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Treatment Outcomes in the Primary Tube Versus Trabeculectomy Study after 1 Year of Follow-up

Steven J. Gedde, MD,[1] *William J. Feuer, MS,*[1] *Wei Shi, MS,*[1] *Kin Sheng Lim, MD,*[2] *Keith Barton, MD,*[3] *Saurabh Goyal, MD,*[4] *Iqbal I.K. Ahmed, MD,*[5] *James Brandt, MD,*[6] *for the Primary Tube Versus Trabeculectomy Study Group**

Purpose: To report 1-year treatment outcomes in the Primary Tube Versus Trabeculectomy (PTVT) Study.

Design: Multicenter, randomized clinical trial.

Participants: Two hundred forty-two eyes of 242 patients with medically uncontrolled glaucoma and no previous incisional ocular surgery, including 125 in the tube group and 117 in the trabeculectomy group.

Methods: Patients were enrolled at 16 clinical centers and assigned randomly to treatment with a tube shunt (350-mm^2 Baerveldt glaucoma implant) or trabeculectomy with mitomycin C (MMC; 0.4 mg/ml for 2 minutes).

Main Outcome Measures: Intraocular pressure (IOP), glaucoma medical therapy, visual acuity, visual fields, surgical complications, and failure (IOP of more than 21 mmHg or reduced by less than 20% from baseline, IOP of 5 mmHg or less, reoperation for glaucoma, or loss of light perception vision).

Results: The cumulative probability of failure during the first year of follow-up was 17.3% in the tube group and 7.9% in the trabeculectomy group ($P = 0.01$; hazard ratio, 2.59; 95% confidence interval, 1.20–5.60). Mean ± standard deviation IOP was 13.8±4.1 mmHg in the tube group and 12.4±4.4 mmHg in the trabeculectomy group at 1 year ($P = 0.01$), and the number of glaucoma medications was 2.1±1.4 in the tube group and 0.9±1.4 in the trabeculectomy group ($P < 0.001$). Postoperative complications developed in 36 patients (29%) in the tube group and 48 patients (41%) in the trabeculectomy group ($P = 0.06$). Serious complications requiring reoperation or producing a loss of 2 Snellen lines or more occurred in 1 patient (1%) in the tube group and 8 patients (7%) in the trabeculectomy group ($P = 0.03$).

Conclusions: Trabeculectomy with MMC had a higher surgical success rate than tube shunt implantation after 1 year in the PTVT Study. Lower IOP with use of fewer glaucoma medications was achieved after trabeculectomy with MMC compared with tube shunt surgery during the first year of follow-up. The frequency of serious complications producing vision loss or requiring reoperation was lower after tube shunt surgery relative to trabeculectomy with MMC. *Ophthalmology 2018;125:650-663 © 2018 by the American Academy of Ophthalmology*

Supplemental material available at www.aaojournal.org.

Despite the recent introduction of several minimally invasive glaucoma surgeries, trabeculectomy and tube shunt implantation remain the most commonly performed glaucoma operations worldwide. These traditional glaucoma procedures are the most effective means of providing substantial, long-term intraocular pressure (IOP) reduction. Trabeculectomy historically has been the initial glaucoma operation of choice, and tube shunts have been reserved for refractory glaucoma.[1] However, tube shunts more recently have been used routinely in eyes at lower risk for filtration failure.

Surveys of the American Glaucoma Society membership indicate a lack of consensus regarding the preferred primary incisional procedure for glaucoma.[2–5] In 2008, the most popular approaches for surgically managing primary open-angle glaucoma in eyes without previous ocular surgery were trabeculectomy with mitomycin C (MMC) in 74% of patients and placement of a tube shunt in 11% of patients.[4] The use of tube shunt surgery as an initial incisional procedure increased to 23% in a repeat American Glaucoma Society survey in 2016, and use of trabeculectomy with MMC decreased to 59%.[5]

The Primary Tube Versus Trabeculectomy (PTVT) Study is a multicenter, randomized clinical trial comparing the safety and efficacy of tube shunt implantation and trabeculectomy with MMC in eyes without prior ocular surgery. Our companion article describes the methodology of the study.[6] This article reports the outcomes of treatment during the first year of follow-up in the PTVT Study.

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Methods

The institutional review board at each clinical center approved the study protocol before recruitment began (see Appendix, available at www.aaojournal.org). Written informed consent was obtained from all subjects for both treatment and participation in the research. The study adhered to the tenets of the Declaration of Helsinki and the provisions of the Health Insurance Portability and Accountability Act. This study is registered at www.clinicaltrials.gov (identifier, NCT00666237). The design and methods of the PTVT Study are described in detail in our companion article,[6] and they are summarized as follows.

Eligibility Criteria

Patients 18 to 85 years of age who had not undergone any previous incisional ocular surgery and who had inadequately controlled glaucoma with IOP of 18 mmHg or more and 40 mmHg or less with tolerated medical therapy were eligible for the study. Exclusion criteria included no light perception vision, pregnant or nursing women, narrow anterior chamber angle, iris neovascularization or proliferative retinopathy, iridocorneal endothelial syndrome, epithelial or fibrous downgrowth, chronic or recurrent uveitis, steroid-induced glaucoma, severe posterior blepharitis, unwillingness to discontinue contact lens use after surgery, previous cyclodestructive procedure, conjunctival scarring from prior ocular trauma or cicatrizing disease precluding a superior trabeculectomy, functionally significant cataract, need for glaucoma surgery combined with other ocular procedures or anticipated need for additional ocular surgery, unwillingness or inability to give consent, unwillingness to accept randomization, or inability to return for scheduled protocol visits. Only 1 eye of eligible patients was included in the study.

Randomization and Treatment

The PTVT Study was conducted at 16 clinical centers. Eligibility was confirmed independently at the statistical coordinating center. Patients enrolled in the study were randomized to placement of a 350-mm^2 Baerveldt glaucoma implant or trabeculectomy with MMC. Randomization was performed with a permuted block design stratified by age, race, and presence of failed filtering surgery in the nonstudy eye, as well as the clinical center. Neither the patient nor the clinician was masked to the randomization assignment during follow-up.

Patient Visits

Baseline demographic and clinical information were collected for enrolled patients. Follow-up visits were scheduled at 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, 18 months, 2 years, 3 years, 4 years, and 5 years after surgery. Data were collected with standardized forms at each follow-up visit. Additional information was collected for patients undergoing a reoperation, including the date of surgery, type of procedure, and IOP level and number of glaucoma medications immediately before reoperation.

Outcome Measures

The primary outcome measure in the PTVT Study is the cumulative rate of surgical failure at 1 year, and secondary outcome measures include IOP, visual acuity (VA), use of glaucoma medical therapy, surgical complications, and visual fields. Failure was defined prospectively as IOP of more than 21 mmHg or reduced by less than 20% from baseline on 2 consecutive follow-up visits after 3 months, IOP of 5 mmHg or less on 2 consecutive follow-up visits after 3 months, reoperation for glaucoma, or loss of light perception vision. Patients who had not failed by the above criteria and were not receiving supplemental medical therapy were considered complete successes. Patients who had not failed but required supplemental medical therapy were categorized as qualified successes. An independent safety and data monitoring committee monitored outcomes in the study.

Reoperation for glaucoma or a complication was defined as additional surgery requiring a return to the operating room. Cyclodestruction also was counted as a reoperation for glaucoma, and a vitreous tap with injection of intravitreal antibiotics was a reoperation for a complication, whether performed in the clinic or operating room. Interventions performed at the slit lamp, such as needling procedures or reformation of the anterior chamber, were not considered reoperations. Early postoperative complications were defined as surgical complications developing within the first month after randomized surgical treatment, and late postoperative complications were complications that occurred more than 1 month after glaucoma surgery. Surgical complications that developed during the first postoperative month and persisted with longer follow-up were counted only as early postoperative complications. Persistent diplopia, persistent corneal edema, and dysesthesia were defined as the postoperative development of these complications and their presence at the 6-month follow-up visit or thereafter. Eyes with a positive Seidel test within the first month of follow-up were classified as having wound leaks, and those with a positive Seidel test occurring after 1 month were categorized as having bleb leaks. Serious complications were defined as surgical complications that produced a loss of 2 lines or more of Snellen VA, required reoperation to manage the complication, or both. Patients who underwent additional surgery were censored from analysis of complications after the reoperation. Cataracts were considered to have progressed if there was loss of 2 Snellen lines or more that was attributed to cataract at the 6-month follow-up visit or thereafter, or if cataract surgery was performed.

Sample Size Calculations

Sample size calculations were performed based on projected differences in failure rates between treatment groups. Enrollment of 88 patients in each treatment group was expected to detect a relative risk of failure of 2.0 at 5 years assuming a 20% failure rate in the lower risk group with a 2-sided significance level of 0.05, a power of 0.80, and analysis with a Yates-corrected chi-square test. A total of 242 patients were recruited for the study to allow for a dropout rate of 6% per year.

Statistical Analysis

Univariate comparisons between treatment groups were performed with the 2-sided Student *t* test for continuous variables and the chi-square test—asymptotic, Yates corrected, or exact permutation as appropriate—for categorical variables. Snellen VA measurements were converted to logarithm of the minimum angle of resolution (logMAR) equivalents for the purpose of data analysis, as reported previously.[7] The time to failure was defined as the time from surgical treatment to reoperation for glaucoma, loss of light perception vision, or the first of 2 consecutive study visits after 3 months in which the patient showed persistent hypotony (i.e., IOP $\leq$5 mmHg) or inadequately reduced IOP (i.e., IOP $>$21 mmHg or reduced $<$20% from baseline). Treatment comparisons of cumulative rate of failure and reoperation for glaucoma or complications were assessed with the stratified Kaplan-Meier survival analysis log-rank test. A *P* value of 0.05 or less was considered statistically significant in our analyses.

Results

Recruitment and Retention

A total of 242 eyes of 242 patients were enrolled and underwent surgical treatment between May 2008 and March 2015, including 125 patients in the tube group and 117 patients in the trabeculectomy group. There were 6 patients in the tube group and 8 patients in the trabeculectomy group who were randomized but did not receive surgical treatment in the study, and they were not included in the analysis of outcomes. The reasons for exiting the study before undergoing surgery involved insurance issues for 2 patients, transfer of care to another surgeon for 2 patients, cancellation of surgery secondary to stroke for 1 patient, death between the time of randomization and scheduled surgery for 1 patient, and unknown reasons for 8 patients.

Figure S1 (available at www.aaojournal.org) shows the progress of patients in the study. In the overall study group, 1 patient (0.4%) died within the first year of enrollment. An additional 16 patients (6.6%) missed their 1-year study visit. During the first year of the study, 3.0% of follow-up visits were missed because of death or loss to follow-up. The visit completion rate did not differ significantly by treatment group ($P = 0.99$, chi-square test).

Protocol Violations

One patient who was randomized to the trabeculectomy group underwent laser-assisted in situ keratomileusis (LASIK) in the study eye and should have been excluded because of previous incisional ocular surgery. Two patients were randomized to the trabeculectomy group but underwent placement of a tube shunt because of surgeon error. All patients were analyzed according to the treatment group to which they were assigned by randomization in an intent-to-treat analysis. None of the 3 patients who violated the study protocol experienced treatment failure or underwent additional ocular surgery.

Baseline Characteristics of Study Population

The baseline characteristics of the study population are provided in Table 1. No significant differences in any of the demographic or ocular features were observed between treatment groups at enrollment. The mean ± standard deviation (SD) age of the study population at enrollment was 61.4±11.8 years, and 160 patients (66%) were men. The mean ± SD IOP of the overall study group was 23.6±5.3 mmHg, and the mean ± SD number of glaucoma medications was 3.2±1.1. The most common diagnosis was primary open-angle glaucoma in 218 eyes (90%). The median Snellen VA was 20/25, and mean ± SD Early Treatment Diabetic Study (ETDRS) VA was 73±20 letters. The mean ± SD mean deviation with Humphrey visual field testing was −14.6±9.9 dB.

Eyes were stratified at enrollment based on several factors including age, ethnicity, and previous failed filtering surgery in the nonstudy eye. Only 13 patients (5%) had undergone glaucoma surgery in the fellow eye that had failed (stratum 2). The remaining patients in the study were approximately equally distributed between the other 2 strata.

Operative Data

Operative data for the tube group are shown in Table S2 (available at www.aaojournal.org). A fornix-based conjunctival flap was used in Baerveldt implantation in 110 eyes (88%). An intraluminal ripcord suture was the most common method for temporary flow restriction, which was used in 84 eyes (67%). Fenestration of the tube was performed in 59 eyes (47%) for early IOP reduction. Pericardium was the patch graft material in 61 eyes (49%), sclera in 38 eyes (30%), cornea in 24 eyes (19%), and other materials in 2 eyes (2%).

Operative data for the trabeculectomy group are presented in Table S3 (available at www.aaojournal.org). A fornix-based conjunctival flap was used in 96 trabeculectomy patients (84%). Approximately half the patients received 3 scleral flap sutures. A tenonectomy was performed in 10 eyes (9%), and 93 eyes (81%) underwent a single-layer closure of the conjunctiva.

Treatment Outcomes

The outcomes of randomized patients unadjusted for follow-up time are presented in Table S4 (available at www.aaojournal.org). All patients who completed 1-year follow-up visits, who experienced a prior failure, or both were included in this analysis. A significantly higher failure rate was seen in the tube group than the trabeculectomy group after 1 year. Treatment failure had occurred in 23 patients (20%) in the tube group and in 9 patients (8%) in the trabeculectomy group at 1 year ($P = 0.02$, logistic regression analysis adjusted for stratum). In the tube group, 16 patients (14%) were classified as complete successes and 78 patients (67%) were qualified successes. In the trabeculectomy group, 64 patients (59%) were complete successes and 36 patients (33%) were qualified successes. The rate of complete success was significantly higher in the trabeculectomy group relative to the tube group ($P < 0.001$, logistic regression analysis adjusted for stratum).

Kaplan-Meier survival analysis also was used to compare failure rates between the 2 treatment groups, and the results are presented in Figure 2. The cumulative probability of failure was 17.3% in the tube group and 7.9% in the trabeculectomy group at 1 year ($P = 0.01$, log-rank test adjusted for stratum; hazard ratio, 2.59; 95% confidence interval, 1.20−5.60). No significant differences in treatment efficacy were found between strata ($P = 0.51$, Cox regression analysis).

Figure 3 presents the failure rates for the 2 treatment groups with alternative outcome criteria. Patients with persistent hypotony, reoperation for glaucoma, or loss of light perception vision were still classified as treatment failures. However, the upper IOP limit distinguishing success from failure was changed. When inadequate IOP reduction was defined as IOP of more than 17 mmHg or reduced by less than 20% from baseline on 2 consecutive follow-up visits after 3 months, the cumulative probability of failure at 1 year was 20.6% in the tube group and 9.6% in the trabeculectomy group ($P = 0.01$, log-rank test adjusted for stratum; hazard ratio, 2.40; 95% confidence interval, 1.19−4.88). When inadequate IOP reduction was defined as IOP of more than 14 mmHg on 2 consecutive visits after 3 months, the cumulative probability of failure was 28.1% in the tube group and 20.0% in the trabeculectomy group at 1 year ($P = 0.15$, log-rank test adjusted for stratum; hazard ratio, 1.47; 95% confidence interval, 0.87−2.50). Higher failure rates were observed in the tube group compared with the trabeculectomy group when more stringent IOP criteria were used to define success and failure. These differences were statistically significant with failure defined as IOP of more than 17 mmHg, but not when failure was defined as IOP of more than 14 mmHg.

Table 5 lists the reasons for classification as a treatment failure. Inadequate IOP reduction (i.e., IOP >21 mmHg or reduced <20% from baseline on 2 consecutive follow-up visits after 3 months) was the most common cause for failure during the first year of follow-up in both treatment groups, occurring in 13 patients in the tube group and 4 patients in the trabeculectomy group. There were 10 patients in the tube group and 4 patients in the trabeculectomy group who failed because they underwent a reoperation for

Table 1. Baseline Characteristics of Primary Tube Versus Trabeculectomy Study Patients

Characteristic	Tube Group (n = 125)	Trabeculectomy Group (n = 117)
Age (yrs)		
Mean ± SD	62.0±11.4	60.8±12.3
Median (range)	62 (28–85)	61 (21–85)
Gender, no. (%)		
Male	84 (67)	76 (65)
Female	41 (33)	41 (35)
Race, no. (%)		
Black	59 (47)	57 (49)
White	50 (40)	45 (39)
Hispanic	9 (7)	6 (5)
Asian	6 (5)	7 (6)
Other	1 (1)	2 (2)
Hypertension, no. (%)	63 (50)	55 (47)
Diabetes mellitus, no. (%)	18 (14)	27 (23)
Study eye, no. (%)		
Right	68 (54)	60 (51)
Left	57 (46)	57 (49)
IOP (mmHg)		
Mean ± SD	23.3±4.9	23.9±5.7
Range	18–40	18–40
Central corneal thickness (μm), mean ± SD	525±37	524±33
Glaucoma medications		
Mean ± SD	3.1±1.1	3.2±1.1
Range	0–6	0–5
Diagnosis, no. (%)		
POAG	109 (87)	109 (93)
CACG	5 (4)	3 (3)
PG	4 (3)	2 (2)
PXFG	4 (3)	1 (1)
Other	3 (2)	2 (2)
Previous ocular laser treatment, no. (%)		
LTP	34 (27)	29 (25)
LPI	11 (9)	2 (2)
Other	9 (7)	5 (4)
ETDRS VA, mean ± SD	73±20	73±20
Snellen VA		
LogMAR, mean ± SD	0.20±0.42	0.25±0.51
Median	20/25	20/25
Range	20/13–HM	20/13–LP
Cataract, no. (%)	76 (61)	65 (56)
Mild	62 (82)	50 (77)
Moderate	13 (17)	14 (22)
Severe	1 (1)	1 (1)
Diplopia, no. (%)	8 (6)	4 (3)
Humphrey visual fields, mean ± SD		
MD	−14.5±10.2	−14.7±9.7
PSD	7.71±3.86	8.19±3.57
Stratum*		
1	55 (44)	53 (45)
2	8 (6)	5 (4)
3	62 (50)	59 (50)

CACG = chronic angle-closure glaucoma; ETDRS = Early Treatment Diabetic Retinopathy Study; HM = hand movements; IOP = intraocular pressure; logMAR = logarithm of the minimum angle of resolution; LP = light perception; LPI = laser iridotomy; LTP = laser trabeculoplasty; MD = mean deviation; PG = pigmentary glaucoma; POAG = primary open-angle glaucoma; PSD = pattern standard deviation; PXFG = pseudoexfoliation glaucoma; SD = standard deviation; VA = visual acuity.
*Stratum 1, no failed glaucoma surgery in fellow eye and age 50 years or older and not black race; stratum 2, failed glaucoma surgery in fellow eye; stratum 3, no failed glaucoma surgery in fellow eye and age younger than 50 years, black race, or both.

glaucoma. Persistent hypotony (i.e., IOP ≤5 mmHg on 2 consecutive visits after 3 months) was the cause for treatment failure in 1 patient in the trabeculectomy group. Loss of VA from baseline was seen in the patient with hypotony failure. No failures occurred in either treatment group because of loss of light perception vision.

Intraocular Pressure Reduction

Baseline and follow-up IOP measurements for the tube and trabeculectomy groups are provided in Table 6, and they are also graphically presented in Figure 4 and in Figure S5 (available at

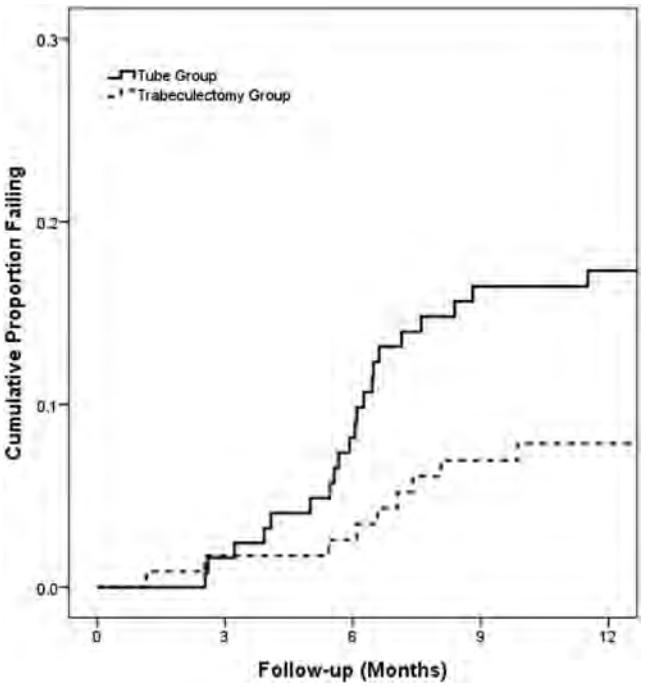

Figure 2. Kaplan-Meier plot showing the cumulative probability of failure in the Primary Tube Versus Trabeculectomy Study.

www.aaojournal.org). Patients who underwent additional glaucoma surgery were censored from analysis after reoperation. Both surgical procedures produced a significant and sustained reduction in IOP. At 1 year, mean ± SD IOP was 13.8±4.1 mmHg in the tube group and 12.4±4.4 mmHg in the trabeculectomy group ($P = 0.01$, Student t test). Among patients who completed 1-year follow-up visits, mean ± SD IOP reduction from baseline was 9.3±6.6 mmHg (37.5%) in the tube group and 11.4±6.6 mmHg (46.0%) in the trabeculectomy group ($P = 0.02$, Student t test). The degree of IOP reduction was significantly greater in the trabeculectomy group compared with the tube group at 1 year. The trabeculectomy group had significantly lower mean IOPs than the tube group at all follow-up visits during the first year of the study. At 1 year, 69 patients (60%) in the tube group and 75 patients (71%) in the trabeculectomy group had an IOP of 14 mmHg or less ($P = 0.11$, chi-square test).

An analysis was performed carrying the last observation forward, which included the last IOP before glaucoma reoperation for patients who underwent additional glaucoma surgery and the last study visit for patients with missing follow-up. At 1 year, mean ± SD IOP was 14.5±4.7 mmHg in the tube group and 12.7±4.7 mmHg in the trabeculectomy group ($P = 0.003$, Student t test) with the last observation carried forward. An assessment of IOP was also made for all patients, including those who underwent further surgery for glaucoma. At 1 year, mean ± SD IOP was 13.9±4.1 mmHg in the tube group and 12.5±4.5 mmHg in the trabeculectomy group ($P = 0.02$, Student t test) taking into account all medical and surgical management.

Medical Therapy

Table 6 shows the number of glaucoma medications in the tube and trabeculectomy groups at baseline and follow-up. Patients who underwent additional glaucoma surgery were censored from analysis after reoperation. A significant reduction in the use of medical therapy was seen in both treatment groups. The mean ± SD number of glaucoma medications decreased from baseline by

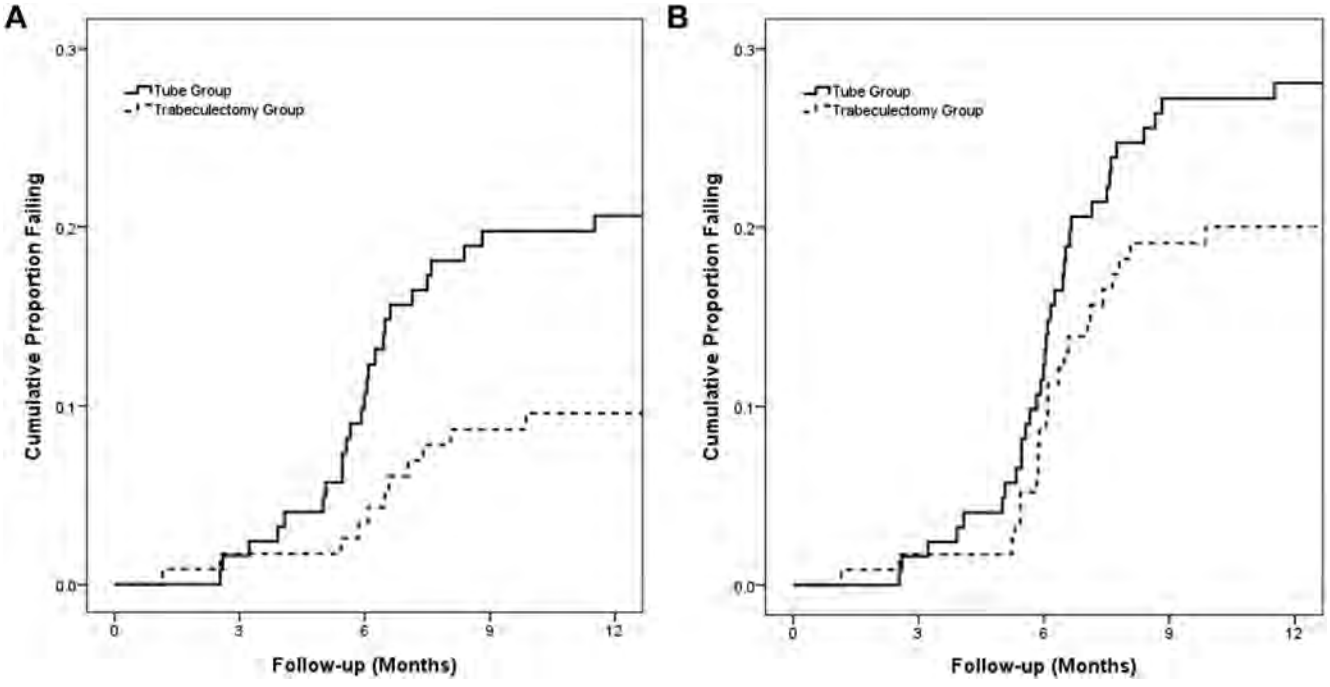

Figure 3. Kaplan-Meier plots showing the cumulative probability of failure in the Primary Tube Versus Trabeculectomy Study defining inadequate intraocular pressure (IOP) reduction as (**A**) IOP of more than 17 mmHg or reduced by less than 20% from baseline or (**B**) IOP of more than 14 mmHg. Inadequate IOP reduction criteria must have been present on 2 consecutive visits after 3 months to qualify as treatment failure. Patients with persistent hypotony, reoperation for glaucoma, and loss of light perception vision were classified as failures.

Table 5. Reasons for Treatment Failure in the Primary Tube Versus Trabeculectomy Study

	Tube Group (n = 23)	Trabeculectomy Group (n = 9)
Inadequate IOP reduction*	13 (57)	4 (44)
Reoperation for glaucoma	10 (43)	4 (44)
Persistent hypotony†	0	1 (11)
Loss of light perception	0	0

IOP = intraocular pressure.
Data are presented as number (percentage). Patients are categorized according to the first-occurring reason for treatment failure. $P = 0.49$ for the difference in distribution of reasons for failure between treatment groups (exact permutation chi-square test).
*Intraocular pressure more than 21 mmHg or reduced by less than 20% from baseline on 2 consecutive follow-up visits after 3 months.
†Intraocular pressure 5 mmHg or less on 2 consecutive follow-up visits after 3 months.

1.0±1.5 in the tube group and 2.2±1.5 in the trabeculectomy group in patients who completed 1-year follow-up visits. Significantly greater use of glaucoma medical therapy was observed in the tube group compared with the trabeculectomy group at all follow-up visits during the first year of the study.

The mean ± SD number of glaucoma medications was 2.1±1.5 in the tube group and 0.9±1.4 in the trabeculectomy group at 1 year ($P < 0.001$, Student t test) with the last observation carried forward. When patients who underwent additional glaucoma surgery were included in the analysis, the mean ± SD number of glaucoma medications was 2.1±1.4 in the tube group and 0.9±1.4 in the trabeculectomy group ($P < 0.001$, Student t test).

Table 6. Intraocular Pressure and Medical Therapy at Baseline and Follow-up in the Primary Tube Versus Trabeculectomy Study

	Tube Group	Trabeculectomy Group	P Value*
Baseline			
IOP (mmHg)	23.3±4.9	23.9±5.7	0.35
Glaucoma medications	3.1±1.1	3.2±1.1	0.56
No.	125	117	
1 day			
IOP (mmHg)	19.0±9.7	16.3±9.2	0.03
No.	125	116	
1 wk			
IOP (mmHg)	18.2±8.5	15.1±9.2	0.007
Glaucoma medications	1.1±1.4	0.1±0.5	<0.001
No.	120	116	
1 mo			
IOP (mmHg)	19.7±7.3	13.1±6.3	<0.001
Glaucoma medications	1.4±1.5	0.2±0.8	<0.001
No.	124	115	
3 mos			
IOP (mmHg)	18.0±5.9	12.5±4.9	<0.001
Glaucoma medications	1.9±1.4	0.6±1.2	<0.001
No.	121	113	
6 mos			
IOP (mmHg)	14.7±4.4	12.8±4.8	0.003
Glaucoma medications	2.1±1.4	0.6±1.2	<0.001
No.	112	109	
1 yr			
IOP (mmHg)	13.8±4.1	12.4±4.4	0.01
Glaucoma medications	2.1±1.4	0.9±1.4	<0.001
No.	108	105	

IOP = intraocular pressure.
Data are presented as mean ± standard deviation unless otherwise indicated. Data censored after a reoperation for glaucoma.
*Student t test.

Reoperation for Glaucoma

The rate of reoperation for glaucoma was similar in both treatment groups. The 1-year cumulative reoperation rate for glaucoma with Kaplan-Meier survival analysis was 6.6% in the tube group and 3.5% in the trabeculectomy group ($P = 0.14$, log-rank test adjusted for stratum). A total of 10 patients in the tube group underwent additional glaucoma surgery, which involved placement of a second tube shunt in 3 patients, trabeculectomy with MMC in 3 patients, transscleral cyclophotocoagulation in 3 patients, and endoscopic cyclophotocoagulation in 1 patient. In the trabeculectomy group, 4 patients underwent glaucoma reoperations, including tube shunt placement in 3 patients and trabeculectomy revision in 1 patient.

Because the surgeon was not masked to the treatment assignment, a potential bias existed in the decision to reoperate for glaucoma. To evaluate for selection bias, the IOP levels were compared between treatment groups in patients who underwent glaucoma reoperation, as well as those who failed because of inadequate IOP reduction but did not undergo additional glaucoma surgery. The mean ± SD IOP was 20.0±2.7 mmHg for the 10 patients in the tube group and 22.8±4.1 mmHg for the 4 patients in the trabeculectomy group at the time of reoperation for glaucoma ($P = 0.17$, Student t test). The IOP levels also were compared between the 13 patients in the tube group and 4 patients in the trabeculectomy group who failed because of inadequate IOP reduction but did not undergo additional glaucoma surgery during the first year of follow-up. In this patient subgroup, the mean ± SD IOP was 17.8±3.6 mmHg in the tube group and 19.5±3.0 in the trabeculectomy group ($P = 0.41$, Student t test). The mean IOP before reoperation for glaucoma was similar in the tube and trabeculectomy groups, and no significant difference was seen between treatment groups in mean IOP among patients who failed because of inadequate IOP reduction but did not undergo additional glaucoma surgery.

Visual Acuity

Table 7 shows VA results in the PTVT Study. Significant decreases in Snellen VA and ETDRS VA were observed in both treatment groups during the first year of follow-up. Among patients who completed 1-year follow-up visits, mean ± SD Snellen VA decreased 0.05±0.22 logMAR units from baseline ($P = 0.02$, paired t test) and mean ± SD ETDRS VA was reduced by 3±15 letters from baseline ($P = 0.02$, paired t test) in the tube group. In the trabeculectomy group, mean ± SD Snellen VA decreased 0.08±0.32 logMAR units ($P = 0.008$, paired t test) and mean ± SD ETDRS VA declined 7±13 letters ($P = 0.001$, paired t test) from baseline to the 1-year follow-up visit. No significant differences in Snellen VA ($P = 0.16$, Student t test) or ETDRS VA ($P = 0.48$, Student t test) were seen between the tube and trabeculectomy groups at 1 year. The changes in Snellen VA ($P = 0.35$, Student t test) and ETDRS VA ($P = 0.07$, Student t test) from baseline also were similar between treatment groups among patients who completed 1 year of follow-up.

The rate of loss of 2 lines or more of Snellen VA was similar in the tube and trabeculectomy groups. At 1 year, 16 patients (13%) in the tube group and 13 patients (11%) in the trabeculectomy

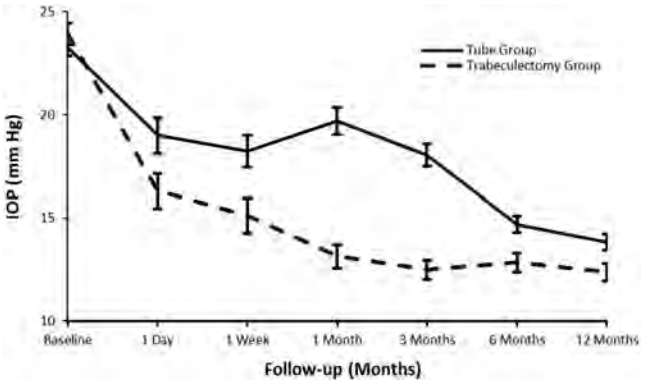

Figure 4. Graph showing intraocular pressure (IOP) at baseline and follow-up in the Primary Tube Versus Trabeculectomy Study. Data are presented as mean ± standard error of the mean and are censored after a reoperation for glaucoma. Note that follow-up time is not on a linear scale.

group had lost 2 Snellen lines or more from baseline ($P = 0.84$, chi-square test). The examining clinician was asked to provide an explanation for this reduction in VA. The most frequent causes of vision loss during the first year of follow-up were cataract in 10 patients in the tube group and 11 patients in the trabeculectomy group, glaucoma in 4 patients in the tube group and 2 patients in the trabeculectomy group, and macular disease in 1 patient in the tube group and 2 patients in the trabeculectomy group. The reason for decreased vision was unknown in 2 patients in the tube group and 1 patient in the trabeculectomy group.

Postoperative Interventions

Postoperative interventions are listed in Table 8. Interventions were performed with similar frequency in the tube and trabeculectomy groups. Postoperative interventions were undertaken in 75 patients (60%) in the tube group and in 74 patients (63%) in the trabeculectomy group ($P = 0.70$, chi-square test). Rip-cord removal and laser suture lysis were the most common interventions in the tube and trabeculectomy groups, respectively. The method of temporary tube occlusion did not influence the rate of surgical success in the tube group. The cumulative probability of failure at 1 year was 18.2% in patients with intraluminal rip-cord sutures and 15.3% in patients with external polyglactin ligatures ($P = 0.86$, log-rank test).

Surgical Complications

Table 9 lists surgical complications encountered during the first year of the PTVT Study. The overall incidence of intraoperative complications was similar between the tube and trabeculectomy groups. A total of 6 patients (5%) in the tube group and 2 patients (2%) in the trabeculectomy group demonstrated complications at the time of surgery ($P = 0.33$, chi-square test). One patient in each treatment group experienced 2 intraoperative complications, and the remaining 6 patients each experienced only 1 intraoperative complication. Hyphema was the most common intraoperative complication in both treatment groups, occurring in 4 patients (3%) in the tube group and in 2 patients (2%) in the trabeculectomy group. No intraoperative complication occurred with significantly higher frequency in either treatment group.

Early postoperative complications developing within the first month after surgery occurred with significantly greater frequency in the trabeculectomy group compared with the tube group. A total of 36 early postoperative complications were reported in 25 patients (20%) in the tube group, and 52 complications were noted in 39 patients (33%) in the trabeculectomy group ($P = 0.03$, chi-square test). Forty-six patients experienced only 1 early postoperative complication. Several patients demonstrated multiple early postoperative complications, including 12 patients with 2 complications, 6 patients with 3 complications, and 1 patient with 4 complications. Wound leak ($P < 0.001$, chi-square test) and encapsulated bleb ($P = 0.009$, chi-square test) were early postoperative complications that were significantly more common in the trabeculectomy group compared with the tube group. No early postoperative complications occurred with significantly greater frequency in the tube group than the trabeculectomy group.

The overall incidence of late postoperative complications occurring more than 1 month after surgery was similar between treatment groups. A total of 22 late postoperative complications were seen in 20 patients (16%) in the tube group, and 20 complications were observed in 18 patients (15%) in the trabeculectomy group ($P = 0.99$, chi-square test). A single late postoperative complication developed in 34 patients, and 4 patients experienced 2 complications. No late postoperative complication occurred with significantly higher frequency in either treatment group.

Several patients in each treatment group demonstrated both early and late postoperative complications. There was a trend toward a higher overall rate of postoperative complications in the trabeculectomy group compared with the tube group, but the difference did not reach the level of statistical significance. During the first year of follow-up, 36 patients (29%) in the tube group and 48 patients (41%) in the trabeculectomy group experienced 1 or more surgical complications after surgery ($P = 0.06$, chi-square test).

Table 10 shows serious complications resulting in reoperation, vision loss, or both. The incidence of serious complications was significantly higher in the trabeculectomy group compared with the tube group. Serious complications were observed in 1 patient (1%) in the tube group and in 8 patients (7%) in the trabeculectomy group ($P = 0.03$, chi-square test). Hypotony maculopathy produced loss of 2 Snellen lines or more in 2 patients in the trabeculectomy group, despite surgical treatment in 1 of these patients.

Reoperation for Complications

The rate of reoperation for complications was significantly higher in the trabeculectomy group compared with the tube group. A total of 7 patients (6%) in the trabeculectomy group and 1 patient (1%) in the tube group underwent additional surgery to manage postoperative complications. The 1-year cumulative reoperation rate for complications from Kaplan-Meier survival analysis was 0.8% in the tube group and 6.0% in the trabeculectomy group ($P = 0.02$, log-rank test), as shown in Figure 6. There were 4 patients in the trabeculectomy group who underwent bleb revision for wound leaks after failing management with a bandage contact lens or suturing at the slit lamp. Trabeculectomy revision was performed in 2 patients for hypotony maculopathy, and 1 patient underwent a trabeculectomy revision and anterior chamber washout for an 8-ball hyphema. One patient in the tube group underwent removal of the tube shunt for exposure of the end plate. A phacoemulsification cataract extraction and endoscopic cyclophotocoagulation was performed at the time of shunt removal, and the patient was classified as a failure because of additional glaucoma surgery.

Cataract Progression

No significant difference in the rate of cataract progression was seen between treatment groups. Cataract surgery was performed in

Table 7. Visual Acuity Results in the Primary Tube Versus Trabeculectomy Study

	Tube Group (n = 125)	Trabeculectomy Group (n = 117)	P Value
ETDRS VA, mean ± SD			
Baseline	73±20	73±20	0.96*
1 yr	73±19	71±19	0.48*
Change†	−3±15	−7±13	0.07*
Snellen VA (logMAR), mean ± SD			
Baseline	0.20±0.42	0.25±0.51	0.42*
1 yr	0.22±0.39	0.31±0.55	0.16*
Change†	0.05±0.22	0.08±0.32	0.35*
Loss of ≥2 Snellen lines, no. (%)‡	16 (13)	13 (11)	0.84§
Cataract	10	11	
Glaucoma	4	2	
Macular disease	1	2	
Unknown	2	1	

ETDRS = Early Treatment Diabetic Retinopathy Study; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation; VA = visual acuity.
*Student *t* test.
†Not all patients seen at baseline returned for 1-year visits, so the baseline mean minus the 1-year mean does not equal the change.
‡Some patients had more than 1 reason for decreased vision.
§Chi-square test.

15 patients (12%) in the tube group and in 12 patients (10%) in the trabeculectomy group during the first year of follow-up ($P = 0.69$, chi-square test). An additional 10 patients (8%) in the tube group and 11 patients (9%) in the trabeculectomy group experienced loss of 2 lines or more of Snellen VA attributed to cataract ($P = 0.87$, chi-square test). Cataract progression occurred in 25 patients (20%) in the tube group and 23 patients (20%) in the trabeculectomy group after 1 year ($P = 1.00$, chi-square test).

Sensitivity Analysis

Although the principal analysis was performed on observed data, we also did a sensitivity analysis in which multiple imputation was used to estimate missing IOP and number of glaucoma medications. In the imputed dataset, the averages by study visit and treatment group differed from the observed ones by 0.1 mmHg or less and 0.1 medication or less. Table 6 shows that all postoperative mean IOPs and numbers of medications were significantly different between treatment groups. Some of these differences were slightly more significant and others were slightly less significant with imputed data, but none had *P* values of more than 0.05. Imputation of IOP added 1 failure to the tube group because IOP was not reduced by 20% from baseline at both the 6-month and 1-year follow-up visits. This resulted in an increase in the cumulative failure rate in the tube group from 17.3% to 17.6% at 1 year, compared with 7.9% in the trabeculectomy group ($P = 0.009$, log-rank test).

Table 8. Postoperative Interventions in the Primary Tube Versus Trabeculectomy Study

	Tube Group (n = 125)	Trabeculectomy Group (n = 117)
Removal of rip-cord	63 (50)	—
Laser suture lysis	22 (18)	34 (29)
5-Fluorouracil injection	0	24 (21)
Removal of releasable suture	—	21 (18)
Needling	0	16 (14)
Anterior chamber reformation	10 (8)	6 (5)
Paracentesis	7 (6)	2 (2)
Suture wound	2 (2)	3 (3)
Bevacizumab injection	0	3 (3)
Subconjunctival steroid injection	0	1 (1)
Laser iridotomy	0	1 (1)
Laser iridoplasty	1 (1)	0
Total no. of patients with postoperative interventions*,†	75 (60)	74 (63)

Data are presented as number (percentage).
*Some patients received more than 1 intervention.
†$P = 0.70$ for the difference in total number of patients with postoperative interventions between treatment groups (chi-square test).

Discussion

The PTVT Study is a multicenter clinical trial that prospectively enrolled patients with medically uncontrolled glaucoma who had not undergone any previous incisional ocular surgery and randomized them to surgical treatment with a 350-mm^2 Baerveldt glaucoma implant or trabeculectomy with MMC. Patients who underwent tube shunt surgery had a higher failure rate compared with those who underwent trabeculectomy with MMC during the first year of follow-up in the study. At 1 year, the cumulative probability of failure was 17.3% in the tube group and 7.9% in the trabeculectomy group.

Both tube shunt surgery and trabeculectomy with MMC were effective in lowering IOP in the PTVT Study. Placement of a Baerveldt glaucoma implant produced a 37.5% reduction in IOP, and trabeculectomy with MMC achieved a 46.0% decrease in IOP in patients who completed 1 year of follow-up. Glaucoma specialists have suggested that low IOP levels generally cannot be achieved with tube shunts, and the IOP typically settles in the high teens after surgery.[8] However, the PTVT Study found a mean IOP of 13.8 mmHg in the tube group at 1 year, and 60% showed an IOP of 14 mmHg or less.

Table 9. Surgical Complications in the Primary Tube Versus Trabeculectomy Study

	Tube Group (n = 125)	Trabeculectomy Group (n = 117)	P Value*
Intraoperative complications			
Hyphema	4 (3)	2 (2)	0.74
Conjunctival buttonhole	3 (2)	0	0.27
Vitreous prolapse	0	1 (1)	0.97
Total no. of patients with intraoperative complications†	6 (5)	2 (2)	0.33
Early postoperative complications‡			
Shallow or flat anterior chamber	13 (10)	11 (9)	0.97
Choroidal effusion	9 (7)	12 (10)	0.54
Wound leak	1 (1)	14 (12)	<0.001
Hyphema	8 (6)	5 (4)	0.65
Encapsulated bleb	0	8 (7)	0.009
Hypotony maculopathy	1 (1)	3 (3)	0.57
Wound dehiscence	2 (2)	0	0.51
Aqueous misdirection	0	1 (1)	0.97
Corneal dellen	1 (1)	0	0.99
Cystoid macular edema	1 (1)	0	0.99
Suture-related infection	0	1 (1)	0.97
Total no. of patients with early postoperative complications†	25 (20)	39 (33)	0.03
Late postoperative complications§			
Encapsulated bleb	10 (8)	11 (9)	0.87
Shallow or flat anterior chamber	3 (2)	3 (3)	0.99
Choroidal effusion	1 (1)	0	0.99
Cystoid macular edema	1 (1)	0	0.99
Dysesthesia	1 (1)	2 (2)	0.95
Iritis	2 (2)	1 (1)	0.99
Diplopia	2 (2)	1 (1)	0.99
Hypotony maculopathy	0	2 (2)	0.45
Plate erosion	1 (1)	—	—
Tube retraction	1 (1)	—	—
Total no. of patients with late postoperative complications†	20 (16)	18 (15)	0.99
Total no. of patients with postoperative complications‖	36 (29)	48 (41)	0.06

Data are presented as number of patients (percentage).
Data censored after a reoperation.
*Chi-square test.
†Some patients experienced more than 1 complication.
‡Onset ≤1 month.
§Onset >1 month.
‖Some patients experienced early and late postoperative complications.

Treatment success was subdivided into complete and qualified successes based on the use of supplemental medical therapy. In addition to a higher overall success rate in the trabeculectomy group, the rate of complete success was higher in the trabeculectomy group relative to the tube group. This is consistent with the observed greater use of supplemental glaucoma medications by the tube group throughout the first year of follow-up. Glaucoma medications are effective only if they are used. Nonadherence to glaucoma medical therapy is well described and potentially could have influenced the study results.[9–12]

The ideal measure of success for any glaucoma therapy is the prevention of further glaucomatous optic nerve damage with preservation of visual function. We recognize that treatment success for individual patients cannot be defined by an arbitrary IOP level, because individuals vary in their susceptibility to the damaging effect of IOP. Nevertheless, currently available glaucoma therapy is directed entirely toward lowering IOP, and no other surrogate measure better reflects therapeutic success for this disease at present. The outcome criteria for the PTVT Study were developed a priori, and our definitions of success and failure are consistent with recommendations by the World Glaucoma Association for the reporting of outcomes in glaucoma surgical trials.[13]

The results of several multicenter randomized clinical trials have suggested that IOP of 21 mmHg or less may not be adequate to prevent glaucomatous progression in many patients.[14–16] To determine if the PTVT Study results changed if more stringent IOP criteria were applied to define success, several analyses were performed using alternative outcome criteria. Higher failure rates in the tube group compared with the trabeculectomy group were still seen when the upper IOP level defining success was reduced from 21 mmHg to 17 mmHg and 14 mmHg, although the difference did not reach the level of statistical significance when defining failure as IOP more than 14 mmHg. Because the differences in treatment outcomes were present using a range of IOP success criteria, the study results seem applicable to patients with the full spectrum of glaucoma from early to advanced damage.

Table 10. Serious Complications Associated with Reoperation, Vision Loss, or Both in the Primary Tube Versus Trabeculectomy Study

	Tube Group (n = 125)	Trabeculectomy Group (n = 117)
Reoperation for complications	1 (1)	7 (6)
8-Ball hyphema	0	1
Hypotony maculopathy	0	2
Plate exposure	1	—
Wound leak	0	4
Vision loss of ≥2 Snellen lines	0	2 (2)
Hypotony maculopathy	0	2
Total no. of patients with serious complications*	1 (1)	8 (7)†

Data are presented as number of patients (percentage). Data censored after a reoperation.
*$P = 0.03$ for the difference in serious complication rates between treatment groups (chi-square test).
†One patient who underwent a trabeculectomy revision for hypotony maculopathy also experienced vision loss.

Although the overall failure rate was higher in the tube group than the trabeculectomy group, the reasons for failure were distributed similarly between treatment groups. Inadequate IOP reduction was the most common reason for failure in both treatment groups. Failure because of persistent hypotony occurred in only 1 patient in the trabeculectomy group. It has been argued that hypotony may be an acceptable outcome of glaucoma surgery if it is not associated with vision loss.[17] It is noteworthy that the patient who experienced hypotony failure in the present study also sustained associated vision loss.

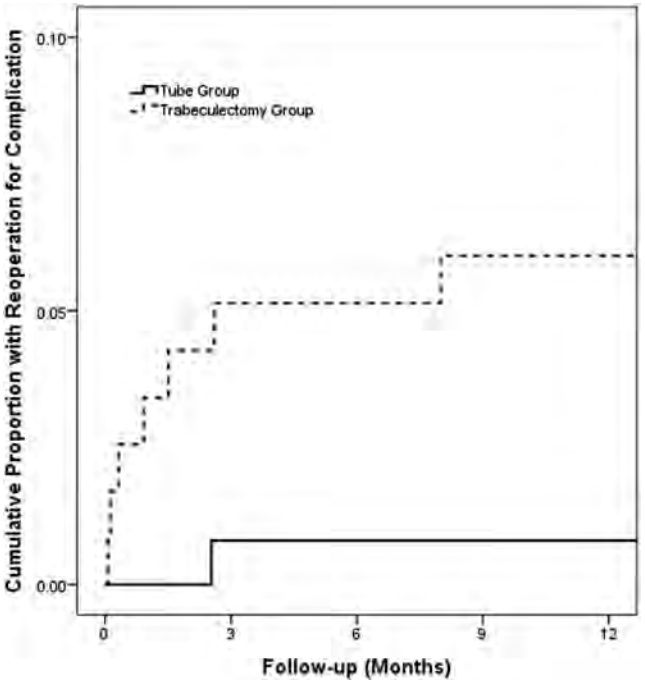

Figure 6. Kaplan-Meier plot showing the cumulative probability of reoperation for complications in the Primary Tube Versus Trabeculectomy Study.

Patients in whom trabeculectomy fails and who need additional glaucoma surgery generally undergo repeat trabeculectomy or placement of a tube shunt. However, additional glaucoma surgery in patients whose tube shunt surgery has failed frequently is more complex and traditionally has involved placement of a second tube shunt or cyclodestruction.[18–20] Trabeculectomy with MMC was performed in 3 patients in the tube group as a reoperation for glaucoma, and filtering surgery may be a feasible approach in some patients who have undergone primary tube shunt implantation. Because investigators in the PTVT Study were not masked to the treatment assignment and the decision to reoperate was left to the surgeon's discretion, a potential for bias existed in the decision to reoperate for glaucoma. We explored the possibility that surgeons may have had a higher threshold to perform additional glaucoma surgery in the tube group than the trabeculectomy group. No significant difference in mean IOP at the time of failure was seen between treatment groups in patients who underwent reoperation for glaucoma or in patients who failed because of inadequate IOP reduction, but did not undergo additional glaucoma surgery. We found no evidence of selection bias for additional glaucoma surgery, although the small number of glaucoma reoperations limits the ability to detect differences between treatment groups.

Reduction of VA occurred in both treatment groups during 1 year of follow-up. Snellen and ETDRS VA were similar in the tube and trabeculectomy groups at 1 year, and no significant difference in the rate of vision loss was observed between treatment groups. All patients in the PTVT Study were phakic at enrollment, and vision loss of 2 Snellen lines or more was attributed most frequently to cataract by the examining clinicians. However, the study did not use methods of grading lens opacities with standard lens photographs, such as the Lens Opacities Classification System II[21] or the Wisconsin System.[22] Cataracts were considered to have progressed in the PTVT Study if there was loss of 2 lines or more of Snellen VA that was attributed to lens opacification or if cataract surgery was performed. Cataract progression was common during the first year of follow-up, but occurred at a similar rate in the tube and trabeculectomy groups. Multiple studies have reported that glaucoma surgery is associated with the development of cataract.[14,23–28]

Several steps in the surgical procedures under investigation were standardized. A dosage of MMC (0.4 mg/ml for 2 minutes) was administered as an adjunct to filtering surgery in all patients randomized to the trabeculectomy group. This was the most common dosage used by glaucoma specialists in primary trabeculectomy in recent surveys of the American Glaucoma Society membership.[4,5] A 350-mm^2 Baerveldt glaucoma implant was placed in the superotemporal quadrant of all patients randomized to the tube group. This implant offers a large surface area with ease of insertion in a single quadrant, and greater IOP reduction has been observed with tube shunts with larger end plates.[29–31] Other aspects of each operation were left to the surgeon's discretion in keeping with his or her usual practice.

Limbus-based or fornix-based conjunctival flaps were allowed for both trabeculectomy and tube shunt surgery. Most surgeons selected a fornix-based conjunctival flap when performing both procedures. A trend toward greater use of fornix-based flaps with diffuse application of MMC in trabeculectomy has been observed in recent years.[32] An intraluminal rip-cord suture was the most popular method for temporary restriction of aqueous flow though the tube, which was used in two thirds of patients undergoing Baerveldt implantation. Approximately half the patients in the PTVT Study underwent tube fenestration at the time of shunt placement, and this technique has been shown to be effective in providing early IOP reduction.[33,34]

Postoperative interventions were performed with similar frequency in both treatment groups. Rip-cord removal and laser suture lysis were the most common interventions in the tube and trabeculectomy groups, respectively. Trabeculectomy is the only incisional glaucoma procedure that allows titration of IOP after surgery. Removal of releasable sutures and laser suture lysis were undertaken to increase filtration and reduce IOP in approximately half of the patients who underwent a trabeculectomy with MMC in the study. Because the Baerveldt glaucoma implant is a nonvalved tube shunt, an intraluminal rip-cord suture or external polyglactin ligature was used to restrict flow temporarily during tube shunt implantation. No difference in treatment outcome was observed based on the method of temporary tube occlusion.

The benefit of a glaucoma procedure in reducing IOP must be interpreted in the context of associated adverse events. Intraoperative complications occurred at a similar rate with tube shunt surgery and trabeculectomy with MMC. No serious intraoperative complications were observed in the PTVT Study, such as suprachoroidal hemorrhage or aqueous misdirection. Early postoperative complications developed more frequently after trabeculectomy with MMC than tube shunt surgery, but no significant difference in the rate of late postoperative complications was seen between both surgical procedures during the first year of follow-up. All surgical complications are not equal in severity. We chose to define serious complications as postoperative events that produced loss of 2 lines or more of Snellen VA, required reoperation to manage the complication, or both, as was done in the Tube Versus Trabeculectomy Study[27] and Ahmed Baerveldt Comparison Study.[28] The incidence of serious complications and reoperation for complications was higher after trabeculectomy with MMC compared with tube shunt surgery.

A large number of surgical complications were observed in the PTVT Study, but most were transient and did not require intervention. High rates of complications also were seen in the Tube Versus Trabeculectomy Study,[27] Ahmed Baerveldt Comparison Study,[28] Ahmed Versus Baerveldt Study,[31] Collaborative Initial Glaucoma Treatment Study,[35] and Advanced Glaucoma Intervention Study.[36] It is not unexpected that prospective studies generally report higher complication rates than retrospective case series. Surgical complications may be overlooked unless attention is directed specifically toward their detection. Moreover, even when complications are observed, they may not be documented in the medical record (especially if they are believed to be insignificant).

The incidences of most postoperative complications in the PTVT Study were similar between treatment groups. Wound leak and encapsulated bleb were the only early postoperative complications that occurred with greater frequency in the trabeculectomy group compared with the tube group. Although nonvalved tube shunt surgery produces delayed drainage of aqueous humor to the equatorial region of the eye, trabeculectomy results in an immediate filtration of aqueous near the conjunctival incision with a greater tendency toward postoperative wound leaks and bleb encapsulation in the early postoperative period. No late postoperative complications were significantly more common in either treatment group. Although many of the differences in complication rates were not statistically different, they may be clinically relevant. For example, the occurrence of hypotony maculopathy in 1 patient in the tube group and 5 patients in the trabeculectomy group is not statistically significant, but raises concern. The power of this study to detect differences in complications with low incidence rates was limited by the sample size.

Several studies have compared trabeculectomy directly with tube shunt surgery. Panarelli et al[37] retrospectively reviewed the outcomes of Baerveldt implant placement and trabeculectomy with MMC in eyes without previous ocular surgery. Similar rates of surgical success and complications were observed with both procedures, but trabeculectomy produced greater IOP reduction with use of fewer glaucoma mediations than Baerveldt implantation after 3 years of follow-up. Molteno et al[38] reported the results of a prospective, nonrandomized study comparing primary trabeculectomy and primary insertion of the Molteno implant (Molteno Ophthalmic Limited, Dunedin, New Zealand). The cumulative rate of failure was higher after trabeculectomy relative to Molteno implant placement during 20 years of follow-up, but no significant differences were seen between the 2 procedures in mean IOP, glaucoma medical therapy, complications, or vision loss. The Tube Versus Trabeculectomy Study was a multicenter randomized clinical trial comparing Baerveldt implantation and trabeculectomy with MMC in eyes that had undergone previous cataract and glaucoma surgery.[39] The rate of surgical success with survival analysis was higher with tube shunt surgery than trabeculectomy with MMC throughout 5 years of follow-up, although similar mean IOPs and use of glaucoma medications were observed with both surgical procedures at 5 years. Early postoperative complications occurred more frequently after trabeculectomy with MMC than tube shunt placement, but both procedures had similar rates of late and serious complications after 5 years.[27] Wilson et al[40] conducted a prospective clinical trial in Sri Lanka randomizing unoperated eyes with primary angle-closure glaucoma and primary open-angle glaucoma to initial trabeculectomy or placement of the Ahmed glaucoma valve (New World Medical, Inc., Rancho Cucamonga, CA). Surgical success, mean IOP, glaucoma medications, VA, and postoperative complications were comparable with both surgical procedures at the

final follow-up period (41−52 months). The differences in study results between the PTVT Study and other studies comparing tube shunts with trabeculectomy and MMC may relate to variations in study design, patient populations, disease stage, surgical technique, length of follow-up, and definitions of success and failure.

There are several limitations to the PTVT Study. The study population was restricted to patients without previous incisional ocular surgery, and several patient types were ineligible for enrollment. Results of the PTVT Study cannot be directly applied to dissimilar patient groups. Several patients were enrolled in the study but withdrew before surgical treatment. These patients were not included in the analysis because they contributed no operative or postoperative data. Patients randomized to the tube group received a 350-mm^2 Baerveldt glaucoma implant, and the study results should not be generalized to different implant types. A standard dosage of MMC was used in all trabeculectomy cases based on results from a survey of the American Glaucoma Society membership,[4] but it is unclear whether a different dosage may have altered the rate of filtration failure because of fibrosis or hypotony failure in the trabeculectomy group. Although aspects of both surgical procedures were standardized, some variation in surgical technique occurred because surgeons were allowed some latitude to perform the operations in a manner with which they were comfortable. The patient and clinician were not masked to the randomized treatment assignment, and this is a potential source of bias.

The PTVT Study does not demonstrate clear superiority of one glaucoma procedure over the other. Both tube shunt surgery and trabeculectomy with MMC were effective in lowering IOP in patients who had not undergone previous incisional ocular surgery. Greater surgical success and IOP reduction were achieved with use of less adjunctive medical therapy after trabeculectomy with MMC compared with tube shunt implantation in the first year of follow-up. However, trabeculectomy also was associated with higher rates of early postoperative complications, serious complications, and reoperation for complications, suggesting a more favorable safety profile for tube shunt surgery over trabeculectomy with MMC. The surgeon's skill and experience with each operation are additional important considerations when selecting a glaucoma surgical procedure.

Several minimally invasive glaucoma procedures have been introduced in recent years. Lower rates of surgical complications have been reported with these procedures compared with trabeculectomy and tube shunt surgery, but they are generally less effective in decreasing IOP.[41] With the expansion of surgical options for managing glaucoma, selecting the most appropriate glaucoma operation involves balancing the risks of adverse events and the benefit of IOP reduction for an individual patient. Comparative studies like the PTVT Study are required to assess the relative efficacy and safety of the various glaucoma procedures available to surgeons. We plan also to report results of the trial after 3 years and 5 years of follow-up, and long-term data are required to evaluate these traditional glaucoma procedures fully.

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Footnotes and Financial Disclosures

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[1] Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida.

[2] Department of Ophthalmology, St. Thomas Hospital, London, United Kingdom.

[3] Department of Ophthalmology, Moorfields Eye Hospital, London, United Kingdom.

[4] Department of Ophthalmology, Queen Mary's Hospital, Sidcup, United Kingdom.

[5] Department of Ophthalmology, University of Toronto, Toronto, Canada.

[6] Department of Ophthalmology, University of California, Davis, Sacramento, California.

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Author Contributions:

Conception and design: Gedde, Feuer, Barton, Brandt

Analysis and interpretation: Gedde, Feuer, Shi, Lim, Barton, Goyal, Ahmed, Brandt

Data collection: Gedde, Feuer, Shi, Lim, Barton, Goyal, Ahmed, Brandt

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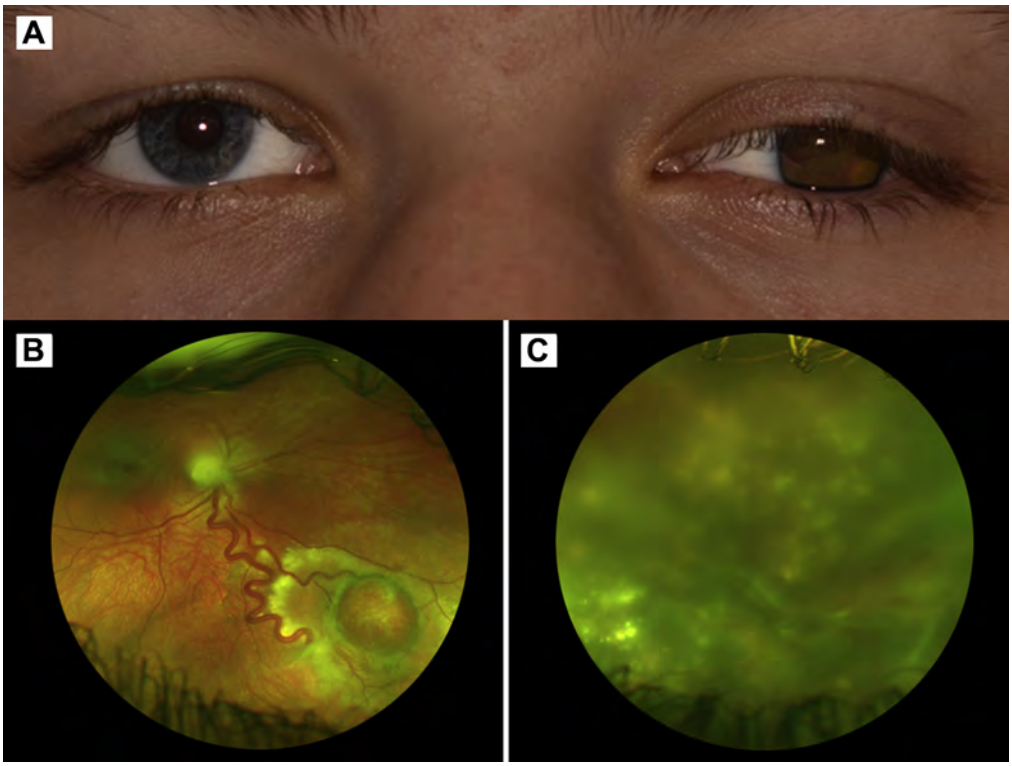
Abbreviations and Acronyms:
ETDRS = Early Treatment Diabetic Retinopathy Study; **IOP** = intraocular pressure; **logMAR** = logarithm of the minimum angle of resolution; **MMC** = mitomycin C; **PTVT** = Primary Tube versus Trabeculectomy; **SD** = standard deviation; **VA** = visual acuity.

Correspondence:
Steven J. Gedde, MD, Bascom Palmer Eye Institute, 900 NW 17th Street, Miami, FL 33136. E-mail: sgedde@med.miami.edu.

Pictures & Perspectives



Von Hippel-Lindau Incidentally Diagnosed in Evaluation of Sporadic Aniridia

A 15-year-old girl with history of unilateral sporadic aniridia presented with decreased vision and eye pain in the left eye (Fig 1**A**). Fundus examination of right eye revealed a capillary hemangioma inferonasally with circumferential exudation consistent with Von Hippel-Lindau Syndrome (VHL) (Fig 1**B**). Examination of the left eye revealed complete chronic exudative retinal detachment and neovascular glaucoma presumed to be due to capillary hemangioma (Fig 1**C**). Genetic testing and a systemic work-up were performed. The patient had a pathogenic variant c.500G>A/p.R167Q (Arg167Gln) in VHL gene. Brain and abdominal magnetic resonance imaging (MRI) revealed a possible 2 mm, right cerebellar hemangioblastoma and a right kidney cyst. The patient underwent grid laser photocoagulation and bevacizumab injection in the right eye for the VHL hemangioma.

Ian C. Holmen, BA[1]
Zackery Oakey, MD[2]
Michael M. Altaweel, MD[2]

[1]University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin; [2]Department of Ophthalmology and Visual Sciences, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin