Trabeculectomy Revision as a Treatment for Failed Trabeculectomy

BY NATHAN M. RADCLIFFE, MD

t first glance, the treatment of glaucoma seems simple: reduce the IOP. Since the introduction of evidence-based medicine to glaucoma, several prospective, randomized trials have shown that lowering the IOP effectively decreases the progression of glaucoma.^{1,2} Despite demonstrated equivalence in several large, prospective, randomized studies sponsored by the National Institutes of Health, topical ocular hypotensive medicines or laser therapy are the preferred initial treatments for glaucoma, whereas incisional surgery is mainly reserved for refractory glaucoma.³⁻⁵ When surgery is performed, trabeculectomy (a guarded filtration procedure) with adjunctive antifibrotic chemotherapy is still the initial procedure of choice for US glaucoma surgeons.⁶

This column will take a closer look at the evidence (or in some cases, lack of evidence) in support of common glaucoma practice patterns. While the field of glaucoma management has recently benefited from a number of large, multicenter, randomized, controlled clinical trials, we have not yet fully arrived at the era of evidence-based medicine. Although such an arrival may neither be imminent nor desirable, perhaps now is a good time to take stock of our current commonly performed procedures and determine which practices might benefit from further investigation.

One commonly performed procedure worthy of our consideration is trabeculectomy revision. Trabeculectomy revision, or incisional removal of episcleral fibrosis at the site of a failed trabeculectomy, may be achieved through a variety of techniques. The appeal of this option for the glaucoma surgeon is multifaceted. The procedure does not sacrifice a new region of fresh conjunctiva. It can (and often must) be repeated. Plus, the revision may be performed at the slit lamp, in a minor procedure room, or in a main OR. However, there are no prospective randomized clinical trials that have evaluated the outcome of this commonly performed surgery. How strong is the evidence in support of its efficacy and safety? Which antifibrotic agent helps most to optimize outcomes, and which patients make the best candidates? This article evaluates the clinical evidence relating trabeculectomy revision that has been published in the peer-reviewed literature.

TRABECULECTOMY AND TRABECULECTOMY FAILURE

Despite its widespread use, trabeculectomy has its limitations. Aside from short-term problems such as a 50% rate of transient perioperative complications, as seen in the Collaborative Initial Glaucoma Treatment Study (CIGTS), trabeculectomy surgery is limited by a suboptimal long-term success rate.⁷ The procedure's success varies with the type of antifibrotic therapy used, but the rate of failure has been reported to be as high as 23% to 51% at 5 years and 52% to 59% at around 15 years, even with adjunctive 5-fluorouracil (5-FU) or mitomycin C (MMC).^{8,9} Unfortunately, without antiscarring chemotherapy, the success rate of trabeculectomy is lower due to unwanted episcleral fibrosis at the site of aqueous humor outflow, resulting in bleb failure in 24% to 74% of cases at 4 years.¹⁰⁻¹²

In the prospective Tube Versus Trabeculectomy (TVT) study, 105 patients were randomized to trabeculectomy, and 30.7% of those surgeries were considered failures (IOP > 21 mm Hg or less than a 20% reduction from



baseline) at 3 years. Of those failures, 19 of the 28 eyes that met a treatment failure endpoint in the trabeculectomy arm had inadequate IOP control or were reoperated for their glaucoma with a mean IOP of 28 mm Hg.¹³ The 3-year cumulative probability of failure in the tube group was 15.1%. The main cause of a failed trabeculectomy is episcleral or subconjunctival fibrosis.¹⁴ When a trabeculectomy procedure fails and cannot be rescued, subsequent procedures include a second trabeculectomy, placement of an aqueous shunt, or a cyclodestructive procedure.

CAN OCULAR COMPRESSION RESCUE A BLEB?

Rather than abandon a failed trabeculectomy, surgeons often attempt other interventions aimed at rescuing or reviving the trabeculectomy. Prior to performing an incisional trabeculectomy revision, some ophthalmologists instruct their patients to perform digital ocular compression in order to enhance the egress of aqueous. Henderer et al from the Wills Eye Institute in Philadelphia conducted a short-term, prospective, randomized, controlled, single-masked trial of 29 patients and compared ocular compression (pressing on the zygomatic arch) to control.¹⁵ Over the course of this 6-month study, two 10-second sets of ocular compressions were performed 5 seconds apart three times daily. All patients in the study had undergone guarded filtration surgery at least 3 months (and on average several years) prior to the initiation of the protocol. At the study's conclusion, the mean change in IOP was 0.25 mm Hg for the ocular compression group compared with -0.44 mm Hg for the control group (P = .7). Although the researchers postulated that the intervention might have been initiated too late (longer than 3 months after surgery) to obtain the full effect of treatment, they conceded that the study did not demonstrate efficacy for this widely used technique.¹⁶

TRABECULECTOMY REVISION

Perhaps the most scientifically rigorous evaluation of trabeculectomy revision was a prospective, observational, noncomparative, interventional case series of 101 patients who underwent postoperative bleb needling with adjunctive 5-FU at several centers (including Moorfields Eye Hospital) in England.¹⁷ This technique involved a slit-lamp-guided passage of a 29-gauge needle into the subconjunctival space, followed by a superior subconjunctival injection of 5-FU (5 mg in 0.2 mL).

On average, IOP was reduced from 26.5 to 15 mm Hg after an average of 1.6 needling procedures, but only

75% of eyes at 1 year's and 52% at 3 years' follow-up had an untreated IOP of less than 22 mm Hg. Given that many glaucoma patients require multiple surgeries over the course of their lifetime and that trabeculectomy itself has a relatively high failure rate, the success rate reported in this series suggests that trabeculectomy revision may play a valuable role in the management of bleb failure.

SELECTING AN ANTIFIBROTIC THERAPY

For trabeculectomy revision, adjunctive antifibrotic chemotherapy can play a role in enhancing surgical success. Anand and Kahn retrospectively evaluated 98 eyes of 95 consecutive patients with at least 1 year of followup after trabeculectomy revision (45 with 0.02 mg of MMC and 53 with 5 mg of 5-FU).¹⁸ Success (defined as an IOP between 5 and 16 mm Hg with no glaucoma medications) was 71% and 45% after 1 year and 61% and 30% after 2 years in the MMC and 5-FU groups, respectively. There was a significantly higher number of needle revisions in the MMC group than in the 5-FU group $(1.9 \pm 1.0 \text{ vs})$ 1.2 \pm 0.5, *P* = .001). In this study, MMC use (hazard ratio [HR], P = .006) and decrease in IOP immediately after needling (HR = 1.06, P = .03) were more likely to result in success. The type of antifibrotic agent used was not associated with a difference in complication rates, although the MMC group had a shorter follow-up than the 5-FU group (33 months vs 53 months, P < .001). Significant limitations of this study were the lack of randomization and the possibility of bias induced by physicians' experience; 5-FU revisions were generally performed earlier, before the physicians transitioned to MMC revisions. Nonetheless, the study supports the possibility that revisions with MMC could be more efficacious than those using 5-FU, with a similar complication rate between groups.

Shin et al found that a preneedling IOP of more than 30 mm Hg, a lack of MMC use during the original trabeculectomy, and a higher IOP immediately after needling were important risk factors for failure in a retrospective review of 30 5-FU needle revisions.¹⁹ Without a truly randomized study that can eliminate selection bias, it is not possible to determine definitively which antifibrotic agent is better, but early evidence suggests that the use of MMC may be associated with a higher success rate.

IS TRABECULECTOMY REVISION SAFE?

Hypotony (and its potentially devastating sequelae), infection, bleeding, and inflammation are potential complications of trabeculectomy and bleb revision. What information is available about the safety of bleb needling? In Anand and Khan's series of 98 consecutive eyes undergoing revision with antifibrotic therapy, 4.5% experienced blebitis, 10.5% experienced a delayed bleb leak, 1% experienced aqueous misdirection, and 1% experienced a suprachoroidal hemorrhage.¹⁸ Broadway et al observed potentially serious complications in 6% of 101 needling procedures using 5-FU, including hyphema (3%), bleb leak (1%), and hypotony with choroidal effusion (2%).¹⁷ However, a higher rate of complications was presented in a series of 81 patients undergoing bleb needling by Rotchford and King.²⁰ When considering all complications (such as subconjunctival hemorrhage and leaking at the needling site without hypotony), 27.9% had complications in that study. Sight-threatening complications typically requiring surgical intervention (such as penetrating keratoplasty or choroidal drainage) occurred in 8.6%.

Although these complication rates may be acceptable given the serious nature of vision loss from glaucoma, it should be noted that a trabeculectomy revision should not be considered a risk-free or low-risk procedure, even if performed in a seemingly innocuous setting such as at the slit lamp. Furthermore, in a prospective trial where study forms specifically query for the presence of complications at each visit, it is possible, if not likely, that the complication rates would be higher than reported in a retrospective chart review.

CAN A FAILING TUBE SHUNT BE RESCUED?

Glaucoma tube shunt surgery is gaining in popularity among glaucoma surgeons.³ Although the 3-year data from the TVT study demonstrated a lower (15.1%) probability of failure in patients receiving a Baerveldt implant (Abbott Medical Optics Inc., Santa Clara, CA), tube shunt procedures have significant challenges as well.¹³ A tube may undergo primary failure when a tense fibrotic capsule forms around the extraocular reservoir, and for such cases, there is a paucity of data regarding the success of needle revision. In the only published retrospective case series on this topic, Chen and Palmberg reviewed the charts on 21 eyes that underwent shunt revision with 5-FU. They reported a short-term (14-month) success rate of 43% with a 5% rate of endophthalmitis.²¹ The issue of whether tube shunts can be revised is of critical importance. The inability to perform revisions would make tube shunt surgery a potential "dead end" compared with trabeculectomy and might limit the former's usefulness, particularly in younger patients who may need a sequence of operations over their life span. High-quality, prospective data on the efficacy and safety of surgical revision for encapsulated tube shunt reservoirs could be an important piece of information in the tube versus trabeculectomy debate.

CONCLUSION

Prospective randomized clinical trials are providing important information to glaucoma surgeons. It will never be the case that every conundrum in glaucoma can be resolved with such evidence-based research, because many patients' situations will be unique. Physicians, however, can now be more critical of the quality of data that guides their therapeutic choices. The available evidence suggests that trabeculectomy revision has a reasonable success rate (probably in the range of 30%-60%) 3 years after the procedure and a serious complication rate of roughly 10% or lower.

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