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

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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;■:1–14 © 2018 by the American Academy of Ophthalmology*

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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.