction form for corneal graft

status during follow-up visits. The number of PAS, presence of graft rejection and/or graft failure was not properly recorded at times. While good IOP control reflects GDD function, corneal graft function was estimated by visual acuity which is a subjective measurement and can be impacted by many other ocular and neurological factors.

Future directions

The potential negative long-term effects on the corneal endothelium and predictability of IOP control have previously hampered the use of GDDs as a primary surgical modality for the treatment of glaucoma [25]. Recent studies have shown that GDD insertion is more likely to maintain IOP control compared to trabeculectomy + MMC in the long term [4,26], while laser trabeculoplasty was shown to have minimal impact on the treatment of post-keratoplasty glaucoma [13]. Newer GDD implant materials, surgical methods and insertion sites (CS/PP) have made the extent of IOP-lowering more predictable. However, studies with endothelial cell counts prior to and post GDD insertion are still relatively uncommon and are focused on AC-GDDs only [27-29].

The utilization of OCT imaging in the AC has allowed better visualization of AC-GDD tube patency, position and direct measurements of endothelial-tube distance [27,30]. Its use has been integral in showing the relationship between endothelial-tube distance and endothelial cell loss [27]. It has also led to more accurate and timely identification of AC-GDD tube complications [27].

DSEK/DMEK grafts have become more popular as they have been shown to have superior visual outcomes and better postoperative recovery times when compared to PK [31,32]. From our results, endothelial grafts comprised of 40% all corneal transplants. Postoperative visual acuity in endothelial grafts compared to PK grafts was not statistically significant (p=0.30). Failure of these endothelial grafts is mostly attributed to graft dislocation rather than rejection [33]. The donor tissue preparation and transplantation into host tissue can be challenging. Studies have shown better surgical outcomes and decreased endothelial cell loss in eyes that used a donor insertion device compared to the Sheets glide technique [34,35].

With PK, Femtosecond laser used in the preparation of donor and host tissue may lead to better visual outcomes [36]. The decreased number of sutures needed may also lead to less angle distortion and decreased incidence of post-PK glaucoma [13].

The constant advancements made towards GDD design and corneal grafting methods are crucial to further improve on IOP control and graft success rate. However, the exact mechanism of endothelial cell damage in the cornea post AC-GDD insertion is still not well understood. A large prospective study looking at the effects of GDD insertion (at different insertion sites) in patients with primary glaucoma who have healthy corneas may help determine the effects of GDD insertion on corneal endothelium [25], and this could help inform decision-making in patients with compromised corneas who require glaucoma surgery.

Conclusion

GDD insertion is an effective means of IOP control post-keratoplasty. CS-GDD (n=2) yielded the best clinical outcomes in terms of IOP control, decreased number of glaucoma medications and visual acuity in the context of keratoplasty. AC-GDD was the most common GDD insertion site for our study. Clinical outcomes for AC-GDDs were similar to PP-GDDs in terms of IOP reduction and decreased number of glaucoma medications postoperatively. Pre-keratoplasty insertion of AC-GDDs were more frequently associated with corneal decompensation compared to the other GDD insertion sites (p=0.19). PP-GDDs were likely to be more successful in the long term (3 years) compared to AC-GDDs (p=0.04). However, PP-GDDs were associated with poorer visual acuity (p=0.02), but this most likely reflects preoperative case selection. PK grafts demonstrated best graft survival when used in conjunction with PP-GDDs (n=8). This study could not determine which GDD insertion site maximised endothelial (DSEK/DMEK) graft success.

Our results did not conclusively show that GDD insertion prior to corneal transplantation was associated with better graft survival. However, intuitively if uncontrolled IOP is present then future graft survival is likely to be compromised and thus control of IOP pre-operatively with glaucoma surgery would be desirable. The inherent limitations of this study meant this question could not be definitively answered, however this case series outlines some important considerations when combining corneal and glaucoma surgery. The data should also be helpful in informing the development of a prospective study with larger numbers that will be able to more definitively identify which types of glaucoma surgery maximise the chance of a good outcome in patients also requiring corneal transplantation.

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