Long-term surgical outcomes of ab externo trabeculotomy in the management of primary congenital glaucoma

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PURPOSE To analyze the long-term results of ab externo trabeculotomy with a Harms trabeculotome at a single, tertiary care pediatric hospital.

METHODS The medical records of pediatric patients operated on between September 2006 and June 2018 were reviewed retrospectively. Kaplan-Meier analysis was performed, with success defined as postoperative intraocular pressure (IOP) of ≤21 mm Hg, >20% reduction from preoperative IOP, and no need for further glaucoma surgery. Risk factors for failure were identified using Cox proportional hazards ratio.

RESULTS A total of 63 eyes of 40 patients were included. The cumulative probability of success rate was 83% at 3 months, 76% at 6, 73% at 12, 72% at 18, and 65% at final visit. Presentation within 3 months of life was associated with a less favorable outcome. Thirty-five eyes (56%) underwent repeat trabeculotomy to treat a different area of the trabecular meshwork because of inadequately controlled IOP after the first session. Of those who needed another session of trabeculotomy, the final success rate was 60.2%. IOP significantly decreased from 29.79 ± 7.67 mm Hg at baseline to 16.13 ± 3.41 mm Hg by final follow-up ($P = 0.001$). Patients were followed for an average of 85.74 ± 32.95 months. IOP and success rates remained stable 18 months after surgery.

CONCLUSIONS In our patient cohort, ab externo trabeculotomy was associated with good long-term results. More extensive trabeculotomy (ie, more than one procedure) was associated with better long-term success rates. (J AAPOS 2019;23:222.e1-5)

Primary congenital glaucoma (PCG) is the most common type of childhood glaucoma and is characterized by high intraocular pressure (IOP) leading to optic nerve head and ocular damage, usually presenting within the first year of life.[1] Most cases of PCG are sporadic and not associated with other ophthalmic or systemic disorders, but there are autosomal recessive cases, particularly in the setting of consanguinity.[1,2] The presumed pathology is angle dysgenesis secondary to the arrested maturation of neural crest cells.[3]

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The ultimate goal of childhood glaucoma management is lifelong IOP control to maintain lifetime visual function.[4] Medications alone are typically ineffective and make surgery the main therapeutic option.[5,6] Traditionally, a staged approach has been favored by many ophthalmologists, starting with angle-based surgery (repeated in case of failure) then proceeding with trabeculectomy or combined trabeculotomy-trabeculectomy for refractory patients and drainage device implantation or cyclodestruction for advanced cases.[7] However, the type of surgery is often dictated by corneal clarity, initial severity of the disease, patients' socioeconomic status (in developing nations), and the surgeon's experience and preference.[4,5,7,8]

Angle surgery aims to restore the physiologic outflow pathway by opening the dysplastic trabecular meshwork and inner wall of Schlemm's canal. Whereas conventional trabeculotomy with a rigid trabeculotome opens about one-third of the angle, the 360-degree passage of a suture through Schlemm's canal can open the angle circumferentially.[9] Although this technique has been shown to yield good results, it is associated with potential complications, including the inability to advance the suture in one pass

with a single scleral cut-down, poor gonioscopic visibility of the suture location in case of corneal opacity, false passage, misdirected suture, hyphema, iris tear, and hypotony due to the development of a cyclodialysis cleft.[9,10] Recent studies have demonstrated that performing 360-degree trabeculotomy using an illuminated microcatheter helps to prevent the most serious consequences of microcatheter misdirection.[11-14] Investigators postulate more angle opening as the reason for improved short-term success rates with 360-degree trabeculotomy. The purpose of this study was to report the long-term outcomes of ab externo trabeculotomy using a Harms trabeculotome in PCG.

Subjects and Methods

The Ann & Robert H. Lurie Children's Hospital of Chicago Institutional Review Board approved this retrospective study, which complied with the regulations of the US Health Insurance Portability and Accountability Act of 1996 and followed the tenets of the Declaration of Helsinki. All patients who underwent ab externo trabeculotomy surgery for primary congenital glaucoma at Ann & Robert H. Lurie Children's Hospital between September 2006 and June 2018 were identified using current procedural terminology codes and included in the study.

Exclusion criteria were previous history of intraocular surgery, combined surgeries, any form of anterior segment dysgenesis, and follow-up of <6 months. There was no case of goniotomy in our center within the time period of this study. Information collected include demographic data, pre- and postoperative IOP, baseline ocular biometric characteristics including axial length (AL), central corneal thickness (CCT), corneal diameter, presence of Haab's striae, number of pre- and postoperative glaucoma medications, type of surgery, and intra- and postoperative complications. At each postoperative visit, IOP, glaucoma medications, and adverse events were recorded. Assessment of the patient's ability to fix and follow an object of interest or best-corrected visual acuity was recorded when assessed.

The diagnosis of PCG was based on the presence of a constellation of typical clinical signs and symptoms (epiphora, photophobia, and blepharospasm), elevated IOP, enlargement and opacification of the cornea, Haab's striae, globe elongation, and optic nerve head cupping.

IOP was measured by handheld tonometer (Tono-Pen XL or Tono-Pen AVIA, Reichert Technologies, NY), Goldmann applanation tonometry (Haag-Streit Diagnostics, Koeniz, Switzerland), or rebound tonometry (iCare Finland Oy, Helsinki, Finland), according to patient age and cooperation.

The primary outcome measure was clinical success, defined as (1) normal IOP ($5 < \text{IOP} \leq 21$ mm Hg), (2) ≥20% reduction of IOP from baseline at two consecutive visits, and (3) no need for further glaucoma surgery (apart from repeat trabeculotmy). Kaplan-Meier survival analysis was used to evaluate the success rates. Secondary outcome measures were IOP, number of glaucoma medications, and complications. Risk factors for success and failure were identified using the Cox proportional-hazards ratio model with multivariate analysis.

Surgical Technique

All surgeries were performed under general anesthesia. A corneal traction suture was passed using a spatulated 7-0 silk suture. A fornix-based localized peritomy was created in the temporal quadrant and hemostasis was achieved using wet-field cautery. A triangular, 3 mm, limbal based, the partial-thickness scleral flap was fashioned followed by a radial incision to expose Schlemm's canal under high magnification. A scleral cut down was performed from the surgical blue zone to the white zone until egress of aqueous humor was noted. The Harms trabeculotome was then passed into each end of Schlemm's canal up to the joint and gently rotated into the anterior chamber through the trabecular meshwork. The scleral flap was sutured with 8-0 polyglactin 910 suture, and knots were buried in the sclera. The conjunctiva was closed using 10-0 polyglactin 910 sutures. Postoperative medications included topical antibiotic, steroid, and cycloplegic drops tapered over 4 weeks. At a minimum, patients were examined postoperatively at 1 day, 1 week, 2 weeks, and 4 weeks, followed by 1- to 3-month intervals based on the clinical course. Examinations under anesthesia were performed as indicated to obtain better evaluations of glaucoma status and provide necessary manipulations such as suture removal. Postoperative examinations under anesthesia included assessment of IOP, corneal clarity, corneal diameter, axial length, optic nerve head evaluation, and refractive errors.

Statistical Analysis

All analyses were performed using SPSS software (SPSS Statistics for Windows, version 25, Armonk, NY, IBM Corporation). Frequency, percent, mean with standard deviation, median, and range were used to describe the data. To compare the change in IOP, we used an interaction analysis within a linear mixed model. To evaluate the baseline differences, we used the t test, χ^2 test, and Fisher exact test. Kaplan-Meier survival plots were constructed to assess the long-term survival rates and compared using the log-rank test. A Cox proportional hazards model was used to find potential risk factors for failure (baseline IOP, axial length, CCT, refraction, age at time of diagnosis, and corneal diameter) and to estimate the adjusted hazard ratio of each factor. Statistical significance was set at $P < 0.05$.

Results

A total of 63 eyes of 40 patients (25 males [63%]) were included. Mean age at diagnosis was 6.9 ± 10.7 months; 31% of the patients were diagnosed before 3 months of age. Mean follow-up time was 85.7 ± 32.9 months. Average baseline IOP was 29.8 ± 7.7 mm Hg. Clinical signs and symptoms at presentation time included epiphora (93%), photophobia (83%), and buphthalmos (64%). Haab's striae were present in 73% of eyes. Mean baseline CCT was 585.4 ± 76.6 μm (Table 1). On average, each patient underwent 9.4 ± 3.4 examinations under anesthesia postoperatively.

Table 1. Baseline characteristics of patients

Clinical characteristics	Result
Sex, male, no. (%)	25 (62.5)
Unilateral disease, no. (%)	17 (42.5)
Age at diagnosis, mos, mean ± SD	6.89 ± 10.68
Follow-up, mos, mean ± SD	85.74 ± 32.95
Baseline IOP, mm Hg, mean ± SD	29.79 ± 7.67
Cup:disk ratio, mean ± SD	0.55 ± 0.22
Corneal diameter, mm, mean ± SD	12.79 ± 1.26
Central corneal thickness, μm, mean ± SD	585.44 ± 76.57
Axial length, mm	22.37 ± 2.50
Baseline refraction, D, mean ± SD	−4.78 ± 5.87
Time of diagnosis by category, no. (%)	
≤3 mos	18 (31)
3 < age ≤ 6 mos	26 (48)
>6 mos	14 (24.1)
Ocular signs, no. (%)	
Presence of Haab striae	45 (72.6)
Buphthalmos	30 (83.3)
Ocular symptoms, no. (%)	
Tearing	30 (93.8)
Photophobia	24 (82.8)

D, diopter; *IOP*, intraocular pressure; *SD*, standard deviation.

Surgical Success and Risk Factors for Failure

The Kaplan-Meier survival curves indicated a mean time to failure of 107.79 ± 9.04 months (Figure 1). Cumulative probability of overall clinical success was 83% at 3 months, 76% at 6, 73% at 12, 72% at 18, and 65% at final visit (Figure 1A). In a Cox proportional hazard ratio model, only age group was associated with the final success. Other baseline characteristics, including baseline IOP, baseline CD, AL, CCT, and corneal diameter were not correlated with increased hazard of the failure (Table 2).

In a subgroup analysis, patients who were diagnosed before 3 months of age had a lower likelihood of achieving overall clinical success compared to patients who were diagnosed at an older age. Mean time to failure was 69.65 ± 12.51 months among subjects ≤3 months of age, compared with 114.76 ± 14.21 months ($P = 0.03$) among patients 3-6 months of age and 119.50 ± 18.25 months ($P = 0.03$) among patients >6 months of age (Figure 1B).

Thirty-five eyes (55.5%) underwent repeat trabeculotomy because of uncontrolled IOP after the first session. The cumulative probability of clinical success for the reoperation was 72.4% at 6 months, 67.2% at 12, 65.3% at 18, and 60.2% at final visit.

Intraocular Pressure

Mean baseline IOP was 29.8 ± 7.7 mm Hg. Mean follow-up IOP was 18.0 ± 5.9 mm Hg at 6 months, 16.8 ± 4.4 at 18 months, 15.3 ± 2.9 at 36 months, and 16.2 ± 3.7 at 60 months (all $P < 0.001$ compared to baseline). At the final follow-up examination, mean IOP was 16.1 ± 3.4 mm Hg, which corresponded to 44% reduction from the baseline (Figure 2). The mean number of glaucoma medications at final follow-up was 1.4 ± 0.5 drops; 23 eyes (36.5%) were off glaucoma medications.

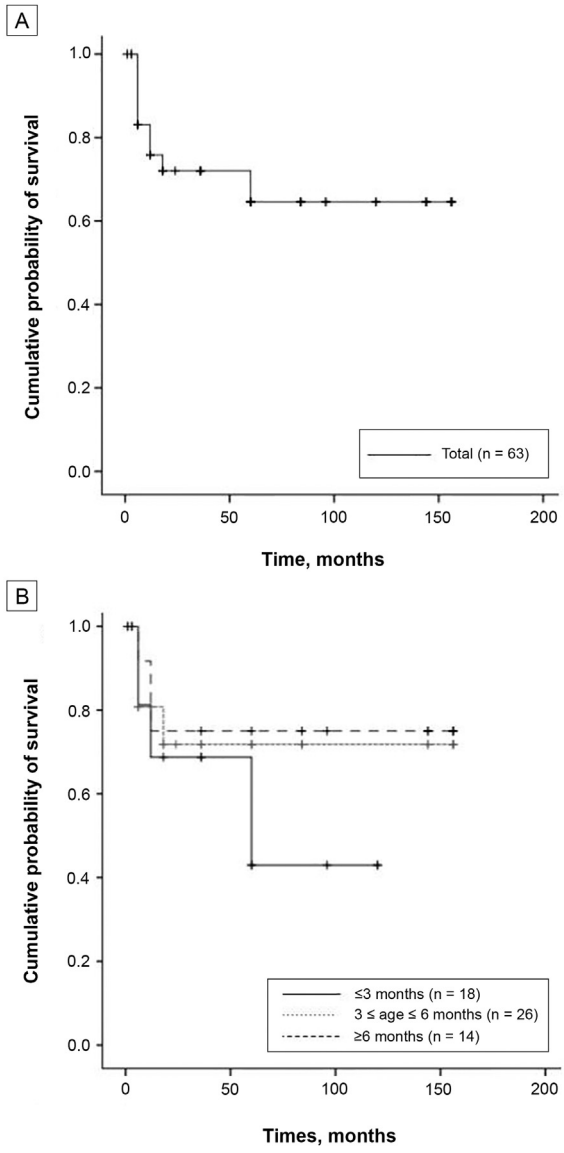

FIG 1. Kaplan-Meier survival plots, with success defined as a final intraocular pressure (IOP) of ≤21 mm Hg and a 20% reduction from baseline. A, Plot for all eyes. B, Separated by age at diagnosis.

Table 2. Cox Proportional hazard ratios for factors affecting survival

Variable	Hazard ratio	*P* Value
Baseline IOP	1.439 (0.5-4.1)	0.495
Axial length	0.324 (0.009-11.50)	0.536
CCT	1.089 (0.96-1.24)	0.192
Refraction	0.328 (0.05-1.97)	0.224
Corneal diameter	1.1 (0.8-1.25)	0.163

CCT, central corneal thickness; *IOP*, intraocular pressure.

Visual Acuity

Mean best-corrected visual acuity of patients was 0.37 ± 0.48 logMAR in the fifth year postoperatively and was 0.51 ± 0.56 logMAR at final follow-up ($P = 0.08$). Mean refraction was −4.78 ± 5.87 D at the

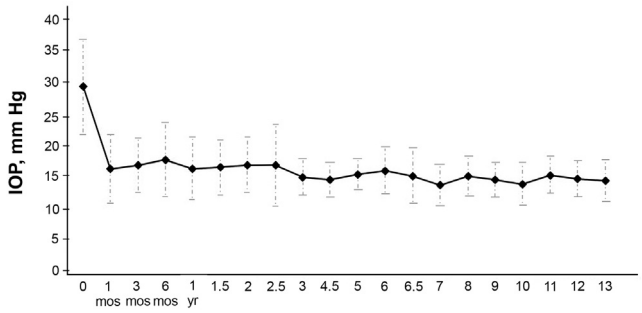

FIG 2. Preoperative and postoperative mean IOP within 13 years' follow-up.

baseline and −2.90 ± 3.83 D at final visit, with a reduction in myopia.

Reoperation and Postoperative Observations

Subsequent glaucoma surgery was performed when IOP could not be controlled within the individual target range or when there was evidence of disease progression. Additional glaucoma surgeries included 7 tube shunt procedures (4 Ahmed and 2 Baerveldt drainage devices). Cyclophotocoagulation was performed in 1 case of failed drainage device surgery. The mean interval between trabeculotomy and reoperation was 6.2 ± 4.4 months.

The most common observation after the procedure was hyphema (reported in 18 eyes [29%]), which was managed conservatively in all cases. Surgical drainage of a suprachoroidal effusion was performed in 1 case. There was one case of a localized, nonprogressive lens opacity that developed as a result of inadvertent injury of the crystalline lens with a 15° blade.

Discussion

In the current study, ab externo trabeculotomy resulted in significant reduction of IOP in primary congenital glaucoma, with a success rate of 65% by final follow-up. Of those that failed to respond to primary surgery, almost 60% had successful long-term outcomes with repeat trabeculotomy. Furthermore, both IOP and success rates tended to stabilize by 18 months postoperatively. Sixty-two percent of our patients were male, which is consistent with several other studies that have shown a male preponderance.[2] The corneal thickness in our study was on the thicker side of the reported range.[15,16]

The ideal approach to PCG surgery is debated. These diverse approaches indicate variations in disease presentation, lack of high-standard randomized clinical trials, and local issues, including access to facilities, types of equipment, and skilled surgeons.[17]

Trabeculotomy involves disrupting the tissue between Schlemm's canal and the anterior chamber using an ab externo approach to create direct communication. Currently, there are at least three different approaches: rigid probe, suture assisted, and illuminated microcatheter.[18] The success of angle surgery is reported to be 65%-85%, with higher success rates achieved when PCG is recognized and treated within the first year of life.[18,19] Zagora and colleagues[20] reported their 10-year outcomes of ab externo trabeculotomy to be 75%, comparable to our 8 year-outcomes.

The suture trabeculotomy was introduced in 1960 and involves passing a nylon suture into the canal and cutting through the trabecular meshwork in a purse string fashion.[21] This method was largely replaced by the rigid probes because of complications such as misdirected suture, false passage, damage to the cornea and lens, hyphema, and chorioretinal damage. To date, there is no randomized controlled trial comparing the outcomes of trabeculotomy performed with a suture versus rigid probe, although several smaller retrospective studies with mostly short-term follow-up offer insight into the efficacy of each technique. The reported long-term success using the suture technique varies between 70%-92%,[10,22] whereas rigid probe trabeculotomy has an overall success of 60%-85% within 1-3 years of follow-up.[5,7,17,23] Almost half of the primary trabeculotomies in our report failed to reduce the IOP, necessitating repeat trabeculotomy, which improved the success rate to 67% at 1 year. To avoid the need for multiple procedures as well as complications of suture-associated trabeculotomy, illuminated microcatheters have been increasingly adopted for circumferential trabeculotomy.[11,12,24] Any misdirection can be thus detected and arrested. Girkin and colleagues[12] have reported higher success rates in cases undergoing illuminated, microcatheter-assisted 360° trabeculotomy compared to goniotomy. In their retrospective study, Neustein and Beck[25] showed a significantly higher success rate using circumferential trabeculotomy (81%) compared with standard trabeculotomy/goniotomy (31%) after 7 years' follow-up. Published rates of short-term success range from 75% to 90% in PCG, which is higher than achieved with a rigid probe and comparable with suture trabeculotomy, but with a reduced risk of intraoperative complications.[11–13,24] The findings of our study are consistent with other studies that increased circumferential opening of the angle is associated with a higher long-term success in PCG. The challenge is to identify the eyes that need more than 120° of trabeculotomy to control the IOP. This may help to improve surgical planning and individualize the therapy. Our analysis failed to identify baseline factors predictive of failure after one or two sessions of trabeculotomy with a rigid probe. It is possible that eyes with success after a single session, 4-clock-hour trabeculotomy procedure may have more developed angle structures because of ongoing outflow maturation. Based on the results of our study and lack of identifiable predictive factors, one could argue in favor of a relatively large opening in the first trabeculotomy. Although the most common approach for trabeculotomy is ab externo, an increasing number of surgeons are adopting ab interno approaches to save the conjunctiva for

probable future glaucoma surgeries.[26,27] These studies demonstrated that gonioscopy-assisted transluminal trabeculotomy was successful in the management of PCG.

Our observation that IOP and success rates decline during the first 18 months after the surgery underscores the need for frequent examinations in the early postoperative period. As seen in previous reports, younger age at the time of diagnosis was associated with a lower success rate. Patients with early-onset PCG typically require more aggressive treatment and examination under anesthesia monitoring.[28]

The definitive role of corneal pachymetry in congenital glaucoma has yet to be determined.[16] Published data regarding the corneal thickness in congenital glaucoma is ambiguous and both thicker[17,29] and thinner[30] pachymetry are reported. PCG eyes in our study had relatively thicker corneas, which could be due to the structural changes, scarring, or edema. It is well established that corneal thickness affects IOP measurements in adult patients; however, the effect of corneal thickness on measurement error is poorly understood in children. We advise against "adjusting" IOP in light of central corneal thickness in children,[29] although it should be considered in the overall context of the examination.

Our study was limited by its retrospective nature, including variable follow-up, different surgeons, and different instruments to measure the intraocular pressure in the postoperative period. Additionally, this study was conducted at a single tertiary academic referral center, and the results cannot easily be generalized to other practices.

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