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Optimising Combination Therapies and Modern MIGS for Early-to-Advanced Glaucoma

Reviewing the Impact of Glaucoma on the Cataract Patient and the Benefits of Earlier Intervention

A range of diagnostic and treatment options are available to manage glaucoma in cataract patients

Simonetta Morselli, MD

Before performing surgery on a patient with glaucoma, we need to determine the disease severity — assessing the optic nerve, extent of visual field damage and the patient's imaging studies — and identify the target intraocular pressure (IOP).

The more damage the patient has, the lower the target IOP should be. In patients with mild disease, IOP should be in the upper teens; moderate disease, mid-teens; and severe disease, low teens. Therefore, postoperative IOP should be nearly 10 or 11mmHg if glaucoma is very severe. The targeted IOP decrease narrows our minimally invasive glaucoma surgery (MIGS) choices, guiding our choice of procedure.

Diagnosis and Treatment

Key tests are used to diagnose glaucoma — visual fields, optical coherence tomography (OCT) and anterior segment OCT. In addition, gonioscopy should be used for planning and to check the angle before surgery. Additional tests include aqueous angiography, ocular surface and tear film assessments, and corneal hysteresis. We also need to check the lens and corneal refractive error.

When I initially see a patient with glaucoma and cataract, my first step is to try to reduce the IOP with drops, considering glaucoma progression. Patient compliance is an important consideration with glaucoma drops. If patients do not adhere to their treatment regimen, glaucoma will progress.[1] We also need to keep in mind the tolerability of topical therapy.[2]

If a patient has cataracts, the second step after topical medication is MIGS, which reduces IOP and takes an ab interno approach with no conjunctival dissection, and the third step is filtering surgeries, in which IOP is reduced through artificial drainage between the anterior chamber and subconjunctival space.

Considering Options

When making a surgical decision, we need to balance safety and efficacy (Figure 1). The risk of the procedure should not exceed the risk of disease.

We use diagnostic testing to stage disease, determine target IOP and decide which MIGS procedures are indicated. It can be overwhelming to choose among the available MIGS procedures, but we cannot ignore them. Ophthalmologists should learn to access all of the spaces of the angle where MIGS devices can be placed. It is also important to understand what you can do and which cases you should refer to colleagues.

Assessing and addressing glaucoma in cataract patients is critical to achieve successful outcomes. Early intervention with a stepwise treatment approach should be considered in all cataract patients with glaucoma.

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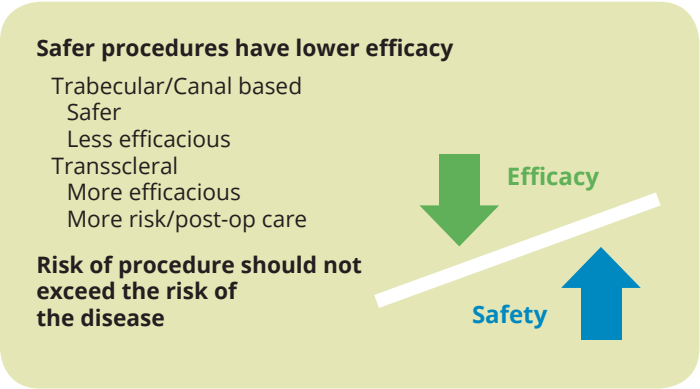

Figure 1. When making surgical decisions, it is important to balance safety with efficacy

What's New in Glaucoma Medical Therapy?

Potential therapies aim to improve patient compliance, efficacy and other factors

Christophe Baudouin, MD, PhD

We are on the brink of a new cycle of innovations in glaucoma medical therapy, and I would like to share a number of these.

Improving Glaucoma Medications

To provide the best medical glaucoma treatments, we need a formulation that efficiently reduces intraocular pressure (IOP); is well tolerated short- and long-term, easy to use and reasonably priced; and has a complementary mode of action.

To improve upon existing medications, we need preservative-free formulations and medications with an increased duration of effect (and decreased number of doses) to increase patient compliance.

Lemij et al. reported that dry eye and meibomian gland symptoms increased after patients began using glaucoma medications.[1] Long-term effects and decreased tolerance will significantly affect compliance and efficacy.

New delivery systems may reduce problems associated with compliance. Researchers are studying conjunctival rings and intracameral implants with bimatoprost; intracameral implants with travoprost; an intraocular drug delivery device with travoprost that bypasses the cornea; a subtarsal implant that can release medication; and a punctum plug containing medication (Figure 2).

Implants*

Bimatoprost sustained-release implant

Now in phase III trials

Phase II (75 eyes):
-7.2 to -9.5 mmHg at M4 (≈bimatoprost 0.03%)

Travoprost intracameral implants

Phase IIA: Implant vs. topical on 28 days:
-6.7 vs. -6.6 mmHg

Intraocular implant with travoprost

Phase II
Reduction of +/-8 mmHg up to 12 months

*These implants showed IOP-lowering effects in some patients up to 1 year. The exact duration of efficacy and strategies for refilling are under investigation

Figure 2. New drug delivery systems may help reduce compliance problems

New Drug Families

Researchers also are investigating new families of drugs. These include cannabinoids to reduce IOP, drugs that act on the trabecular matrix and inhibitors of actin polymerisation. Latanoprostene bunod, combining latanoprost acid and nitric oxide, was approved by the US Food and Drug Administration (FDA) in 2017.[2]

In the rho-kinase inhibitor (ROCK) family, three medications have been developed that are administered once daily: netarsudil and netarsudil plus latanoprost, which are both FDA approved; and ripasudil, which is available in Japan. The combination of ROCK with latanoprost increases the effect compared with latanoprost alone.

The combined drug properties of netarsudil and netarsudil plus latanoprost affect secretion, outflow and episcleral vein pressure. By decreasing the pressure, it increases the gradient of outflow and uveal scleral outflow.

Protecting the Optic Nerve

The goal of glaucoma therapy is to protect the optic nerve from degeneration by controlling IOP. However, we do not have a treatment that protects and regenerates the damaged optic nerve. Many targets could be developed addressing neuroprotection because glaucoma neuropathy results from many stresses. Pharmacologic, cellular and gene therapies are being studied.

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MIGS Options for the Advanced and Refractory Glaucoma Patient

Evolving technologies enable surgeons to tailor treatment approaches to each case

Julian García-Feijoo, MD, PhD

In patients with glaucoma, our goal is not to treat an intraocular pressure (IOP) but preserve visual function. To achieve this goal in our patients, we have to balance the risks vs benefits of procedures.

MIGS Devices

Safety is a primary concern and is the concept behind minimally invasive glaucoma surgery (MIGS). The procedure ideally should use physiological outflow pathways. With different MIGS devices, we can enhance the trabecular or suprachoroidal drainage or take a subconjunctival approach with a bleb.

We treat some patients more aggressively, depending on the patient's age, disease stage, rate of progression and other risk factors. MIGS allows us to tailor our approach (Figure 3).

Trabecular or suprachoroidal (bleb-less) surgery does not decrease intraocular pressure (IOP) as significantly. Within the first one or two years, IOP will be in the mid or high teens. Trabecular or suprachoroidal devices may decrease IOP enough in mild glaucoma but not advanced cases.

However, a suprachoroidal drainage pathway may provide another option. In a study, we used a CyPass Microstent in patients scheduled for trabeculectomy, and it effectively reduced IOP in approximately 80% after one year.[1] CyPass is no longer available due to corneal endothelial damage, but we will have other suprachoroidal devices.

Advanced Cases

If we want to achieve very low IOP, we most likely need a bleb. However, we know that hypotony, inflammation and bleb-related adverse effects may occur.

Minimally penetrating glaucoma surgery (MPEGS) devices create a new pathway, rather than using the physiologic outflow pathways.

The InnFocus Microstent was launched recently. It could be an alternative to trabeculectomy in certain cases. In one study, the mean IOP was approximately 11 or 12mmHg and IOP was lower than 14mmHg in a significant number of patients.[2] In our study, using a lower mitomycin C dose, mean IOP was approximately 14mmHg.[3]

We also can obtain low pressures with Xen; however, the needling rate is 20-30%.

With these MPEGS procedures, we need more evidence and long-term data (success, adverse effects, mitomycin C dosing and bleb management).

In the past, we have used trabeculectomy in cases requiring significant IOP decreases; however, MPEGS may be less invasive and aggressive and could be an alternative in some cases.

We have numerous options, so we need to carefully consider each patient's case and characteristics and the patient's concerns and opinion when choosing our treatment strategy.

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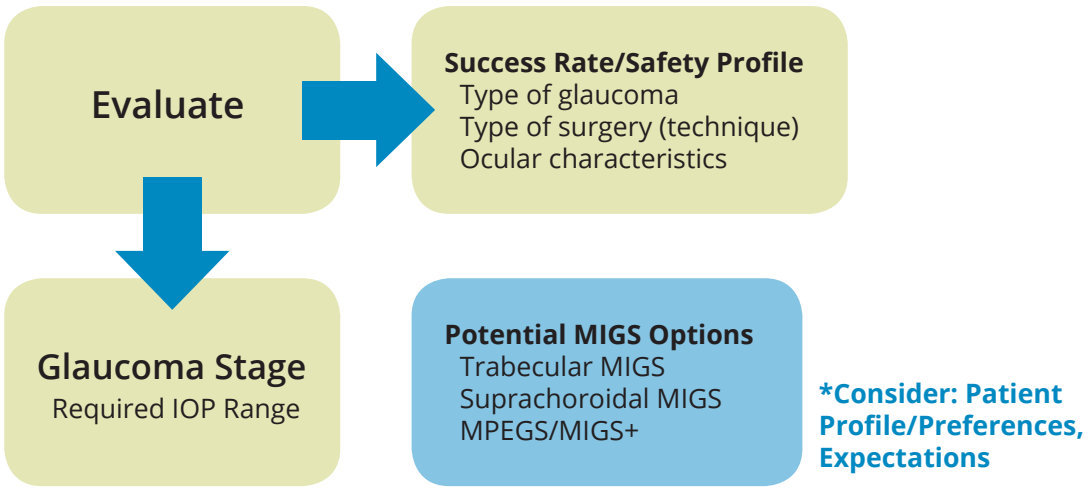

Figure 3. Considerations when selecting a glaucoma procedure

MIGS Options for the Early-to-Moderate Glaucoma Patient

The array of MIGS technologies continues to expand

Boris Malyugin, MD, PhD

The typical candidate for minimally invasive glaucoma surgery (MIGS) needs cataract surgery and uses one or two medications, but intraocular pressure (IOP) is not low enough. Combining MIGS with cataract surgery helps reduce medications while gaining better IOP control. It is also prophylaxis for early IOP spike.

Examining Options

Figure 4 shows factors that should be considered when examining a potential MIGS candidate.

In most European countries, patients pay out-of-pocket for MIGS because it is not covered by insurance. Therefore, we need to discuss this with patients, along with the benefits, expected long-term results in terms of IOP efficacy and safety issues.

There are a number of challenges when performing cataract surgery in patients with glaucoma, including comorbidities in the posterior and anterior segments of the eye. Loose zonules and small pupils are the most frequent issues for anterior segment surgeons. We also have to be vigilant with regard to postoperative IOP spikes. Advanced optic nerve damage results in low visual potential. We also need to weigh the challenges of glaucoma procedures in terms of technique, safety, and effectiveness.

Trabecular Bypass

Several trabecular bypass approaches can be used during cataract surgery. With iStent, a heparin-coated non-ferromagnetic titanium implant, we can enhance the IOP-lowering effect by increasing the number of stents.[1] Another generation of this implant, iStent Inject, is smaller. Several can be used during cataract surgery, and it can be used for a standalone procedure. It is not available yet in all countries.

The Hydrus Microstent, a scaffold made of nitinol, helps expand Schlemm's canal and reduces IOP, with varying results reported.

Standalone Bypass

Trabecular bypass also is performed as a standalone procedure, and trabeculotomy is a cost-effective alternative to implant-based technologies.

The Kahook dual blade mechanically opens the trabecular meshwork. The Trabectome uses microelectrocautery, allowing 180 degrees of treatment.

Several other technologies are based on excising Schlemm's canal, with some treating 360 degrees, such as the Visco360, Trab360 and GATT.

> **We need to monitor the development of this technology and master it because it is promising and continues to evolve**

Ongoing Research

I believe MIGS devices are best for early and moderate glaucoma. We need to monitor the development of this technology and master it because it is promising and continues to evolve.

The classical pathway of outflow through the trabecular meshwork, Schlemm's canal, collector channels and episcleral veins is affected by the segmental outflow of aqueous humour from MIGS. Therefore, if we implant the MIGS device where there is no outflow, it will have no effect. Consequently, we need to aim for functionally active portions of Schlemm's canal to achieve better results.

Factors to Consider

- Target IOP
- Rate of progression / degree of damage
- Ocular health
- Lens status
- Age / life expectancy
- Compliance with / ability to instill drops

Figure 4. Factors to consider when examining a potential MIGS candidate

Reference

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