Rate of Corneal Grafting Post-Glaucoma Drainage Device Use in Pediatric and Adult Patients

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Précis: Kaplan-Meier analysis was used to compare the rate of corneal grafting after glaucoma drainage device (GDD) placement in pediatric and adult patients. Adults were at an increased risk of receiving a corneal graft after device placement.

Purpose: The goal of this study was to compare the rate of corneal graft implantation after GDD placement in pediatric and adult patients.

Patients: Patients receiving a GDD between January 1, 1985 and December 31, 2017 were selected from the medical records. Patients receiving their first device while <18 years of age were considered children for the extent of the study.

Methods: We compared the rate of receiving a corneal graft after GDD implantation using Kaplan-Meier analysis. Baseline patient characteristics and surgical characteristics were compared using a generalized estimating equation.

Results: Corneal grafting occurred in 8.6% of adults and 4.7% of children from the original cohort. The rate of receiving a corneal graft at 5, 10, and 15 years was 9.4%, 16.8%, 39.4% and 1.6%, 1.6%, 12.5% for adults and children, respectively. However, certain characteristics were different between the 2 groups.

Conclusion: Adult patients were more likely to receive a corneal graft after GDD placement. However, pediatric and adult patients differed in the prevalence of preexisting corneal disease, GDD type, GDD type used, and types of previous surgeries. Elucidation of the impact of these factors on corneal graft rate requires a larger cohort size.

Key Words: glaucoma drainage device, corneal decompensation, pediatric glaucoma

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The use of glaucoma drainage devices (GDDs) is increasing. However, GDDs are associated with reduced endothelial cell density and corneal decompensation. Many studies have looked at the frequency of corneal decompensation after GDDs. However, there is limited data that compares the frequency of corneal decompensation after GDDs between adults and children.

Mandalos and Sung found no statistically significant difference in the rate of corneal decompensation between children and adults. However, their study was limited in its power because of their small sample size. Furthermore, given that the primary purpose of their study was to characterize the outcomes of GDD placement between children and adults, survival analysis was not used to characterize the risk of corneal decompensation, which adjusts for variable follow-up time.

The mechanism for corneal decompensation associated with GDD placement is not known. However, biochemical and mechanical mechanisms including promotion of turbulent flow or the introduction of inflammatory or oxidative mediators into the anterior chamber leading to endothelial cell damage may play a role. In addition, corneal edema and subsequent decompensation may occur in children due to their active lifestyle which may increase intermittent tube-corneal contact. This can be complicated by impaired detection of early corneal edema because of difficulty examining a child. Furthermore, children have a more elastic sclera which can result in greater changes in tube position. The tube position may also change as the child’s eye grows with age. Given these risk factors, we hypothesized that children may be more likely to receive cornea graft implantation after GDD placement. The purpose of this study was to characterize the rate of corneal grafting in children and adults using survival analysis.

METHODS

Patient Selection

This was a retrospective cohort study at a single institution which included adult and pediatric patients that underwent surgery for GDD implantation between January 1, 1985 and December 31, 2017. Any patient that received a GDD while <18 years old was classified as a pediatric patient for the extent of the study. Patients receiving a corneal graft before GDD placement and those with a keratoprosthesis were excluded. For surgeries completed outside Mayo Clinic with a missing date, the surgical date was estimated using available exam information. One patient with a prior GDD placed at an outside institution was excluded as no reasonable estimate could be made.

Surgery

GDD type used and tube position were decided by the operating surgeon. GDD implants were the Baerveldt Glaucoma Implant (Advanced Medical Optics, Santa Ana,
CA), Ahmed glaucoma valve (AGV) (New World Medical Inc., Rancho Cucamonga, CA), and Scheck tube. All of the GDD surgeries for the pediatric patients used in this study were conducted by staff physicians. A total of 530 of the GDD surgeries in adult patients were conducted by staff physicians and 27 were conducted by outside surgeons.

### Outcome Measures
Baseline characteristics of patients including sex, race, age, prior surgeries, preexisting corneal disease, and glaucoma type were recorded. Rate of corneal grafting after GDD placement was the outcome of interest.

### Statistical Analysis
Categorical variables are presented with the frequency and the percentage. Continuous variables are summarized using the mean and standard deviation, unless noted otherwise. Baseline characteristics were compared between the groups using generalized estimating equation models. These models were used to attempt to account for the potential correlation between eyes from the same patient. The rate of corneal grafting was estimated using Kaplan-Meier method. Potential risk factors of corneal grafting were assessed using Cox proportional hazards models. Sandwich estimators were used to account for the multiple eyes in the analysis for some of the patients. All analysis was completed using SAS version 9.4 (Cary, NC).

### RESULTS
A total of 621 eyes (64 pediatric and 557 adult) were included from 481 adult and 44 pediatric patients. The median age (standard deviation) was 68 (17) years for adults and 8 (6) years for children. The median follow-up time (standard deviation) for adult and pediatric patients was 34 (52) months and 94 (61) months, respectively. A majority of adult (89%) and pediatric (88%) patients were white. The median age (standard deviation) was 34 (52; 0-287) years for adult and 34 (52; 0-102) years for children. The proportion of female and male patients between the 2 groups was similar and evenly distributed ($P=0.40$, Table 1). However, glaucoma type differed between the 2 groups. Open-angle glaucoma ($P=0.05$) was more common in adults, while congenital glaucoma ($P<0.001$) and uveitic glaucoma ($P<0.001$) were more common in children. In this cohort, the most common diagnosis for adults was open-angle glaucoma, while uveitic glaucoma was the most common diagnosis in pediatric patients (Table 2). A greater proportion of adults (22%) had preexisting corneal disease (Table 3, $P=0.05$). Furthermore, adults had a greater number of laser surgeries for glaucoma (ie, selective laser trabeculoplasty, argon laser trabeculoplasty, laser peripheral iridotomy) (mean number 0.51 vs. 0.03 in adults and children, respectively, Table 4, $P<0.001$).

There was a significant difference in GDD type used in pediatric and adult patients. Baerveldt 350 ($P<0.001$) and Ahmed FP7 ($P=0.01$) implants were more common in adults, while the Baerveldt 250 ($P<0.001$) and Ahmed S2 ($P<0.001$) implants were more common in pediatric patients (Table 5). The superior temporal position was preferred for plate placement for both children and adults (Table 5). The tube was most commonly placed in the anterior chamber and no difference was noted in the proportion of pediatric (86%) and adult patients (86%) with anterior tube placement (data not shown, $P=0.99$).

Corneal grafting occurred in 48 eyes (8.6% of the original cohort) in the adult group and 3 eyes (4.7% of the original cohort) in the pediatric group. The risk of corneal grafting after GDD implantation was greater in adult patients (Fig. 1, $P=0.006$). The rate of receiving a corneal graft at 5, 10, and 15 years was 9.4%, 16.8%, 39.4% and 0.70, respectively. A similar distribution of sex and race were seen in the pediatric and adult cohorts. STD indicates standard deviation.

### Table 1. Patient Characteristics

|              | Adults (N = 557) | Children (N = 64) | P   |
|--------------|------------------|-------------------|-----|
| Sex          |                  |                   |     |
| Male         | 265 (48)         | 28 (44)           | 0.78|
| Female       | 292 (52)         | 36 (56)           |     |
| Race         |                  |                   | 0.40|
| White        | 495 (89)         | 56 (88)           |     |
| Other        | 62 (11)          | 8 (12)            |     |
| Median age (STD; range) | 68 (17; 18-102) | 8 (6; 0-17)       |     |
| Follow-up time median in months (STD; range) | 34 (52; 0-287) | 94 (61; 0-241)   |     |

### Table 2. Glaucoma Type in Pediatric and Adult Patients

| Glaucoma Type         | Adults (N = 557) | Children (N = 64) | P   |
|-----------------------|------------------|-------------------|-----|
| Angle closure         | 38 (7)           | 0                 |     |
| Congenital            | 7 (1)            | 18 (28)           | <0.001|
| Ocular hypertension   | 3 (1)            | 0                 |     |
| Open angle            | 189 (34)         | 1 (2)             | 0.05|
| Pigmentary            | 13 (2)           | 0                 |     |
| Pseudoxefoliation     | 57 (10)          | 0                 |     |
| Steroid induced       | 12 (2)           | 1 (2)             |     |
| Uveitic               | 29 (5)           | 23 (36)           | <0.001|
| Mixed mechanism       | 36 (6)           | 3 (5)             |     |
| Steroid induced, uveitic | 6 (1)         | 1 (2)             |     |
| Neovascular           | 57 (10)          | 1 (2)             |     |
| Secondary             | 27 (5)           | 5 (8)             |     |
| Other                 | 83 (15)          | 11 (17)           | 0.70|

### Table 3. Frequency of Preexisting Corneal Disease in Adult and Pediatric Patients

| Preexisting Corneal Disease | Adults (N = 557) | Children (N = 64) | P   |
|-----------------------------|------------------|-------------------|-----|
| Yes                         | 120 (22)         | 8 (12)            | 0.05|
| Fuchs’ dystrophy            | 18 (3)           | 0                 |     |
| Herpes simplex virus        | 10 (2)           | 0                 |     |
| Trauma                      | 22 (4)           | 0                 |     |
| Pseudoxanthoma              | 19 (3)           | 0                 |     |
| Elasticum                   |                  |                   |     |
| Other                       | 51 (9)           | 8 (12)            |     |
| No                          | 437 (78)         | 56 (88)           |     |
TABLE 4. Number of Previous Surgeries Differed Between Pediatric and Adult Patients

| Surgeries Before GDD | Mean Number (SD) | Adults (N = 557) | Children (N = 14) | P |
|----------------------|------------------|------------------|-------------------|---|
| Incisional glaucoma  | 0.65 (1.05)      | 0.78 (0.93)      | 0.32              |
| surgery              |                  |                  |                   |
| Incisional surgery   | 0.72 (0.92)      | 0.70 (0.94)      | 0.73              |
| (nonglaucoma)        |                  |                  |                   |
| Laser (glaucoma)     | 0.51 (0.83)      | 0.03 (0.25)      | < 0.001           |
| Laser (nonglaucoma)  | 0.27 (0.59)      | 0.13 (0.65)      | 0.06              |

Incisional glaucoma surgeries: goniotomy, IStent, trabectome, 360 trabeculotomy, bleb revision.
Incisional nonglaucoma surgeries: cataract surgery, vitrectomy.
Laser glaucoma surgeries: selective laser trabeculoplasty, argon laser trabeculoplasty, laser peripheral iridotomy.
Laser nonglaucoma surgeries: YAG laser capsulotomy, panretinal photocoagulation.
GDD indicates glaucoma drainage device.

1.6%, 1.6%, 12.5% for adults and children, respectively (Table 6). The median time to graft was 36 months in adults and 163 months in pediatric patients. When comparing GDD tube location in the anterior chamber versus pars planar, sulcus, or unknown placement, a statistically significant difference is observed in the rate of corneal grafting between adult and pediatric patients with placement in the anterior chamber (Fig. 2A, \( P = 0.02 \)) but not between the 2 groups when the tube is placed outside the anterior chamber (Fig. 2B, \( P = 0.73 \)).

DISCUSSION
In our study, adults were more likely to have a corneal graft after GDD implantation. Mandalos and Sung conducted a study that compared the frequency of corneal decompensation between children and adults directly. Their study did not show a difference in the frequency of corneal decompensation between children and adults, but was limited in power.5 Most previous studies calculate the raw frequency of corneal decompensation to be between 2.2% and 11.9% for children1–5 and 2.1% to 16% in adults.5,7,10–12 However, this method does not control for loss to follow-up. The frequency of corneal grafting in our cohort was similar to some of these studies (8.6%). However, since this method is impacted by follow-up, a longer follow-up time could result in detecting a greater number of events. Survival analysis allows for correcting for loss to follow-up to reduce the impact of differences in follow-up times.

Using Kaplan-Meier analysis, adults were found to be more likely to have a corneal graft following GDD placement. A previous study had a 3.3% 5-year cumulative risk of corneal decompensation;2 This is lower than the 9.4% 5-year cumulative risk of corneal grafting in our study. However, our study contains patients that were referred after GDD placement. It is possible that this difference could be because of a referral bias with more complicated cases being at a greater risk of corneal decompensation. When adults are stratified based on where they received their surgery, no difference is noted in the probability of receiving a corneal graft (\( P = 0.13 \), data not shown). However, it is possible that the higher rate of corneal grafting could be because of a selection bias where more complicated patients are remaining within the health system for follow-up and those less likely to receive a graft are lost to follow-up.

Given the presence of a foreign body in the anterior chamber, it is believed that anterior chamber placement of the GDD tube is likely to increase the likelihood of corneal decompensation and subsequent need for a corneal graft compared with pars planar or sulcus placement of the GDD tube.

TABLE 5. GDD Location and GDD Type Used for the Patient’s First GDD Surgery

| GDD location | Adults (N = 557) | Children (N = 64) | P |
|--------------|------------------|-------------------|---|
| Superior nasal | 6 (1)            | 2 (3)             | 0.42†|
| Superior temporal | 507 (91) | 56 (88)           |       |
| Inferior nasal | 10 (2)           | 0                 |       |
| Inferior temporal | 7 (1)            | 0                 |       |
| Multiple      | 15 (3)           | 4 (6)             |       |
| Unspecified   | 12 (2)           | 2 (3)             |       |
| GDD type      |                  |                   |       |
| Baerveldt 250 | 58 (10)          | 20 (31)           | < 0.001*|
| Baerveldt 350 | 303 (54)         | 16 (25)           | < 0.001*|
| Ahmed FP7     | 129 (23)         | 5 (8)             | 0.01*|
| Ahmed S2      | 47 (8)           | 18 (28)           | < 0.001*|
| Sclerotic tube | 4 (1)            | 0                 |       |
| Ahmed B1      | 15 (3)           | 4 (6)             |       |
| Unspecified   | 1 (< 1)          | 1 (2)             |       |

*Comparing specified group against all others between pediatric and adult patients.
†Comparing superior temporal position against all other groups between pediatric and adult patients.
GDD indicates glaucoma drainage device.

TABLE 6. Probability of Receiving a Corneal Graft After GDD

| Years after GDD | Adults (N = 557) (%) | Children (N = 64) (%) |
|-----------------|----------------------|-----------------------|
| 5               | 9.4                  | 1.6                   |
| 10              | 16.8                 | 1.6                   |
| 15              | 39.4                 | 12.5                  |

GDD indicates glaucoma drainage device.
in pediatric patients.\(^5\) As such, we attempted to stratify factor between the groups, GDD type may impact outcomes confounding factor. In addition to being a confounding important to consider the GDD type used as a potential makes sense given the smaller eye size in children,\(^5\) it is pediatric patients were more likely to receive an Ahmed S2 or a Baerveldt 250 implant (Table 4). While this preference pediatric and adult patients. Adults were more likely to receive a Baerveldt 350 or an Ahmed FP7 implant and pediatric and adult patients. However, the groups differed on the number of previous surgeries (Table 4) and glaucoma type (Table 2). The impact that these factors have on the probability of corneal grafting cannot be ruled out.

Our study was limited by the number of events in each group; thus, determining the impact the variables discussed above had on the probability of grafting was not possible. While we cannot rule out the impact that these variables have on graft probability, the strength of our study was in utilizing survival analysis to compare the rate of corneal grafting between pediatric and adult patients. From these results, it appears that adults are at a higher risk of receiving a corneal graft after GDD implantation in comparison to children when the GDD tube is placed in the anterior chamber regardless of history of corneal disease. Given that children have a longer predicted life span, characterizing the rate of corneal grafting after GDD, one of the most common complications of GDD implantation, can hold important clinical and prognostic utility when treating this patient population.

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