

Evaluating glaucoma surgeries in the MIGS context

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Abstract

The challenges of glaucoma management are many: the disease is chronic, progressive, often asymptomatic, and very often, the quality of life and costs of treatment is unacceptable to the patient. This is true for both medical therapy and conventional glaucoma surgery. The choice of therapy, especially the transition from the former to the latter, is now being bridged by Minimally Invasive Glaucoma Surgeries (MIGS). Choosing from the several options now available in the surgical armamentarium requires a deeper understanding of the available modalities. This review aims to provide an overview of the decision-making process, keeping in mind age, type of glaucoma, life expectancy, socioeconomic status, patient expectations, and coexisting cataract.

Keywords: glaucoma, minimally invasive glaucoma surgery, MIGS, trabeculectomy, glaucoma drainage device

Introduction

Glaucoma surgeries, unlike cataract surgeries, are not one-time procedures. There is a frequent need of stringent postoperative follow-up for the management of various early and late post-operative complications and repeated procedures because of gradual decrease in the efficacy of procedure over time. Despite refinements of the surgical technique, and the introduction of newer surgical procedures, the outcomes of glaucoma surgery remain suboptimal.

In the quest for the perfect glaucoma surgery, a lot of innovations and devices have come into market. These are collectively labelled MIGS (Minimally Invasive Glaucoma Surgery) and are ab-interno glaucoma procedures often sparing the conjunctiva, and thought to be less aggressive than the standard glaucoma surgical

procedures, namely, trabeculectomy and glaucoma drainage devices (GDD) (**Table 1**) [1].

Even though surgical success criteria have been defined by WGA (World Glaucoma Association) consensus in 2011, the criteria for success of many surgeries have been variably defined in different trials (**Table 2**). Even over the last decade, there has also been a growing understanding that the criteria for success cannot be generalized and have too many variables. These include the purpose of procedure, its efficacy as well as safety, patient age, stage of glaucoma, etc. In a present scenario, there are many surgical options for patients as well as for surgeons and there is a demand of tailored management for each patient. This review aimed to critically evaluate each of these, making the surgical decision process a little less ambiguous.

Table 1. Available MIGS devices and mechanism of action

Mechanism	Example	Outflow Pathway	FDA approval
Increase in trabecular outflow	1. iStent/ iStent inject 2. Hydrus implant	Implant is inserted through trabecular meshwork to Schlemm's canal	<ul style="list-style-type: none"> Mild-moderate open angle glaucoma (OAG) in conjunction with cataract surgery
	3. Ab-interno trabeculotomy with Trabectome device or Kahook dual blade	Removes the trabecular meshwork and inner wall of Schlemm's canal	<ul style="list-style-type: none"> Medically uncontrolled primary or secondary OAG with or without cataract extraction
	4. Gonioscopy assisted transluminal trabeculotomy (GATT)	Gonioscopic guided ab-interno trabeculotomy using microcatheter (iTrack) or sutures (prolene/ nylon) after performing a 1-2 mm goniotomy	
	5. Ab-interno canaloplasty using iTrack	Ab-interno viscodilatation of Schlemm's canal	<ul style="list-style-type: none"> Mild-moderate POAG with or without cataract surgery
		Cypass	
Increase in uveoscleral outflow	Solx Gold shunt	Implants are inserted into suprachoroidal space after creating a localized cyclodialysis	<ul style="list-style-type: none"> Not yet approved
	iStent supra		<ul style="list-style-type: none"> CE approved for mild-moderate POAG with or without cataract surgery, but not yet FDA approved Medically uncontrolled POAG, pseudoexfoliation or pigmentary glaucoma patients or refractory glaucoma after failed previous surgery with or without cataract surgery
	Xen implant,		Implant is inserted through trabecular meshwork to subconjunctival space
Innfocus	<ul style="list-style-type: none"> Refractory glaucoma with or without cataract surgery In medically controlled glaucoma in combination with cataract surgery 		
Decrease in aqueous humour production	Endolaser Cyclophotocoagulation	Ab-interno cyclophotocoagulation to ablate ciliary processes by direct visualization	<ul style="list-style-type: none"> Refractory glaucoma with or without cataract surgery In medically controlled glaucoma in combination with cataract surgery

Table 2. Criteria used for defining surgical success in evaluating glaucoma surgery

Surgery	Success criteria
Trabeculectomy	<ul style="list-style-type: none"> • IOP 6-21 mmHg and at least 30% IOP reduction [2] • IOP 5-21 mmHg and IOP decrease of $\geq 20\%$ [3,4] • IOP $\geq 6 - \leq 18$ mmHg [5] • IOP $> 5 - \leq 18$ mmHg or 20% reduction [6,7] • IOP 6-16 mmHg without medication (complete success), $\geq 6 - \leq 16$ mmHg with one antiglaucoma medicine or needling (Qualified success) [8] • IOP ≤ 15 mmHg [9]
Glaucoma Drainage Devices	<ul style="list-style-type: none"> • IOP ≤ 21 or $> 20\%$ IOP reduction, success rates at IOP levels $\leq 17, \leq 14$ mmHg also evaluated [10,11] • IOP $\leq 21, \leq 16$ mmHg [12], qualified success - up to 2 topicals • 5-21 or $\geq 25\%$ IOP reduction [13] • IOP $\geq 5 - \leq 18$ mmHg [14]
Deep Sclerectomy	<ul style="list-style-type: none"> • IOP reduction $> 25\%$ [15] • IOP of < 18 mmHg and at least 20% IOP reduction [16]
MIGS	<ul style="list-style-type: none"> • IOP reduction $\geq 20\%$ on the same or fewer medications in a study on Xen implant without cataract surgery [17] • IOP reduction and medicine reduction in a study on Trabecular bypass stents in combination with cataract surgery [18]

Which surgery to choose?

Glaucoma surgery is no longer considered the last-ditch effort to decrease intraocular pressure (IOP) in the end stage glaucoma, or in patients not effectively controlled by maximal medical treatment. Patients, and doctors alike, are increasingly considering surgery for patient comfort, when patients do not want to use eye drops, and choose a safer surgical option for a better quality of life. But not a single surgery fits every patient. The choice of surgery can be guided by several factors like:

a. Desired IOP level: Without doubt the single most important criteria to evaluate a glaucoma surgery remains its efficacy in controlling the IOP. That said, there is a need to realize that the criteria for success of IOP control ≤ 21 mmHg with or without medications (qualified or complete success respectively) might not be valid in each case. IOP level < 21 mmHg might not be good for moderate-advanced glaucoma or with Trab/ tube surgeries, whereas the same might be considered excellent for MIGS when performed in early glaucoma. Similarly, in cases of MIGS, if a patient still has to use medicines, when the surgery was performed early on in the disease to ensure freedom from eye drops, the procedure would be considered a failure.

b. Type of glaucoma and age of the patient:

Early and Moderate Primary Open Angle Glaucoma (POAG)

In early POAG, medical or laser treatment are usually effective options, however, some patients who are intolerant/ non-compliant to medicines or not very well controlled with medical/ laser treatment, MIGS (for example iStent, Trabectome, Hydrus, endolaser cyclophotocoagulation) are good surgical options in terms of reduction in IOP, as well as the number of glaucoma medications, especially since they are conjunctiva sparing and have lesser complications. However, some MIGS devices are ab-interno procedures but are implanted subconjunctivally like Xen implant or Innfocus, which might not be the first choice in these patients, as they involve conjunctiva and have bleb related complications similar to trabeculectomy.

Trabeculectomy may also not be a good option in these cases because of the significantly higher risk of post-operative complications, increase in cataract formation, higher failure rates because of strong healing response in young [19]. If the trabeculectomy in this scenario results in qualified success with persistent need of medicines, it would actually be considered a failure.

In a young patient, with early glaucoma, safety of a procedure is the main priority and the procedure has to be effective on long-term without vision threatening complications. Conjunctiva sparing surgeries should be preferred so as to preserve the conjunctiva for future surgery if needed. At present, there is no ideal surgery that is safe and conjunctival sparing with long-term efficacy. This is especially relevant since the long-term outcome with MIGS is yet to be ascertained [20,21].

On the other hand, in elderly patients with limited life expectancy, MIGS can be offered with good safety profile over trabeculectomy. Non-penetrating deep sclerectomy (NPDS) is another safer option with similar success rates as of trabeculectomy, but with fewer complications [22,23].

Severe POAG

Severe cases usually require lower target IOPs and MIGS might not be a good option in these cases as many of the stents (Schlemm canal based) are unable to maintain lower levels of IOP because of downstream resistance and episcleral venous pressure [24]. Trabeculectomy and deep sclerectomy, or even suprachoroidal shunts, may be better surgical options in these cases.

Primary tube surgery is considered another good option in view of good success rates with fewer complications compared to trabeculectomy (Trab) with Mitomycin-C (MMC), as has been reported in Primary Tube versus Trabeculectomy (TVT) study (overall success 81% vs. 92% and complete success 14% vs. 59% respectively, in Baerveldt implant versus Trab MMC, low rate of serious vision threatening complications or reoperation for complications like hypotony maculopathy, bleb leak, hyphaema (1% vs. 7% respectively) [11].

Secondary glaucomas

They are a heterogenous group and the surgical results in each of these may vary as per etiology. In the absence of active inflammation, and in patients with healthy conjunctiva, Trab MMC has good success rates as in steroid induced, traumatic and post keratoplasty glaucoma (73% success rate at 22 months) [25], however, in neovascular glaucoma (NVG) or uveitic glaucoma, trabeculectomy has poor success rates (overall success rate 54%, 9%

complete, 45% qualified in NVG) [26] and GDDs are more useful in these cases. MIGS are not good options in these cases although steroid induced glaucoma or pseudoexfoliative glaucoma may be managed with MIGS; currently, there is insufficient literature on their efficacy.

Angle closure disease

Angle closure glaucoma is not amenable to treatment by MIGS unless the angle is adequately open after iridotomy/ iridoplasty/ cataract extraction. These patients can be managed with cataract extraction or trabeculectomy in isolation or combined phacotrabeculectomy.

Co-existent cataract and glaucoma

In angle closure disease, cataract surgery alone helps in IOP control, however, in few cases of angle closure disease and in open angle glaucoma, combined surgery is required [27]. In combination with cataract surgery, MIGS have been reported to have good success rates and can be preferred in both types of glaucoma if the angle is fairly open to visualize structures, whereas phacotrabeculectomy is less often performed and less preferred because of longer surgical time, high chances of intraoperative complications and poor success rates compared to stepwise surgery [28].

c. Surgeon expertise: Contrary to popular opinion, MIGS procedures have a relatively steep learning curve. They require training in direct gonioscopy, clear identification of angle structures and hands on training for angle-based procedures. Similarly, the deep sclerectomy procedure, which is often considered safer compared to conventional trabeculectomy because of its non-penetrating nature, also has a steep learning curve. The procedure may be complicated by inadvertent rupture of Descemet's membrane (3.5-7% of the cases) changing the procedure to a penetrating one, similar to Trab [29].

d. Feasibility of procedure and contraindications: There are several conditions when MIGS cannot be used, as in cases with poor visibility of the angle because of extensive anterior synechiae, corneal opacity, and ocular surface disease. Surgery is difficult in patients with narrow palpebral apertures, cervical spine abnormalities, and in unco-operative patients who are not able to follow commands.

Many of these procedures including iStent and Hydrus are approved in conjunction with cataract surgery, which may not be appropriate in young patients or patients having very early cataract. So, in these cases, conventional trabeculectomy is still the first choice of surgery, however, it must be kept in mind that trabeculectomy surgery leads to progression of cataract [30]. There are several MIGS, including Trabectome, Xen implant, gonioscopy assisted transluminal trabeculotomy, which can be performed alone without cataract surgery. Thus, an informed decision has to be made in these circumstances after a discussion with the patient. Availability of devices and the additional cost of the surgery represent another major concern with regard to the feasibility of MIGS.

e. Safety of the procedure and complications: Safety is of utmost importance and risk-benefit ratio must be considered in deciding the type of procedure. The complications that are relatively more acceptable in patients with advanced disease, might not be so in patients with an early disease. Therefore, complications that may be considered acceptable can vary according to the procedures.

MIGS and deep sclerectomy are considered safer options and MIGS are better in terms of sparing the conjunctiva and avoiding the use of anti-metabolites. Similarly, hypotony after DS may be acceptable as it doesn't lead to hypotony maculopathy, however, this may not be the case with trabeculectomy. Though MIGS procedures are presumed to have lesser complications, they can have unique complications of stent malpositioning or obstruction apart from the complications of immediate postoperative rise in IOP, hyphaema, hypotony, etc., which are usually transient and not vision threatening. If the same procedure results in a complication that can have a long-term impact on vision, it should not be acceptable. Because of this reason, Cypass shunt was voluntarily withdrawn from the market by Alcon in 2018, because of unacceptably high endothelial cell loss even though a significant loss occurs with trabeculectomy and GDD procedures as well [31]. **Table 3** summarizes the complications associated with different procedures.

Table 3. Complications following glaucoma surgery: A comparative overview

	Trab	Trab with express shunt	Baerveldt	AGV	NPDS	MIGS
Hypotony	16.8 - 39.3% [32-34]	10.5% [35]	13% [32,36]	2% [36]	4.3-9.9% [34,37]	13.8% with Cypass [38] 15.3% with Xen [39]
Hypotony maculopathy	5.18% [35]	3.17% [35]	1% [32]	Rare reports [40,41]	0-2.1% [42,43]	1.08% with Xen [44] 1.3% with Cypass [45]
Hyphaema	14.9-17.2% [33,34]	1.6% [35]	5% [46]	18.3% [33]	7.4-12.4% [34,37]	24.3% with Xen [47] 0.02% for iStent [48,49] 19.04% for Hydrus [50] 2.7% for Cypass [45]
Shallow anterior chamber	11.8-32.1% [33,34]	4.74% [35]	3% [46]	11.11% [33]	2.9-8.9% [34,37]	0-2.3% [51]
Choroidal detachment	3.2-15.9% [34,52]	10.38% [35]	3% [46]	12% [53]	8.6-10.2% [34,37]	15.3% with Xen [39]

Progressive cataract	29-35% [30,34]	12% at 2 years [54]	8% [36]	8% [36]	6.6-12.7% [34,37]	12.2% with Cypass [55] 11.1% with iStent [56]
Loss of light perception	2% [32]	3.2% [57]	26% [36]	12% [36]		No reports yet [17]
Bleb leak	6.7-13.6% [33,35,44]	16.8% [35]				1.93% with Xen [44]
Endophthalmitis	1.6% [35]	1.6% [35]	0.5-1.4% [58,59]	1.7% [60]	Rare, isolated reports of blebitis [61]	0.5% with Xen [62]
Endothelial cell loss	-3±8% to 9.6% at 1 year [39, 63]	-10±8% at 12 months [39]	Mainly with anterior chamber implantation 7.2% at 6 months 12% at 1 year [64] 4.54% per year [65]	9% at 6 months to 12% at 1 year [66]	4.5% at 1 year [63]	2.1% in one month with Xen implant in cases with dynamic corneal contact [67], 18.4% with Cypass at 5 years in Compass-XT study (unpublished data)
Stent malpositioning						12.2% with Xen [47]
Stent obstruction						4% with iStent [68] 2.4-5.4% with Cypass [38,45]
Need of needling	23-30.76% over 3 years [44,69]	15.9% over 30 months follow-up [69]				43.24% [44]
Need of Re-surgery	7-28% over a 5-year period [53,70]	5.12% during 1st year [71], 30.6% at 3 years [72]	5.4-17% over 5 years [33,73]	17-40% over 5-year period [36,53]	3.7-5.4% after 1-3 years [74,75]	14.1% with Xen after 12 months of surgery [17] 4.3% with InnFocus at 3 years [76] 7.4% with iStent [39]

f. Survival of surgery: The longevity and survival of the procedure is yet another confounding factor. For surgeries that are minimally invasive and repeatable, the longevity thought extremely desirable, is not absolutely imperative. Especially since a lot of these surgeries are conjunctiva sparing, they do not preclude more definitive surgeries at a later date. For example, iStent has been reported to decrease IOP of up to 40% at 1 year and 16.3% at 5 years with reduction in medication load in up to 85% of the cases at 1 year and 43% at 5

years [77,78]. Thus, if they offer a few drug free years to the patient, they must be considered successes. Survival of surgery on long-term is of less importance when choosing it for elderly patients with a limited life expectancy, where their quality of life impact and morbidity should be considered more important.

g. Ancillary procedures: Procedures like needling and goniotomy are not considered failures of trabeculectomy and NPDS respectively, but merely ancillary procedures. Similarly, the hypertensive phase of the Ahmed

Glaucoma valve (AGV) is considered par for course, as is the two-stage surgery for Baerveldt like devices. In the case of MIGS, a second surgery may also be similarly considered an ancillary procedure since the surgery is not very invasive, except for the significant costs involved. In case of MIGS, multiple MIGS with different sites of action can be performed simultaneously or sequentially as a safer alternative to a more invasive glaucoma surgery [79].

h. Health economics: Cost effectiveness is yet other criteria that must be kept in mind when judging a procedure. For a glaucoma surgery, the cost factor has to be considered in terms of cost of the surgery, efficacy of the procedure in terms of the decrease in drugs use or follow-up visits and the comparison of the cost of one-time procedure with the overall cost of drugs for that period of time. For example, adding the express shunt to trabeculectomy increases its cost significantly, does not increase its longevity, and in fact, turns a surgery that can be used in both POAG and PACG into a surgery that can only be used in open angles [7]. Thus, its success criteria need to be significantly more stringent. Another thing to remember concerning the health economics of glaucoma is the high cost of the minimally invasive devices. Unless they result in a significant economic saving by significantly decreasing or eliminating the use of anti-glaucoma medication for a significant period of time, or decreasing postoperative follow-ups, their use cannot be justified in terms of costs. Trabecular bypass shunts have been shown to be cost effective over standard care with improvement in quality of life [80]. Long-term data regarding cost-effectiveness is currently inexistent. Trabeculectomy is still the cheapest surgical option amongst all glaucoma procedures and the most commonly performed procedure [81,82].

i. Quality of Life, QoL: The QoL impact of each of these surgeries must also be part of the success criteria. Bleb dysesthesias, multiple interventions by needlings and complicated treatment regimens postoperatively, complication rates, etc., may significantly affect the QoL of a patient following trabeculectomy. Therefore, its use in a patient with early disease may not be justified. Regarding MIGS, QoL data is not available as there are limited studies at

present. A study has reported comparable QoL in patients undergoing MIGS (iStent, Trabectome) or trabeculectomy at 6 months postoperatively, however, better social functioning, color vision, and postoperative day 1 visual acuity, were seen in MIGS group, but the trabeculectomy group required lesser topical antiglaucoma medicines [83].

Consensus amongst glaucoma surgeons

A survey of American Glaucoma society (AGS) published in 2017 for preferred practice preferences for the type of glaucoma surgery among AGS members has also reported that Trab MMC, GDD and MIGS constituted 59±30%, 23±23% and 14±20% respectively as an initial surgery in POAG. Although the use of GDD surgery has increased and trabeculectomy has decreased from 1996 to 2016 [81], Trab MMC was still the most popular primary glaucoma surgery among surgeons.

MIGS are emerging devices that are expected to have improved safety, however, there is a need of more randomized controlled trials and long-term results are awaited. They definitely have a future in patients who are non-compliant or intolerant to medications and can act as a bridge between medical/ laser treatment and conventional glaucoma surgeries, having different indications compared to conventional glaucoma surgeries. A tailored approach depending on the patient profile, type of glaucoma, and life expectancy can help in the better management of glaucoma patients.

Conclusion

Glaucoma is a continuum from early to end stage, thus each surgery has a unique space with respect to success and failure criteria applicable. With the introduction of the newer surgical procedures, the algorithm for the choice glaucoma surgery has become more complex. However, this also implies that better and safer surgical procedures, which may be better suited to the needs of the individual, are now available. In addition, a combination of surgical procedures may be performed for any patient during his or her clinical lifetime in order to best preserve their quality of life.

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Conflict of interest

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