

Three-Year Follow-up of the Tube Versus Trabeculectomy Study

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- **PURPOSE:** To report 3-year results of the Tube Versus Trabeculectomy (TVT) Study.
- **DESIGN:** Multicenter randomized clinical trial.
- **METHODS:** **SETTING:** Seventeen clinical centers. **STUDY POPULATION:** Patients 18 to 85 years of age who had previous trabeculectomy, cataract extraction with intraocular lens implantation, or both and uncontrolled glaucoma with intraocular pressure (IOP) ≥ 18 mm Hg and ≤ 40 mm Hg on maximum tolerated medical therapy. **INTERVENTIONS:** A 350-mm² Baerveldt glaucoma implant or trabeculectomy with mitomycin C (MMC 0.4 mg/ml for 4 minutes). **MAIN OUTCOME MEASURES:** IOP, visual acuity, use of supplemental medical therapy, surgical complications, and failure (IOP > 21 mm Hg or not reduced by 20%, IOP ≤ 5 mm Hg, reoperation for glaucoma, or loss of light perception vision).
- **RESULTS:** A total of 212 eyes of 212 patients were enrolled, including 107 in the tube group and 105 in the trabeculectomy group. At 3 years, IOP (mean \pm standard deviation [SD]) was 13.0 ± 4.9 mm Hg in the tube group and 13.3 ± 6.8 mm Hg in the trabeculectomy group ($P = .78$). The number of glaucoma medications (mean \pm SD) was 1.3 ± 1.3 in the tube group and 1.0 ± 1.5 in the trabeculectomy group ($P = .30$). The cumulative probability of failure during the first 3 years of follow-up was 15.1% in the tube group and 30.7% in the trabeculectomy group ($P = .010$; hazards ratio, 2.2; 95% confidence interval, 1.2 to 4.1). Postoperative complications developed in 42 patients (39%) in the tube group and 63 patients (60%) in the trabeculectomy group ($P = .004$). Surgical complications were associated with reoperation and/or loss of ≥ 2 Snellen lines in 24 patients (22%) in the tube group and 28 patients (27%) in the trabeculectomy group ($P = .58$).
- **CONCLUSIONS:** Tube shunt surgery had a higher success rate compared to trabeculectomy with MMC during the first 3 years of follow-up in the TVT Study. Both procedures were associated with similar IOP reduction and use of supplemental medical therapy at 3 years. While the inci-

dence of postoperative complications was higher following trabeculectomy with MMC relative to tube shunt surgery, most complications were transient and self-limited. (Am J Ophthalmol 2009;148:670–684. © 2009 by Elsevier Inc. All rights reserved.)

THE CURRENT TREATMENT OF GLAUCOMA IS DIRECTED toward lowering intraocular pressure (IOP) to prevent or slow progressive optic nerve damage. Glaucoma surgery is indicated when medical therapy and appropriate laser treatment do not provide adequate IOP reduction. Trabeculectomy is the most commonly performed incisional glaucoma procedure worldwide. However, concern about bleb-related complications such as leaks and infections has contributed to an increase in the use of tube shunts (or aqueous shunts) as an alternative to trabeculectomy. Tube shunts have traditionally been reserved for refractory glaucomas at high-risk of failure with trabeculectomy. A growing experience with these devices has prompted their use in eyes at lower-risk of trabeculectomy failure.

Medicare data show a steady decline in the number of trabeculectomies performed and a concurrent rise in tube shunt surgery from 1995 to 2004.¹ Recent surveys of the American Glaucoma Society membership have also demonstrated a progressive increase in the proportion of practitioners using tube shunts and a decrease in the popularity of trabeculectomy, particularly in eyes with previous ocular surgery.^{2,3} Despite these trends, there is no clear consensus among glaucoma surgeons regarding the preferred surgical approach for managing glaucoma in eyes that have previously undergone cataract or glaucoma surgery, with some surgeons favoring an antifibrotic augmented trabeculectomy and others preferring a tube shunt.^{2,3}

The Tube Versus Trabeculectomy (TVT) Study was designed to prospectively compare the safety and efficacy of tube shunt surgery and trabeculectomy with mitomycin C (MMC) in eyes with prior ocular surgery. Patients with uncontrolled glaucoma who had previously undergone cataract extraction with intraocular lens (IOL) implantation and/or failed filtering surgery were enrolled in this multicenter clinical trial and randomized to receive either a 350-mm² Baerveldt glaucoma implant or a trabeculectomy with MMC. The goal of this investigator-initiated study is to provide information that will assist in surgical decision making in similar patient groups. The baseline

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characteristics, outcomes by prospectively defined failure criteria, risk factors, and surgical complications during the first postoperative year were described in previous publications.⁴⁻⁶ The present report provides the 3-year follow-up data on these patients.

METHODS

THE DESIGN AND METHODS OF THE TVT STUDY WERE previously described in detail,⁴ and they are summarized as follows:

- ELIGIBILITY CRITERIA:** Patients 18 to 85 years of age who had previous cataract extraction with IOL implantation and/or trabeculectomy with IOP ≥ 18 mm Hg and ≤ 40 mm Hg on maximum tolerated medical therapy were eligible for the study. Exclusion criteria included no light perception vision, pregnant or nursing women, active iris neovascularization or proliferative retinopathy, iridocorneal endothelial syndrome, epithelial or fibrous downgrowth, aphakia, vitreous in the anterior chamber (AC) for which a vitrectomy was anticipated, chronic or recurrent uveitis, severe posterior blepharitis, unwillingness to discontinue contact lens use after surgery, previous cyclodestructive procedure, prior scleral buckling procedure, presence of silicone oil, conjunctival scarring precluding a superior trabeculectomy, and need for glaucoma surgery combined with other ocular procedures or anticipated need for additional ocular surgery. Only 1 eye of eligible patients was included in the study.

- RANDOMIZATION:** Patients enrolled in the study were randomized to placement of a 350-mm² Baerveldt glaucoma implant or a trabeculectomy with MMC (0.4 mg/ml for 4 minutes). Randomization was performed using a permuted block design stratified by clinical center and qualifying previous intraocular surgery. Neither the patient nor the clinician was masked to the randomization assignment.

- PATIENT VISITS:** Baseline demographic and clinical information were collected for enrolled patients. Follow-up visits were scheduled 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, 18 months, 2 years, 3 years, 4 years, and 5 years postoperatively. Each examination included measurement of Snellen visual acuity (VA), IOP, slit-lamp biomicroscopy, Seidel testing, and ophthalmoscopy. Humphrey perimetry, Early Treatment Diabetic Retinopathy Study (ETDRS) VA, and quality of life using the National Eye Institute–Visual Function Questionnaire (NEI VFQ-25) were assessed at baseline and at the annual follow-up visits. A formal motility evaluation was performed in all patients at baseline and at the 1-year and 5-year follow-up visits, and at any visit after 3 months in which the patient reported diplopia. Postoperative interventions and surgical

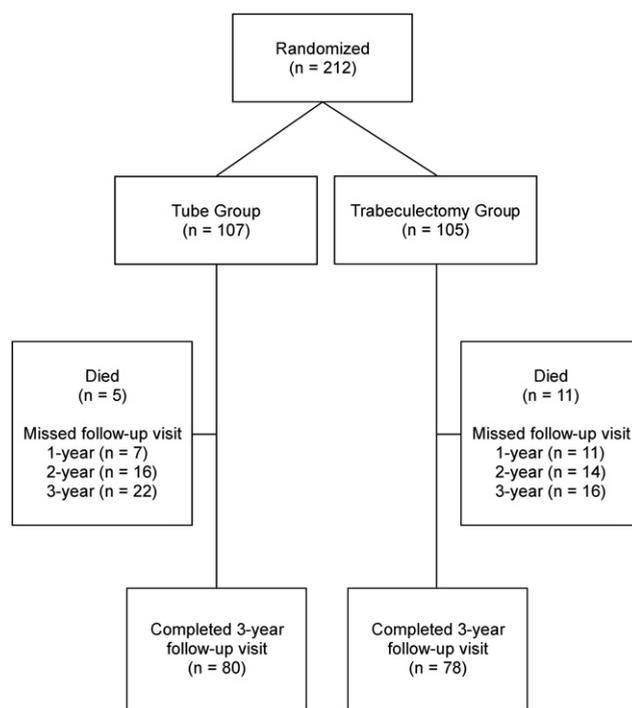


FIGURE 1. Flowchart of patient progress in the Tube Versus Trabeculectomy (TVT) Study.

complications were documented at each follow-up visit. Investigators provided a reason for loss of 2 or more lines of Snellen VA at follow-up visits after 3 months.

- OUTCOME MEASURES:** Outcome measures assessed in the TVT Study include IOP, VA, reoperation for glaucoma, use of supplemental medical therapy, surgical complication rates, visual fields, and quality of life. Failure was prospectively defined as IOP > 21 mm Hg or less than 20% reduction below baseline on two consecutive follow-up visits after 3 months, IOP ≤ 5 mm Hg on 2 consecutive follow-up visits after 3 months, reoperation for glaucoma, or loss of light perception vision. All eyes that had not failed by the above criteria and were not on supplemental medical therapy were considered complete successes. Eyes that had not failed but required supplemental medical therapy were defined as qualified successes. The study outcomes were monitored by an independent Safety and Data Monitoring Committee.

Reoperation for glaucoma or a complication was defined as additional surgery requiring a return to the operating room. Cyclodestruction was also counted as a reoperation for glaucoma, and a vitreous tap with injection of intravitreal antibiotics was a reoperation for a complication. Interventions performed at the slit-lamp, such as needling procedures or reformation of the AC, were not considered reoperations. Serious complications were defined as surgical complications that were associated with loss of 2 or more lines of Snellen VA and/or reoperation to manage

TABLE 1. Baseline Characteristics of Tube Versus Trabeculectomy Study Patients

	Tube Group (n = 107)	Trabeculectomy Group (n = 105)	P value
Age (years), mean ± SD	70.9 ± 11.0	71.1 ± 9.9	.89 ^a
Gender, n (%)			.055 ^b
Male	43 (40)	57 (54)	
Female	64 (60)	48 (46)	
Race, n (%)			.53 ^c
White	52 (49)	43 (41)	
Black	40 (37)	42 (40)	
Hispanic	12 (11)	18 (17)	
Other	3 (3)	2 (2)	
Diabetes mellitus, n (%)	31 (29)	36 (34)	.49 ^b
Hypertension, n (%)	61 (57)	63 (60)	.76 ^b
IOP (mm Hg), mean ± SD	25.1 ± 5.3	25.6 ± 5.3	.56 ^a
Glaucoma medications, mean ± SD	3.2 ± 1.1	3.0 ± 1.2	.17 ^a
Diagnosis, n (%)			.057 ^c
POAG	88 (82)	84 (80)	
CACG	7 (7)	11 (10)	
PXFG	7 (7)	1 (1)	
PG	1 (1)	0 (0)	
Other	4 (4)	9 (9)	
Lens status, n (%)			.85 ^c
Phakic	24 (22)	21 (20)	
PCIOL	80 (75)	80 (76)	
ACIOL	3 (3)	4 (4)	
Previous intraocular surgery			.35 ^a
Mean ± SD	1.3 ± 0.5	1.2 ± 0.5	
Range	1 to 3	1 to 4	
Interval (months), mean ± SD ^e	54 ± 50	60 ± 55	.42 ^a
ETDRS VA, mean ± SD	62.7 ± 24.1	64.4 ± 19.6	.56 ^a
Snellen VA			
Median	20/30	20/40	
Range	20/17 – HM	20/20 – 2/200	.76 ^d
LogMAR mean ± SD	0.42 ± .54	0.37 ± 0.38	.40 ^a
Humphrey visual fields			
MD, mean ± SD	-16.0 ± 10.2	-15.8 ± 9.6	.87 ^a
PSD, mean ± SD	7.1 ± 3.5	6.9 ± 3.5	.73 ^a

ACIOL = anterior chamber intraocular lens; CACG = chronic angle-closure glaucoma; ETDRS = Early Treatment Diabetic Retinopathy Study; HM = hand motion; IOP = intraocular pressure; LogMAR = logarithm of the minimal angle of resolution; MD = mean deviation; PCIOL = posterior chamber intraocular lens; PG = pigmentary glaucoma; POAG = primary open-angle glaucoma; PSD = pattern standard deviation; PXFG = pseudoexfoliation glaucoma; SD = standard deviation; VA = visual acuity.

^aStudent *t* test.

^b χ^2 test.

^cExact permutation χ^2 test.

^dMann-Whitney *U* test.

^eInterval between last intraocular surgery and surgical treatment in study.

the complication. Persistent diplopia and corneal edema, as well as dysesthesia, were defined as the postoperative development of these complications and their continued presence at the 6-month follow-up visit or after. Eyes that tested Seidel positive within the first month of follow-up were classified as wound leaks, and those occurring after 1

month were categorized as bleb leaks. Patients who underwent additional glaucoma surgery were censored from analysis of complications after the reoperation for glaucoma. Cataracts were considered to have progressed if there was loss of 2 or more lines of Snellen VA that was attributed to cataract, or if cataract surgery was performed.

TABLE 2. Intraocular Pressure and Medical Therapy at Baseline and Follow-up in the Tube Versus Trabeculectomy Study^a

	Tube Group	Trabeculectomy Group	P value ^b
Baseline			
IOP (mm Hg)	25.1 ± 5.3	25.6 ± 5.3	.56
Glaucoma medications	3.2 ± 1.1	3.0 ± 1.2	.17
N	107	105	
6 months			
IOP (mm Hg)	13.5 ± 4.2	12.8 ± 5.9	.32
Glaucoma medications	1.2 ± 1.2	0.6 ± 1.1	<.001
N	102	93	
1 year			
IOP (mm Hg)	12.5 ± 3.9	12.7 ± 5.8	.73
Glaucoma medications	1.3 ± 1.3	0.5 ± 0.9	<.001
N	97	87	
18 months			
IOP (mm Hg)	13.5 ± 4.5	12.2 ± 4.8	.093
Glaucoma medications	1.3 ± 1.3	0.6 ± 1.0	<.001
N	94	74	
2 years			
IOP (mm Hg)	13.4 ± 4.8	12.1 ± 5.0	.101
Glaucoma medications	1.3 ± 1.3	0.8 ± 1.2	.016
N	82	72	
3 years			
IOP (mm Hg)	13.0 ± 4.9	13.3 ± 6.8	.78
Glaucoma medications	1.3 ± 1.3	1.0 ± 1.5	.30
N	74	67	

IOP = intraocular pressure; N = number of patients.

^aData presented as mean ± standard deviation. Data censored after a reoperation for glaucoma.

^bStudent *t* test.

• **STATISTICAL ANALYSIS:** Univariate comparisons between treatment groups were performed using the two-sided Student *t* test for continuous variables and the χ^2 test, Fisher exact test, or exact permutation χ^2 test for categorical variables. Snellen VA measurements were converted to logarithm of the minimal angle of resolution (logMAR) equivalents for the purpose of data analysis, as reported previously.⁷ The time to failure was defined either as the time from surgical treatment to reoperation for glaucoma, or as the time from surgical treatment to the first of two consecutive study visits after 3 months in which the patient had persistent hypotony (IOP ≤5 mm Hg) or inadequately reduced IOP (IOP >21 mm Hg or not reduced by 20% below baseline). Treatment comparisons of time to failure, time to reoperation for glaucoma, time to reoperation for complications, and time to VA loss were assessed with stratified Kaplan-Meier survival analysis log-rank test. A *P* value of .05 or less was considered statistically significant in our analyses.

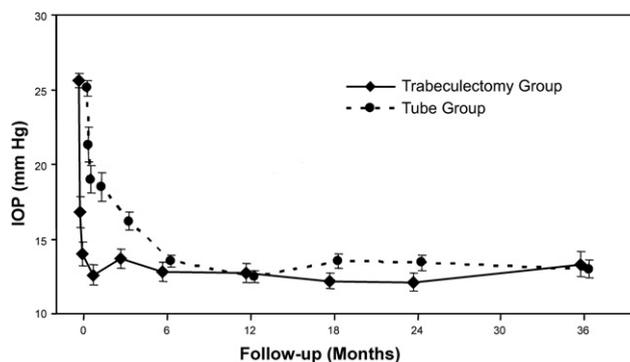


FIGURE 2. Distribution of intraocular pressure (IOP) at baseline and follow-up in the TVT Study. Data are presented as mean ± standard error of the mean and are censored after a reoperation for glaucoma.

RESULTS

• **RECRUITMENT AND RETENTION:** The TVT Study enrolled a total of 212 patients at 17 clinical centers between October 1999 and April 2004. Randomization assigned 107 patients to placement of a 350-mm² Baerveldt glaucoma implant and 105 patients to a trabeculectomy with MMC. All patients received their assigned treatment.

The progress of patients in the study is shown in Figure 1. In the overall study group, 16 patients (7.5%) died within 3 years of enrollment. There were 38 other patients (18%) who missed the 3-year follow-up visit, but 13 of these patients (34%) returned for subsequent follow-up visits. Excluding deaths, 93% of follow-up visits were completed during the first 3 years of the study. The visit completion rate did not differ by treatment group (*P* = .36, χ^2 test). During the first 3 years of follow-up, 10% of study visits were missed because of deaths and losses to follow-up.

• **BASILINE CHARACTERISTICS:** The baseline characteristics of study patients are presented in Table 1. No significant differences in any of the demographic or clinical features were observed between treatment groups at baseline. Additional information on randomized patients was provided in a previous publication.⁴

• **INTRAOCULAR PRESSURE REDUCTION:** Baseline and follow-up IOP measurements for the tube and trabeculectomy groups are reported in Table 2 and Figure 2. Patients who underwent additional glaucoma surgery were censored from analysis after reoperation. Both surgical procedures produced a significant and sustained reduction in IOP. Among patients who completed 3-year follow-up visits, IOP (mean ± standard deviation [SD]) decreased 11.7 ± 6.5 mm Hg from baseline in the tube group (*P* < .001, paired *t* test) and was reduced 11.4 ± 8.9 mm Hg from baseline in the trabeculectomy group (*P* < .001, paired *t* test). No significant difference in mean IOP was seen

TABLE 3. Treatment Outcomes After Three Years of Follow-up in the Tube Versus Trabeculectomy Study

	Tube Group, n (%) (n = 85)	Trabeculectomy Group, n (%) (n = 82)
Stratum 1 – previous cataract extraction		
Failure	5 (14)	16 (40)
Qualified success	20 (56)	10 (25)
Complete success	11 (31)	14 (35)
Stratum 2 – previous trabeculectomy or combined procedure without an antifibrotic agent		
Failure	6 (30)	5 (31)
Qualified success	11 (55)	6 (38)
Complete success	3 (15)	5 (31)
Stratum 3 – previous trabeculectomy with 5-FU or combined procedure with 5-FU or MMC		
Failure	0	2 (17)
Qualified success	6 (40)	4 (33)
Complete success	9 (60)	6 (50)
Stratum 4 – previous trabeculectomy with MMC		
Failure	4 (29)	5 (36)
Qualified success	9 (64)	1 (7)
Complete success	1 (7)	8 (57)
Overall group		
Failure ^a	15 (18)	28 (34)
Qualified success	46 (54)	21 (26)
Complete success ^b	24 (28)	33 (40)

5-FU = 5-fluorouracil; MMC = mitomycin C.

^a*P* = .019 for the difference in failure rates between treatment groups (χ^2 test adjusted for stratum).

^b*P* = .10 for the difference in complete success rates between treatment groups (χ^2 test adjusted for stratum).

between treatment groups after 3 months. At 3 years, 46 patients (62%) in the tube group and 39 patients (58%) in the trabeculectomy group had an IOP of 14 mm Hg or less. No significant difference was found in the proportion of patients with IOP \leq to 14 mm Hg between treatment groups (*P* = .76, χ^2 test). Greater variability in IOP was observed in the trabeculectomy group compared with the tube group at 1 year (*P* = .027, Levene's test for equality of variance), and a similar trend was noted at 3 years (*P* = .052, Levene's test for equality of variance) but did not reach statistical significance.

An additional intent-to-treat analysis was performed, which included patients who required further surgery for glaucoma. At 3 years, IOP (mean \pm SD) was 13.0 \pm 4.8 mm Hg in the tube group and 13.1 \pm 6.5 mm Hg in the trabeculectomy group. No significant difference in mean IOP was present between treatment groups taking into account all medical and surgical management during the first 3 years of follow-up (*P* = .91, Student *t* test).

• **MEDICAL THERAPY:** Table 2 shows the number of glaucoma medications in the tube group and the trabeculectomy group at baseline and follow-up. Patients who

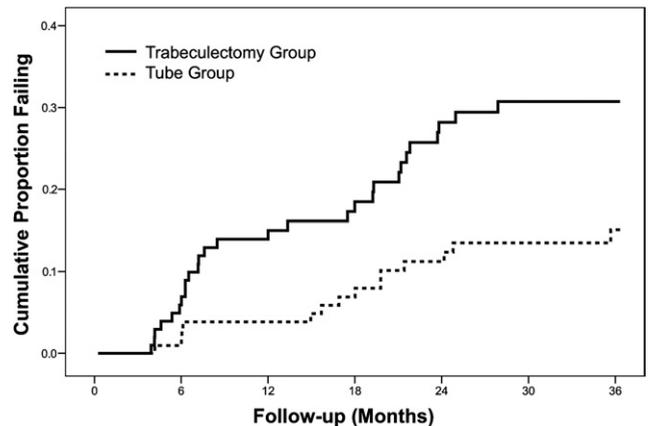


FIGURE 3. Kaplan-Meier plots of the probability of failure in the TVT Study.

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. Among patients who completed 3-year follow-up visits, the number of glaucoma medications (mean \pm SD)

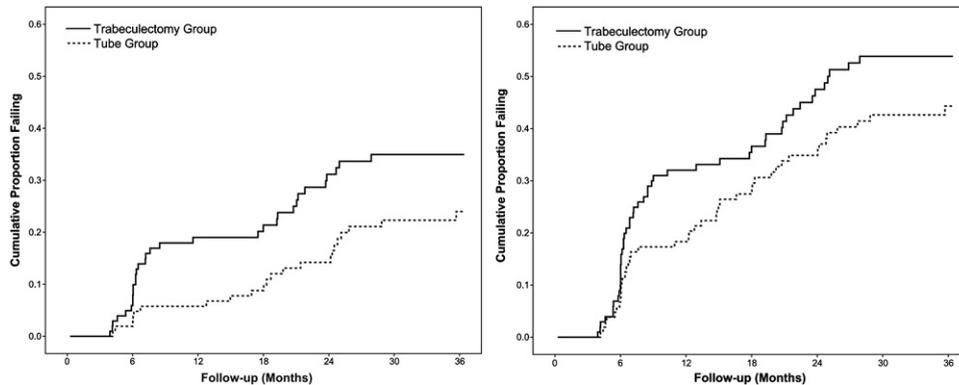


FIGURE 4. Kaplan-Meier plots of the cumulative probability of failure in the TVT Study defining inadequate intraocular (IOP) reduction as IOP >17 mm Hg or not reduced by 20% below baseline (Left) or IOP >14 mm Hg (Right). Inadequate IOP reduction criteria must be present on two consecutive visits after 3 months to qualify as failure. Patients with persistent hypotony, reoperation for glaucoma, and loss of light perception vision are classified as failures.

TABLE 4. Reasons for Treatment Failure During Three Years of Follow-up in the Tube Versus Trabeculectomy Study^a

	Tube Group, n (%) (n = 15)	Trabeculectomy Group, n (%) (n = 28)
Inadequate IOP reduction ^b	7 (47)	10 (36) ^d
Reoperation for glaucoma	6 (40)	9 (32)
Persistent hypotony ^c	2 (13)	8 (29)
Loss of light perception	0	1 (4)

IOP = intraocular pressure.

^a $P = .71$ for the difference in distribution of reasons for failure between treatment groups (exact permutation χ^2 test).

^bIOP >21 mm Hg or not reduced by 20% below baseline on two consecutive follow-up visits after 3 months.

^cIOP ≤ 5 mm Hg on two consecutive follow-up visits after 3 months.

^dThree patients underwent reoperation for glaucoma subsequent to failure because of inadequate IOP reduction.

TABLE 5. Reoperations for Glaucoma During Three Years of Follow-up in the Tube Versus Trabeculectomy Study

	Tube Group (n = 107)	Trabeculectomy Group (n = 105)
Tube shunt	3	10
Trans-scleral cyclophotocoagulation	3	1
Endocyclophotocoagulation and cataract extraction	1	0
Bleb revision and tube shunt	0	1
Trabeculectomy with 5-FU	0	1
Total number of patients (cumulative percentage) with reoperation for glaucoma ^a	6 ^b (6)	12 ^b (13)

5-FU = 5-fluorouracil.

^a $P = .091$ for the difference in 3-year cumulative reoperation rates for glaucoma between treatment groups from Kaplan-Meier analysis (log-rank test adjusted for stratum).

^bOne patient had two different types of reoperations for glaucoma.

decreased by 2.0 ± 1.7 in the tube group ($P < .001$, paired t test) and 1.8 ± 2.0 in trabeculectomy group ($P < .001$, paired t test) from baseline. A significantly greater use of supplemental medical therapy was observed in the tube group compared with the trabeculectomy group at all follow-up visits during the first 2 postoperative years. However, no significant difference in the mean number of medications was present between treatment groups at 3 years ($P = .30$, Student t test).

The mean number of medications was 1.3 ± 1.2 in the tube group and 1.1 ± 1.5 in the trabeculectomy group at 3 years in an intent-to-treat analysis. No difference in the mean number of medications was seen between treatment groups after 3 years of follow-up when patients who underwent additional glaucoma surgery were included in the analysis ($P = .46$, Student t test).

• **TREATMENT OUTCOMES:** Table 3 presents the outcomes of randomized patients, unadjusted for follow-up time. All patients who completed 3-year follow-up visits and/or had a prior failure were included in this analysis. At 3 years, treatment failure had occurred in 15 patients (18%) in the tube group and 28 patients (34%) in the trabeculectomy group. A significantly higher failure rate was seen in the trabeculectomy group than the tube group after 3 years of follow-up ($P = .019$, χ^2 test adjusted for stratum). In the tube group, 24 patients (28%) were classified as complete successes and 46 patients (54%) were qualified successes. In the trabeculectomy group, 33 patients (40%) were complete successes and 21 patients (26%) were qualified successes. While the tube group had a higher overall success rate after 3 years, the rates of

TABLE 6. Visual Acuity Results in the Tube Versus Trabeculectomy Study

	Tube Group	Trabeculectomy Group	P value
ETDRS VA, mean ± SD (n)			
Baseline	63 ± 24 (107)	64 ± 20 (105)	.56 ^c
3 years	55 ± 30 (56)	59 ± 24 (51)	.52 ^c
Snellen VA, logMAR mean ± SD (n)			
Baseline	0.42 ± 0.54 (107)	0.37 ± 0.38 (105)	.40 ^c
3 years	0.61 ± 0.73 (80)	0.57 ± 0.64 (77)	.72 ^c
Loss of ≥2 Snellen lines, n (%) ^{a,b}			
	38 (31)	39 (34)	.65 ^d
Glaucoma	8	10	
Macular disease	10	6	
Cataract	3	6	
Other	15	15	
Unknown	4	5	

ETDRS = Early Treatment Diabetic Retinopathy Study; LogMAR = logarithm of the minimal angle of resolution; SD = standard deviation; VA = visual acuity.

^aThree-year rate of visual acuity loss from Kaplan-Meier analysis.

^bSome patients had more than one reason for decreased vision.

^cStudent *t* test.

^dLog-rank test.

complete success were not statistically different between treatment groups ($P = .10$, χ^2 test adjusted for stratum).

Kaplan-Meier survival analysis was also used to compare failure rates between the two treatment groups, and the results are shown in Figure 3. The cumulative probabilities of failure in the tube group were 3.8% at 1 year, 6.9% at 18 months, 11.2% at 2 years, and 15.1% at 3 years. The failure rates in the trabeculectomy group were 13.9% at 1 year, 18.5% at 18 months, 28.2% at 2 years, and 30.7% at 3 years ($P = .010$, log-rank test adjusted for stratum). A significantly higher rate of failure was observed in the trabeculectomy group compared with the tube group after 3 years of follow-up using Cox survival analysis adjusted for stratum (hazards ratio, 2.2; 95% confidence interval, 1.2 to 4.1). There were no significant differences in treatment efficacy between strata ($P = .450$, test of treatment-stratum interaction).

Figure 4 presents the failure rates for the two treatment groups using 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 greater than 17 mm Hg or not reduced by 20% from baseline on two consecutive follow-up visits after 3 months, the cumulative probability of failure at 3 years was 24.0% in the tube group and 35.0% in the trabeculectomy group ($P = .057$, log-rank test adjusted for stratum). When inadequate IOP reduction was defined as IOP greater than 14 mm Hg on two consecutive visits after 3 months, the cumulative probability of failure was 44.3% in the tube group and 53.9% in the trabeculectomy group at 3 years ($P = .12$,

log-rank test adjusted for stratum). Higher failure rates were observed in the trabeculectomy group compared with the tube group when more stringent IOP criteria were used to define success and failure, but these differences were not statistically significant.

The reasons for treatment failure are listed in Table 4. The most common cause for failure during the first 3 years of follow-up in both treatment groups was inadequate IOP reduction (IOP >21 mm Hg or not reduced by 20% below baseline on two consecutive follow-up visits after 3 months). There were 3 patients in the trabeculectomy group who failed because of inadequate IOP reduction and subsequently underwent reoperation for glaucoma. There were 6 patients in the tube group and 9 patients in the trabeculectomy group who had a reoperation for glaucoma before meeting the failure criteria for inadequate IOP reduction. Among the patients who failed because of inadequate IOP reduction or glaucoma reoperation, the number of medications (mean ± SD) at the time of failure was 2.5 ± 1.2 in the tube group and 2.4 ± 1.2 in the trabeculectomy group ($P = .77$, Student *t* test). No significant difference in the distribution of reasons for failure was present between treatment groups ($P = .71$, exact permutation χ^2 test).

• **REOPERATION FOR GLAUCOMA:** Table 5 presents the reoperations that were performed for glaucoma. A total of 12 patients in the trabeculectomy group had reoperations for glaucoma, which involved placement of a tube shunt in 10 patients, a trabeculectomy with 5-fluorouracil in 1 patient, and a bleb revision with tube shunt placement in 1 patient. All of the patients in the trabeculectomy group who underwent tube shunt surgery as a glaucoma reopera-

TABLE 7. Postoperative Complications During Three Years of Follow-up in the Tube Versus Trabeculectomy Study^a

	Tube Group, n (%) (n = 107)	Trabeculectomy Group, n (%) (n = 105)
Early postoperative complications^b		
Choroidal effusion	15 (14)	14 (13)
Shallow or flat anterior chamber	11 (10)	10 (10)
Wound leak	1 (1)	12 (11)
Hyphema	2 (2)	8 (8)
Aqueous misdirection	3 (3)	1 (1)
Suprachoroidal hemorrhage	2 (2)	3 (3)
Vitreous hemorrhage	1 (1)	1 (1)
Decompression retinopathy	0	1 (1)
Cystoid macular edema	0	1 (1)
Late postoperative complications^c		
Persistent corneal edema	10 (9)	6 (6)
Dyesthesia	1 (1)	8 (8)
Encapsulated bleb	2 (2)	6 (6)
Choroidal effusion	2 (2)	4 (4)
Cystoid macular edema	5 (5)	1 (1)
Hypotony maculopathy	1 (1)	4 (4)
Persistent diplopia	5 (5)	0
Bleb leak	0	5 (5)
Tube erosion	5 (5)	—
Endophthalmitis/blebitis	1 (1)	3 (3)
Chronic or recurrent iritis	2 (2)	1 (1)
Tube obstruction	3 (3)	—
Retinal detachment	1 (1)	1 (1)
Corneal ulcer	0	1 (1)
Shallow or flat anterior chamber	1 (1)	0
Total number of patients with postoperative complications ^{d,e}	42 (39)	63 (60)

^aData censored after a reoperation for glaucoma.
^bOnset ≤1 month.
^cOnset >1 month.
^dSome patients had more than one complication.
^e*P* = .004 for the difference in total number of patients with postoperative complications between treatment groups (χ^2 test).

tion had placement of a 350-mm² Baerveldt implant in the superotemporal quadrant. One of the patients who received a tube shunt subsequently underwent a trans-scleral cyclophotocoagulation in the study eye as a second reoperation for glaucoma. In the tube group, 6 patients underwent additional glaucoma surgery, including placement of a second tube shunt in 3 patients, trans-scleral cyclophotocoagulation in 2 patients, and endocyclophotocoagulation performed in conjunction with cataract surgery in 1 patient. Among the patients in the tube group who received another tube shunt as a glaucoma reoperation, the second implant was a 350-mm² Baerveldt implant placed in the inferonasal quadrant in 2 patients and a 250-mm² Baerveldt implant positioned in the inferotemporal quadrant in 1 patient. Repeat trans-scleral cyclophotocoagula-

TABLE 8. Serious Complications Associated With Reoperation and/or Vision Loss During Three Years of Follow-up in the Tube Versus Trabeculectomy Study^a

	Tube Group, n (%) (n = 107)	Trabeculectomy Group, n (%) (n = 105)
Reoperation for complications	15 (14)	9 (9)
Vision loss of ≥ 2 Snellen lines	17 (16)	23 (22)
Total number of patients with serious complications ^{b,c}	24 (22)	28 (27)

^aData censored after a reoperation for glaucoma.
^bSome patients had both a reoperation for a complication and vision loss.
^c*P* = .58 for the difference in serious complication rates between treatment groups (χ^2 test).

tion was performed in the patient who had endocyclophotocoagulation. While it is notable that the 3-year cumulative reoperation rate for glaucoma was greater in the trabeculectomy group (13%) than the tube group (6%) using Kaplan-Meier survival analysis, this difference did not reach statistical significance (*P* = .091, log-rank test adjusted for stratum).

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 and those who failed because of inadequate IOP reduction but did not have additional glaucoma surgery. The IOP (mean ± SD) was 21.5 ± 6.6 mm Hg for the 6 patients in the tube group and 27.9 ± 9.6 mm Hg for the 12 patients in the trabeculectomy group at the time of reoperation for glaucoma. The IOP levels were also compared between the 7 patients in the tube group and 7 patients in the trabeculectomy group who failed because of inadequate IOP reduction but did not undergo additional glaucoma surgery during the first 3 years of follow-up. In this patient subgroup, the IOP (mean ± SD) was 21.4 ± 5.4 mm Hg in the tube group and 20.6 ± 2.8 mm Hg in the trabeculectomy group. The mean IOP prior to reoperation for glaucoma was similar in the tube group and trabeculectomy group (*P* = .12, Student *t* test), 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 (*P* = .74, Student *t* test).

• **VISUAL ACUITY:** VA results are shown in Table 6. A significant decrease in Snellen VA and ETDRS VA was observed in both treatment groups during the first 3 years of follow-up. Among patients who completed 3-year follow-up visits, logMAR Snellen VA (mean ± SD) decreased 0.24 ± 0.58 units from baseline (*P* < .001, paired

TABLE 9. Reoperations for Complications During Three Years of Follow-up in the Tube Versus Trabeculectomy Study^a

	Tube Group (n = 107)	Trabeculectomy Group (n = 105)
Penetrating keratoplasty	3	3
Pars plana vitrectomy	6	0
Tube shunt revision with patch graft	4	—
Bleb revision	0	3
Drainage of choroidal effusion	2	1
Drainage of suprachoroidal hemorrhage	0	1
Vitreous tap with injection of intravitreal antibiotics	0	1
Lysis of iris adhesions to tube and cataract extraction	1	—
Tube shunt revision with patch graft and cataract extraction	1	—
Removal of tube shunt	1	—
Trabeculectomy revision and tube shunt	—	1
Total number of patients (cumulative percentage) with reoperations for complications ^b	15 ^c (15)	9 ^c (10)

^aData censored after a reoperation for glaucoma.

^b $P = .24$ for the difference in 3-year cumulative reoperation rates for complications between treatment groups from Kaplan-Meier analysis (log-rank test adjusted for stratum).

^cSome patients had more than one type of reoperation for complications.

t test) and ETDRS VA (mean \pm SD) was reduced by 9 ± 22 letters from baseline ($P = .007$, paired *t* test) in the tube group. In the trabeculectomy group, logMAR Snellen VA (mean \pm SD) decreased 0.26 ± 0.58 units from baseline to the 3-year follow-up visit ($P < .001$, paired *t* test) and ETDRS VA (mean \pm SD) declined 11 ± 23 letters from baseline ($P = .001$, paired *t* test). No significant differences in Snellen VA ($P = .72$, Student *t* test) or ETDRS VA ($P = .52$, Student *t* test) were seen between the tube group and the trabeculectomy group at 3 years. The changes in Snellen VA ($P = .91$, Student *t* test) and ETDRS VA ($P = .57$, Student *t* test) from baseline were also not significantly different between treatment groups.

Kaplan-Meier survival analysis showed that 31% of patients in the tube group and 34% of patients in the trabeculectomy group lost 2 or more lines of Snellen VA from baseline at 3 years, and this difference in rate of vision loss between treatment groups was not statistically significant ($P = .65$, log-rank test). The examining clinician was asked to provide a reason for reduction of 2 or more lines of Snellen VA from baseline. The most frequent causes of vision loss after 3 years of follow-up were glaucoma (in 8 patients in the tube group and 10 patients in the trabeculectomy group), macular disease (in 10 patients in the tube group and 6 patients in the trabeculectomy group), and cataract (in 3 patients in the tube group and 6 patients in the trabeculectomy group). Other miscellaneous causes for reduced vision in 15 patients in the tube group included corneal edema, diabetic retinopathy, posterior capsular opacification, central retinal vein occlusion, endophthalmitis, and ocular surface disease. Other causes of vision loss in 15 patients in the trabeculectomy

group included corneal edema, hypotony, suprachoroidal hemorrhage, ischemic optic neuropathy, diabetic retinopathy, retinal detachment (RD), corneal scarring, and ocular surface disease. The reason for decreased vision was unknown in 4 patients in the tube group and 5 patients in the trabeculectomy group.

• **POSTOPERATIVE COMPLICATIONS:** Table 7 lists postoperative complications. A total of 74 complications in 42 patients (39%) were reported in the tube group, and 91 complications in 63 patients (60%) were noted in the trabeculectomy group. Significantly more patients in the trabeculectomy group experienced postoperative complications compared with the tube group ($P = .004$, χ^2 test). There were 61 patients who had only 1 postoperative complication. Many patients developed more than 1 postoperative complication, including 32 patients with 2 complications, 8 patients with 3 complications, and 4 patients with 4 complications.

Several complications occurred exclusively in the early or late postoperative periods. All cases of wound leak, hyphema, aqueous misdirection, suprachoroidal hemorrhage, vitreous hemorrhage, and decompression retinopathy developed during the first month after surgery. Complications presenting at least 1 month following surgery included persistent corneal edema, dysesthesia, encapsulated bleb, hypotony maculopathy, persistent diplopia, bleb leak, tube erosion, endophthalmitis/blebitis, chronic or recurrent iritis, tube obstruction, RD, and corneal ulcer. Most choroidal effusions were observed in the early postoperative period. However, 2 patients in the tube group developed choroidal effusions after 1 month

presumably related to opening of the tube, and there was concurrent shallowing of the AC in 1 patient. There were 4 patients in the trabeculectomy group who developed choroidal effusions after 1 month, and this was associated with laser suture lysis in all patients. Cystoid macular edema was seen in 1 patient at 1 month, and this complication was identified at later follow-up visits in 6 other patients.

Wound leaks ($P = .004$, χ^2 test), dysesthesia ($P = .018$, Fisher exact test), and bleb leaks ($P = .028$, Fisher exact test) occurred with significantly greater frequency in the trabeculectomy group than the tube group. No postoperative complications were significantly more common in the tube group compared with the trabeculectomy group. Trends toward a higher incidence of hyphema in the trabeculectomy group ($P = .058$, Fisher exact test) and persistent diplopia ($P = .060$, Fisher exact test) and tube erosion ($P = .060$, Fisher exact test) in the tube group were observed, but these differences did not reach statistical significance.

Serious complications resulting in reoperation and/or vision loss are shown in Table 8. There were 24 patients (22%) in the tube group and 28 patients (27%) in the trabeculectomy group who had surgical complications that were associated with loss of 2 or more lines and/or reoperation to manage the complication. The incidence of serious complications was similar between the tube and trabeculectomy groups ($P = .58$, χ^2 test).

• **REOPERATION FOR COMPLICATIONS:** Table 9 presents the reoperations that were performed for complications. A total of 15 patients in the tube group and 9 patients in the trabeculectomy group underwent additional surgery to manage surgical complications. The 3-year cumulative rate of reoperation for complications was similar between the tube group (15%) and the trabeculectomy group (10%) using Kaplan-Meier survival analysis ($P = .24$, log-rank test adjusted for stratum). There were 3 patients in each treatment group who had persistent corneal edema requiring a penetrating keratoplasty, and 1 patient in the tube group underwent a repeat penetrating keratoplasty in the study eye. A pars plana vitrectomy was performed in 6 patients in the tube group, including 2 patients for aqueous misdirection, 2 patients for vitreous obstruction of the tube, 1 patient for endophthalmitis, and 1 patient for a RD. Revision of the tube shunt with placement of a new patch graft was performed in 4 patients in the tube group for tube erosion, and 1 additional patient had this procedure in conjunction with cataract extraction. One of these patients required a second tube revision followed by removal of the tube shunt for recurrent exposure. There were 3 patients in the trabeculectomy group who had a bleb revision, including 2 patients for bleb leaks and 1 patient for hypotony maculopathy. The patient with hypotony maculopathy subsequently underwent a trabeculectomy revision and placement of a 350-mm² Baerveldt

glaucoma implant for persistent hypotony. Drainage of a choroidal effusion was performed in 2 patients in the tube group and 1 patient in the trabeculectomy group, and 1 patient in the trabeculectomy group had drainage of a suprachoroidal hemorrhage. In the tube group, 1 patient had lysis of iris adhesions obstructing the tube that was performed with cataract extraction. Bleb-related endophthalmitis was treated with a vitreous tap with injection of intravitreal antibiotics in 1 patient in the trabeculectomy group.

• **CATARACT DEVELOPMENT AND CATARACT SURGERY:** The incidence of cataract progression during the first 3 years of the study was examined in the 24 phakic eyes in the tube group and the 21 phakic eyes in the trabeculectomy group. Worsening of cataract occurred in 14 patients (58%) in the tube group, including 11 patients who had cataract surgery and 3 patients who experienced loss of 2 or more lines of Snellen VA attributed to cataract. Cataract progression developed in 12 patients (57%) in the trabeculectomy group, including 6 patients who underwent cataract extraction and 6 patients who had loss of 2 or more lines of Snellen VA from cataract. No significant differences in the frequency of cataract surgery ($P = .38$, χ^2 test) or cataract progression ($P > .99$, χ^2 test) were observed between treatment groups.

DISCUSSION

THE TVT STUDY IS A MULTICENTER CLINICAL TRIAL THAT enrolled patients with medically uncontrolled glaucoma in eyes that had previously undergone cataract extraction with IOL implantation and/or failed filtering surgery and randomized them to surgical treatment with a 350-mm² Baerveldt glaucoma implant or a trabeculectomy with MMC. Patients who underwent tube shunt surgery were more likely to achieve IOP control and avoid persistent hypotony, reoperation for glaucoma, or loss of light perception vision compared to trabeculectomy during the first 3 years of follow-up in the study. At 3 years, the cumulative probability of failure was 15.1% in the tube group and 30.7% in the trabeculectomy group. The 1-year follow-up data also demonstrated a lower failure rate of 3.9% in the tube group compared to 13.5% in the trabeculectomy group.⁵ The TVT Study shows a persistent treatment benefit of tube shunt surgery over trabeculectomy through the third postoperative year.

Both tube shunt surgery and trabeculectomy with MMC were effective in lowering-IOP. Among patients who completed 3-year follow-up visits, placement of a Baerveldt glaucoma implant produced a 48% decrease in IOP and trabeculectomy with MMC achieved a 47% reduction in IOP. No significant difference in mean IOP was observed between treatment groups after 3 months of follow-up. Similar mean IOPs were seen between treat-

ment groups, despite a higher failure rate in the trabeculectomy group than the tube group. This counterintuitive observation relates to a greater variability in IOP in the trabeculectomy group compared with the tube group. More patients in the trabeculectomy group had extremes of high- and low-IOP resulting in classification as failures because of inadequate IOP reduction or persistent hypotony. The patients who failed because of hypotony had the effect of reducing the mean IOP. Even though the patients who failed because of inadequate IOP reduction had higher IOP levels, they represented a small proportion of the total treatment group that was used to calculate mean IOP. Among the patients who failed because of inadequate IOP reduction or glaucoma reoperation, the mean number of medications at the time of failure was similar between treatment groups. This observation suggests that the higher failure rate in the trabeculectomy group was not related to inadequate treatment with medical therapy.

Based upon a systematic review of the published literature on tube shunts, a panel of glaucoma specialists concluded that low IOP levels usually cannot be attained with these devices, and the IOP typically settles in the high teens postoperatively.⁸ Our results contradict these assertions, as evidenced by a mean IOP of 13.0 mm Hg and IOP of 14 mm Hg or less in 62% of patients in the tube group at 3 years. Additionally, this same panel suggested that the rate of failure of tube shunts averages 10% per year,⁸ while we observed a rate of failure of approximately 5% per year in the tube group. The more favorable results of tube shunt surgery in the TVT Study compared with previous studies may relate to differences in study populations, refinements in surgical technique, and/or variations in the definitions of success and failure. The TVT Study excluded several secondary glaucomas with poor surgical prognoses (eg, neovascular glaucoma) that were included in other case series of tube shunts, and this study enrolled patients considered to be at lower-risk of surgical failure than have traditionally undergone tube shunt surgery (eg, prior clear cornea cataract extraction alone).

Treatment success was subdivided into complete and qualified successes, based on the use of supplemental medical therapy. While the overall success rate was higher for the tube group after 3 years of follow-up, the rates of complete success were not statistically different between treatment groups. This is consistent with the observed similar use of supplemental glaucoma medications by both treatment groups at 3 years. The trabeculectomy group had a progressive increase in adjunctive medical therapy during the first 3 postoperative years, while the use of glaucoma medications remained relatively constant in the tube group.

The outcome criteria for the TVT Study were developed prospectively, and our definitions of success and failure are similar to previous studies involving the surgical treatment of glaucoma, thereby facilitating comparison with published results.^{7,9-39} We recognize that the ideal measure of

success for any glaucoma therapy is the prevention of further glaucomatous optic nerve damage and visual field loss with preservation of visual function. 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, IOP-lowering remains the primary goal of all current glaucoma therapy and no other surrogate measure better reflects therapeutic success for this disease at the present time.

The results of several recent multicenter randomized clinical trials have suggested that IOP of 21 mm Hg or less may not be adequate to prevent glaucomatous progression in many patients.⁴⁰⁻⁴² To determine if the TVT Study results changed if more stringent IOP criteria were applied to define success, several post hoc analyses were performed using alternative outcome criteria. Higher failure rates in the trabeculectomy group compared with the tube group were still seen when the upper IOP level defining success was reduced from 21 mm Hg to 17 mm Hg and 14 mm Hg, although the level of statistical significance progressively declined as the IOP level defining success was reduced.

While the overall failure rate was higher in the trabeculectomy group than the tube 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, and a subset of these patients underwent additional glaucoma surgery. There was a tendency for patients in the trabeculectomy group to require more reoperations for glaucoma compared with the tube group after 3 years of follow-up. Patients who fail trabeculectomy and need additional glaucoma surgery will generally undergo repeat trabeculectomy or placement of a tube shunt.^{2,3} However, additional glaucoma surgery in eyes that have failed tube shunt surgery is more complex and usually involves placement of a second tube shunt or cyclodestruction.^{12,13} Investigators in the TVT Study were not masked to the treatment assignment, and there was a potential for bias in the decision to reoperate for glaucoma. We explored for the possibility that surgeons may have had a higher threshold to perform additional glaucoma surgery in the tube group than the trabeculectomy group. The mean IOP prior to reoperation for glaucoma was similar in the tube group and trabeculectomy group, and no significant difference was noted between treatment groups in mean IOP among patients who failed because of inadequate IOP reduction but did not undergo additional glaucoma surgery. These observations suggest that there was no selection bias for additional glaucoma surgery.

Patients in the TVT Study were stratified by type of previous ocular surgery. It is interesting that the greatest difference in failure rates between treatment groups was observed in patients with previous cataract extraction alone (stratum 1), although there were no significant differences in treatment efficacy between strata. This stratum was expected to have the lowest rate of surgical

failure when the study was designed, and patients in this subgroup are the most dissimilar to those who historically have been selected for tube shunt surgery. The lower failure rate of tube shunts compared with trabeculectomy with MMC in eyes with prior cataract surgery alone supports the need to further evaluate the use of tube shunts in nonrefractory glaucomas. The Primary Tube Versus Trabeculectomy (PTVT) Study is an ongoing multicenter randomized clinical trial comparing the safety and efficacy of tube shunt surgery using a 350-mm² Baerveldt glaucoma implant to trabeculectomy with MMC (0.4 mg/ml for 2 minutes) as the initial surgical procedure in patients with glaucoma considered at low-risk for failure.

Wilson and associates compared the Ahmed glaucoma valve implant (Model S-2) (New World Medical Inc, Rancho Cucamonga, California, USA) to trabeculectomy with or without an antifibrotic agent in a randomized clinical trial involving 117 patients.⁹ With a mean follow-up of 9.7 months, lower mean IOP was observed in the trabeculectomy group, and the Ahmed group had a greater adjunctive medication requirement. The cumulative probabilities of success (IOP <21 mm Hg and at least 15% reduction in IOP from preoperative level) were similar between the two treatment groups. This study was performed in Saudi Arabia and Sri Lanka, and included patients with all glaucoma types and some eyes that had undergone previous ocular surgery. A follow-up study continued enrollment in Sri Lanka to a total of 123 patients with primary open-angle glaucoma and angle-closure glaucoma without previous ocular surgery.¹⁰ With a mean follow-up of 31 months, mean IOPs and success rates were comparable between the trabeculectomy group and the Ahmed group. The difference in study results between the TVT Study and the studies by Wilson and associates may relate to differences in study populations, success and failure criteria, and retention during follow-up. The TVT Study also used the Baerveldt implant for patients randomized to the tube group, and the end-plate of this implant has a larger surface area than the Ahmed implant. There is evidence suggesting that implants with larger plates produce greater pressure reduction.^{8,11}

Visual acuity decreased in both treatment groups during the first 3 years of follow-up. Snellen and ETDRS VA were similar between treatment groups at 3 years, and no significant differences in the rates and reasons for vision loss were present in the tube and trabeculectomy groups. Many of the causes of loss of 2 or more Snellen lines were not directly attributable to the surgical procedures under study (eg, diabetic retinopathy, ischemic optic neuropathy). The development of cataract was a frequent cause of vision loss, although many of these patients regained VA with subsequent cataract surgery. There is strong evidence that glaucoma surgery increases cataract incidence and progression.⁴³ No significant difference in the rates of cataract progression or cataract surgery were observed between treatment groups.

The benefit of tube shunt surgery or trabeculectomy with MMC in reducing IOP must be interpreted in the context of adverse events associated with these procedures. A large number of surgical complications were seen in the TVT Study, but most were transient and did not require intervention. A similar high rate of complications in the early postoperative period was also reported in the Collaborative Initial Glaucoma Treatment Study.⁴⁴ More patients in the trabeculectomy group experienced postoperative complications than the tube group in the TVT Study. However, all surgical complications are not equal in severity, and the rate of serious complications associated with reoperation and/or vision loss was similar in both treatment groups. Dysesthesia, wound leaks, and bleb leaks occurred with greater frequency in the trabeculectomy group compared with the tube group. There was a trend toward a higher incidence of diplopia and tube erosion in the tube group and hyphema in the trabeculectomy group, but these differences did not reach statistical significance. Although many of the differences in complications were not statistically significant, they may be clinically relevant. For example, the development of endophthalmitis or blebitis in 1 patient in the tube group and 3 patients in the trabeculectomy group is not statistically significant, but these findings raise concern. The power of this study to detect differences in complications with low rates of occurrence was limited by the sample size.

Stein and associates recently evaluated the rates of postoperative complications after glaucoma surgery among Medicare beneficiaries.⁴⁵ The rates of adverse outcomes were higher after tube shunt surgery than primary trabeculectomy or trabeculectomy with scarring. The authors of the study⁴⁵ and accompanying Editorial⁴⁶ acknowledged the limitations of data derived from Medicare claims, including the possibility of misattributing adverse events from the fellow eye. Tube shunts have historically been reserved for patients who have failed or are more prone to fail standard filtering surgery, and the results of this study are likely related to differences in case severity among the glaucoma procedures that were compared. In contrast, patients who underwent tube shunt surgery and trabeculectomy with MMC in the TVT Study had similar characteristics as a result of the randomization process, and included lower-risk patients than have traditionally had tube shunt surgery.

There are several limitations to the TVT Study. The study enrolled patients who met specific inclusion and exclusion criteria, and they received a standardized trabeculectomy with MMC or 350-mm² Baerveldt glaucoma implant. The study results cannot be generalized to different patient groups or other implant types. The low incidence of certain complications and the small size of many patient subgroups limits the power of the study to detect significant differences. There were no standardized definitions or quantification of surgical complications. A limbus-based conjunctival flap was used in most patients randomized to the trabeculectomy group, and MMC (0.4

mg/ml) was applied intraoperatively for 4 minutes. A trend toward use of fornix-based conjunctival flaps with a more diffuse application of MMC at a lower dosage has developed since the TVT Study was initiated.⁴⁷ This modification in surgical technique may result in lower rates of hypotony and bleb-related complications after trabeculectomy.⁴⁸ A subgroup of patients enrolled in the TVT Study (ie, those with a history of prior trabeculectomy with MMC) had already failed one treatment arm of the study, and potentially could have introduced bias in favor of the tube group. We felt that the study question of whether one surgical procedure was superior to the other was clinically relevant in eyes that had failed a MMC trabeculectomy, and a separate stratum (stratum 4) was created for these eyes to facilitate data analysis and address concerns about possible bias. No significant differences in treatment efficacy were observed between strata.

The 3-year results of the TVT Study provide further evidence that the role of tube shunts should be expanded in the surgical management of glaucoma. Although these devices have traditionally been reserved for refractory glaucomas at high-risk of failure with standard filtering surgery, this study enrolled eyes at lower-risk of surgical

failure. In eyes with previous cataract and/or glaucoma surgery, the TVT Study found that tube shunt surgery was more likely to maintain IOP control and avoid persistent hypotony, reoperation for glaucoma, or loss of light perception vision compared to trabeculectomy with MMC during the first 3 years of follow-up. Both surgical procedures were associated with similar IOP reduction and use of supplemental medical therapy at 3 years. The incidence of postoperative complications was higher after trabeculectomy with MMC compared with tube shunt surgery, but serious complications associated with reoperation and/or vision loss occurred with similar frequency with both surgical procedures. The TVT Study does not demonstrate clear superiority of one glaucoma operation over the other. There are other factors that must be considered when selecting a surgical procedure in patients with medically uncontrolled glaucoma, including the surgeon's skill and experience with both operations, the patient's willingness to undergo repeat glaucoma surgery, and the surgeon's planned surgical approach should failure occur. Additional follow-up is needed to fully assess the risks and benefits of tube shunt surgery and trabeculectomy with MMC in similar patient groups.

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THE TUBE VERSUS TRABECULECTOMY STUDY GROUP

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