Will Surgery Become the First Line of Glaucoma Treatment in the United States?

It is highly unlikely.

BY SHAN C. LIN, MD

Surgery is very unlikely to become the preferred first line of treatment for glaucoma. In some parts of the world, including England, surgery has been considered the optimal initial therapy to prevent visual field loss. Furthermore, there is evidence that surgery has been considered the optimal initial therapy for primary open-angle glaucoma. The rates of serious complications and reoperations also were not substantially lower in the preferred first-line approach. We need to do better.

**Efficacy**

What about the current crop of new glaucoma surgeries that purportedly possess an improved safety profile and are associated with fewer complications? In a recent ophthalmology technology assessment, the American Academy of Ophthalmology reviewed many novel surgeries for glaucoma. They included the Fugi blade (Medisurg Ltd., Norristown, PA), the Ex-Press Glaucoma Filtration Device (Alcon Laboratories, Inc., Fort Worth, TX), the Solsa Gold Shunt (Sols, Inc., Boston, MA; not available in the United States), canaloplasty (SciVision Interventional, Menlo Park, CA), trabeculectomy by an internal approach (Trabectome; NeoMedix Corporation, Tustin, CA), and a trabecular microbypass stent (Stent; Glaukos Corporation, Laguna Hills, CA; not available in the United States). Thus far, no prospective, randomized trials have compared these new techniques to the reference standard for glaucoma surgery—trabeculectomy. Quite likely, none of them will have greater efficacy than trabeculectomy in terms of reducing patients’ IOP and their need for medication.

Consequently, the potential benefits of these new procedures are fewer complications such as a shallower/flat anterior chamber, hypotony, blephitis/endophthalmitis, and ocular dysesthesia. In these situations where the efficacy is mild but the complications are relatively low, the clinician needs to decide if the cost-benefit ratio is in the patient’s best interest. Given the efficacy and safety of current drugs such as the prostaglandin analogues, the scale tips toward medication as the best first-line treatment.

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Safer, more efficacious procedures will mean earlier surgery.

BY GARRY P. CONDON, MD

Why shouldn’t we ophthalmologists consider the possibility that incisional surgery will eventually replace medications as first-line therapy for established primary open-angle glaucoma here in the United States? The answer has come down to safety. None of us doubts the historic efficacy of trabeculectomies and tube shunts when it comes to dramatically lowering IOP; but we cannot shake our concerns about safety and predictability. For that reason, to this day, we continue to relegate our questionably compliant patients to the often expensive, frequently ineffective realm of medical therapy despite the potential for adverse reactions. For many patients, medication is neither the answer nor the best first-line approach. We need to do better.

**Improvements Already**

For many of us, compared with argon laser trabeculectomy, selective laser trabeculoplasty represents a more refined and less traumatic nonincisional surgical modality that we are willing to use as first-line therapy for early glaucoma. Can we move toward creating a disconnection between the increased risks inherent in traditional incisional surgery while achieving its historical efficacy? That is a work in progress.

Although armed with patients with advanced disease, the Tube Versus Trabeculectomy (TVT) Study validated the safety and efficacy of tubes to the extent that a new study is underway to compare these two approaches as primary surgery. Three-year data on canaloplasty (Science Interventional, Menlo Park, CA) as primary surgery or in combination with cataract surgery point to a 30% reduction in IOP with a low rate of complications. Other recent work suggests that modifying trabeculectomy by incorporating the Ex-Press Glaucoma Filtration Device (Alcon Laboratories, Inc., Fort Worth, TX) can lead to faster visual recovery while being as effective as standard trabeculectomy. Clearly, we are improving on traditional surgical approaches.

The appeal of minimally invasive glaucoma surgery (MIGS) is its proven safety relative to the old standby surgical procedures. The goal is reducing complications. George Sparth, MD, once said to me, “An operation that works half the time, with few complications, can be a great operation for glaucoma.” That thought underscores the growing interest in MIGS. New surgical approaches aim to access the indigenous outflow system or the supraciliary space. Examples of the former include the Trabectome (Stent, and Hydrus [respectively, NeoMedix Corporation, Tustin, CA; Glaukos Corporation, Laguna Hills, CA; and Iantes Inc., Irvine, CA; Stent and Hydrus not available in the United States]). The latter include the Transcend CyPass System and Sols Gold Shunt (respectively, Transcend Medical, Menlo Park, CA, and Sole Inc., Wal-tham, MA; neither available in the United States). Effective nontransscleral approaches with low complications would be attractive, especially considering how easily they could be combined with standard cataract surgery.

In addition to their safety profiles, what makes MIGS procedures attractive as a means of intervening early in a patient’s disease is that they do not prevent us from performing more traditional surgery at a later date, if needed.

**Compliance**

I believe that patients experience less long-term IOP fluctuation when their pressure is lowered surgically rather than medically. That is because we cannot expect our patients to adhere to prescribed topical therapy as ideally as do subjects in a clinical trial. I ask my patients to estimate how closely they are following their drug regimen, because I want an idea of their real-life experience. Patients who tell me they miss their drops more often than they take them may benefit from surgical intervention.
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A Combined Approach

There is a trend toward conducting studies that compare a new glaucoma procedure in conjunction with cataract surgery using phacoemulsification to cataract surgery alone.\(^6,7\) The combined procedure often provides a marginal added benefit in terms of reducing IOP and the need for medication. Can surgery truly be considered the first line in this situation, however, when the overriding reason to perform surgery in many of these cases was to remove the cataract to improve visual acuity? Also, the cataract surgery by itself often lowers the IOP and can reduce the patient’s need for glaucoma medications postoperatively. Perhaps phacoemulsification, then, can be considered a reasonable and safe first-line treatment for mild glaucoma.

The Ideal

Certainly, the possibility exists that future developments in incisional surgery will yield a technique that is nearly as efficacious as trabeculectomy but is much safer and more predictable. Ideally, surgery would also be long lasting, have a fast recovery time, and allow for repeatability and other potential surgeries such as trabeculectomy. Given such requirements, the likelihood of such a procedure’s being developed in the next 5 years is low.

THE DRAWBACKS OF TOPICAL THERAPY

A clear downside of topical medication is noncompliance. Eye drops are difficult to administer, and the elderly often forget to use them. An obvious advantage of surgery is that the ophthalmologist performs the treatment rather than the patient, but the continued development of newer and more potent medications will help to reduce the problem of noncompliance. The availability of prostaglandin analogues is an example of this progression in drug development. This class of medication is very potent, enduring (once-a-day dosing), and systemically safe. Several new classes of medications are already in clinical trials, including rho kinase inhibitors, serotonin receptor antagonists, and EP receptor agonists. Their approval might help physicians prevent progressive visual field loss.

Also on the horizon are better methods of delivering medication. Slow-release depots of prostaglandins and other drugs are already being tested. Potential areas for these depots include the punctal, subconjunctival, sub-Tenon, anterior chamber, and vitreous spaces. Successful developments in this arena, rather than in the surgical field, are more likely to result in future advances in the initial treatment of glaucoma.

ECONOMICS

Are there particular situations or social/economic circumstances in which incisional surgery is a reasonable first-line option? Certainly. In a recent case of neovascular glaucoma at my county hospital, the patient’s IOP was 80 mm Hg and did not respond to maximal medical therapy over the course of 6 hours. Because the patient’s visual acuity was in the usable range, he was taken to the OR for the urgent placement of a tube. The patient’s IOP decreased to the teens, and his visual acuity was stabilized.

Additionally, in some parts of the world, medications are not readily available and/or are too expensive. Although not an incisional surgery, transscleral cyclophotocoagulation was used with some success in Ghana as a first-line treatment.\(^8\)

CONCLUSION

Medications will probably remain the predominant first-line therapy for the treatment of glaucoma in the developed world. Current surgical techniques have not reached a level of safety and efficacy that justifies their use as initial treatment in the vast majority of cases. Future advances in medical treatment and delivery are likely to outpace surgical development, so drug therapy will remain the mainstay of first-line treatment.

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A LITTLE NOW OR A LOT LATER?

The chief criticism of the new MIGS procedures is that they are less efficacious than trabeculectomy. Incrementally lowering a patient’s IOP earlier in the course of the disease, however, can increase his or her chance of maintaining visual function longer. MIGS may delay this patient’s need for riskier surgery. Moreover, many individuals with glaucoma do not need an IOP below the mid-teens. In fact, I see patients with pressures of 10 mm Hg who do not see well, because their IOP is too low.

LOOK FORWARD, NOT BACKWARD

In the long term, will our overall rate of surgical complications be lower? That is the subject of current study. Certainly, my level of confidence in surgical intervention is far higher than it was 15 years ago. I am more comfortable intervening earlier in the disease process than in the past. A current problem of glaucoma surgery, however, is that we are performing it on eyes with advanced disease. MIGS may allow us to intervene before the outflow system can no longer be revived.

Ophthalmologists who lack enthusiasm for MIGS bemoan the absence of well-structured studies—research that really has just begun. It does not benefit our field or our patients to trash the new procedures from the sidelines. What we need is more experience performing MIGS so that we can attempt to improve the procedures’ efficacy without compromising safety. Ideally, the results will improve to the point that we need not justify performing these surgeries by combining them with other interventions such as cataract extraction. ☐

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