

# ADVANCEMENTS IN GLAUCOMA THERAPY: FROM MEDICATIONS TO MINIMALLY INVASIVE SURGERY

## Abstract

Glaucoma is a prevalent eye condition typically associated with an elevated intraocular pressure that damages the optic nerve. It has the potential to result in permanent vision loss if not identified and addressed promptly. In the majority of instances, early-stage glaucoma presents with minimal or absent symptoms. The treatment approach varies depending on the extent of the condition's impact. Regarding the management, medical intervention continues to be the mainstay, and significant progress has been made in the advancement of medical therapy for this condition. This article will explore the advancements in glaucoma treatment, encompassing the transition from medication-based approaches to minimally invasive surgeries.

**Keywords:** Glaucoma, condition's Intensity, Treatment obstacles, Therapy advancements, Medications, surgeries, Benefits, Outcomes.

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## I. INTRODUCTION

Glaucoma encompasses a collection of optic neuropathies distinguished by the gradual deterioration of retinal ganglion cells. This degeneration of the nerve cells leads to the development of cupping, a distinctive manifestation observed in the optic disc. It occurs as a result of increased pressure within the eye, known as intraocular pressure (IOP), which in turn leads to damage to the optic nerve and loss of visual field [1]. While elevated IOP may not always be a conclusive sign of glaucoma, it serves as a significant risk factor and plays a causative role in the development of this condition. The individual may also experience a growing challenge with nocturnal vision. As the disease progresses to its advanced stages, visual impairment for the patient typically begins in the peripheral areas and gradually extends to affect the central vision.

It is categorized based on anatomical characteristics as either open-angle, where the anterior chamber angle of the eye remains unblocked, or angle-closure, where there is closure of the anterior chamber angle. The primary classification of glaucoma applies when the eye does not have any preexisting conditions [2].

Secondary glaucoma can occur as a consequence of factors such as injury, specific medications like corticosteroids, inflammation, tumors, or conditions like pigment dispersion or pseudo-exfoliation.

## II. CHALLENGES IN GLAUCOMA TREATMENT

It encompasses the subsequent challenges such as

- 1. Early detection and assessment of the condition** are significant for the structural and functional alterations caused by glaucoma are predominantly permanent; hence, timely identification of the disease remains a crucial approach to avert visual impairment [3]. This has been accomplished by evaluating the structure of the optic nerve using imaging devices and assessing optic nerve function via perimetry.
- 2. The Establishment of intraocular pressure (IOP) goals** is significant for setting up the criteria in which intraocular pressure has been recognized as the sole adjustable risk factor, and reducing IOP to impede glaucoma progression is now the cornerstone of glaucoma treatment. Increasing evidence indicates that not only the average decrease in IOP is significant, but also the management of IOP fluctuations has a substantial impact on preserving vision and visual fields [4]. Determining the target intraocular pressure (IOP) is one of the critical stages of treatment. Typically, it is presumed that aiming for a minimum 30% reduction from the initial pressure, where the damage occurred, serves as a practical and arbitrary approach to reach the initial target IOP. The determination of the target intraocular pressure relies on several factors including the extent of glaucoma damage, the IOP level when the damage occurred, the patient's life expectancy, the condition of the other eye and the family's glaucoma history. It is recommended that the target IOP be monitored so that it is accessible on consecutive patient visits.

- 3. Additional recommendations for the target intraocular pressure** may include categorization of each patient as normal, suspicious, early-stage, moderate-stage or advanced-stage glaucoma based on assessments of the optic nerve and/ or visual field.

Establish the maximum value within the initial range of target intraocular pressure for each eye during the initial visit and subsequently reassess the range at each visit to consider the stability or changes observed in the structure and function of the optic nerve [5].

### III. TRADITIONAL METHODS FOR TREATING GLAUCOMA

Exploring the utilization of natural substances possessing antioxidant and anti-inflammatory properties could potentially serve as a viable strategy for treating glaucoma. Herbal medications are the most prevalent alternative treatment, accompanied by dietary adjustments and vitamin/mineral supplements. Acupuncture, a component of traditional Chinese medicine, has been utilized for over two millennia to address a variety of medical conditions. Acupuncture, an ancient medical practice that originated in China over two millennia ago, stands as one of the oldest known therapeutic procedures worldwide [6]. The precise mechanism underlying the effects of acupuncture is still not well-defined. Certain individuals diagnosed with glaucoma may consider acupuncture as a complementary or substitute approach to their conventional management of the condition.

### IV. MEDICAL ATTENTION TO GLAUCOMA

- 1. Choice of Treatment:** The selection of treatment relies on the classification of glaucoma, specifically distinguishing between open-angle and closed-angle glaucoma.
  - **For open-angle glaucoma:** This particular form of glaucoma is frequently encountered and is typically addressed through the use of medications, laser interventions (such as laser trabeculoplasty), or surgical measures (such as trabeculectomy).
  - **For angle-closure glaucoma:** Laser peripheral iridotomy is the initial treatment approach for angle closure, involving the creation of a complete hole in the iris to eliminate pupillary blockage.

The medical treatment of glaucoma involves the use of topical anti-glaucoma medications, laser peripheral iridotomy, or laser trabeculoplasty to reduce intraocular pressure (IOP) [7]. Surgical interventions for managing glaucoma include trabeculoplasty and glaucoma drainage devices. These surgical options carry various intraoperative and postoperative complications, necessitate extended follow-up periods, and may entail a prolonged recovery period. The term MIGS, which stands for minimally invasive glaucoma surgery, has been introduced to categorize this set of procedures. Patients diagnosed with mild-to-moderate glaucoma, which do not adhere to or cannot tolerate topical medications, are considered optimal candidates for MIGS (minimally invasive glaucoma surgery).

- 2. Anti-Glaucoma Medications:** In the management of glaucoma, the therapeutic objective is to prevent or alter the risk factors, particularly intraocular hypertension, through the administration of hypotensive medication and these are used in the treatment of glaucoma and are categorized based on their pharmacological properties [9].

S. NO	Drug Class	Name of The Drugs	Formulation	Indications
1.	$\alpha$ -adrenergic agonists	Dipivefrin, Apraclonidine and Brimonidine	Eye drops	For chronic open-angle glaucoma.
2.	$\beta$ -adrenergic antagonists	Betaxolol (selective) and Timolol and levobunolol (non-selective)	Eye drops	Treatment of chronic open-angle glaucoma.
3.	Carbonic anhydrase inhibitors	Brinzolamide, Dorzolamide and Acetazolamide.	Eye drops Powder for injection 500 mg PO/IV, followed by 125-250 mg PO q4hr  Sustained-release: 500 mg PO q12hr	Individuals with chronic open-angle glaucoma and acute angle-closure glaucoma before surgery  For Secondary glaucoma.
4.	Cholinergic agent	Pilocarpine, Aceclidine, Carbacholine (direct-acting agents) Demecarium bromide (indirect-acting agents)	Solution/drops	Short-term management of some angle-closure glaucomas. Contra-indicated for secondary glaucoma.
5.	Prostaglandin analogs	Bimatoprost, Latanoprost, Travoprost and Tafluprost,	Eye drops	Lowering elevated intraocular pressure in individuals diagnosed with open-angle glaucoma.
6.	Osmotic agents	Glycerol and	Oral solution (1 to 2 grams per kg of	Can be utilized to terminate a sudden onset of glaucoma attack.

		Mannitol.	body weight taken one time. Injectable solution <ul style="list-style-type: none"> <li>• 5%</li> <li>• 10%</li> <li>• 15%</li> <li>• 20%</li> <li>• 25%</li> </ul>	
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When single-drug therapy proves inadequate in controlling intraocular pressure, combination therapy is employed. The combined effect is achieved when drugs with different mechanisms of action are used together, leading to enhanced efficacy. Furthermore, compliance tends to improve with combination therapy, resulting in fewer side effects [10]

**3. Minimally Invasive Glaucoma Surgery (MIGS):** The term MIGS, which stands for minimally invasive glaucoma surgery or micro-invasive glaucoma surgery has been introduced to categorize this set of procedures. Over the past few years, this surgery has brought about a significant transformation in the management of glaucoma. It is an emerging and rapidly growing field for glaucoma treatment [10].

- **Goals:**

- To minimize reliance on eye drops during traditional phacoemulsification surgery, particularly in patients with well-controlled glaucoma,
- To offer a highly favorable safety profile facilitating rapid postoperative recovery and ensuring consistent reduction in intraocular pressure (IOP).
- To bridge the gap between conservative medical and laser therapies, and more invasive surgical interventions and provide the patients with an opportunity for an earlier and safer transition towards surgical management of their condition.

- **Benefits:**

- It offers enhanced safety with minimized chances of complications such as choroid detachment, hypotony, hemorrhage, and effusion.
- It enhances the natural outflow of aqueous humor by causing minimal disruption to the structures within the angle of the eye.
- Patients experience a favorable postoperative recovery with minimal bedtime following the procedure.
- It presents a highly effective option as an alternative to conventional angle surgery for reducing intraocular pressure (IOP).

- **Patients Selection Criteria:**

- Glaucoma patients who had not recovered from eye drops
- Glaucoma patients who had not recovered from traditional surgeries such as trabeculectomy

- Patients with extreme fluid drainage inside the eye due to high intraocular pressure

**4. Classification:** Based on its mechanism, it encompasses four primary methods- To achieve a reduction in intraocular pressure (IOP), it works by:

- Circumventing the trabecular meshwork
- Enhancing the drainage of aqueous humor via Schlemm's canal
- Boosting the uveoscleral outflow
- Creating an aqueous shunt through the subconjunctival space or
- By ablating the ciliary body.

S.NO	Mechanism	Techniques Involved	Indication
1.	Circumventing the trabecular meshwork and Enhancing the drainage of aqueous humor via Schlemm's canal (Trabecular bypass)	<ul style="list-style-type: none"> <li>• IStent</li> <li>• iStent inject</li> <li>• Hydrus</li> </ul>	For individuals who have undergone cataract surgery : • Adults • Individuals with mild to moderate open-angle glaucoma • Those who are currently using medication to lower intraocular pressure
2.	Boosting the uveoscleral outflow	<ul style="list-style-type: none"> <li>• CyPass micro-stent</li> </ul>	Initially employed in 2016 and received FDA approval for the management of glaucoma. The device led to increased endothelial cell loss, resulting in its withdrawal from the market in 2018.
3.	Creating an aqueous shunt through the subconjunctival space	<ul style="list-style-type: none"> <li>• Xen implant</li> </ul>	Use in patients with open-angle glaucoma in the moderate to advanced stages, resistant to treatment, following an unsuccessful trabeculectomy procedure, and in individuals with either phakic or pseudophakic glaucoma.
4.	Ablating the ciliary body.	<ul style="list-style-type: none"> <li>• Endocyclopho tocoagulation</li> </ul>	Use in patients with mild to moderate glaucoma, in combination with cataract removal while preserving the conjunctiva, as well as for individuals with refractory open-angle glaucoma, pediatric glaucoma, and neovascular glaucoma. It should be avoided in cases of active inflammation

Trabecular meshwork micro-bypass stents are minute implants inserted into the eye's drainage system, establishing a new pathway for fluid to exit, thereby decreasing intraocular pressure.

5. **Trabeculectomy:** It is a surgical procedure that involves creating an opening, known as an ostium, in the anterior chamber of the eye. This is achieved by making a partial thickness sclera flap, allowing the aqueous fluid to drain out of the eye. The drained fluid typically accumulates in the subconjunctival space, resulting in the elevation of the conjunctiva, in which a small fluid-filled blister is commonly referred to as a filtering bleb forms on the surface of the eye beneath the eyelid [11].
6. **Laser peripheral iridotomy:** It also known as laser iridotomy or iridotomy, is a medical intervention that employs laser technology to form an aperture in the iris. This opening enables the direct passage of aqueous humor from the back to the front chamber of the eye, effectively alleviating pupillary blockage. The purpose is to facilitate the expansion of the drainage angle and address angle-closure glaucoma. Although the created aperture is not perceptible without magnification, it can potentially contribute to delaying or halting the advancement of the disease [12].
7. **Canaloplasty** is a minimally invasive surgical procedure recognized for its high effectiveness in treating open-angle glaucoma. It operates by reestablishing the proper functioning of the eye's natural outflow system. The procedure boasts an exceptional safety record and exhibits long-term efficacy, making it a suitable choice for a wide range of glaucoma patients. It can be combined with current drug-based glaucoma treatments, implemented following laser or alternative forms of surgical interventions, and does not hinder or influence the outcome of future surgical procedures. Additionally, pediatric patients diagnosed with congenital glaucoma have experienced positive outcomes with Canaloplasty [13]. The procedure has demonstrated both safety and efficacy in patients who are undergoing cataract surgery or who wear contact lenses. Moreover, it can be effectively performed in patients who have had unsuccessful trabeculectomy procedures, with Schlemm's canal remaining intact from previous filtration surgeries.
8. **Laser Trabeculoplasty:** The utilization of a laser in this procedure aims to enhance the outflow of fluid from the eye by targeting the drainage angle. In specific cases, it is recommended as the primary treatment option. This is especially applicable when patients either have difficulties tolerating topical medications or are unable to administer them. It is also applicable in situations where there is a significant risk of noncompliance. These are of two types. Argon laser trabeculoplasty and selective laser trabeculoplasty. The low-energy laser used in this procedure selectively focuses on pigmented cells, minimizing unintended harm to surrounding tissues. It demonstrates comparable efficacy in reducing intraocular pressure as the traditional argon laser trabeculoplasty. Moreover, when considering a second treatment, repeat selective laser trabeculoplasty exhibits efficacy levels that are similar to those observed during the initial treatment. Selective laser trabeculoplasty is a secure procedure with minimal occurrence of adverse effects [14]. These effects typically involve mild inflammation in the anterior chamber and temporary spikes in intraocular pressure. However, these effects can generally be prevented or reduced by administering prophylactic medication to lower intraocular pressure before the procedure.

**9. Phacotrabeculectomy: Traditional Combined Cataract and Glaucoma Surgery:** In the context of combined cataract and glaucoma procedures, phacotrabeculectomy is regarded as the preferred treatment option for individuals who have both open-angle glaucoma and cataracts [16]. When glaucoma and cataract surgeries are performed together, they result in superior long-term control of intraocular pressure compared to cataract surgery alone [ It is anticipated that these combined procedures can lead to a reduction in intraocular pressure ranging from 5 to 8 mm Hg. While phacotrabeculectomy is a secure and efficient choice for individuals with open-angle glaucoma, it is important to explore alternative surgical options for patients who have both cataracts and chronic angle-closure glaucoma[17]. Certain patients may not be suitable candidates for combined phacotrabeculectomy surgery due to either excessively high risks of postoperative complications or suboptimal conditions for intensive postoperative follow-up visits. In such cases, these patients may derive advantages from undergoing a concurrent glaucoma surgery that is either less invasive or necessitates less rigorous postoperative monitoring[18].

**10. Endocyclophotocoagulation (ECP):** This procedure is recommended for cases of mild to moderate glaucoma, in conjunction with cataract removal while preserving the conjunctiva. It is also suitable for refractory open-angle glaucoma cases, pediatric glaucoma, and neovascular glaucoma, and should be avoided in the presence of active inflammation. As a result of ciliary body ablation, there is a decrease in the production of aqueous humor, leading to a reduction in intraocular pressure (IOP). The mechanism involves the localized shrinkage of the ciliary processes and temporary occlusive vasculopathy. The procedure is performed using the pars plana approach and is preceded by pars plana vitrectomy. Reported adverse effects include secondary glaucoma, hyphema (blood in the anterior chamber of the eye), post-operative inflammation, retinal detachment, choroidal detachment, cystoid macular edema, intraocular lens (IOL) dislocation, and capsular opacification. On average, it leads to a reduction of approximately 35% in intraocular pressure (IOP) for patients who are taking one medication.

## V. COMPLICATIONS AND RISKS IN MIGS

Temporary hyphema (blood in the anterior chamber of the eye) and temporary spikes in intraocular pressure are frequently encountered complications in this group of MIGS procedures [22]. However, more severe adverse events, such as the formation of a cyclodialysis cleft, can also occur. Other Possible side effects encompass intraocular bleeding, transient changes in intraocular pressure post-operation, corneal edema, infection susceptibility, and potential visual disruptions like diplopia.

## VI. COMPARISON OF TRADITIONAL SURGERIES AND MINIMALLY INVASIVE GLAUCOMA SURGERY:

Minimally invasive glaucoma surgery (MIGS) is a recently developed method of addressing glaucomacomprising a range of minimally invasive techniques;



1. **Safety and Efficacy:** MIGS presents alternative surgical choices for glaucoma treatment that pose fewer risks compared to conventional glaucoma surgeries. Due to its minimally invasive nature, MIGS allows for a quicker recovery period in comparison to traditional glaucoma surgery [23]. Apart from reducing intraocular pressure and decelerating optic nerve deterioration, MIGS also provides advantages to patients such as minimizing trauma to ocular tissues and demonstrating an outstanding safety record.
2. **Cost- Effectiveness:** According to a recent study, MIGS demonstrated lower cost-effectiveness when compared to traditional glaucoma surgeries suggesting that the latter may be a more favorable choice for patients prioritizing cost considerations

## VII. CONCLUSION

Advancements in glaucoma therapy have witnessed a transformative shift from relying solely on medications to embracing the emergence of minimally invasive glaucoma surgeries (MIGS). It also expands the treatment options available, allowing for tailored therapy with either anti-glaucoma medications or combined surgery and directly addressing the underlying cause of elevated intraocular pressure, providing a more focused and precise method of treatment. Highlighting the significant progress made in glaucoma therapy, marking a promising transition from medication-centric approaches to the adoption of minimally invasive surgical interventions.

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