



Journal of
Clinical Medicine

Special Issue Reprint

Clinical Debates in Minimally Invasive Glaucoma Surgery (MIGS)

Edited by
Etsuo Chihara

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Clinical Debates in Minimally Invasive Glaucoma Surgery (MIGS)

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Guest Editor

Etsuo Chihara



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This is a reprint of the Special Issue, published open access by the journal *Journal of Clinical Medicine* (ISSN 2077-0383), freely accessible at: https://www.mdpi.com/journal/jcm/special_issues/R32N37E24U.

For citation purposes, cite each article independently as indicated on the article page online and as indicated below:

Lastname, A.A.; Lastname, B.B. Article Title. <i>Journal Name</i> Year , Volume Number, Page Range.
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ISBN 978-3-7258-8573-2 (Hbk)

ISBN 978-3-7258-8574-9 (PDF)

<https://doi.org/10.3390/books978-3-7258-8574-9>

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Reprinted from: *J. Clin. Med.* **2024**, *13*, 4564, <https://doi.org/10.3390/jcm13154564> **145**

About the Editor

Etsuo Chihara

Etsuo Chihara is Clinical Professor at Sensho-kai Eye Institute in Uji, Kyoto, and Shimane University in Izumo, Shimane, Japan. His academic and clinical research has focused primarily on glaucoma surgery and ophthalmic imaging. He received his Medical Degree from Kyoto University in 1974 and his PhD from Kyoto University in 1982. He currently serves as President of the Sensho-kai Eye Institute and as Clinical Professor of Ophthalmology at Shimane University. His previous academic appointments include Assistant Professor of Ophthalmology at Miyazaki Medical College (1986–1989) and Kyoto University (1989–1992), as well as Vice President and Associate Professor in the Department of Ophthalmology at Kyoto University (1992–1993). Since 2009, he has served as President of the Japanese Tube Surgeons Association. Professor Chihara has supervised five doctoral theses, directed nine competitively funded research projects, authored more than 100 peer-reviewed publications, co-edited nine books, and contributed 31 chapters to ophthalmology textbooks. Moreover, he has been invited to speak at more than 100 national and international conferences. In 2012, he delivered the Suda Memorial Lecture, one of the most prestigious glaucoma lectures in Japan, and was elected an Emeritus Member of the Japanese Glaucoma Society in 2015. He currently serves on the editorial boards of the *Journal of Clinical Medicine* (2022–), *Annals of Eye Science* (2024–), and *Graefe's Archive for Clinical and Experimental Ophthalmology* (2026–). He has developed surgical devices for glaucoma surgery named T-hook and CAPT device, respectively, and holds related intellectual property registrations. Through his sustained academic leadership and clinical contributions, Professor Chihara has played a significant role in advancing glaucoma surgery and clinical practice in Japan.

Preface

Glaucoma surgery is entering the era of precision glaucoma surgery. Rather than relying on a single standard procedure, surgeons can now select from a wide range of surgical options tailored to the individual patient's disease characteristics and therapeutic goals. For patients with mild glaucoma and modestly elevated intraocular pressure (IOP), microinvasive glaucoma surgery (MIGS) has become an important treatment strategy. These tissue-sparing procedures offer effective IOP reduction with a favorable safety profile and have transformed the surgical management of early-stage glaucoma.

Recent advances have also expanded the spectrum of glaucoma surgery beyond MIGS. Lens extraction plays an important role in opening the anterior chamber angle in eyes with primary angle closure. Minimally invasive bleb surgery (MIBS), using subconjunctival microshunts such as the PreserFlo MicroShunt and XEN Gel Stent, provides controlled aqueous outflow and helps reduce the risk of postoperative overfiltration. When very low postoperative IOP is required, trabeculectomy, the traditional gold standard, remains an essential option. Likewise, aqueous shunt surgery continues to be indispensable for eyes with severe conjunctival scarring, extensive peripheral anterior synechiae due to uveitis, or neovascular glaucoma. Endoscopic or transscleral cyclophotocoagulation may also serve as valuable adjunctive procedures to achieve additional IOP reduction in selected cases. Because the majority of patients with glaucoma have mild or early-stage disease, effective treatment during the early stages is of paramount importance. This reprint focuses on MIGS, which has become one of the most important surgical approaches for managing early glaucoma while preserving ocular tissues and minimizing surgical trauma.

Etsuo Chihara

Guest Editor



Editorial

Clinical Debates in Minimally Invasive Glaucoma Surgeries (MIGSs)

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I am pleased to introduce this Special Issue of the *Journal of Clinical Medicine*, dedicated to “Clinical Debates in minimally Invasive Glaucoma Surgeries (MIGSs)”, which address current and emerging topics in glaucoma surgery.

Glaucoma is one of the leading causes of blindness worldwide [1,2]. Reduction in intraocular pressure (IOP) remains the only evidence-based and modifiable treatment strategy for glaucoma. Medical therapy and laser procedures are considered first-line approaches for lowering IOP; however, when these treatments fail to achieve adequate IOP control, surgical intervention becomes necessary.

Traditionally, trabeculectomy has been regarded as the gold standard surgical treatment for glaucoma. However, this procedure is associated with a high risk of postoperative complications, including bleb leaks, infection, postoperative hypotony, and deterioration of visual acuity [3,4].

To address the shortcomings of trabeculectomy, minimally invasive glaucoma surgeries (MIGSs) have been developed. Over the past decade, substantial advances have been made in understanding the mechanism of IOP reduction, as well as the safety profile and surgical efficacy of MIGS procedures. This Special Issue covers a broad spectrum of topics, including the historical evolution of MIGS, recent trends in surgical decision making, advances in surgical devices and technologies, and tissue responses following MIGS procedures.

There are several types of MIGSs, among which canal-opening surgery (COS) is one of the most widely used subtypes. There has been a long-standing debate regarding the mechanism of action and clinical outcomes of COS. Chihara and Hamanaka (Contribution 1) reviewed the historical development of MIGS and critically discussed the mechanism of action underlying COS. It took considerable time to understand the differences in tissue responses between experimental monkey eyes, where the trabecular opening closes shortly after surgery due to tissue regeneration [5], resulting in limited improvement in outflow facility [6], and human eyes, in which canal opening tends to persist [7] and IOP reduction is maintained over a long period [8]. The long-term debate on the clinical outcome of COS in human eyes is extensively reviewed in a review article of this series (Contribution 1).

There are several types of MIGS. Among them, canal opening surgeries, which originated from trabeculotomy ab externo, have recently evolved and are now widely used for the treatment of mild to moderate open angle glaucoma (OAG). With respect to postoperative visual acuity, there is a clear contrast between COS and trabeculectomy. The advantage of MIGS in preserving and restoring visual acuity was elegantly demonstrated by Kasahara et al. (Contribution 2), which is one of the key reasons COS is increasingly selected for patients with mild to moderate OAG.

An increasing trend in the use of MIGS has been reported in several studies [9,10], and this trend was further confirmed by Iwasaki et al. (Contribution 3) in this Special Issue. The extent of canal opening and the type of device used to open Schlemm's canal may influence surgical outcomes. Sugihara et al. (Contribution 4) reported that IOP reduction after 120-degree canal opening did not differ significantly from that after 240-degree canal opening using the Tanito microhook. This finding is consistent with the report by Ćwiklińska-Haszcz et al. (Contribution 5), in which IOP reduction after 180-degree canal opening using the GATT procedure was not significantly greater than that achieved with canal opening exceeding 190 degrees. These results also align with findings from other large-scale studies [11]. Nevertheless, caution is warranted, as other investigators have reported superior IOP reduction with 360-degree canal opening compared with sectorial canal opening [12,13]. Given the heterogeneity in sample size, follow-up duration, and surgical techniques across studies, this issue remains an important topic for future investigation. Ćwiklińska-Haszcz et al. (Contribution 5) also reported that the number of previous trabeculectomies and the performance of combined cataract surgery did not significantly affect surgical outcomes, a finding that aligns with some previous reports [14,15]. However, conflicting results have been reported by other investigators with several studies suggesting positive additive effects of combined cataract surgery on IOP reduction [16]. Thus, the impact of combined cataract surgery on the outcome of MIGS remains controversial and warrants further study.

When performing iStent surgery, the type of gonio-lens used can influence the surgical time required for implantation of the iStent inject. W, Fujii et al. (Contribution 6) reported that the use of the Ahmed gonio-lens was associated with more efficient implantation and recommended it for this procedure.

The Hydrus Microstent represents a different class of microstent, designed not only to bypass the trabecular meshwork but also to dilate Schlemm's canal. Although this device effectively reduces IOP, precise insertion into Schlemm's canal may be technically challenging. Zimmermann et al. (Contribution 7) investigated postoperative positioning of the Hydrus Microstent using a NIDEK GS-1 automated 360° gonioscope and demonstrated substantial variability in postoperative implant positioning. Even though postoperative IOP was successfully reduced in all cases, the distal tip of the nitinol stent was located behind the trabecular meshwork in five cases, in the anterior chamber in one case, and was not visible in seven cases. The long-term clinical implications of Hydrus malpositioning may be a subject for future studies.

Minimally invasive bleb surgery (MIBS) represents another category of glaucoma surgery that is increasingly applied in patients with moderately severe OAG. With respect to the XEN Gel Stent, the device may be implanted via an ab interno or ab externo approach. Jin et al. (Contribution 8) studied the outcome of XEN in the treatment of refractive glaucoma and reported superior results with the ab externo open-conjunctival approach combined with adjunctive Ologen, compared with simple ab interno implantation.

PreserFlo MicroShunt is another type of MIBS; however, when used in the eyes with exfoliation glaucoma, the probability of surgical success at 48 weeks was approximately 50%, and needed reoperation in 30%. Wakuda et al. (Contribution 9) highlighted this limited success probability in exfoliation glaucoma. The long-term outcomes of MIBS therefore remain an important subject for future studies.

Although MIGS and MIBS are generally considered safe procedures with a lower risk of complications, and their effects on corneal deformation are mild, these are not entirely free of adverse effects. Asaoka et al. (Contribution 10) evaluated corneal stiffness using Corvis ST parameters and demonstrated that corneal stiffness was more significantly reduced in eyes undergoing MIGS compared with those undergoing cataract surgery alone.

Overall, this Special Issue highlights the advantages of MIGS and MIBS procedures; however, surgeons must be fully aware of their respective benefits and limitations. Differences in surgical techniques and clinical outcomes should be carefully considered when applying these procedures in clinical practice.

I extend my sincere gratitude to all authors who contributed to this Special Issue and demonstrated outstanding commitment to advancing this important topic. I hope that this Special Issue serves as a valuable resource and stimulates further research into the surgical treatment of OAG.

Conflicts of Interest: The author declares no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

MIGS	Minimally invasive glaucoma surgery
COS	Canal opening surgery
IOP	Intraocular pressure
GATT	Gonioscopy-assisted transluminal trabeculotomy
MIBS	Micro-invasive bleb surgery
OAG	Open-angle glaucoma

List of Contributions:

1. Chihara, E.; Hamanaka, T. Historical and Contemporary Debates in Schlemm's Canal-Based MIGS. *J. Clin. Med.* **2024**, *13*, 4882. <https://doi.org/10.3390/jcm13164882>.
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Review

Historical and Contemporary Debates in Schlemm's Canal-Based MIGS

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Abstract: Glaucoma is one of the primary causes of blindness worldwide. Canal opening surgery, a type of minimally invasive glaucoma surgery (MIGS) applied in cases of mild to moderate glaucoma, has gained increasing popularity in recent years due to its efficacy in reducing the intraocular pressure, its safety profile, the simplicity of its technique, and the reduced likelihood of compromised vision. Nevertheless, the existing body of histopathological studies remains insufficient for a comprehensive understanding of post-surgical wound healing. Consequently, debates persist among researchers regarding the mechanism through which Schlemm's canal opening surgery reduces the intraocular pressure, as well as the surgical techniques that may impact the outcomes and the factors influencing surgical success. As the history of MIGS is relatively short and lacks sufficient systemic reviews or meta-analyses evaluating the influence of individual factors, this review was conducted to illuminate the disparities in researchers' opinions at the current stage of research.

Keywords: minimally invasive glaucoma surgery (MIGS); Schlemm's canal opening surgery; trabeculotomy; trabeculectomy; canaloplasty; Kahook dual blade; trabectome; Tanito micro-hook; surgical success; history; T hook

1. Introduction

Ideally, glaucoma surgery must be safe and effective in reducing the intraocular pressure and maintaining the patient's visual function. Filtering surgeries are effective in reducing the IOP; however, the deterioration of post-surgical visual acuity is common [1,2], and many problems occur, such as post-surgical hypotension, bleb leaks, infection, and others. Because of these problems and the complexity of postoperative care, there has been a shift from filtering surgery to non-filtering surgery. Canal opening surgery (Schlemm's canal-based MIGS) is a type of minimally invasive glaucoma surgery (MIGS) that has gained popularity in recent years. However, the history of MIGS is short, and controversies remain unresolved. This study provides an overview of the history and clinical controversies of canal opening surgery.

2. History of Canal Opening Surgery

2.1. Evolution of Trabeculotomy Ab Externo

As early as 1873, it was established that the trabecular meshwork is the main site of aqueous humor outflow resistance in glaucoma eyes [3]. In 1954, Barany and Scotchbrook found that the injection of testicular hyaluronidase significantly increased the aqueous outflow [4].

In 1947, Barkan hypothesized that incising the trabecular meshwork, which was postulated as the primary site of outflow resistance, could reduce the intraocular pressure [5]. He introduced the concept of goniotomy. This technique offered great relief for refractory congenital glaucoma patients [6]. However, at that time, the absence of appropriate surgical

microscopes posed a significant challenge in accessing and incising the trabecular meshwork from inside the eye. Consequently, goniotomy was primarily indicated for congenital glaucoma, which was associated with poor outcomes after filtration surgery.

Subsequently, in England, Smith achieved success by opening Schlemm's canal through a blunt incision in the trabecular meshwork [7]. This was accomplished by inserting a thread into Schlemm's canal and pulling it; this technique was also reported by Burian around the same period [8].

Nine years later, Smith provided an update on his continued efforts. He said, "I have been performing Nylon filament trabeculotomy for seven years, but I've been holding back from writing papers in the meantime. The reason for this was that I was not sure whether the surgery was really benefiting the patient". Subsequently, he detailed the outcomes. The outcomes of 26 cases of suture trabeculotomy and 27 cases of filtering surgery (nine iridencleisis, eight Scheie, six trephine, and four Stallard surgeries) were compared. The results indicated a more favorable decrease in intraocular pressure with suture trabeculotomy [9].

Trabeculotomy using a thread was technically challenging in the era before the development of surgical microscopes. Subsequently, trabeculotomy using metal probes was invented in Germany, and it became a widely adopted technique [10–12].

2.2. Trabeculotomy Ab Externo: A Time of Hardship

Outflow surgery was a prominent topic at that time. A comprehensive exploration of the histopathological aspects of outflow surgery took place during the 76th American Academy of Ophthalmology (AAO) meeting (Symposium: Microsurgery of the outflow channels), held in Las Vegas from 20 to 24 September 1971. The symposium presented the results of histopathological studies on trabeculectomy, sinusotomy, and trabeculotomy.

During the same symposium, it was demonstrated that aqueous outflow is a passive process and that the outflow ability ($\mu\text{L}/\text{min}/\text{mmHg}$) is enhanced by trabeculotomy. However, the opening of Schlemm's canal in normal monkey eyes closed within 28 weeks after surgery [13], and the ability to enhance the outflow diminished over time. Grant suggested that leaks from the flap and inadvertent cyclodialysis may lead to post-surgical hypotension [14]. Trabeculotomy ab externo was reported as a challenging procedure that carried the risk of the misinsertion of the probe outside Schlemm's canal [15].

Despite the AAO's critical debate on the promotion of trabeculotomy, the publication of studies recommending trabeculotomy ab externo did not stop [16–18]. Dannheim subsequently reported a stable reduction in intraocular pressure for 4 years following trabeculotomy surgery [19] and reported the facilitation of aqueous outflow using tonography [20]. Mackensen noted that "even though effects of trabeculotomy in pressure-reducing is inferior to that of fistulizing surgery, authors prefer trabeculotomy because this preserves the unaffected meshwork" [21].

Despite the favorable clinical reports, the negative impact of the experimental studies, which demonstrated the early closure of the trabecular opening after trabeculotomy and no improvement in the rate of aqueous humor outflow in monkeys, was substantial [19,22,23]. Due to these negative results, the validity of trabeculotomy ab externo as a treatment for adult-onset primary open-angle glaucoma (POAG) was questioned at that time.

2.3. Trabeculotomy Ab Externo: Exploring a Means to Survive as a Treatment for Congenital Glaucoma

In a prospective study, Luntz et al. treated 19 cases of adult-onset glaucoma with a mean intraocular pressure (IOP) of 41 mmHg using trabeculotomy ab externo, achieving a success rate of 70%. In contrast, trabeculotomy in 19 cases of congenital glaucoma with a mean IOP of 34 mmHg achieved success in 18 out of 19 eyes (95%). The authors concluded that trabeculotomy was a procedure for congenital glaucoma and not for adult-onset POAG [24].

Subsequently, trabeculotomy ab externo gained recognition as a viable option for the treatment of congenital glaucoma and infantile glaucoma. It was acknowledged as being equally effective as goniotomy, solidifying its status as a treatment for children at that time.

The disparity in efficacy between adult-onset POAG, which showed poor results, and infantile or congenital glaucoma, which exhibited positive outcomes, was attributed to the presence of rich elastic fibers in the infantile angle, which could increase the gaping of elastic tissue in the angle structure [25].

3. Historical Controversy (Part I): Clinical Aspects

3.1. *Goniotomy vs. Trabeculotomy Ab Externo; Which Is the Optimal Approach for Congenital Glaucoma?*

As previously mentioned, trabeculotomy ab externo gained recognition as a viable treatment for congenital glaucoma in Europe and the United States. As a next step, the debate on the comparative merits of trabeculotomy and conventional goniotomy came to a focal point.

Some of the authorities argued that congenital glaucoma patients should undergo at least one goniotomy before considering trabeculotomy [26].

McPherson compared the surgical outcomes for congenital glaucoma between trabeculotomy using a modified Harms Trabectome and goniotomy. The study concluded that the outcomes of trabeculotomy ab externo yielded superior results compared to traditional goniotomy. Additionally, the success rate of trabeculotomy was higher in congenital glaucoma cases than in adolescent glaucoma cases [27–29].

Rothkoff introduced a modified surgical technique that excised the deeper flap of the doubled flap and reported improved outcomes [30].

Glaucoma authorities of this era also reported that trabeculotomy was the recommended surgical approach for congenital and developmental glaucoma. Quigley and Anderson reported that trabeculotomy and goniotomy exhibited comparable performance, with fewer complications in the case of childhood glaucoma. Furthermore, they documented that trabeculotomy ab externo had an advantage when dealing with cloudy cornea. Both researchers also highlighted the correlation between a child's age and the success of the outcomes [31,32].

Subsequently, particularly in the United States, trabeculotomy gained recognition as a viable treatment option for congenital and juvenile glaucoma. At the same time, it was recognized that the outcomes deteriorated as the patient aged. This concept had widespread acceptance both within and outside the USA [33].

Before the widespread adoption of internal trabeculotomy (trabeculectomy), external trabeculotomy was frequently employed for congenital glaucoma. However, as internal trabeculotomy gained popularity, there was a shift from external to internal trabeculotomy, and it is becoming the preferred method over external trabeculotomy [34–43].

3.2. *Historical Controversy (Part II): Is Trabeculotomy Ab Externo Effective for Adult POAG?*

Before the introduction of the Trabectome in 2005, Lamers [18], Dannheim et al. [19], and Nagata et al. [44,45] reported the long-term success of trabeculotomy ab externo in controlling the intraocular pressure in adult-onset POAG.

In the “Tübingen Study”, Weder and others compared the surgical outcomes between trabeculotomy ab externo and goniotrephination. They concluded that trabeculotomy should be considered as an alternative operation for elderly patients with glaucoma simplex to avoid hypotonia. Their study revealed that two thirds of 80 POAG cases were controlled without medication, and 89% achieved qualified success [46]. In 1999, Quaranta and others reported that trabeculotomy could be applied in adult-onset POAG. They compared the outcomes between trabeculotomy and trabeculectomy augmented with mitomycin C in adult POAG, finding no statistically significant difference in the IOP from the 6th to the 24th postoperative month between the two groups [47].

Before 2004, the clinical effectiveness of external trabeculotomy was mainly highlighted in Japan, with multiple publications supporting its effectiveness in adult POAG and PEG [48–58]. A user-friendly probe for trabeculotomy, invented by Nagata, might have facilitated the widespread adoption of this technique in the country. In 2002, Tanito et al. utilized Cox multivariate analysis and reported that advanced age is a favorable prognostic factor for the successful control of the IOP through trabeculotomy ab externo. Their findings also demonstrated a good post-surgical visual acuity prognosis, highlighting that elderly POAG patients with a concomitant cataract are well suited for combined phacoemulsification aspiration, the implantation of an IOL, and trabeculotomy ab externo surgery [59]. At that time, the efficacy of trabeculotomy ab externo was widely accepted and it was adopted as a standard treatment for mild to moderate POAG in Japan. Around 2008, trabeculotomy ab externo accounted for 38% of the total number of glaucoma surgeries performed in Japan [60].

In spite of these reports, canal opening surgery was not recognized as an effective treatment for POAG in adults globally until 2005. The shift towards canal opening surgery in the United States began to emerge in 2005. In 2005, the invention of the Trabectome[®] by Minckler marked the initiation of internal trabeculotomy, which was later named MIGS [25,61].

In a review article, Godfrey and others introduced canal surgeries such as the Trabectome procedure, canaloplasty, and trabeculotomy ab externo as effective treatments for adult glaucoma. They noted that “in other parts of the world, where canal surgery is more popular, trabeculotomy remains an option to filtering surgery for adult and juvenile glaucoma [62]”.

Following the publication of this review article, it appears that many glaucoma surgeons have embraced the view that canal opening is an effective treatment for adult patients with POAG or PEG.

4. Historical Controversy (Part III): Histological Aspects

Debate in Histological Findings after Trabeculotomy: Difference in Tissue Response between Monkeys and Humans

In an earlier study, Dannheim and colleagues investigated the post-surgical regenerative closure of Schlemm’s canal opening in monkey eyes following external trabeculotomy using a metal probe. They observed cellular regeneration in 17 healthy monkeys and noted that this regeneration was initiated between 6 and 8 weeks after the opening of the trabecular meshwork. The trabecular opening closed within 28 weeks due to the regenerated trabecular lamellae and trabecular endothelium, ultimately forming a dense scar [23]. In their study, the Schlemm’s canal opening was filled with fibrous tissue, and the IOP did not decrease in healthy monkey eyes. The closure of the Schlemm’s canal opening in their study might have been considered a potential cause of the poor reduction in IOP.

Ito and colleagues [63] conducted an electron microscope study of the regeneration of the trabecular meshwork following trabeculotomy ab externo in 10 monkey eyes. Their research revealed that the regeneration of the trabecular meshwork begins with the regeneration of the corneo-scleral meshwork and endothelium, eventually progressing to the regeneration of the uveal meshwork. After one year, the defects were almost completely repaired by newly formed trabecular tissue, which closely resembled normal trabecular tissue. Notably, there was no direct communication between Schlemm’s canal and the anterior chamber at the one-year mark.

In contrast to the reports by Dannheim [23] and Ito [63], Hamanaka and colleagues conducted a study of the histopathological changes in the trabecular meshwork (TM) and Schlemm’s canal of human eyes where trabeculotomy ab externo had been unsuccessful [64–66]. They reported that, in 10 out of 31 eyes, Schlemm’s canal remained open to the anterior chamber even six years after trabeculotomy ab externo [65,66]. In these cases, the inner wall of Schlemm’s canal was either covered or filled with fibrous tissue or the regenerated endothelium of Schlemm’s canal (Figure 1). This finding aligns with the

histopathology observed in human eyes by d'Epiney [67], who used electron microscopy to investigate the histopathology of the angle following trabeculotomy in two human eyes with congenital glaucoma. They found that Schlemm's canal contained abundant erythrocytes, and the inner wall of the canal exhibited an encroached endothelium. In the trabecular area, the trabecular structures were lost and were replaced by cell- and fiber-rich tissue.

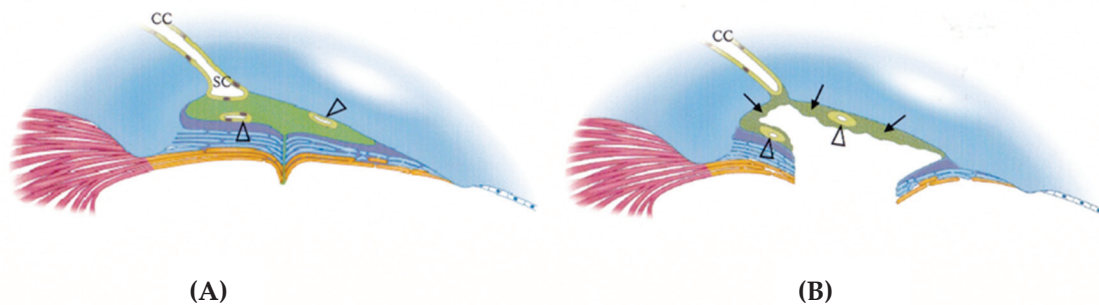


Figure 1. A schematic drawing depicting the histopathology of human eyes following an unsuccessful trabeculotomy [66]. Surgical opening of the trabecular meshwork resulted in closure in 14 of 31 eyes (A) and it remained open in 10 of 31 eyes (B) to the anterior chamber six years (ranging from 3.4 to 22.6 years) after external trabeculotomy. These specimens were obtained during subsequent trabeculectomy after the initial trabeculotomy ab externo. In 10 eyes, in which Schlemm's canal (SC) remained open to the anterior chamber, the inner wall of the SC was lined with extended Schlemm's canal endothelium and/or fibrous proliferation. In 14 eyes with a closed SC, the trabecular meshwork showed sign of fibrous degeneration. Additionally, the intracanalicular space might be filled with fibrous proliferation, leading to the shrinkage of the SC space. In four eyes, the trabecular meshwork was covered by Schlemm's canal endothelial cells, and, in three eyes, peripheral anterior synechiae covered the trabecular meshwork. Open triangles indicate lumens surrounded by the extended endothelium of Schlemm's canal. Arrows point to fibrotic tissue surrounding the expanded Schlemm's canal. (Copyright License #5796400157661 by Exp. Eye Res. Elsevier).

These findings indicate potential differences between monkey eyes and human eyes.

Notably, the presence of an endothelial layer covering the uveal meshwork was observed in individuals who underwent laser trabeculoplasty; these findings may align with post-trabeculotomy observations [68].

It is crucial to emphasize a key distinction between monkey eyes and human eyes. In monkey eyes, the Schlemm's canal opening closes within 28 weeks, whereas this phenomenon does not occur in the human eye.

Regarding the functional aspects of the trabecular meshwork, the outflow after trabeculotomy did not change significantly in "normal" monkey eyes [22]. In contrast, clinical studies in humans have indicated that the reduction in IOP persists for a long period of time [19,48–58].

From a clinical perspective, when eyes are examined using gonioscopy following canal opening surgery, it is common to observe a rough-surfaced, pigmented, membrane-like tissue that covers the inner surface of Schlemm's canal following internal trabeculotomy and internal trabeculectomy. Despite the formation of this membrane on the inner surface of Schlemm's canal, delayed-onset hyphema may occur after internal trabeculotomy or trabeculectomy. This finding suggests direct communication between the anterior chamber and collector channel [69–73].

The enhancement of the episcleral venous fluid wave (EVFW) in the aqueous vein serves as a sign of activated aqueous outflow following canal surgery [74].

In normal eyes, the reported number of collector channels (CCs) is approximately 80 [75]. The inferior half of the CCs drain 87% and the inferior nasal CCs drain 56% of the total outflow [76]. If the orifice of the CC becomes sealed by regenerated endothelium and/or fibrous tissue, there is potential for an elevation in the IOP (Figure 1).

Currently, we lack sufficient information regarding the degree or number of closed CCs that is crucial to impair the normal aqueous outflow. In a previous report, it was suggested that only one or two active aqueous veins may be sufficient to drain enough aqueous humor from the eye [77,78]. The regeneration and fibrosis of the TM tissue, along with the sealing of CCs by fibrous tissue or Schlemm's canal endothelium, may lead to a gradual increase in the post-surgical IOP [79].

It is important to note that any type of surgical intervention can impact the morphology of the trabecular meshwork [68,80].

5. Evolution of Internal Trabeculotomy in Minimally Invasive Glaucoma Surgery (MIGS)

5.1. Evolution of 360-Degree Suture Trabeculotomy (Complete Trabeculotomy)

Suture trabeculotomy was first reported by Smith in 1960 [7]. With this technique, the trabecular meshwork is not excised. A nylon thread is inserted into Schlemm's canal and pulled to open the trabecular meshwork by blunt trauma. In 1987, Lynn and Fellman gave an oral presentation on a 360-degree suture trabeculotomy. Subsequently, in 1987, Beck et al. conducted a study on the outcomes in 26 eyes of 15 patients [81]. In 2012, Chin and others reported a positive 2-year outcome of 360-degree suture trabeculotomy using a 5-0 nylon suture from outside the eye [82].

Two years later, Grover and others introduced a technique named gonioscopy-assisted transluminal trabeculotomy (GATT), whereby a microcatheter or suture is used for a complete 360-degree trabeculotomy from inside the eye. They identified the "trabecular shelf" as a sign of an opened Schlemm's canal [83].

In 2014, Sato and others reported a modified technique involving the simple insertion of a nylon thread without the need for any special instruments [84].

The GATT technique encountered challenges during its initial introduction [85], and it was necessary to undergo a learning curve to acquire proficiency; however, it is now widely accepted as a viable option for the treatment of both adult POAG and childhood glaucoma. Many reports have attested to the long-term success of GATT in effectively controlling the IOP [86–102]. Recently, the combination of internal trabeculotomy and canaloplasty has been reported [103–106]. It will be interesting to see whether the combined approach of canaloplasty and trabeculotomy yields improved outcomes.

The histopathology of the angle after 360-degree suture trabeculotomy was reported by Hamanaka and others. In their study of 11 cases with unsuccessful IOP control, Schlemm's canal remained open in 9 out of 11 eyes at 4 years after surgery. The identified cause of failure was the fibrous proliferation and elongation of the Schlemm's canal endothelium (SCE), which was not associated with the closure of the orifice of the Schlemm's canal opening [66].

There is an ongoing debate regarding whether the outcomes of a 360-degree circumferential trabecular meshwork opening surpass those achieved with a canal opening in the range of 90–150 degrees (see Section 6.2 for further details).

5.2. Evolution of Trabectome® and Kahook Dual Blade

The Trabectome®, which was introduced by Minckler and others in 2005, stands as the pioneering device for the ablation of the trabecular meshwork from inside, leading to the evolution of MIGS [25,61]. They introduced a hand piece featuring a 19-gauge infusion sleeve and a 25-gauge aspiration port with a moderately sharp triangular tip. The inner wall of the trabecular meshwork was ablated in a manner similar to bipolar cautery [25]. With this technique, the conjunctiva is completely preserved, and, in the case of failure, it permits subsequent filtering surgeries, such as trabeculectomy and tube shunt surgery.

As a next-generation internal trabeculectomy device, the Kahook dual blade was invented; it enabled the excision of the trabecular meshwork through the use of a dual-blade tip.

Some have raised questions about the effectiveness of internal trabeculectomy [107]; however, numerous reports have documented the efficacy of Trabectome procedures [108–149] and Kahook dual blade (KDB) surgery [150–180] in maintaining the long-term control of the IOP (Figure 2).



Figure 2. The Kahook dual blade is a device to excise the trabecular meshwork (internal trabeculectomy) between two parallel blades near the tip (product of New World Medical Rancho Cucamonga, CA).

5.3. Evolution of Internal Trabeculotomy, Which Opens Trabecular Meshwork without Excising Tissue

The Tanito micro-hook (TMH, Figure 3) is a device for internal trabeculotomy that pushes away the trabecular meshwork to create an opening in Schlemm’s canal. The surgical outcomes of the TMH are comparable to those achieved with the Trabectome, KDB, and trabeculotomy ab externo [141,181–193] and it may surpass the efficacy of the iStent [194–196].



Figure 3. Tanito micro-hook for internal trabeculotomy: A device inserted into Schlemm’s canal to push away trabecular meshwork tissue (product of Inami, Tokyo).

The T-hook (Figure 4) is a novel device designed to permit the bidirectional opening of the trabecular meshwork without injuring the outer wall tissue of Schlemm’s canal [197].



Figure 4. Chihara T-hook for internal trabeculotomy. The T-shaped head allows the bidirectional opening of the trabecular meshwork. The tip of this device is rounded and designed not to injure outer wall of Schlemm’s canal (product of Inami Tokyo; Handaya Tokyo; and AOI: Advanced Ophthalmic Innovations, Singapore).

Additionally, there are other new devices that have recently been invented to push away trabecular meshwork tissue [198].

5.4. Effects of Canal Expansion (Canaloplasty) without Opening the Trabecular Meshwork

Canaloplasty facilitates aqueous outflow by expanding Schlemm's canal, and this technique has gained widespread adoption, primarily in Europe. The fundamental mechanism underlining IOP reduction in canaloplasty may be explained by four theories, one of which is the hinge–valve theory [199]. The tension of the conduits traversing Schlemm's canal regulates both the aqueous inflow from the anterior chamber into Schlemm's canal and the outflow from Schlemm's canal to the collector channel. The proposed entry site for the aqueous chamber is a funnel-shaped canal inlet, and the regulator of the aqueous outlet is a hinged collagen flap. If Schlemm's canal expands, the tension of the conduit increases, and the hinged collagen flap is pulled, opening the outlet valve. Another theory suggests that Schlemm's canal ruptures under high pressure, resulting in multiple defects in the inner and outer walls of Schlemm's canal [200,201]. The third theory involves the herniation of the inner wall of Schlemm's canal into the collector channel. In other theories, this procedure effectively reduces the IOP by dilating the collapsed Schlemm's canal, cleaning the collector channel, and stretching the trabecular meshwork. Even now, debate continues regarding the basic mechanism of IOP reduction following canal expansion.

The technique involves the viscodilation of Schlemm's canal, the insertion of a microcatheter (such as iTrack, OMNI, etc.), and the stretching of the trabecular meshwork using a 10-0 prolene thread, facilitating aqueous outflow. Additionally, the creation of an intrascleral lake may provide an alternative drainage route into the intrascleral and suprachoroidal space [202]. Planned goniopuncture can further enhance the outflow. In the case of failure following canaloplasty, trabeculotomy may be employed as the next step [203].

External trabeculectomy is more efficient than canaloplasty in reducing the IOP; however, the probability of success when using canaloplasty is not inferior to that of trabeculectomy, according to several meta-analysis studies [204–206].

In one report, conventional canaloplasty achieved better outcomes than viscocanalostomy [207]. There are numerous reports on the effects of canaloplasty [98,103–106,208–264]. Essentially, classic canaloplasty is performed externally and is not considered an MIGS procedure [203,208–224,226–231,235,236,239,241,242,245,249,250,255,256,261–264]. However, recent ab interno techniques using specific devices (such as iTrack, OMNI, etc.) are categorized as MIGS [98,103–106,225,232–234,237,238,240,243,244,246–248,251–260]. In the latest advancement of canaloplasty, Schlemm's canal is “unroofed” [103–106,203,253,259,265]. If Schlemm's canal is disrupted under high intracanal pressure [200,201], the difference between GATT or suture trabeculotomy and canaloplasty becomes unclear [265].

5.5. Streamline[®] and Hydrus[®]

Streamline[®] expands Schlemm's canal using a viscoelastic material [266], while Hydrus, a Schlemm's canal scaffold, combines elements of canaloplasty and the iStent to dilate Schlemm's canal and establish a connection between the anterior chamber and Schlemm's canal [260]. Both methods are considered to be techniques that are associated with canaloplasty. These reduce the IOP without significant complications.

5.6. iStent

The iStent, a popular tool for canal surgery, offers a low risk of complications and a mild reduction in IOP. This is a type of stenting surgery that does not open the canal. There are many review papers that compare the outcomes between the iStent and canal opening MIGS [267–272]; therefore, it is not extensively reviewed in this study.

5.7. Others

Viscocanalostomy is a technique that externally modulates Schlemm's canal. It is not included in MIGS and not commented upon in this study [273]. Recently, viscocanalostomy has been largely replaced by canaloplasty [207]. High-frequency deep sclerectomy creates an intrascleral pocket internally and facilitates the uveo-scleral pathway, but it is not included in canal opening surgery [267].

6. Clinical Controversies Regarding Internal Canal Opening Surgery

6.1. Differences between Internal Canalectomy and Canalotomy

6.1.1. Open or Closed? Does It Matter?

When Minckler and colleagues introduced the "Trabectome", the device was designed to create the permanent unroofing of the TM [25]. They believed that permanent unroofing was important for long-lasting IOP reduction, a concept that was later advanced by the Kahook dual blade (KDB) [274]. In contrast, trabeculotomy ab externo opens Schlemm's canal through blunt trauma using a nylon filament or metal probe. This concept was succeeded by GATT and internal suture trabeculotomy, which creates a "shelf" in the angle. Similarly, new devices such as the Tanito micro-hook (TMH) and the T-hook push the TM tissue away and do not excise the TM, creating a double-door opening in the TM.

When post-surgical wounds were studied using anterior segment OCT, the size of the wound was found to be greater in cases of internal trabeculectomy, such as that with the KDB, compared to internal trabeculotomy, such as that with the TMH. However, no significant difference in post-surgical IOP was noted [275].

From a clinical standpoint, no discernible difference in surgical outcomes was observed between the internal trabeculectomy cases, such as those involving the Trabectome and KDB, and the trabeculotomy cases, such as those involving trabeculotomy ab externo, GATT [83], the TMH [189], the T-hook [197], and 360-degree suture trabeculotomy [82,141,184,197,276–280].

This raises the question of whether the surgical outcomes after internal trabeculotomy differ from those after internal trabeculectomy.

However, there is still insufficient research to determine whether the long-term observations reveal distinctions between the two procedures [271,281]. The clinical findings and the histopathological studies conducted by Hamanaka and others [66] suggest that the issue regarding whether Schlemm's canal is opened or closed may not be the critical factor; instead, the sealing of the inner surface of the canal is the issue.

On the other hand, there is a debate regarding whether the meridional extent of the canal opening affects the surgical outcomes (see Section 6.2). Some believe that a larger opening is beneficial for a greater IOP reduction [101,282–284], while others hold the contrary view.

6.1.2. Comparison between Conventional Trabeculectomy and MIGS

Meta-analysis is a desirable approach for the evaluation of the efficacy of new surgical techniques; however, the number of randomized clinical trials in the area of MIGS is not sufficient [285].

Several reports indicate that ab interno trabeculotomy provides a similar IOP reduction to trabeculectomy, with a lower risk of complications [128,286]. The post-surgical IOP outcomes for the Ahmed glaucoma valve and Baerveldt implant may be comparable [121,123]. However, others suggest that conventional trabeculectomy has greater efficacy in reducing the IOP compared to internal trabeculotomy [287]. Most reports agree that trabeculectomy also carries a higher risk of complications [288].

6.2. Does the Extent of the Canal Opening Area Impact the Surgical Outcomes?

In a clinical study, the area of active circumferential flow in Schlemm's canal was restricted. Fellman and Grover reported that downstream episcleral vein bleaching is confined to two clock hours from the edge of the Trabectome incision. In their report,

the bleaching of the episcleral veins was shown to occur within 41 degrees infero-nasally and 13 degrees supero-nasally from the incisional end using the Trabectome [289]. This may explain why the effects of the iStent on the IOP are inferior to those of other internal trabeculotomy techniques [130,167,195,290–293]. In a meta-analysis study, the outcome of the iStent was inferior to that of the Hydrus [271].

Ellingsen and Morton found that the aqueous outflow was better when a wide area of the trabecular meshwork was opened [294]. Rosenquist and others confirmed the better IOP reduction with a wider Schlemm's canal opening in cadaver eyes [295]. Several clinical reports also suggest that the wider opening of the canal leads to a better IOP reduction [97,101,282,296,297].

However, when the canal opening extends beyond 90 degrees, the effects of widening the canal opening on the post-surgical intraocular pressure do not exhibit a consistent trend. Several studies indicate that there is no significant difference in the extent of IOP reduction when the canal opening exceeds 90 degrees [182,298–303]. In a hypothetical model, the decrease in outflow resistance was greater in eyes with a 4 h incision than those with a 1 h incision. However, the effects of expanding the incision on the post-surgical IOP reached a saturation point when the excision area exceeded 90 degrees [304]. In eyes where the canal opening is expanded to 360 degrees, there is no further decrease in outflow resistance [304]. The wider the canal opening, the greater the intracameral bleeding and obstruction of collector channels [305].

It has been reported that only one or two active aqueous veins are enough to drain a sufficient amount of aqueous humor to maintain a normal IOP [77,78]. Thus, the survival of only a few active collector channels may be sufficient to sustain normal intraocular pressure. After the canal opening surgery, the gradual coverage of the collector channel opening due to the elongation of the Schlemm's canal endothelium, along with the proliferation of fibrous tissue, constitutes a slowly progressing phenomenon and may lead to a gradual elevation in IOP [66]. It may require a long time for the complete obstruction of 80 collector channels to occur.

If the collector channel at the site of the canal opening is intact, a localized opening may be sufficient to obtain clinical success; however, it is difficult to estimate the clinical integrity of the intra-scleral outflow before surgery. If the outflow resistance is abnormal in a specific meridian, the opening of Schlemm's canal in the affected area may not yield a good outcome. From this perspective, "complete trabeculotomy" (360-degree canal opening) may offer an advantage in achieving constant results in eyes with a localized impairment in the outflow system. When comparing the surgical outcomes between complete trabeculotomy (360-degree canal opening) and "partial trabeculotomy" (less than 360-degree canal opening), several reports demonstrate better outcomes with complete trabeculotomy [97,101,296,297], although others do not [299,300,303].

It is still unclear whether a wide canal opening is beneficial to the restoration of the active aqueous vein or not. A prospective and long-term follow-up study is needed to address this question.

6.3. Does the Type of Glaucoma Affect Canal Opening Surgery Outcomes?

6.3.1. Steroid-Induced Glaucoma

In steroid-induced glaucoma, an abnormal extracellular matrix (ECM), consisting of abnormal collagen and dense homogenous material, accumulates adjacent to the inner wall of Schlemm's canal. These ECM characteristics are different from those observed in POAG [306]. Cellular proliferation and migration in the sclera are restricted, while the cell size may be increased after steroid administration [307]. Clinically, Schlemm's canal and CC are generally unaffected by steroids, and a favorable response to the canal opening surgery is expected. Many reports indicate positive outcomes following internal trabeculotomy or internal trabeculectomy [114,181,245,261,284,308–311]. Therefore, steroid-induced glaucoma may be considered a suitable candidate for internal canal surgeries.

6.3.2. Secondary Glaucoma: Uveitic Glaucoma

When inflammatory cells obstruct the trabecular meshwork, the intraocular pressure increases. In the case of prolonged inflammation, scar tissue is formed, which impairs the aqueous outflow. In canal surgery, post-surgical inflammation may promote the post-surgical proliferation of fibrous tissue and induce the elongation of the SCE [181,308].

However, when the inflammation was mitigated and the post-Schlemm's canal route was preserved, positive outcomes were reported in canal surgeries for secondary glaucoma [185,312,313]. Some cases of uveitic glaucoma may respond similarly to POAG or steroid-induced glaucoma [100,284].

6.3.3. Pseudoexfoliation (Exfoliation) Glaucoma

In contrast to POAG, (pseudo-)exfoliation glaucoma (PEG) is characterized by a higher IOP, faster visual field deterioration, a poor response to medical therapy, and an increased need for surgical intervention. While some reports demonstrate positive outcomes with canal surgeries in PEG cases [17,52,55], others do not.

The reduction in IOP through canal surgery in PEG cases is significant [17,52,102,115, 139,314,315], often surpassing that observed in POAG [55,316], or an equivalent outcome between PEG and POAG is shown [94,119,317]. However, it is noteworthy that the pre-surgical IOP is typically higher in PEG cases, which may contribute to a greater IOP reduction following canal surgery. This substantial IOP reduction in PEG cases may simply reflect the inherent nature of canal surgery, which tends to achieve a higher IOP reduction in cases with a high preoperative IOP. Consequently, the final IOP in PEG might remain high, potentially leading to a poor final outcome [181]. In addition to the final IOP, the fluctuation of the IOP level may cause nerve damage. Therefore, the efficacy of canal surgery in treating PEG remains unclear.

6.4. How High Can the Preoperative Intraocular Pressure Be to Indicate Canal Opening Surgery?

In many reports, the surgical reduction in the IOP in canal surgery is more pronounced in eyes with a higher pre-surgical IOP [181,183,192,318–320]. Tanito reported the following association: (percentile IOP reduction) = $2.1 \times (\text{preoperative IOP}) - 15.7$ [183]. A clear correlation exists between the pre-surgical IOP and the extent of IOP reduction [183]. We reported a marginal association between the pre-surgical IOP and post-surgical IOP in phaco-trabeculotomy cases, reporting the following regression equation: (post-surgical IOP) = $12.812 + 0.166 \times (\text{pre-surgical IOP})$, $p = 0.0629$. In this study, the critical pre-surgical IOP required to achieve 18 mmHg was 31.3 mmHg [319]. However, the association between the pre- and post-surgical IOP was weak and it may not follow a linear regression line; thus, it requires further elucidation. The upper limit of the pre-surgical IOP for consideration of canal opening surgery has not yet been determined.

6.5. Do Pre- and Post-Surgical Eye Drops Affect Outcomes?

The use of certain drugs may influence or alter the surgical outcome. A parasympathomimetic drug is employed to prevent post-surgical peripheral anterior synechia (PAS) formation, although its effects have not been comprehensively assessed [321]. It should be noted that parasympathomimetic drugs may induce post-surgical inflammation, potentially leading to PAS formation.

The application of a vasoconstrictive agent may potentially limit intracameral bleeding [322]. The use of Rho-associated coiled-coil-containing protein kinase (ROCK) inhibitors may modulate the contractile elements of the collector channel and positively impact the post-surgical IOP. However, the available data are limited, and additional studies are needed to validate these findings [323,324]. The response to ROCK inhibitors may be useful in predicting the outcome of MIGS, while the prolonged or multiple use of anti-glaucoma medications may adversely affect the outcome [325–327].

6.6. Does the Combination of Cataract Surgery Benefit the Outcomes of Canal Opening Surgery?

The extraction of the lens results in the retro-positioning of the iris diaphragm and increases the tension on the trabecular meshwork [199]. Simple lensectomy widens the angle and intensifies the tension of the trabecular meshwork, consequently reducing the IOP [328–331]. In angle-closure glaucoma, lens extraction has a favorable impact on the post-surgical IOP [137,329].

On the other hand, the results of a meta-analysis of the outcomes of standalone Trabectome (39% reduction) and a combined phacoemulsification–Trabectome (27% reduction) were not conclusive [332]. Regarding POAG cases, there is ongoing debate concerning the effects of concomitant cataract surgery and canal surgery in terms of their impacts on the post-surgical IOP. While several studies indicate positive effects [97,314,315,320,333–337], conflicting findings are reported by others [83,93,303,338–342].

It is worth noting that combined cataract surgery negatively affects the outcomes of trabeculectomy; however, this is not the case in canal surgeries [102].

6.7. How Does a Post-Surgical IOP Spike and Intracameral Bleeding Affect MIGS Outcomes?

Here, we must be careful to note the difference between simple hyphema and clot formation. Surgical trauma to vascular tissue triggers the release of von Willebrand factor, initiating a cascade of events from platelet adherence and the conversion of fibrinogen to fibrin, which leads to peripheral anterior synechia (PAS) formation and the potential occlusion of the collector channel orifice [92,343]. Rao reports that the development of PAS is associated with a spike in the IOP [92].

Even though the trabecular meshwork tissue is rich in tissue plasminogen activator [344] and facilitates the dissolution of a blood clot to enhance aqueous humor drainage, once a clot is formed, it may worsen the tissue adhesion. Ishida and colleagues have reported a close correlation between clot formation and a subsequent elevation in the post-surgical IOP [196]. Shi, Quan, and others have emphasized that a spike in the IOP constitutes a risk factor for poor IOP control [89–91]. In other reports, clot formation is highlighted as a significant risk factor for re-operation [305] and may lead to a gradual increase in the post-surgical IOP [79].

6.8. Does Prior Selective Laser Trabeculoplasty (SLT) or LTP Affect MIGS Outcomes?

A modest reduction in IOP is achieved with selective laser trabeculoplasty, without any significant complications. This may not affect the surgical outcome of the canal surgery [345,346]; however, others report adverse effects of SLT [148,336,347]. After a failed SLT, canal opening surgery is a viable candidate option to reduce the IOP [348–350]. However, caution is necessary, as there is a report suggesting that SLT may not be useful as a subsequent step following failed canal surgery [351].

6.9. What Are the Risk Factors for the Failure of Canal Surgery?

As mentioned previously, uveitic glaucoma and pseudoexfoliation glaucoma, a history of SLT and LTP [347], and post-surgical PAS or spikes are risk factors for failure. Neovascular glaucoma is contraindicated for canal surgery, with the exception of one report [88].

When the preoperative IOP is high, the decline in IOP is large; however, the final IOP value is often high, so a high preoperative IOP is a risk factor for failure [181,320,352,353]. Regarding traumatic glaucoma, we do not have enough evidence, and it is therefore difficult to comment on. A younger age [87,336,354] was shown to be a risk factor for failure, except in one report [86]. This finding may contrast with the findings of older studies, in which the outcome of trabeculotomy ab externo was better in congenital glaucoma than in juvenile-onset glaucoma [31,32].

A high central corneal thickness [353,354] and myopia [355–357] were listed as risk factors, except in one study [358]. Being male may affect the outcome [359]. It is noteworthy

that better outcomes are reported in Hispanic individuals [315]. However, the Black ethnicity was associated with a higher risk of reoperation [320].

6.10. Risk of Postoperative Ciliary Effusion

Canal-based MIGS procedures do not typically result in severe post-surgical hypotension and are generally considered safe. Ciliary effusion is a rare complication, although it may occasionally be observed [187,360–362]. This complication can be triggered by inadvertent damage to the pectinate ligament and the formation of a ciliary cleft. Precise opening of the trabecular meshwork is crucial in minimizing the risk of post-surgical ciliary effusion.

7. Conclusions

This review explores the history of canal opening surgery, the several types of procedures available, the clinical controversies surrounding them, and the risk factors associated with their failure.

External trabeculotomy, since its inception, has faced numerous challenges and has not gained global acceptance for the treatment of adult-onset POAG. It was later modified into internal trabeculotomy, which has recently become more popular. Initial experiments on normal monkey eyes indicated the excessive regeneration of the trabecular meshwork, casting doubt on the efficacy of external trabeculotomy and hindering its widespread adoption in clinical practice. However, more recent studies showing mild histopathological tissue responses in humans, combined with numerous clinical success stories, have led to a shift in perspective. Currently, canal opening surgeries, classified as minimally invasive glaucoma surgeries (MIGS), have gained popularity. Nevertheless, distinctions from other procedures, such as canaloplasty and stenting surgeries, have sparked significant debate. Additionally, there remains a debate concerning the surgical outcomes based on the surgical method, type of glaucoma, preoperative intraocular pressure levels, effects of concurrent cataract surgeries, impacts of postoperative anterior chamber hemorrhage, effects of treatments such as SLT, and risk factors associated with the surgery.

Future Directions: Canal opening surgery currently offers good postoperative visual acuity and an effective IOP reduction, making it a promising treatment for mild to moderate glaucoma. While there are several surgical methods and devices available, they are being improved annually and should be explored to ensure that they become more cost-effective and user-friendly in the future.

Author Contributions: Conceptualization, E.C.; Resources, E.C.; Writing, E.C.; Review and Supervision, T.H. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Acknowledgments: This review is part of a series of studies: “Clinical Debates in Minimally Invasive Glaucoma Surgery (MIGS)”. For histopathological debates, please refer to the review titled “Effect of Canal Opening Surgery on Reducing Intraocular pressure from Physio-pathological Aspect”, by Hamanaka T and Chihara E. The authors extend their profound appreciation to Murrey Johnstone for generously providing valuable insights into prior physiological and histological glaucoma research endeavors. We used ChatGPT to correct grammatical errors.

Conflicts of Interest: The authors declare no conflicts of interest.

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Review

Visual Function After Schlemm's Canal-Based MIGS

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Abstract

Filtration surgery is highly effective in lowering intraocular pressure; however, it is associated with a higher risk of severe complications. Visual dysfunction may persist in relatively uneventful cases because of induced astigmatism or worsening optical aberrations. Therefore, for early- to moderate-stage glaucoma, an increasing number of surgeons are prioritizing surgical safety and preserving postoperative visual function by opting for minimally invasive glaucoma surgery (MIGS). Among the various MIGS techniques, canal-opening surgery—targeting aqueous outflow through the Schlemm's canal (Schlemm's canal-based MIGS, CB-MIGS)—has gained increasing popularity. Unlike filtration surgery, CB-MIGS does not require creating an aqueous outflow pathway between the intraocular and extraocular spaces. Consequently, it is considered a minimally invasive procedure with a reduced risk of severe complications and is increasingly being chosen for suitable cases. Although this surgical technique has limitations in lowering intraocular pressure, it avoids the manipulation of the conjunctiva or sclera and is primarily performed through a small corneal incision. Therefore, a minimal impact on induced astigmatism or postoperative refractive changes is expected. However, few reviews comprehensively summarize postoperative changes in visual function. Therefore, this study reviews the literature on visual function after CB-MIGS, focusing on changes in best-corrected visual acuity (BCVA), refraction, astigmatism, and the effectiveness of visual field preservation to assess the extent of these postoperative changes. Hyphema is the primary cause of early postoperative vision loss and is often transient in cases in which other complications would have led to visual impairment. Severe complications that threaten vision are rare. Additionally, compared with filtration surgery, postoperative visual recovery tends to be faster, and the degree of induced astigmatism is comparable to that of standalone cataract surgery. When combined with cataract surgery, the refractive error is at the same level as that of cataract surgery alone. However, in some cases, mild hyperopic shifts may occur because of axial length shortening, depending on the extent of intraocular pressure reduction. This possibility has been highlighted in several studies. Regarding the effectiveness of slowing the progression of visual field defects, most studies have focused on short- to medium-term postoperative outcomes. Many of these studies have reported the sufficient suppression of progression rates. However, studies with large sample sizes and long-term prospective designs are limited. To establish more robust evidence, future research should focus on conducting larger-scale, long-term investigations.

Keywords: minimally invasive glaucoma surgery (MIGS); Schlemm's canal-opening surgery; trabeculotomy; canaloplasty; Kahook Dual Blade; trabectome; tanito microhook; visual acuity; visual field; astigmatism

1. Introduction

Glaucoma is the leading cause of blindness worldwide [1]. As the global population continues to age, the number of patients with glaucoma is projected to increase from 76 million in 2020 to 95.4 million by 2030 [2]. Elevated intraocular pressure (IOP) is a major risk factor for disease onset and progression [3,4], and lowering the IOP slows disease progression [5,6]. First-line treatments for reducing IOP include topical medications and selective laser trabeculoplasty [7,8]. However, when these conservative treatments fail to provide long-term control or prevent disease progression, glaucoma surgery should be considered. Glaucoma surgery aimed to lower IOP in a safe and sustained manner over the long term. Although filtration surgery is highly effective in reducing IOP, it is associated with a high risk of severe complications. Even in patients with an uneventful postoperative course, a long recovery period is often required to restore visual acuity. In addition, refractive changes, increased astigmatism, and the exacerbation of optical aberrations may result in reduced unaided visual acuity or persistent visual impairment [9,10].

Therefore, in early- to moderate-stage glaucoma, surgical safety, the speed of postoperative visual recovery, and the preservation of long-term visual function are often prioritized. Consequently, minimally invasive glaucoma surgery (MIGS) has been increasingly used in such cases. Among the MIGS techniques, canal-opening surgery, which targets aqueous outflow through the Schlemm's canal, is classified as Schlemm's canal-based MIGS (CB-MIGS). Depending on the mechanism used to enhance aqueous outflow through the main drainage pathway, CB-MIGS can be further categorized into several surgical methods, each utilizing different devices.

A common feature of these device-based procedures is that they are minimally invasive, have a lower risk of severe complications [11–13], are relatively simple and quick to perform, and do not typically require conjunctival incisions, thereby preserving the possibility of future filtration surgery. Due to their mechanism of action, CB-MIGS cannot lower IOP beyond episcleral venous pressure. However, unlike filtration surgery, CB-MIGS rarely results in excessively low single-digit IOP. Moreover, because it is primarily performed through small corneal incisions without manipulating the conjunctiva or sclera, a minimal impact on induced astigmatism or postoperative refractive changes is expected.

Another important focus is how effectively CB-MIGS can slow the postoperative progression of visual field defects, although it generally achieves less IOP reduction than filtration surgery. While numerous reports and reviews have examined the IOP-lowering effects and complications of CB-MIGS, relatively few comprehensive reviews have detailed the changes in visual function, such as best-corrected visual acuity (BCVA), refraction, astigmatism, or maintenance of visual fields after surgery.

This review summarizes the existing literature on visual function outcomes after CB-MIGS. Two authors (M.K. and N.S.) independently conducted the literature search in October 2024. The search was performed using PubMed and targeted full-text articles or abstracts written in English. Articles published in peer-reviewed journals over the past 20 years were selected if they were relevant to the topic of this review and contributed to a deeper understanding of the visual function after CB-MIGS. Relevant studies cited in the references of the retrieved articles were also included. In cases where the authors had differing opinions on the relevance of a study, a disputed study was included.

2. Types and Characteristics of CB-MIGS

CB-MIGS can be broadly classified into three categories based on their underlying principles. Ab interno trabeculotomy (AIT), a procedure involving incising or excising the trabecular meshwork, bypassing the trabecular meshwork using implantable devices, which involves placing stents to bypass the anterior chamber and Schlemm's canal, and Ab

interno canaloplasty (ABiC) is a procedure performed ab interno to expand the Schlemm's canal without incising or excising the trabecular meshwork.

2.1. AIT

The Trabectome[®], introduced by Minckler et al. in 2005 [14], represents the first device specifically designed to internally ablate the trabecular meshwork, marking a significant milestone in MIGS development. The device features a handpiece equipped with a 19-gauge infusion sleeve, a 25-gauge aspiration port, and a moderately sharp triangular tip. The inner wall of the trabecular meshwork was ablated using a mechanism resembling bipolar cautery [14].

Subsequently, the Kahook Dual Blade (KDB) was developed as an alternative. Although it does not include a cauterization function, the KDB does not require expensive equipment and allows the excision of the trabecular meshwork using its dual-bladed tip. Numerous studies have demonstrated the safety and efficacy of both the Trabectome (TOM) [15–55] and KDB procedures [56–86].

The Tanito Microhook (TMH), developed to incise rather than excise the trabecular meshwork, differs from TOM and KDB because it is a reusable device, offering superior cost-effectiveness. The IOP-lowering effects of TMH are comparable to those of TOM, KDB, and trabeculotomy ab externo (exLOT) [47,87–99].

In 2014, Grover introduced gonioscopy-assisted transluminal trabeculotomy (GATT), a procedure that uses a microcatheter or suture to achieve a 360-degree incision in the trabecular meshwork ab interno. The safety and efficacy of GATT have been well established [100–118]. Regarding the extent of the incision, whether performing a 360-degree incision offers superior IOP reduction compared with a 90–150-degree incision remains unclear. Some studies suggest that a larger incision area results in greater IOP reduction [106,119–121], whereas others report no significant difference in IOP reduction beyond a 90-degree incision [97,122–127]. This is currently an area of ongoing research.

2.2. Bypassing the Trabecular Meshwork Using Implantable Devices

The iStent (Glaukos Corporation, San Clemente, CA, USA) and Hydrus (Alcon Laboratories, FortWorth, TX, USA) are the most widely used micro-implantable devices in the market. The first-generation design was a single nonferromagnetic titanium stent with an inlet attached at a 40-degree angle to an intracanalicular half-cylinder coated with heparin to prevent fibrosis [128]. The second-generation iStent injection comprises two button-shaped titanium stents delivered through an updated delivery system. The stents feature a head that resides in the Schlemm's canal, a thorax that anchors in the trabecular meshwork, and a rear flange that resides in the anterior chamber. Third-generation iStent Injection W represents an iterative improvement, featuring a wider rear flange designed to reduce the risk of overimplantation. The iStent, which does not involve incising the trabecular meshwork, is minimally invasive and effective [129–134]. However, its efficacy may be lower compared with AIT [135–137].

In contrast, the Hydrus, a Schlemm's canal scaffold, combines elements of canaloplasty and the iStent to dilate Schlemm's canal and establish a connection between the anterior chamber and Schlemm's canal [138]. The stent is made of a nonferromagnetic nickel–titanium alloy and features a curved, flexible, open structure with windows and spines designed to dilate approximately 8 mm of the Schlemm's canal to four to five times its physiological diameter. Moreover, its efficacy and safety have been well documented [138–142].

2.3. ABiC

Rather than creating a wide incision in the Schlemm's canal, canaloplasty facilitates aqueous outflow by expanding the canal and has gained widespread adoption, particularly

in Europe. The procedure involves the viscodilation of the Schlemm's canal, the insertion of a microcatheter, and the stretching of the trabecular meshwork using a 10-0 prolene thread, thereby improving aqueous outflow.

Traditional canaloplasty is performed externally and is not classified as MIGS. However, more recently, ABiC, which uses specific devices, such as iTrack (Ellex Inc., Minneapolis, MN, USA) and OMNI (Sight Sciences Inc, Menlo Park, CA, USA), has been considered a form of MIGS. Numerous studies have reported their safety and efficacy [115,138,143–161]. Additionally, OMNI enables AIT to be performed after canaloplasty [162–167].

A common feature of CB-MIGS is that these procedures are performed through a small corneal incision using the ab interno approach. These outflow reconstruction surgeries redirect the aqueous humor to the collector channels and episcleral veins. Consequently, CB-MIGS can lower the IOP; however, it cannot reduce it below the episcleral venous pressure (8–10 mmHg) or the resistance levels of the distal outflow pathways. In contrast, CB-MIGS rarely causes severe complications associated with filtration surgeries, such as hypotony-related issues, infections, or expulsive hemorrhages. This positions CB-MIGS as a safe and reliable surgical option [11–167].

3. Surgical Indications for CB-MIGS

It is essential to observe the anterior chamber angle intraoperatively, with a Shaffer grade between 2 and 4. Additionally, the trabecular meshwork at the incision or implant site should ideally be free of peripheral anterior synechia (PAS). However, in AIT, a small tent-shaped PAS can be released using the instrument tip during the incision. The target intraocular pressure (IOP) is in the mid-10 mmHg range, making cases with an IOP exceeding 20 mmHg ideal candidates. However, surgery may also be considered for patients with an IOP in the 10 mmHg range, depending on medication adherence, side effects, and IOP fluctuations. For example, surgery may be appropriate for elderly patients with dementia who struggle with eye drop adherence, those experiencing severe keratitis or blepharitis from eye drops, or individuals with systemic symptoms—such as fatigue, loss of appetite, or a history of urinary stones—that hinder acetazolamide therapy. Significant IOP fluctuations, particularly with nighttime elevation, may also indicate the need for surgery. Conversely, surgery is not actively recommended for patients who can manage eye drops and maintain an IOP in the mid-to-high 10 mmHg range, even if visual field defects continue to progress. In cases where the visual field defect is already in the late stage or beyond, filtration surgery may be a more suitable option.

4. Visual Acuity After CB-MIGS

Visual acuity often declines after trabeculectomy (TLE), and recovery can take considerable time. Moreover, some cases experience permanent visual impairment [9,10]. In a study conducted by the authors on visual changes following TLE in 292 eyes, 4.45% of the patients exhibited a decline in BCVA of two or more lines on the Snellen chart that did not recover by 3 months postoperatively [168]. Similarly, Francis et al. analyzed data on 301 eyes that underwent TLE and reported that 64.5% of cases experienced a decline in three or more Snellen chart lines within 6 months postoperatively. Of these, 56.5% recovered within 6 months, while 8.0% did not recover [169].

However, the proportion of cases in which BCVA declines by two or more Snellen chart lines after CB-MIGS is 0–5% for AIT [15–18,39,56–59,70,92,170–175], 0–9.7% for micro-implantable devices [139–142,176–195], and 1.2–3% for ABiC [146,148,196,197], which is lower than that of TLE. Additionally, many studies have reported no severe complications that significantly affect visual function.

Additionally, reports showing a $\geq 7\%$ incidence of visual decline identified several causes. These included the progression of pre-existing cataracts during long-term follow-up after iStent implantation [183] and a transient two-line or greater decrease on the Snellen chart due to corneal edema from an IOP spike and hyphema on the day after Hydrus implantation [140]. Variations in observation time points, unclear reporting, and the inclusion of simultaneous cataract surgery make accurate result interpretation challenging.

When proposing CB-MIGS, it is crucial to understand whether the postoperative BCVA reduction is due to direct surgical complications and whether such reductions are temporary or permanent. A long-term decline in visual acuity may occur when the procedure is performed in advanced cases with severe preoperative sensitivity loss near the fixation point. Moreover, the progression of cataracts or the development of other diseases that affect visual acuity can contribute to a decline in BCVA. Therefore, reviews that merely quantify the percentage of BCVA reduction are limited. It is critical to first explain the extent, types, and frequency of complications that may influence visual acuity in the chronological order of their occurrence.

5. Visual Decline Due to Complications

5.1. Hyphema

Hyphema is the most common complication causing early postoperative visual decline after CB-MIGS. When the IOP temporarily drops below the episcleral venous pressure postoperatively, reflux bleeding can result in hyphema. In the absence of intraoperative iris trauma or damage to the angle vessels, postoperative hyphema serves as evidence that the outflow pathway beyond the collector channels has been connected to the episcleral veins. This is also considered a positive indicator of IOP reduction.

Hyphema is not limited to AIT or micro-implantable devices; it is also a common complication of ABiC, where the partial incision of the trabecular meshwork during the expansion of Schlemm's canal can lead to bleeding. The reported incidence of hyphema varies depending on the procedure used. For iStent and iStent injections, the incidence ranged from 0 to 11.4%, whereas it ranged from 1.9 to 6.5% for Hydrus. Procedures, such as the KDB, have reported an incidence of 0–34.9%, whereas the TOM has a wider range of 4.7–95.0%. For TMH, the incidence is 14–41%, while that for GATT ranges from 2.0 to 100.0%. Similarly, the incidence of ABiC ranges from 1.0 to 47.0% (Table 1).

Table 1. Summary of Principal Complications (%) Leading to Visual Decline by Device Type.

Surgical Technique	Hyphema (%)	IOP Spikes (%)	Corneal Edema (%)	CME (%)	Severe Complications (e.g., Endophthalmitis, Suprachoroidal Hemorrhage) (%)
iStent/iStent inject	1.1–22.2	0–11.4	0–10.0	1.0–1.3	Not specified
Hydrus	1.9–6.5	1.9–6.5	0–3.2	2.0	Not specified
AIT (KDB, TOM, TMH)	0–95.0	1.0–28.9	0–17.2	1.8–7.0	0.01% (Endophthalmitis)
GATT	2.0–100.0	0–49.0	0–14.7	0–6.2	0–1.1% (Suprachoroidal Hemorrhage)
ABiC	1.0–47.0	0–42.0	0–4.9	0–4.9	Not specified

IOP = intraocular pressure, CME = Cystoid macular edema, AIT = ab interno trabeculotomy, KDB = Kahook Dual Blade, TOM = Trabectome, TMH = Tanito Microhook, GATT = gonioscopy-assisted transluminal trabeculotomy, ABiC = ab interno canaloplasty.

Visual acuity naturally reduces, whereas hyphema persists postoperatively. However, in most cases, bleeding resolves spontaneously within approximately 1 week, and visual acuity returns to baseline [34,59,68,71,78,80,103,115].

In rare cases, massive or prolonged bleeding may require anterior chamber irrigation because such conditions can lead to elevated IOP or adverse effects on the corneal endothelium. Reports indicate that anterior chamber irrigation was required

in 0–9.0% of cases following AIT [21,84,88,92,93] and in 0–10.9% of cases following GATT [102,105,112,114,116,198]. However, no previous studies have identified this as a direct cause of permanent visual impairment. However, MIGS aims to promote early visual recovery, and bleeding should ideally be avoided or, if it occurs, should remain minimal and resolve spontaneously within a short period.

Regarding the speed of visual recovery in CB-MIGS alone, Tanito et al. reported postoperative visual outcomes in 159 eyes treated with TMH alone [92]. The preoperative logMAR BCVA was 0.11 ± 0.39 . Postoperatively, the BCVA was 0.30 ± 0.68 at 1–2 weeks ($p < 0.0001$), 0.15 ± 0.48 at 1 month ($p = 0.02$), and 0.07 ± 0.29 at 3 months ($p = 0.83$). These results indicate that while visual acuity recovered to levels close to the preoperative values after 1 month, a statistically significant difference remained at that point. In contrast, reports on iStent and iStent injections suggest that, unlike AIT, these procedures do not require an incision of the trabecular meshwork. Consequently, early postoperative complications, including hyphema, are less frequent [130,133,134,137], and early postoperative visual recovery is often expected [133].

In a comparative study of TMH, Harano et al. evaluated 78 eyes of 39 patients who underwent simultaneous cataract surgery with TMH in one eye (TMH group) and iStent injection of W in the contralateral eye (injection W group) [136]. The incidence of hyphema in the injection of W group was 5%, which was significantly lower than that in the TMH group (26%; $p = 0.025$). Additionally, the BCVA in the injection of W group was significantly better at 2 weeks ($p = 0.005$) and 1 month ($p < 0.0001$) postoperatively, whereas no significant difference in BCVA was observed between the two groups at 3 months postoperatively.

These characteristics make them particularly suitable for patients requiring early postoperative visual recovery in order to facilitate a quick return to social and occupational activities.

The frequency and severity of hyphema vary not only between different surgical techniques but also considerably within the same technique across various reports. This discrepancy can be attributed to three main factors. First, the definition of hyphema has not been standardized. Although many studies define hyphema as the formation of a blood niveau in the anterior chamber [88,92,93], some reports, although not explicitly stated, may include coagulated blood clots in their definition. Furthermore, hyphema does not always present as blood niveau; it can also manifest as individual red blood cells floating in the anterior chamber. This flutter-type hyphema is challenging to quantify and is often omitted from reports. However, it is believed to have an impact on visual acuity reports. Sugihara et al. reported that when flutter-type hyphema was included, hyphema was observed in 97% of cases after TMH with a nasal incision alone and in 100% of cases after TMH with both nasal and temporal incisions [97].

Second, differences in the extent of the incision may influence the frequency and severity of hyphema. In procedures like TOM and KDB, it is common to incise or excise the trabecular meshwork over a range of approximately 90–120 degrees through a single corneal port [20,21,26,56,199]. In contrast, TMH with curved hooks allows for a broader incision range. Incisions may cover 90–240 degrees using one or two corneal ports [88,89,97,200,201], whereas GATT typically involves a 360-degree incision of the trabecular meshwork [100,101,105,112].

Reports of hyphema persisting beyond 1 week postoperatively or even beyond 1 month, requiring additional anterior chamber irrigation, are more prominent in studies involving 360-degree incisions than in those involving 120-degree incisions [102,105,112,114,116]. However, reports of anterior chamber irrigation have also been noted in studies on TOM, TMH, and KDB [21,84,88,92,93], making it challenging to compare techniques based on retrospective studies.

Several studies have compared the incidence of hyphema based on different incision ranges when using TMH for AIT. Okada et al. compared the 120-degree and 180-degree incisions [200], whereas Mori et al. compared the 120-degree and 240-degree incisions [201]. In all these studies, no significant differences in IOP reduction were observed between the groups. However, broader incision ranges were associated with a higher incidence of hyphema [97,200,201]. It is important to consider the potential for delayed visual recovery when choosing surgical techniques involving extensive TM incisions.

Third, differences in IOP settings at the time of wound closure may influence the degree of reflux bleeding from the episcleral veins. Although no studies have directly compared the incidence of hyphema based on IOP levels at closure, the difference in hyphema incidence between ab externo and ab interno trabeculotomy techniques may provide some insights.

Kanda et al. compared the incidence of hyphema between AIT and exLOT and found that hyphema occurred in 33% of cases with exLOT and 11% with AIT, with the incidence being significantly lower in AIT ($p < 0.01$) [96]. The higher incidence of hyphema in exLOT may be attributed to the use of a sinusotomy, which facilitates aqueous humor filtration into the external environment, making achieving a low IOP more likely and predisposing patients to reflux bleeding. By contrast, AIT may reduce the likelihood of reflux bleeding from the episcleral veins by setting a higher IOP during hydrosealing at wound closure.

As IOP settings at the time of closure vary, depending on the surgeon's preferences and individual cases, this factor may contribute to differences in the incidence of hyphema in CB-MIGS. To reduce the frequency of hyphema, the surgeons routinely aimed to complete a procedure with relatively higher IOP settings at the time of wound closure.

In GATT combined with cataract surgery, Loayza-Gamboa et al. reported a low incidence of hyphema (9.3%) [202], whereas Cubuk et al. reported a much higher incidence (89.1%) [203]. Cubuk et al. attributed the high frequency of hyphema to the omission of filling the anterior chamber with viscoelastic material at the end of the procedure [203], suggesting that this step may help prevent postoperative hyphema [100]. Additionally, recent studies have identified exfoliation glaucoma (XFG) as a risk factor for increased hyphema incidence [84,204,205]. Many patients with glaucoma are elderly and often receive anticoagulants, while some studies have found no association between anticoagulant and hyphema incidence [84,205,206]. Chihara et al., in their study of exLOT, reported a significant difference in hyphema incidence between patients who discontinued the anticoagulant therapy and those who did not. They further noted that patients who continued anticoagulant therapy experienced prolonged hyphema, required more anterior chamber irrigation, and showed differences in early safety and complications compared with those who discontinued the therapy [207].

However, they also reported no significant difference in IOP 1 year postoperatively between the two groups. Given the potential risk of ischemic systemic diseases such as stroke or myocardial infarction, which could affect life expectancy, the decision to discontinue anticoagulant therapy remains unclear.

5.2. IOP Spikes and Corneal Edema

In addition to hyphema, corneal edema is another postoperative complication that can affect early visual recovery [29,56,68,70,75,104]. Baykara et al. reported transient corneal edema in five eyes (6.2%) in their study on the outcomes of GATT using TRAB360 (Sight Sciences Inc, Menlo Park, CA, USA) in 81 eyes with primary open-angle glaucoma (POAG) [105]. Corneal edema can occur when surgery is prolonged because of technical challenges, in cases with pre-existing endothelial dysfunction, or because of postoperative IOP spikes. Sakamoto et al. identified long axial length as a

risk factor for IOP spikes [85]. The reported incidence of IOP spikes varies by procedure, with rates of 1.0–28.9% for AIT [15–18,39,56–59,70,88,92,93,95,170–175], 0–49.0% for GATT [100,104,105,113,202,208–212], 1.1–22.2% for iStent and iStent inject [176–194], 1.9–6.5% for Hydrus [139–142,195], and 0–42.0% for ABiC [146,148,196,197]. In most cases, IOP spikes are transient and can be managed by adding IOP-lowering medications. However, in advanced cases with preoperative sensitivity loss extending near the fixation point, such spikes may exacerbate the sensitivity loss and potentially lead to permanent visual impairment. Therefore, careful consideration is necessary when determining surgical indications for such patients [52].

5.3. Cystic Macular Edema (CME)

CME is a frequently observed complication, with a reported incidence of 1.8–7.0% [31,39,55,57,65,68–70,81,86,88,93,107,213]. While some cases of CME are triggered by intraoperative inflammation, others are induced by pre-existing ischemic retinal conditions such as retinal vein occlusion or inflammatory diseases. Most cases are temporary and improve with treatment.

Luebke et al. reported clinically significant postoperative CME (defined as CME associated with visual impairment or confirmed by optical coherence tomography) in three (2.2%) of 137 eyes that underwent TOM combined with cataract surgery [213]. Of these cases, two eyes were diagnosed with exfoliation glaucoma, and one eye had primary open-angle glaucoma. Local corticosteroid therapy, topical non-steroidal anti-inflammatory agents, and systemic acetazolamide were administered for 6 weeks, resulting in the improvement of both CME and visual acuity in all three eyes.

In contrast, the study examined a control group of 1704 eyes that underwent standalone cataract surgery and reported a 1.9% incidence of CME in this group. Cataract surgery alone has been previously associated with a 20–30% incidence of CME, as detected by angiography [214], with clinically significant CME affecting visual acuity reported in 1–2.4% of cases [215,216]. These findings suggest that the cataract procedure may influence CME incidence in CB-MIGS combined with cataract surgery. In previous reports that specified whether CME occurred after standalone CB-MIGS or simultaneous cataract surgery, most cases were associated with cataract surgery [31,65,68,69,81,86,88,213].

In our study, 2 out of 46 eyes that underwent standalone AIT developed CME [55]. One case was linked to central retinal vein occlusion (CRVO), which occurred incidentally two months postoperatively, while the cause in the other case remained unclear. However, after a subtenon triamcinolone acetonide injection, visual acuity recovered to baseline. Additionally, a separate report documented one case of CME among 53 eyes that underwent standalone KDB, though the cause was unspecified [57]. Another study reported one case of CME among 22 standalone KDB cases, where the patient had a history of multiple intraocular surgeries and eventually developed uncontrollable iritis, presumed to be the cause of CME. Although the incidence of CME following standalone CB-MIGS appears to be much lower than with simultaneous cataract surgery, it remains a potential complication.

5.4. Complications Potentially Leading to Severe Visual Impairment

Although severe and permanent visual loss due to CB-MIGS complications is extremely rare, it can still occur. Kaplowitz et al. reported that [217] the incidence of hypotony < 5 mmHg after TOM was 0.09% [174,218]. Most cases are believed to result from intraoperative errors, leading to angle disinsertion. In cases where macular folds persist, treatment options, such as the injection of viscoelastic agents into the anterior chamber or laser therapy, may be considered [219].

In addition, the risk of endophthalmitis, a complication often associated with filtration surgery, is extremely low in CB-MIGS performed using small corneal incisions. One reported case of postoperative endophthalmitis caused by *Enterococcus faecalis* was detected through culture, with a meta-analysis indicating an incidence of 0.01% [220]. However, at our facility, we experienced one case of endophthalmitis [18]: a patient with severe atopic dermatitis, associated lagophthalmos, and a history of multiple intraocular surgeries. Fortunately, following vitrectomy and antibiotic therapy, the patient's vision was recovered, and the IOP was well controlled.

Patients with atopic dermatitis are highly likely to harbor resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* or methicillin-resistant *Staphylococcus epidermidis*, in their conjunctival sacs [221]. Therefore, careful monitoring for postoperative endophthalmitis is essential.

Similarly, suprachoroidal hemorrhage, another serious complication of filtration surgery, is exceedingly rare in CB-MIGS, with a reported incidence of 0.01% [222]. In a recent study, Waldner et al. compared the outcomes of superior and inferior hemi-section GATT in 297 eyes and reported two cases of suprachoroidal hemorrhage. However, both cases were rapidly resolved with appropriate management [114].

5.5. Delayed-Onset Hyphema

Delayed-onset hyphema is a complication that may occur > 2 months after surgery, often resulting in mild visual decline. Patients typically present with a sudden blurring of vision after an extended postoperative period. On slit-lamp examination, floating red blood cells (flutter-type hyphema) are often observed in the anterior chamber, and gonioscopy frequently reveals mild hyphema localized inferiorly.

To date, 12 cases of delayed-onset hyphema occurring > 2 months after TOM have been reported [223]. Other cases have also been documented, including one case occurring 6 months after GATT [100], one 13 months after iStent implantation [224], and one 4 years after TMH [225]. The proposed mechanisms for these events include an increase in episcleral venous pressure due to physical exertion or sudden decompression caused by ocular compression during sleep [223].

However, delayed-onset hyphema following CB-MIGS is generally mild and self-limiting. Management typically involves observation rather than aggressive intervention. If a transient mild increase in IOP is observed, the addition of IOP-lowering medications is recommended.

Given that the distal outflow pathways beyond the collector channels connected to the episcleral veins remain functional, recognizing the potential for delayed-onset hyphema, even in the long-term postoperative period, is essential.

5.6. Cataract Progression

Since CB-MIGS is an intraocular procedure, cataract progression leading to postoperative visual decline may occur if the crystalline lens is preserved during surgery [51,113,115,178]. Particular attention should be paid to uveitic glaucoma (UG) as it poses a higher risk of cataract progression than other types of glaucoma [113,226,227].

Kijima et al. conducted a study involving 51 eyes with UG and 51 eyes with POAG that underwent the GATT. They reported that in the UG group, 29% of cases required additional cataract surgery within 12 months postoperatively, which was significantly higher than the 1.9% in the POAG group ($p < 0.01$) [113].

When performing surgery alone for UG, informing patients about the potential risk of postoperative cataract progression is essential.

5.7. Reduction in Corneal Endothelial Cell Density (ECD)

A reduction in ECD is a potential complication that can lead to visual decline in the long-term postoperative period. Among prior reports, no CB-MIGS procedures exist aside from the CyPass supraciliary stent, which was withdrawn from the market owing to high postoperative ECD loss [228], raising significant concerns regarding substantial ECD reduction [19,88].

The authors conducted a study of 159 eyes to evaluate changes in ECD before and after TOM. The findings indicated no significant reduction in ECD over 3 years, even when measured in six peripheral directions, 3 mm from the central cornea [229]. Although procedures involving device implantation may raise concerns about accelerated ECD loss, a report by Hydrus indicated that, while surgical trauma may initially reduce ECD, the rate of ECD loss beyond 3 months postoperatively was not significantly different from that observed in standalone cataract surgery [228].

5.8. Glaucoma Progression

Although severe complications that threaten vision are rarely observed in advanced cases, there remains a significant possibility of visual decline due to glaucoma progression. Regarding long-term visual outcomes after CB-MIGS, Kitamura et al. studied 96 eyes treated with TOM alone and reported that the BCVA significantly decreased at 1 week postoperatively. However, no significant differences in BCVA were observed between the preoperative and postoperative periods from 2 weeks to 57 months [53].

Conversely, Un et al. evaluated 60 eyes that underwent TOM with a mean follow-up period of 59.4 ± 14.3 months. They reported a significant deterioration in BCVA, which worsened from a preoperative logMAR value of 0.41 ± 0.49 to 0.61 ± 0.75 at the final follow-up ($p = 0.02$). However, during follow-up, five eyes developed other ocular conditions, such as age-related macular degeneration, diabetic maculopathy, or branch retinal vein occlusion [51], leaving it unclear whether the visual decline was due to glaucoma progression alone. In a study involving 305 eyes with a follow-up period of approximately 72 months after TOM [18], a relatively high proportion of advanced cases were included, and 44% of the eyes ultimately required additional filtration surgery. Although some cases involved the re-elevation of IOP, many also exhibited progressive visual field loss or the worsening of visual acuity despite relatively good IOP control.

Notably, cases requiring additional surgery were excluded from subsequent analyses, which may have limited the ability of such studies to fully reflect the true course of visual outcomes following CB-MIGS. Moreover, several recent reports have raised concerns regarding the long-term efficacy of CB-MIGS [18,52]. This is particularly true in advanced cases with preoperative sensitivity loss near the fixation point, where the limited effectiveness of CB-MIGS renders it unsuitable. In such cases, CB-MIGS should be avoided as a treatment option [18,52,53].

6. Refractive Changes

Previous studies have highlighted that patients with glaucoma are at a higher risk of refractive shifts during cataract surgery [230,231], and the accuracy of intraocular lens (IOL) power calculation tends to be low in these patients [232,233]. Furthermore, in filtration surgery, it is common for the IOP to drop to single-digit levels, which results in postoperative axial length shortening [234].

Francis et al. conducted a study of 39 eyes that underwent TLE and 22 eyes with Baerveldt glaucoma implants. At 3 months postoperatively, the mean IOP reduction and axial length shortening were -12.8 ± 1.5 mmHg and -0.16 ± 0.03 mm in the TLE group, and -10.7 ± 1.9 mmHg and -0.15 ± 0.03 mm in the Baerveldt group, respectively. In both

groups, the axial length was significantly shorter than the preoperative values ($p < 0.001$). Additionally, the extent of axial length shortening beyond 3 months postoperatively was associated with postoperative IOP levels and the magnitude of IOP reduction ($p < 0.05$) [235].

Regarding the refractive impact of filtration surgery, Cherecheanu et al. reported on 21 eyes that underwent TLE at least 6 months after cataract surgery. They observed a $0.40 \pm 0.13\%$ reduction in axial length and an average hyperopic shift of 0.34 ± 0.44 D at 12 months postoperatively ($p = 0.002$) [236]. During filtration surgery, in addition to axial length shortening due to IOP reduction, anatomical changes such as shifts in the effective lens position (ELP) and anterior chamber depth (ACD) may also occur. Therefore, the potential for postoperative refractive abnormalities should be carefully considered when performing combined cataract and filtration surgery [235,237–239].

In CB-MIGS, the reduction in IOP is not as dramatic as that observed with filtration surgery, and the impact on axial length and refractive changes is considered less significant. However, in cases with high preoperative IOP, some patients experience IOP reductions > 10 mmHg, which could potentially influence the axial length.

In a study involving 53 eyes, Tekcan et al. reported that the mean axial length was significantly shortened after GATT combined with cataract surgery [240]. Similarly, Kanda et al. conducted a detailed analysis of IOP reduction and axial length changes in 52 eyes that underwent TMH combined with cataract surgery (TMH group) and 67 eyes that underwent cataract surgery alone (cataract group) [241]. In the TMH group, preoperative IOP decreased from 19.0 ± 6.0 mmHg to 12.2 ± 2.3 mmHg at 1 month postoperatively ($p < 0.001$), and axial length shortened from 23.98 ± 1.17 mm preoperatively to 23.82 ± 1.16 mm postoperatively. In the cataract group, the preoperative IOP decreased from 14.7 ± 2.5 mmHg to 13.3 ± 2.6 mmHg at 1 month postoperatively ($p = 0.002$), while the axial length changed from 23.79 ± 1.06 mm preoperatively to 23.68 ± 1.08 mm postoperatively.

Although no statistically significant differences in axial length were observed between the group pre- and postoperatively, the TMH group exhibited a significantly greater reduction ($p < 0.001$) when the magnitude of axial length changes between the groups was compared. Furthermore, the extent of IOP reduction was correlated with the degree of axial length shortening ($p = 0.01$) [241].

In addition to axial length, anatomical factors, such as ELP and ACD, can potentially affect refractive changes. However, CB-MIGS reduces IOP by bypassing the trabecular meshwork, causing minimal alterations to the surrounding structures. This contrasts with filtration surgery, in which significant anatomical changes are more likely. Consequently, CB-MIGS impacts on the target refractive error should be minimal, even in combined cataract surgery [242].

7. Recent Advances in Target Refractive Error in Cataract Surgery

The target refractive error in standalone cataract surgery has steadily decreased in recent years owing to advancements in diagnostic devices and IOL power calculation [243–249]. Reports from 1992 to 2006 indicated that the percentage of eyes achieving a target refractive error within ± 1.0 D is 72.3–87.0% [243–246]. However, between 2007 and 2017, it increased to 89.6–97.3% [247–249]. Regarding combined CB-MIGS and cataract surgery, Scott et al. compared 76 eyes that underwent iStent implantation combined with cataract surgery with 50 eyes that underwent cataract surgery alone. They reported that the percentage of eyes achieving a target refractive error within ± 0.50 D was 80% in both groups, while the percentage within ± 1.0 D was 95% and 94%, respectively, with no significant difference between the groups ($p > 0.05$) [250] (Table 2). Rho et al. examined 36 eyes that underwent iStent inject implantation combined with cataract surgery and found an absolute predicted error (APE) of 0.33 ± 0.26 D, with 83.3% achieving a target refractive error within ± 0.50 D.

This was comparable to a control group of 100 eyes that underwent standalone cataract surgery, with no significant differences between the groups [251]. Similarly, Ioannidis et al. evaluated 106 eyes that underwent iStent inject implantation (Glaukos Corporation, San Clemente, CA, USA) combined with cataract surgery and reported an APE of 0.36 ± 0.25 D. In this study, 73.9% of eyes achieved a target refractive error within ± 0.50 D, and 98.9% were within ± 1.0 D [252]. Furthermore, no significant correlation was observed between preoperative IOP or IOP fluctuation and the postoperative refractive target ($p > 0.05$). The refractive error following combined iStent or iStent injection implantation with cataract surgery is nearly equivalent to that following standalone cataract surgery [230]. However, it cannot be ruled out that the minimal IOP reduction achieved in these cases influenced the favorable outcomes.

Table 2. Summary of Refractive Changes After CB-MIGS Combined with Cataract Surgery.

Study	Procedure	Sample Size	APE (D)	% Within ± 0.50 D	% Within ± 1.0 D	Significant Difference vs. Standalone Cataract Surgery
Scott et al. [250]	iStent	76	Not specified	80%	95%	No
Rho et al. [251]	iStent Inject	36	0.33 ± 0.26	83.3%	97.2%	No
Ioannidis et al. [252]	iStent Inject	106	0.36 ± 0.25	73.9%	98.9%	No
Luebke et al. [213]	TOM	137	0.53 ± 0.44	60.6%	86.9%	No
Sieck et al. [242]	KDB	76	Not specified	73.7%	93.4%	No
Tekcan et al. [240]	GATT	53	0.38 ± 0.32 (SRK/T) 0.36 ± 0.30 (Barrett) 0.32 ± 0.28 (Hill-RBF) 0.30 ± 0.28 (Kane)	66.0% (SRK/T) 69.8% (Barrett) 73.6% (Hill-RBF) 79.2% (Kane)	100.0%	Not Compared
Kanda et al. [241]	TMH	52	0.46 ± 0.42 (Barrett) 0.62 ± 0.55 (SRK/T) 0.76 ± 0.57 (Haigis)	63.5% (Barrett) 57.7% (SRK/T) 38.5% (Haigis)	Not specified	Yes (P = 0.04 for Barrett, P = 0.01 for SRK/T)

APE = Absolute Prediction Error, TOM = Trabectome, KDB = Kahook Dual Blade, GATT = gonioscopy-assisted transluminal trabeculotomy, TMH = Tanito Microhook, SRK/T = Sanders-Retzlaff-Kraft/theoretical, Barrett = Barrett Universal II, Hill-RBF: Hill-radial basis function.

In contrast to the iStent, AIT often achieves greater IOP reduction. Luebke et al. reported that the APE in 137 eyes that underwent TOM combined with cataract surgery was 0.53 ± 0.44 D. No significant difference was observed compared with the control group, which underwent cataract surgery alone, with 86.9% of eyes achieving a target refractive error within ± 1.0 D [213]. However, in three eyes (2.2%), the refractive error exceeded ± 2.0 D.

This study, published in 2015, used the SRK/T formula for IOL power calculation in 131 eyes with axial lengths between 21.0 and 26.0 mm, while the Haigis formula was used for six eyes with axial lengths > 26.0 mm. The authors suggested that using formulas that are less affected by axial length might have yielded different results.

Similarly, Sieck et al. reported that the target refractive error in eyes undergoing KDB combined with cataract surgery was within ± 0.5 D in 73.7% of cases and within ± 1.0 D in 93.4%, with no significant difference compared to cataract surgery alone [242]. In a multi-variate analysis of risk factors for refractive errors exceeding ± 1.0 D, KDB combined with cataract surgery was not identified as a risk factor (adjusted odds ratio: 0.5, 95% CI: 0.2–1.2, $p = 0.32$). However, a higher preoperative IOP was identified as a significant risk factor (adjusted odds ratio: 1.6, 95% CI: 0.8–3.5, $p = 0.03$). The authors speculated that axial length changes related to IOP reduction may have influenced these results, although postoperative axial length measurements were not included in the study. For GATT, which involves a 360° incision in the trabecular meshwork, Tekcan et al. analyzed 53 eyes that underwent GATT combined with cataract surgery. They reported significant postoperative axial length shortening; however, the APE using the Barrett Universal II formula was 0.36 ± 0.30 D [240]. In a comparative study of multiple procedures, Shaheen et al. evaluated 150 eyes that underwent angle incision surgery (84 GATT and 66 non-GATT), 395 eyes that underwent

stent implantation (316 iStent and 79 Hydrus), and 7815 eyes that underwent cataract surgery alone. At 1 month postoperatively, the spherical equivalent was -0.36 ± 0.91 D for angle incision surgery, -0.31 ± 0.85 D for stent implantation, and -0.39 ± 0.88 D for standalone cataract surgery ($p = 0.019$). Although a slight statistical difference was observed between the groups, the authors concluded that this was unlikely to be clinically significant [253].

Most studies suggest that the impact of CB-MIGS combined with cataract surgery on postoperative target refractive error is minimal, with little difference compared with cataract surgery alone. However, Kanda et al. compared 52 eyes that underwent TMH combined with cataract surgery (TMH group) with 67 eyes that underwent cataract surgery alone (CAT group) [241]. At 1 month postoperatively, axial length was shortened by 0.16 mm in the TMH group and by 0.11 mm in the CAT group. The APE with the Barrett formula was 0.46 ± 0.42 D and 0.33 ± 0.24 D, respectively, while with the SRK/T formula, it was 0.62 ± 0.55 D and 0.42 ± 0.32 D, respectively. The APE was significantly larger in the TMH group compared with the CAT group ($p = 0.04$ for Barrett; $p = 0.01$ for SRK/T). For the TMH group, the APE with different IOL power calculation formulas was 0.46 ± 0.42 D for Barrett, 0.62 ± 0.55 D for SRK/T, and 0.76 ± 0.57 D for Haigis. The refractive predicted error (RPE) was 0.09 ± 0.62 D, 0.34 ± 0.76 D, and 0.65 ± 0.69 D, respectively, with Barrett yielding the lowest RPE. Compared with the CAT group, the TMH group showed a greater hyperopic refractive error, which the authors speculated could be influenced by changes in IOP and axial length. However, the magnitude of the refractive error was not significant enough to undermine the validity of TMH combined with cataract surgery. Considering the findings of Sieck et al. that a high preoperative IOP is a risk factor for postoperative refractive error [242], it may be advisable to select IOLs with a more myopic refractive target for patients with a high preoperative IOP, particularly when a significant reduction in IOP is anticipated. Furthermore, when performing CB-MIGS combined with cataract surgery, it is preferable to use IOL power calculation formulas that are less influenced by the corneal refractive power and axial length. The Universal II (Barrett) formula, which has been increasingly used in recent years, is less affected by axial length [254–257] and may be a suitable choice for CB-MIGS combined with cataract surgery. Moreover, eyes with extremely long axial lengths were often excluded from previous studies, as such eyes are known risk factors for the development and progression of glaucoma [258], frequently necessitating glaucoma surgery. Investigating the impact of IOP and axial length changes on the refractive error after CB-MIGS combined with cataract surgery is crucial and warrants further research.

7.1. Surgically Induced Astigmatism (SIA)

In filtration surgery, when cataract surgery is performed simultaneously, the incidence of postoperative refractive abnormalities and SIA is reportedly higher [237]. Additionally, SIA is induced in the direction of the surgical flap [259–261]. The possible mechanism of SIA after TLE may be tissue contraction around the TLE site secondary to extensive scleral cautery and suture, the removal of the second scleral flap, the wound-healing process of the subconjunctiva [261], and corneal steepening provoked by the pressure of a large drainage bleb under the eyelid [262]. Delbeke et al. reported that lower IOPs achieved after filtration surgery were associated with higher SIA and worse visual acuity [263].

In contrast, regarding exLOT, which requires conjunctival incisions and flap creation similar to TLE and CB-MIGS, which are performed using corneal incisions, Kanda et al. compared 52 eyes treated with TMH with 42 eyes treated with exLOT [96]. In the TMH, two corneal ports were created at the 1–2 o'clock, and 10–11 o'clock positions, and the trabecular meshwork was incised at 120–150°. At 1 week postoperatively, the SIA was 0.34 ± 0.67 diopters (D) (88 ± 18 de-

degrees) in the TMH group and 0.28 ± 1.06 D (96 ± 20 degrees) in the exLOT group, with a significant difference observed between the two groups ($p = 0.003$). However, after 1 month, no significant differences were observed between the two groups, and at 3 months postoperatively, the residual SIA was minimal in both groups, measuring 0.06 ± 0.59 D (90 ± 17 degrees) in the TMH group and 0.07 ± 0.77 D (118 ± 18 degrees) in the exLOT group.

Although a scleral incision in exLOT results in unavoidable SIA during the first postoperative week, this is considered a temporary complication that resolves to a negligible level within 1 month. Similar findings were reported by Tanito et al. [264].

Numerous studies have reported the impact of CB-MIGS on SIA [241,251,252,265–267]. Regarding investigations involving the insertion of two iStent inject devices, Ioannidis et al. reported that in 106 eyes that underwent combined cataract surgery, no postoperative worsening of astigmatism was observed, and 73.8% of cases had residual refractive astigmatism of ≤ 0.5 D [252]. Rho et al. compared combined cataract surgery with cataract surgery alone and found no significant differences in SIA between the two groups [251].

Regarding AIT, Kanda et al. reported that in 52 eyes that underwent TMH combined with cataract surgery, the SIA was 0.22 ± 0.85 D (78 ± 19 degrees), which was not significantly different from the SIA in the control group of 67 eyes that underwent only cataract surgery [241]. Similarly, Hirabayashi et al. reported comparable findings in a study using the KDB [265].

Regarding SIA after ABiC, Byszewska et al. examined 37 eyes that underwent ABiC combined with cataract surgery. They reported that the centroid of astigmatism (mean cylinder with axis) was 0.79 D ($172^\circ \pm 1.10$) preoperatively, 0.75 D ($166^\circ \pm 1.01$) at 6 months postoperatively, and 0.64 D ($164^\circ \pm 1.11$) at 24 months postoperatively. No visually significant astigmatism was observed, the mean direction of astigmatism remained stable, and the degree of astigmatism showed no significant changes throughout the 24-month observation period [266].

Furthermore, Wilczynski et al. investigated the differences in SIA caused by different cataract surgical techniques. They compared 58 eyes in which IOLs were implanted through a 1.8 mm temporal corneal incision with coaxial CB-MIGS (coaxial group) and 50 eyes in which IOLs were implanted using a bimanual technique through a 1.7 mm corneal incision and a 1.5 mm side port for an irrigating chopper, followed by CB-MIGS (bimanual group). Based on vector analysis, the SIA was 0.42 ± 0.29 in the coaxial group and 0.50 ± 0.24 in the bimanual group, with no significant difference between the two groups ($p > 0.05$) [267].

Thus, because CB-MIGS is performed using small corneal incisions, SIA caused by the corneal incisions is minimal. Even in combined surgeries, accounting for additional SIA from CB-MIGS beyond the SIA associated with cataract surgery is considered unnecessary [242,265].

7.2. Using Toric IOLs During CB-MIGS Combined with Cataract Surgery

Tanito et al. compared the SIA at 3 months postoperatively across four surgical procedures, TLE, EX-PRESS® shunt (EXP), exLOT, and TMH, with 20 eyes analyzed for each procedure. The reported SIA values were as follows: 1.01 ± 2.27 D ($56 \pm 26^\circ$) for TLE, 0.62 ± 1.20 D ($74 \pm 24^\circ$) for EXP, 0.23 ± 1.04 D ($112 \pm 17^\circ$) for exLOT, and 0.12 ± 0.75 D ($97 \pm 21^\circ$) for TMH. TLE showed a significantly greater SIA than other procedures ($p = 0.0001$) [265].

Additionally, TLE exhibited significant variability in SIA between cases, making it nearly impossible to predict SIA. Consequently, toric IOLs are rarely used in combined cataract surgery. In contrast, for CB-MIGS, accounting for SIA from the procedure itself, beyond the SIA caused by cataract surgery, is unnecessary. Therefore, the use of toric IOLs during CB-MIGS combined with cataract surgery should be considered in cases of pre-existing regular corneal astigmatism.

Ichioaka et al. investigated the outcomes of toric IOL implantation in eyes with pre-existing regular corneal astigmatism $> 1.5\text{D}$. They compared nine eyes (nine patients) implanted with toric IOLs during combined cataract surgery with an iStent (toric group) and nine eyes (nine patients) implanted with non-toric IOLs (non-toric group) [268]. In the toric group, uncorrected visual acuity (UCVA) improved to -0.21 ± 0.06 (logMAR) ($p = 0.02$), and refractive astigmatism improved to $+1.72 \pm 0.25\text{D}$ ($p = 0.0039$). Furthermore, 78% of eyes in the toric group achieved a refractive astigmatism of -1.0D , compared with only 11% in the non-toric group.

Similarly, Takai et al., from the same group, reported on 10 eyes (10 patients) with pre-existing regular corneal astigmatism $> 1.5\text{D}$. They compared eyes implanted with toric IOLs during combined cataract surgery with TMH (toric group) with eyes implanted with non-toric IOLs (non-toric group) [269]. At 3 months postoperatively, the mean UCVA in the toric group was 0.23 ± 0.25 (logMAR), significantly better than 0.45 ± 0.26 (logMAR) in the non-toric group ($p < 0.05$). The mean absolute residual refractive cylinder in the toric group was $1.30 \pm 0.68\text{D}$, which was significantly smaller than $2.25 \pm 0.62\text{D}$ in the non-toric group ($p < 0.05$). However, SIA was $0.77 \pm 0.43\text{D}$ in the toric group and $0.60 \pm 0.32\text{D}$ in the non-toric group, with no significant difference observed. Based on these results, the authors concluded that while toric IOLs improve outcomes compared with non-toric IOLs, some residual astigmatism remains.

Ichioaka et al. reported similar findings under comparable conditions [270]. Their results slightly favored the toric group compared with those of Takai et al., suggesting that toric IOL implantation may lead to better visual outcomes in eyes with pre-existing regular corneal astigmatism.

SIA includes not only corneal astigmatism but also factors such as toric IOL rotation, tilt, or decentration of the lens capsule or IOL, and unknown ocular components [271]. In eyes with high myopia and loose capsules or in those with zonular weakness associated with XFG, the IOL and capsule tend to rotate and tilt [271,272]. In Takai et al.'s study of the 10 patients in the toric group, two patients with high myopia and XFG exhibited a slight worsening of absolute refractive astigmatism postoperatively compared to preoperative values. Although postoperative toric IOL rotation was not assessed, making the details unclear, the authors speculated that IOL rotation or tilt may have occurred in these two cases.

Whether the procedural steps involved in CB-MIGS or the reduction in IOP contribute to toric IOL rotation or tilt remains uncertain, as there is currently insufficient research on this topic. Further studies involving larger numbers of patients are required to clarify this issue. However, based on previous reports, the use of toric IOLs during CB-MIGS combined with cataract surgery appears to be a reasonable option for patients with significant corneal astigmatism.

In contrast, in patients with high myopia or XFG—conditions that are common indications for glaucoma surgery—preoperative astigmatism may not be effectively corrected. Moreover, if these patients undergo TLE, the resulting optical aberrations could negatively affect their vision [269]. Therefore, the decision to use toric IOLs in such cases requires the careful consideration of factors such as patient age, disease stage, and disease type.

8. Effectiveness in Slowing the Progression of Visual Field Defects

Numerous studies have reported that the postoperative progression of visual field defects can be significantly delayed in filtration surgery [5,273–276]. In contrast, Bao et al. conducted a long-term study with an average follow-up period of 8 years (with a minimum of 6 years of observation) and reported that exLOT was inferior to TLE regarding both IOP control and effectiveness in slowing the progression of visual field defects [277].

Several studies have examined the effect of CB-MIGS in slowing the progression of visual field defects. These studies consistently reported that the progression rate after CB-MIGS was slow; however, most were short term and retrospective [92,193,278,279]. Kitamura et al. conducted a relatively long-term study evaluating the progression of visual field defects over 4 years after trabeculotomy using TOM in 250 eyes (POAG, 63%; XFG, 16%; others, 21%) [53].

Using the Humphrey visual field analyzer SITA-standard 24-2 program (HFA24-2), they reported that the mean deviation (MD) values were 10.5 ± 7.0 dB preoperatively and 11.4 ± 7.8 dB at 4 years postoperatively, with no significant worsening observed at any observation point compared to preoperative values. However, 62% of the patients underwent simultaneous cataract surgery, and the number of cases observed after the third postoperative year was less than half of the initial sample size, which requires a careful interpretation of the results.

Weber et al. reported on 264 eyes (POAG: 64%; XFG: 20%; others: 16%) with a mean follow-up period of 45.3 months after trabeculotomy using the TOM [52]. The rate of visual field progression remained relatively stable over 5 years, with MD values measured using the HFA24-2 reported as -11.1 dB preoperatively and -11.0 dB at 4 years postoperatively, showing no significant worsening.

Notably, this study maintained a relatively large sample size for long-term follow-up compared with other reports, with 142 eyes analyzed at 3 years postoperatively, 97 eyes at 4 years, and 68 eyes at 5 years. However, 74 patients (28.0%) required additional glaucoma surgery at a mean of 18.3 months postoperatively; these patients were excluded from further analysis, introducing a potential selection bias.

In addition, 40% of the patients underwent TOM alone, whereas 60% underwent combined cataract surgery. At all time points during the follow-up period, no significant differences in the MD values were observed between the two groups, except at the final five-year follow-up. At this time point, the MD value in the combined cataract surgery group (-10.35 dB) was significantly better than in the TOM-alone group (-12.04 dB) ($p = 0.016$).

Regarding KDB, Vasu et al. examined 90 eyes and reported MD values of -3.56 dB preoperatively and -5.32 dB at 6 years postoperatively using HFA24-2 [280]. Although a statistically significant difference was observed ($p = 0.02$), the progression rate was not considered to be clinically rapid.

Regarding ABiC, Koerber et al. reported on 27 eyes treated with the iTrack micro-catheter, evaluating visual field changes over a maximum of 4 years [157]. The MD values using HFA24-2 were -7.86 ± 6.90 dB preoperatively and -6.95 ± 5.72 dB postoperatively, with no significant worsening observed ($p = 0.634$). However, caution is warranted when interpreting these results because of unclear details regarding the final observation points and the inclusion of cases that underwent combined cataract surgery.

In contrast, prospective randomized controlled trials (RCTs) have reported changes in the visual field after Hydrus device implantation. Montesano et al. conducted a multi-center RCT comparing a group of 352 eyes that underwent combined Hydrus and cataract surgery (Hydrus group) with a group of 165 eyes that underwent cataract surgery alone (CAT group). The study used 5-year visual field data collected during the prospective, randomized, multicenter HORIZON trial. The MD slope > 5 years in the Hydrus group was -0.26 dB/year, which was significantly slower than -0.49 dB/year in the CAT group (95% confidence interval [CI]: $-0.63, -0.34$; $p = 0.014$) [281].

However, differences in mean daytime IOP control accounted for only 17% of the difference in progression rates between the groups (-0.04 dB/year, 95% CI: $-0.06, -0.02$; $p < 0.0001$), leaving a large and significant unexplained difference in progression rates (-0.19 dB/year, 95% CI: $-0.37, -0.02$; $p = 0.0328$, comprising 83% of the total difference).

One potential explanation for this residual difference is that the reduction in diurnal IOP fluctuations achieved by the device placement may have contributed to the slower progression rate. However, this hypothesis needs to be confirmed through 24-hour IOP monitoring [282].

In another report on micro-implantable devices, Gillmann et al. conducted a meta-analysis of 1115 eyes that underwent iStent surgery. The weighted mean follow-up period was 37.9 months (range: 12–96 months), and the baseline weighted mean IOP was 19.0 ± 3.1 mmHg, which showed a mean reduction of 26.6% at the end of follow-up (range: 15.2–42.3%). The weighted mean MD values during the follow-up period changed from -5.76 ± 5.68 dB to -5.91 ± 5.82 dB, with an overall MD slope (MDS) of -0.024 ± 0.34 dB/year. In the cataract-combined surgery group, the MDS was -0.01 ± 0.42 dB/year, while the iStent-alone group was -0.07 ± 0.62 dB/year [283].

This rate of progression is comparable to that reported in normal, non-glaucomatous eyes [284,285] and slower than that reported in glaucomatous eyes treated with medications [284–288], making it a remarkable finding. Gillmann et al. hypothesized that this result may be attributed to a reduction in IOP fluctuations achieved by surgery and improved patient compliance due to early surgical intervention.

However, issues such as the reliability of visual field test results, the impact of disease severity, and the exclusion of cases requiring additional glaucoma surgery introduce several unavoidable biases. Whether device implantation has a greater effect in slowing visual field progression than incisional procedures remains unclear owing to the lack of reliable comparative studies. Although a definitive interpretation cannot be made yet, future research is needed to clarify whether placing a stent to maintain a stable, enclosed space within Schlemm's canal is superior to incising and opening the canal or whether differences in diurnal IOP fluctuations between the two techniques play a role.

Regarding differences in visual field preservation based on disease type, Weber et al. reported 168 eyes with POAG and 52 eyes with XFG in a study with a mean follow-up of 45.3 months after TOM. They found no significant difference in the rate of visual field progression between the two groups during the observation period [52]. However, a separate report investigating the rate of visual field progression over 5.8 years in untreated cases found that XFG progressed at a rate of -1.13 dB/year, which was faster than the rates for normal-tension glaucoma (-0.22 dB/year) and POAG (-0.46 dB/year) [289]. These findings suggest that XFG requires careful monitoring as a high-risk disease.

In our analysis, the cumulative survival rate for 63 eyes with XFG treated with TOM was relatively favorable during the first 2–3 years postoperatively but showed a sharp decline after 4 years. While some cases involve IOP elevation, many others experience the progression of visual field defects or the deterioration of visual acuity despite relatively good IOP control, necessitating additional filtration surgery and ultimately being deemed treatment failures [18].

As a limitation of LOT-type surgeries for XFG, Honjo et al. showed that visual field defects may progress even when IOP is well controlled after exLOT [290], and Konstas et al. suggested that factors other than IOP may contribute to disease progression [291]. For XFG, even when IOP is relatively well controlled following CB-MIGS, a close follow-up with scheduled visual field testing at shorter intervals is necessary to carefully monitor disease progression.

9. Conclusions

Numerous studies have shown that CB-MIGS has a strong safety profile, with a low incidence of complications leading to severe visual impairment. Additionally, many studies support its effectiveness in preserving visual acuity and slowing the progression

of visual field defects. However, recent reports have raised concerns about its long-term efficacy. In advanced cases where preoperative sensitivity near the fixation point has already deteriorated, there is a risk of irreversible postoperative vision loss, highlighting the need for careful patient selection. While some studies have conducted relatively long follow-ups, most are retrospective, and in many cases, fewer than half of the preoperative cohort have data available beyond three to four years postoperatively. Given the current research, it remains difficult to definitively confirm that CB-MIGS provides sustained benefits in preserving visual acuity and slowing visual field progression. Moving forward, long-term prognostic reports from prospective randomized controlled trials (RCTs) are urgently needed.

Author Contributions: Conceptualization, M.K.; methodology, M.K.; validation, M.K.; formal analysis, M.K.; investigation, M.K. and N.S.; resources, M.K.; data curation, M.K.; writing—original draft preparation, M.K. and N.S.; writing—review and editing, M.K.; visualization, M.K.; supervision, M.K. and N.S.; project administration, M.K. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

ABiC	Ab interno canaloplasty
ACD	Anterior chamber depth
AIT	Ab interno trabeculotomy
APE	Absolute predicted error
BCVA	Best-corrected visual acuity
CAT	Cataract surgery alone
CB-MIGS	Canal-based minimally invasive glaucoma surgery
CI	Confidence interval
CME	Cystic macular edema
ELP	Effective lens position
ExLOT	Trabeculotomy ab externo
GATT	Grover introduced gonioscopy-assisted transluminal trabeculotomy
IOL	Intraocular lens
IOP	Intraocular pressure
KDB	Kahook dual blade
MD	Mean deviation
MIGS	Minimally invasive glaucoma surgery
POAG	Primary open-angle glaucoma
RCT	Randomized controlled trial
RPE	Refractive predicted error
SIA	Surgically induced astigmatism
TLE	Trabeculectomy
TMH	Tanito Microhook
TOM	Trabectome
UCVA	Uncorrected visual acuity
XFG	Exfoliation glaucoma

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Article

Clinical Practice Preferences for Glaucoma Surgery in Japan in 2024

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Abstract

Objectives: This study evaluated the clinical preferences of glaucoma specialists regarding glaucoma surgery and postoperative management in Japan in 2024. **Methods:** A survey about clinical practice preferences regarding glaucoma surgery and postoperative care was administered among 50 glaucoma specialists who were councilors in the Japan Glaucoma Society. **Results:** Minimally invasive glaucoma surgery (MIGS) plus phacoemulsification was the most preferred procedure for nonoperated mild to moderate cases of primary open-angle glaucoma (POAG) (94.6%) and normal tension glaucoma (NTG) (67.3%) associated with cataract. Microhook surgery was the most preferred among the MIGS procedures. Meanwhile, PreserFlo MicroShunt (PMS) surgery is emerging as a popular option for cases of POAG and NTG, especially in advanced-stage pseudophakic eyes that underwent prior corneal incision phacoemulsification (40.1%). Long-tube shunt surgeries were predominantly preferred for POAG after two failed trabeculectomies (69.4%) and for neovascular glaucoma with prior vitrectomy after a failed trabeculectomy (73.0%). Among long-tube shunt surgeries, the Ahmed glaucoma valve (AGV) was preferred over the Baerveldt glaucoma implant. Trabeculectomy required the most frequent follow-up visits within the first postoperative year, whereas PMS and long-tube shunt surgeries required comparatively fewer follow-up visits. Overall, MIGS involved less frequent follow-up visits versus filtering surgeries. **Conclusions:** MIGS is currently the procedure of choice for primary glaucoma surgery in Japan. Among glaucoma specialists of the Japan Glaucoma Society, PMS surgery is becoming popular for cases of POAG and NTG. Refractory glaucoma is commonly treated with long-tube shunt surgeries, especially the AGV.

Keywords: glaucoma surgery; surgical preferences; trabeculectomy; PreserFlo MicroShunt; long-tube shunt surgery; minimally invasive glaucoma surgery

1. Introduction

Trabeculectomy is a filtering surgery widely performed worldwide for cases of glaucoma with medically uncontrollable intraocular pressure (IOP), but is commonly associated with severe postoperative complications related to visual impairment [1]. Trabeculectomy is highly effective in lowering IOP; however, due to its high complication rate and complex postoperative management, it is a procedure that is preferably avoided when possible. To address this, less invasive surgical techniques have been recently developed, with a variety of procedures now available. For example, the iStent inject W (Glaukos Corporation, San Clemente, CA, USA) and the Hydrus Microstent (HMS) (Alcon Inc., Geneva, Switzerland) were newly approved for use in Japan. The iStent inject W was first approved in combination with phacoemulsification in October 2019, and then as a standalone procedure in July

2024. Similarly, the HMS plus phacoemulsification was approved in June 2024. Therefore, minimally invasive glaucoma surgery (MIGS), which includes these procedures, has gained global popularity as a primary option for glaucoma surgery [2–6] due to its favorable safety profile and shorter recovery time [7,8]. Meanwhile, the PreserFlo MicroShunt (PMS) (Santen Pharmaceutical Company, Osaka, Japan) is a microinvasive filtration surgical device that was approved for use in Japan in February 2022. PMS surgery is a type of glaucoma filtration surgery that is less invasive than trabeculectomy because it does not require the creation of a scleral flap or iridectomy [9]. Additionally, long-tube shunt surgeries using a Baerveldt glaucoma implant (BGI) (Johnson & Johnson Vision, Jacksonville, FL, USA) and an Ahmed glaucoma valve (AGV) (New World Medical, Rancho Cucamonga, CA, USA) have also become increasingly popular for refractory glaucoma [4,10].

Several studies have surveyed surgical preferences for glaucoma in the United States and the United Kingdom [11–13], but no recent reports are available. In Japan, surgical preferences for glaucoma have not been recently evaluated. In 2019, we previously reported the clinical preferences of Japan Glaucoma Society specialists regarding glaucoma surgery and postoperative management, but this was not updated with recent advancements in the field [4]. Although recent studies have shown trends in surgical procedures for glaucoma in Japan using a nationwide administrative database [14,15], these do not capture the current specific clinical preferences of glaucoma specialists. Considering the rapid advancements in glaucoma surgery over the past five years, especially with the emergence of new surgical options, this study aimed to evaluate the updated clinical preferences of glaucoma specialists regarding the surgical and postoperative management of glaucoma in Japan in 2024. Given the lack of recent reports from the United States and the United Kingdom, this report provides a particularly valuable reference for surgical decision-making and the postoperative management of glaucoma in similar clinical scenarios.

2. Materials and Methods

Institutional review board approval was waived by the ethics committee of the University of Fukui Hospital, Fukui, Japan, because patients were not involved. Survey questions were emailed to 50 glaucoma specialists who were council members of the Japan Glaucoma Society in November 2024. Participants were asked about their years of experience as ophthalmologists and whether they were actively performing glaucoma surgeries at the time of the survey. Active surgeons were then presented with 20 clinical scenarios and asked to indicate their preferred surgical approach for each (Supplemental Table S1). Among these questions, the severity of glaucoma was classified based on the mean deviation (MD) score: mild to moderate ($MD > -12$ dB) and advanced ($MD \leq -12$ dB). Each answer was assigned 1 point; if a participant selected multiple answers to a question, this 1 point was divided by the number of answers. Finally, participants were asked about the frequency of follow-up visits for each type of glaucoma surgery during the first postoperative year.

3. Results

The survey was completed by all 50 glaucoma specialists, with a mean of 30.5 ± 5.8 years (range: 14–42) of experience as ophthalmologists. Among them, 42 were actively performing glaucoma surgery at the time of the survey; these specialists answered questions regarding their preferences for glaucoma surgery. Supplemental Table S2 summarizes the overall surgical preferences for each type of glaucoma across all clinical settings.

3.1. Surgical Choices for Primary Open-Angle Glaucoma

Table 1 shows participants' surgical choices for primary open-angle glaucoma (POAG) across eight clinical settings.

Table 1. Surgical preferences for primary open-angle glaucoma.

Type of Glaucoma Surgery	Unoperated Eyes with Cataract		Unoperated Eyes Without Cataract		Pseudophakic Eyes with a Corneal Incision Phaco		Pseudophakic Eyes with a Previous Failed Trabeculectomy		Pseudophakic Eyes with Two Failed Trabeculectomies	
	Mild to Moderate (%)	Advanced (%)	Mild to Moderate (%)	Advanced (%)	Mild to Moderate (%)	Advanced (%)	Advanced (%)	Advanced (%)	Advanced (%)	Advanced (%)
Microhook+Phaco	51.8	24.8	2.4	2.4	0.0	0.0	0.0	0.0	0.0	0.0
Microhook	0.0	0.0	50.8	5.9	48.4	4.7	0.8	0.8	0.8	0.8
iStent inject W+Phaco	18.1	3.3	1.2	1.2	0.0	0.0	0.0	0.0	0.0	0.0
iStent inject W	0.0	0.0	0.8	0.8	0.8	0.8	0.0	0.0	0.0	0.0
KDB+Phaco	7.1	3.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
KDB	0.0	0.0	9.5	0.0	7.2	0.0	0.0	0.0	0.0	0.0
Suture trabeculectomy+Phaco	6.7	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Suture trabeculectomy	0.0	0.0	6.7	1.6	7.9	1.6	0.8	0.8	0.6	0.6
HMS+Phaco	6.1	2.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Other MIGS+Phaco	4.8	1.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Other MIGS	0.0	0.0	6.0	0.8	4.8	0.8	0.0	0.0	0.0	0.0
PMS+Phaco	4.8	28.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
PMS	0.0	1.6	17.5	32.9	23.4	40.1	18.2	18.2	7.1	7.1
Trabeculectomy+Phaco	0.0	20.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Trabeculectomy	0.6	9.7	5.1	52.0	7.5	49.6	57.2	57.2	15.7	15.7
ExPRESS+Phaco	0.0	2.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
ExPRESS	0.0	0.0	0.0	2.4	0.0	2.4	2.4	2.4	0.0	0.0
AGV	0.0	0.0	0.0	0.0	0.0	0.0	10.7	10.7	49.0	49.0
BGI	0.0	0.0	0.0	0.0	0.0	0.0	4.8	4.8	20.4	20.4
Bleb revision or needling	0.0	0.0	0.0	0.0	0.0	0.0	5.1	5.1	1.6	1.6
MP-TSCPC	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.8	4.8

AGV, Ahmed glaucoma valve; BGI, Baerveldt glaucoma implant; HMS, Hydrus Microstent; KDB, Kahook dual blade; MIGS, minimally invasive glaucoma surgery; MP-TSCPC, micropulse transscleral cyclophotocoagulation; Phaco, phacoemulsification; PMS, PreserFlo MicroShunt.

3.1.1. Mild to Moderate Cases ($MD > -12$ dB)

For unoperated eyes with cataract, the most preferred procedure was microhook plus phacoemulsification (51.8%), followed by the iStent inject W plus phacoemulsification (18.1%). Overall, 94.6% preferred MIGS plus phacoemulsification as the first-line surgical approach for mild to moderate cases of POAG. For unoperated eyes without cataract and pseudophakic eyes, microhook surgery alone was the most commonly chosen procedure (50.8% and 48.4%, respectively) followed by PMS surgery alone (17.5% and 23.4%, respectively).

3.1.2. Advanced Cases ($MD \leq -12$ dB)

For unoperated eyes with cataract, the most preferred procedure was MIGS plus phacoemulsification (36.7%), but PMS surgery plus phacoemulsification was frequently selected as well (28.8%). For unoperated eyes without cataract, trabeculectomy alone was the predominant choice (52.0%). For pseudophakic eyes, the most commonly selected procedure was trabeculectomy (49.6%), followed by PMS surgery (40.1%). For pseudophakic eyes with a previous failed trabeculectomy, trabeculectomy remained the most frequently selected option (57.2%), but after two failed trabeculectomies, long-tube shunt surgeries were chosen, with a preference for the AGV (49.0%) followed by the BGI (20.4%).

3.2. Surgical Choices for Normal Tension Glaucoma

Table 2 summarizes participants' surgical preferences for normal tension glaucoma (NTG) across six clinical settings.

Table 2. Surgical preferences for normal tension glaucoma.

Type of Glaucoma Surgery	Unoperated Eyes with Cataract		Unoperated Eyes Without Cataract	Pseudophakic Eyes with a Corneal Incision Phaco	Pseudophakic Eyes with a Previous Failed Trabeculectomy	Pseudophakic Eyes with Two Failed Trabeculectomies
	Mild to Moderate (%)	Advanced (%)	Advanced (%)	Advanced (%)	Advanced (%)	Advanced (%)
Microhook+Phaco	37.5	21.6	1.2	0.0	0.0	0.0
Microhook	0.0	0.0	4.5	0.8	0.8	0.8
iStent inject W+Phaco	14.5	4.1	1.2	0.0	0.0	0.0
iStent inject W	0.0	0.0	0.8	0.8	0.0	0.0
KDB+Phaco	4.8	2.4	0.0	0.0	0.0	0.0
Suture trabeculectomy+Phaco	2.0	0.6	0.0	0.0	0.0	0.0
Suture trabeculectomy	0.0	0.0	0.8	0.8	0.8	0.8
HMS+Phaco	6.1	2.4	0.0	0.0	0.0	0.0
Other MIGS+Phaco	2.4	0.0	0.0	0.0	0.0	0.0
Phaco only	2.4	0.0	0.0	0.0	0.0	0.0
PMS+Phaco	20.2	17.3	0.0	0.0	0.0	0.0
PMS	2.4	0.8	19.1	25.8	11.1	9.9
Trabeculectomy+Phaco	7.1	36.3	0.0	0.0	0.0	0.0

Table 2. Cont.

Type of Glaucoma Surgery	Unoperated Eyes with Cataract		Unoperated Eyes Without Cataract	Pseudophakic Eyes with a Corneal Incision Phaco	Pseudophakic Eyes with a Previous Failed Trabeculectomy	Pseudophakic Eyes with Two Failed Trabeculectomies
	Mild to Moderate (%)	Advanced (%)	Advanced (%)	Advanced (%)	Advanced (%)	Advanced (%)
Trabeculectomy	0.6	12.1	72.4	69.4	75.0	18.7
ExPRESS+Phaco	0.0	2.4	0.0	0.0	0.0	0.0
ExPRESS	0.0	0.0	0.0	2.4	2.4	2.4
AGV	0.0	0.0	0.0	0.0	2.4	34.1
BGI	0.0	0.0	0.0	0.0	2.4	20.6
Bleb revision or needling	0.0	0.0	0.0	0.0	5.1	9.5
MP-TSCPC	0.0	0.0	0.0	0.0	0.0	3.2

AGV, Ahmed glaucoma valve; BGI, Baerveldt glaucoma implant; HMS, Hydrus Microstent; KDB, Kahook dual blade; MIGS, minimally invasive glaucoma surgery; MP-TSCPC, micropulse transscleral cyclophotocoagulation; Phaco, phacoemulsification; PMS, PreserFlo MicroShunt.

3.2.1. Mild to Moderate Cases ($MD > -12$ dB)

For unoperated eyes with cataract, MIGS plus phacoemulsification was preferred by 67.3%. Among the different types of MIGS, the most preferred was microhook surgery plus phacoemulsification (37.5%), followed by PMS surgery plus phacoemulsification (20.2%), while trabeculectomy plus phacoemulsification was less frequently preferred (7.1%).

3.2.2. Advanced Cases ($MD \leq -12$ dB)

For unoperated eyes with cataract, trabeculectomy plus phacoemulsification was the most preferred procedure (36.3%), followed by microhook surgery plus phacoemulsification (21.6%). In this scenario, 31.1% generally preferred MIGS plus phacoemulsification. For unoperated eyes without cataract, the most dominant choice was trabeculectomy alone (72.4%) followed by PMS surgery alone (19.1%). For pseudophakic eyes, the preferred procedure was trabeculectomy (69.4%) followed by PMS surgery (25.8%). For pseudophakic eyes with a previous failed trabeculectomy, trabeculectomy remained the most commonly selected procedure (75.0%), but after two failed trabeculectomies, long-tube shunt surgeries were chosen, with a preference for the AGV (34.1%) followed by the BGI (20.6%).

3.3. Surgical Choices for Uveitic Glaucoma

Table 3 outlines participants' surgical choices for uveitic glaucoma (UG) across four clinical settings. For unoperated eyes with cataract, surgeons preferred trabeculectomy plus phacoemulsification (32.5%) followed by microhook surgery plus phacoemulsification (20.2%), and then trabeculectomy alone (20.2%). In such cases, 33.7% preferred MIGS plus phacoemulsification. For unoperated eyes without cataract, the dominant choice was trabeculectomy alone (62.7%), while microhook surgery and PMS surgery alone were preferred by 14.3% and 10.7%, respectively. For pseudophakic eyes, the preferred procedure was trabeculectomy (57.2%) followed by microhook surgery (13.9%) and PMS surgery (11.5%). For pseudophakic eyes with a previous failed trabeculectomy, trabeculectomy remained the dominant choice (53.7%) followed by AGV surgery (20.8%) and PMS surgery (13.1%).

Table 3. Surgical preferences for uveitic glaucoma.

Type of Glaucoma Surgery	Unoperated Eyes with Cataract	Unoperated Eyes Without Cataract	Pseudophakic Eyes	Pseudophakic Eyes with a Previous Failed Trabeculectomy
Microhook+Phaco	20.2	1.2	0.0	0.0
Microhook	2.4	14.3	13.9	3.2
iStent inject W	0.0	0.0	0.8	0.0
KDB+Phaco	4.8	0.0	0.0	0.0
KDB	0.0	2.4	2.4	0.0
Suture trabeculectomy+Phaco	5.1	0.0	0.0	0.0
Suture trabeculectomy	0.0	4.3	5.1	0.6
HMS+Phaco	1.2	0.0	0.0	0.0
Other MIGS+Phaco	2.4	1.2	0.0	0.0
Other MIGS	0.0	2.4	2.4	0.0
PMS+Phaco	7.2	0.0	0.0	0.0
PMS	2.4	10.7	11.5	13.1
Trabeculectomy+Phaco	32.5	0.0	0.0	0.0
Trabeculectomy	20.2	62.7	57.2	53.7
AGV+Phaco	1.6	0.0	0.0	0.0
AGV	0.0	0.8	7.5	20.8
BGI	0.0	0.0	0.0	4.8
Bleb revision or needling	0.0	0.0	0.0	3.8

AGV, Ahmed glaucoma valve; BGI, Baerveldt glaucoma implant; HMS, Hydrus Microstent; KDB, Kahook dual blade; MIGS, minimally invasive glaucoma surgery; Phaco, phacoemulsification; PMS, PreserFlo MicroShunt.

3.4. Surgical Choices for Neovascular Glaucoma

Table 4 presents the surgical preferences of participants for neovascular glaucoma (NVG) in two clinical settings. For pseudophakic eyes with prior vitrectomy, the most frequently selected procedure was trabeculectomy (47.2%) followed by an AGV (34.1%). Conversely, for pseudophakic eyes with prior vitrectomy and a failed trabeculectomy, the preferred option was long-tube shunt surgery with an AGV (62.7%), while the preference for trabeculectomy decreased to 19.8%.

Table 4. Surgical preferences for neovascular glaucoma.

Type of Glaucoma Surgery	Pseudophakic Eyes with Prior Vitrectomy and Panretinal Photocoagulation	Pseudophakic Eyes with Prior Vitrectomy, Panretinal Photocoagulation, and a Previous Failed Trabeculectomy
PMS	8.4	4.8
Trabeculectomy	47.2	19.8
ExPRESS	1.2	0.0
AGV	34.1	62.7
BGI	9.1	10.3
Bleb revision or needling	0.0	2.4

AGV, Ahmed glaucoma valve; BGI, Baerveldt glaucoma implant; PMS, PreserFlo MicroShunt.

3.5. Postoperative Management

Figure 1 illustrates the follow-up intervals for each type of glaucoma surgery. After trabeculectomy, more than 80% of surgeons held follow-up sessions at 1 day, 3 days, 1 week, 2 weeks, 1 month, 2 months, and 3 months postoperatively, then every 2 or 3 months. After PMS surgery and long-tube shunt surgeries, more than 80% of surgeons held follow-up sessions at 1 day, 1 week, 2 weeks, 1 month, 2 months, and 3 months postoperatively, then

every 2 or 3 months. These procedures tended to require fewer early postoperative visits compared to trabeculectomy. After the iStent, Hydrus, and other types of MIGS, more than 80% of surgeons held follow-up sessions at 1 day, 1 week, 1 month, 3 months, 6 months, and 1 year postoperatively. These findings suggest that fewer postoperative visits are required after MIGS compared to filtering surgery.

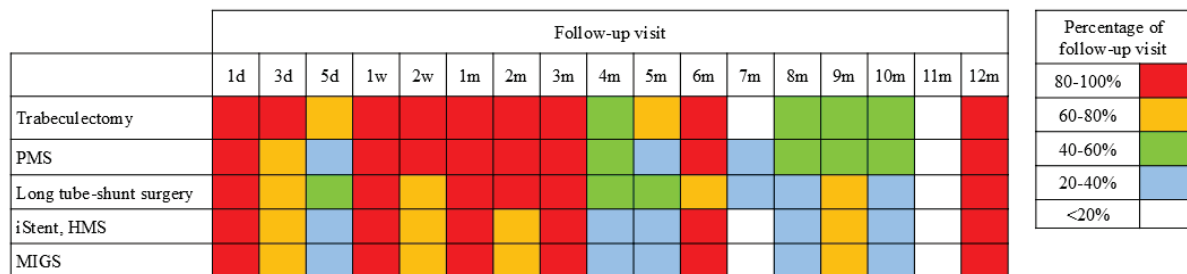


Figure 1. Frequency of postoperative follow-up for each type of glaucoma surgery. d, day; w, week; m, month; HMS, Hydrus Microstent; MIGS, minimally invasive glaucoma surgery; PMS, PreserFlo MicroShunt.

4. Discussion

This article provides a comprehensive overview of the current surgical preferences and postoperative management strategies of glaucoma specialists in Japan. The findings indicate a significant shift toward MIGS as the preferred primary surgical intervention, particularly in mild to moderate cases of POAG and NTG associated with cataracts. MIGS, when combined with cataract surgery, provides excellent IOP-lowering effects [16,17]. Therefore, it is a preferred option for patients with both glaucoma and cataracts. Among the different types of MIGS, microhook surgery was the most preferred option, similar to our previous survey's findings [4]. This preference for microhook surgery could be attributed to its lower cost due to the reusable device, as well as its well-established effectiveness in clinical practice [18], making it an appealing option for many surgeons.

PMS surgery has also increased in popularity, particularly for advanced cases of POAG and NTG in pseudophakic eyes. Similar to long-tube shunt surgeries, PMS surgery causes greater endothelial cell loss when the tube is positioned closer to the corneal endothelium [19,20]. Therefore, it is likely preferred in pseudophakic eyes with a deeper anterior chamber rather than in phakic eyes. PMS surgery is frequently selected in cases wherein trabeculectomy was previously favored, indicating a trend toward the adoption of less invasive filtration surgery with potentially fewer complications [9,21]. Moreover, the preference for PMS surgery in advanced glaucoma cases without prior surgical intervention further underscores its perceived efficacy and safety among glaucoma specialists. However, because of its superior IOP-lowering effect versus PMS surgery [21], trabeculectomy remains the procedure of choice in cases requiring intense IOP reduction, particularly in advanced NTG eyes. In Japan, NTG is the most common type of glaucoma [22] wherein the effectiveness of trabeculectomy has been reported [23,24]. Furthermore, trabeculectomy remains the preferred surgical option for POAG and NTG eyes with a previously failed trabeculectomy, as well as for UG or NVG eyes as a primary glaucoma surgery. Thus, even with the shift toward less invasive surgical techniques, trabeculectomy continues to play a crucial role.

For refractory glaucoma cases, including those with multiple failed trabeculectomies, long-tube shunt surgeries remain the preferred choice, with the AGV being favored over the BGI. The results also suggest that long-tube shunt surgery with an AGV is preferred for NVG with prior vitrectomy and a previous failed trabeculectomy, thus reinforcing its role in managing complex and high-risk glaucoma cases. In contrast, our 2019 survey revealed

that the BGI and AGV had comparable selection rates in similar scenarios [4]. This shift can be attributed to the safety and ease of the procedure with an AGV, despite having a weaker IOP-lowering effect than the BGI [25,26]. The AGV features a valved mechanism that provides immediate IOP control and reduces the risk of postoperative hypotony [25]. The AGV tends to cause less postoperative visual loss than the BGI [26]. Additionally, the AGV has a small plate, is easy to implant, and requires only one quadrant, which allows for potential additional glaucoma surgeries in the future.

There were notable variations in the frequency of postoperative follow-up depending on the type of surgery performed. Trabeculectomy requires the most frequent early postoperative visits, which is appropriate because of the higher risk of complications (e.g., bleb leaks, hypotony, and infections) and the need for proactive and reactive bleb management to achieve better postoperative outcomes [27,28]. In contrast, PMS and long-tube shunt surgeries require fewer early follow-up visits, likely due to their more predictable postoperative course. Meanwhile, MIGS procedures, including the iStent inject W and the HMS, require the least frequent follow-up because of their minimally invasive nature and rapid recovery time.

The trends observed in this study are consistent with global shifts in glaucoma surgical practice [2,3,5,6,29]. Surveys in the United States and the United Kingdom have similarly reported an increasing adoption of MIGS, shifting away from traditional trabeculectomy as a first-line surgical intervention. In Japan, both patients and surgeons have come to prefer less invasive procedures such as MIGS and PMS due to their safety, consistent IOP-lowering effects, and simplified postoperative management. However, the preference for trabeculectomy in advanced glaucoma cases remains strong among Japanese specialists. This suggests that despite the emergence of newer techniques, traditional filtering surgery continues to be a mainstay for managing severe glaucoma. In the United States, endoscopic cyclophotocoagulation (ECP) and micropulse transscleral cyclophotocoagulation (MP-TSCPC) are types of MIGS that are commonly used as primary surgical treatments for glaucoma [2,6,30,31]. In Japan, ECP is currently available at a limited number of facilities and is primarily used for extremely refractory cases of glaucoma. Meanwhile, MP-TSCPC is also used for eyes with refractory glaucoma in Japan, but its surgical indication remains low.

Despite these valuable insights, this study had certain limitations. First, the study population included only 50 glaucoma specialists who are council members of the Japan Glaucoma Society, and thus these data may not fully represent the broader population of glaucoma surgeons in Japan. Second, because the survey was conducted shortly after the approval of new procedures, namely the standalone iStent inject W and the HMS, some of these specialists may have limited experience with them. Third, this study relied on survey responses rather than clinical outcome data. There may have been bias regarding individual preferences, as objective efficacy metrics were not considered. In actual clinical practice, the choice of surgery varies based on patient-specific factors such as age, daily activities, socioeconomic status, access to care, and home environment. Fourth, we did not inquire about the reasons for selecting specific devices within similar surgical procedures (e.g., among MIGS or long-tube shunt surgeries), so the details of surgical preferences remain unclear. Future studies incorporating real-world patient characteristics, clinical outcomes, and long-term follow-up data can provide a more comprehensive understanding of the different types of glaucoma surgery.

In conclusion, this study highlights the evolving trends in glaucoma surgery among Japanese specialists. Notably, there was a strong preference for MIGS in mild to moderate cases, increasing adoption of PMS for advanced cases, and continued reliance on long-tube shunt surgeries for refractory cases. These findings provide valuable guidance for clinical

decision-making and highlight the importance of continued research and innovation in the surgical management of glaucoma.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/jcm14062039/s1>, Table S1. Which glaucoma surgeries had you performed for the following clinical scenarios in 2024? Table S2: Surgical preferences for each type of glaucoma across all clinical settings.

Author Contributions: Conceptualization, K.I. and M.I.; methodology, K.I. and M.I.; formal analysis, K.I.; investigation, K.I., S.A. and M.I.; data curation, K.I., S.A. and Y.T.; writing—original draft preparation, K.I.; writing—review and editing, K.I., Y.T. and M.I. All authors have read and agreed to the published version of the manuscript.

Funding: This work was partly supported by the Japan Society for the Promotion of Science (KAKENHI) (Grant numbers 22K16967, 20H03840, 22K19582).

Institutional Review Board Statement: Institutional review board approval was waived by the ethics committee of the University of Fukui Hospital, Fukui, Japan, because patients were not involved.

Informed Consent Statement: Patient consent was waived due to patients were not involved.

Data Availability Statement: Data are fully available upon reasonable request to the corresponding author.

Acknowledgments: The authors would like to thank the council members of the Japan Glaucoma Society for their cooperation in the survey.

Conflicts of Interest: The authors declare no conflicts of interest.

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Article

Comparison of Standalone Tanito Microhook Trabeculotomy Between Unilateral and Bilateral Incision Groups

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Abstract

Background/Objectives: Trabeculotomy using the Tanito microhook (TMH) is a minimally invasive glaucoma surgery (MIGS) technique that effectively reduces intraocular pressure (IOP). The optimal incision extent for standalone TMH remains unclear. This study aimed to compare the surgical efficacy and safety of unilateral (120-degree) and bilateral (240-degree) incisions in standalone TMH for primary open-angle glaucoma or late-onset juvenile open-angle glaucoma in patients without a history of intraocular surgery. **Methods:** This retrospective study analyzed 81 eyes of 48 patients who underwent standalone TMH at Shimane University Hospital. Patients were categorized into unilateral (29 eyes) or bilateral (52 eyes) incision groups. The primary outcomes were IOP reduction and medication score changes over 12 months. Secondary outcomes included best-corrected visual acuity (BCVA), anterior chamber (AC) flare, corneal endothelial cell density (CECD), and postoperative complications, particularly hyphema, assessed using the Shimane University Postoperative Hyphema Scoring System (SU-RLC). Multivariate mixed-effects regression and Kaplan–Meier survival analyses were performed. **Results:** At 12 months, IOP reduction was comparable between the unilateral (23%) and bilateral (28%) groups ($p = 0.29$). The unilateral group had a significantly lower medication score at postoperative day 3 ($p = 0.0057$) and week 2 ($p = 0.033$). No significant differences were observed in BCVA, AC flare, CECD, or visual field mean deviation (MD). However, the bilateral group had significantly higher hyphema scores ($p = 0.017$), with more cases of layered hyphema. **Conclusions:** Unilateral standalone TMH achieved equivalent IOP and medication score reductions compared to bilateral incisions, with a lower risk of early postoperative hyphema. The unilateral approach may be preferable for faster visual recovery.

Keywords: microhook ab interno trabeculotomy; goniotomy; Tanito microhook (TMH); intraocular pressure; minimally invasive glaucoma surgery; surgical complication; hyphema

1. Introduction

Glaucoma is a progressive neurodegenerative eye disease that results in optic nerve damage, visual field loss, and eventual vision impairment [1,2]. Elevated intraocular pressure (IOP) remains a primary risk factor for disease progression, and the only established treatment strategy involves reducing IOP through pharmacological therapy, laser interventions, or surgical procedures. Among the various surgical options, minimally invasive glaucoma surgery (MIGS) has gained popularity due to its balance between efficacy and

safety [3–5]. One such MIGS technique, the Tanito microhook ab interno trabeculotomy (TMH), employs a metal hook to incise the trabecular meshwork and has been shown to effectively lower IOP while reducing the dependence on antiglaucoma medications [6].

Initially, TMH was performed by creating incisions in both the nasal and temporal trabecular meshwork, achieving a total incision angle of approximately 240 degrees. Previous research on cadaveric eyes suggested that the extent of trabeculotomy may influence postoperative IOP reduction [7]. While some clinical studies have reported a correlation between surgical extent and the magnitude of IOP reduction [8–10], others have found no significant difference [11–16]. Many of these studies compared different surgical techniques or included patient populations with varying preoperative IOP levels and baseline characteristics, which may introduce bias [8–10,13,16]. Additionally, some studies were limited by small sample sizes [11,14].

While the relationship between cataract extraction and IOP reduction remains inconclusive [6,17,18], some studies suggest that cataract removal at the time of trabeculotomy/goniotomy may contribute to greater IOP reduction [19]. This highlights the challenge of assessing the isolated effect of trabecular meshwork incision when cataract surgery is performed simultaneously. In a previous study, we compared the surgical efficacy and safety of 120-degree versus 240-degree TMH in eyes undergoing combined TMH and cataract surgery [20]. The results suggested that IOP reduction following TMH was comparable between unilateral and bilateral incisions. However, in MIGS procedures, the additional IOP-lowering effect of cataract surgery must be considered [21–25]. Thus, an ideal approach to evaluating the impact of incision extent in trabeculotomy should focus solely on standalone trabeculotomy cases.

In the present study, we conducted a comprehensive comparison of surgical outcomes between unilateral (approximately 120-degree) and bilateral (approximately 240-degree) incisions in standalone TMH. To minimize confounding variables, we included only patients with open-angle glaucoma who had no prior history of intraocular surgery.

2. Subjects and Methods

2.1. Subjects

This research was conducted in accordance with the principles outlined in the Declaration of Helsinki and received approval from the institutional review board (IRB) of Shimane University Hospital (IRB No. 20200517-1, revised protocol issued on 22 July 2024). Written informed consent for the surgical procedure was obtained from all participants prior to surgery. However, individual written consent for publication was not mandated by the IRB; instead, the study protocol was publicly posted within the study institutions to inform participants. Only de-identified data were used for statistical analysis.

A retrospective review identified eligible participants based on the following inclusion criteria: individuals who underwent surgery at Shimane University Hospital between April 2018 and August 2023, performed by one of two surgeons (K.S. or M.T.); those who underwent trabeculotomy using a microhook (TMH) as the sole surgical procedure; individuals aged 18 years or older; and those diagnosed with primary open-angle glaucoma (POAG) or late-onset juvenile open-angle glaucoma (JOAG) without any history of prior intraocular or glaucoma surgeries, with a minimum postoperative follow-up of 12 months. No explicit exclusion criteria were established. A total of 81 eyes from 48 participants were identified in our institutional database. At our institution, bilateral incisions were the predominant approach until 2019, whereas from 2021 onward, a nasal-only incision became the preferred technique. This transition allowed for the collection of data on both unilateral and bilateral incision approaches, with 29 eyes from 17 participants categorized

into the unilateral group and 52 eyes from 31 participants assigned to the bilateral group for comparative analysis.

2.2. Parameters

Clinical parameters were extracted from medical records, including age, sex, glaucoma classification, surgical approach, preoperative and postoperative best-corrected visual acuity (BCVA), intraocular pressure (IOP), number of antiglaucoma medications, anterior chamber (AC) flare (measured using the FM-600 laser flare meter, Kowa, Nagoya, Japan), corneal endothelial cell density (CECD) (measured with the EM-3000 specular microscope, Tomey, Nagoya, Japan), axial length (measured using the OA-2000 optical biometer, Tomey, Nagoya, Japan), visual field mean deviation (MD) (central 30-2 program, Humphrey Visual Field Analyzer, Carl Zeiss Meditec, Dublin, CA, USA), and postoperative follow-up duration. Decimal BCVA values were converted to the logarithm of the minimum angle of resolution (logMAR) VA. The following values were assigned for low-vision states: counting fingers (0.0025), hand motions (0.002), light perception (0.0016), and no light perception (0.0013) [26]. IOP was measured using Goldmann applanation tonometry, except on postoperative day 3, when the iCARE rebound tonometer (M.E. Technica, Tokyo, Japan) was used. The medication score was calculated by assigning one point per topical medication component or per tablet of oral acetazolamide.

Details regarding the trabeculotomy site, perioperative complications, complication management, and additional glaucoma surgeries were extracted from surgical and medical records. Postoperative time points were categorized as follows: postoperative day (POD) 3 (1–3 days), postoperative week (POW) 2 (1–3 weeks), postoperative month (POM) 3 (2–4 months), POM 6 (5–7 months), POM 9 (8–10 months), and POM 12 (11–14 months).

The Shimane University Postoperative Hyphema Scoring System (SU-RLC) [27] was utilized to quantify hyphema severity. This system employs slit-lamp examination to assess three components: red blood cells (RBCs) (R), layering (L), and clot formation (C). RBCs are graded from 0 (no visible floating RBCs in the AC) to 3 (dense floating RBCs obscuring the iris pattern). Layering is scored from 0 (absent) to 3 (layering above the lower pupillary margin). Clot formation is rated as 0 (absent) or 1 (present). The cumulative SU-RLC score ranges from 0 to 7, providing an overall assessment of hyphema severity. The highest SU-RLC score observed during follow-up was used for analysis, with most cases reaching peak severity within the first three postoperative days.

2.3. Surgical Techniques

The surgical approach has been described in detail in previous work [6,28]. In brief, TMH was performed using specifically designed spatula-shaped microhooks (M-2215S, 2215R, and 2215L, Inami, Tokyo, Japan). Viscoelastic material (1% sodium hyaluronate or Opegan Hi) was introduced into the AC through corneal ports created with a 20-gauge microvitrectomy knife at the 2–3 o'clock and 9–10 o'clock positions. A microhook was inserted into the AC via a corneal port, and the opposite angle was visualized using a Swan-Jacob gonioscope lens. The microhook tip was inserted into Schlemm's canal and advanced circumferentially to incise the inner wall of Schlemm's canal and trabecular meshwork for at least three hours, either at the nasal site or at both nasal and temporal locations. Following TMH, viscoelastic material was removed, and corneal ports were sealed by stromal hydration. At the conclusion of surgery, a subconjunctival injection of 2 mg of betamethasone sodium phosphate was administered, and 0.3% ofloxacin ointment was applied. Postoperatively, topical 1.5% levofloxacin and 0.1% betamethasone were prescribed four times daily for 3–4 weeks.

2.4. Statistical Tests

Comparative analyses between the unilateral and bilateral incision groups were conducted using unpaired *t*-tests for continuous variables, Fisher's exact test for categorical variables, and the Cochran–Armitage trend test for ordinal data. To address potential biases due to age and sex differences among the subjects, as well as the inclusion of bilateral eyes from individual participants, mixed-effects regression analyses were performed to evaluate the impact of the surgical approach on IOP, medication score, BCVA, AC flare, CECD, and MD.

Kaplan–Meier survival analysis was conducted to estimate the probability of maintaining controlled IOP. Successful IOP control was assessed by defining failure based on multiple criteria: IOP exceeding 18 mmHg (criterion A, D), 15 mmHg (criterion B, E), or 12 mmHg (criterion C, F) after three months postoperatively; an IOP reduction of less than 20% (criteria A–C) or 0% (criteria D–F) after three months postoperatively; the need for additional glaucoma surgery at any point; or loss of light perception. Cases that did not meet the failure criteria were considered to have survived and treated as censored. Since prolonged hypotony was not observed, failure related to hypotony was not included in the survival analysis definition. Antiglaucoma medication use was not factored into survival curve analysis, as most patients continued medication postoperatively. Log-rank tests were employed to compare survival distributions between the surgical groups. Cox proportional hazards regression models were used to identify factors associated with IOP control under each criterion (A–F).

Missing values were imputed using the last observation carried forward (LOCF) method. If no prior observation was available, the next observation carried backward (NOCB) method was applied. For cases requiring additional glaucoma surgery, postoperative IOP and medication scores were considered missing beyond the surgical intervention, while other parameters were included for the full follow-up period. A *p*-value of <0.05 was deemed statistically significant. Statistical analyses were performed using JMP Pro version 17.2 (SAS Institute, Inc., Cary, NC, USA).

3. Results

The baseline characteristics of the study participants, including age, sex, laterality, glaucoma type, BCVA, IOP, medication score, axial length, AC flare, CECD, and preoperative MD values, are summarized in Table 1. The mean ages in the unilateral and bilateral incision groups were 47.5 and 50.9 years, respectively, with males comprising 41% and 68% of each group. The total trabecular meshwork incision width averaged 3.6 clock hours in the unilateral group and 7.1 clock hours in the bilateral group. Apart from this, no significant differences were observed in any other demographic parameters between the two surgical groups.

In this study, data from both eyes were included in the analysis for cases in which bilateral surgery was performed to ensure an adequate sample size. To adjust for potential bias introduced by selecting both eyes from the same patient, a mixed-effects model was applied. This model also accounted for age and sex as covariates. The results of the analysis assessing the impact of incision extent on various parameters are presented in Table 2. IOP, medication score, and AC flare demonstrated significant associations with postoperative duration, indicating that these factors were influenced by the surgical intervention. In contrast, no significant association was found between incision extent (i.e., unilateral or bilateral incision) and IOP, medication score, BCVA, CECD, or MD. Additionally, no significant interaction was detected between postoperative duration and incision extent for any of these parameters.

Table 3 presents a comparison of IOP between the unilateral and bilateral incision groups. The preoperative IOP, which was 22.3 mmHg in the unilateral group and 22.1 mmHg in the bilateral group, decreased to 17.1 mmHg (a 23% reduction) in the unilateral group and 16.0 mmHg (a 28% reduction) in the bilateral group at 12 months postoperatively. At the 3-month postoperative mark, the bilateral group had a significantly lower IOP than the unilateral group. However, at all other time points up to 12 months, no significant difference in IOP was observed between the two groups.

Table 1. Baseline characteristics of study participants.

Parameters	Unilateral Incision	Bilateral Incision	<i>p</i> -Value
N, subjects	17	31	
Age, years			
Mean $\pm$ SD	47.5 $\pm$ 12.3	50.9 $\pm$ 9.4	0.29
95% CI	69.2, 72.7	70.0, 73.2	
Sex, n (%)			
Male	7 (41)	21 (68)	0.13
Female	10 (59)	10 (32)	
N, eyes	29	52	
Incision extent, clock hours			
Nasal	3.6 $\pm$ 0.5	3.6 $\pm$ 0.5	0.61
Temporal		3.5 $\pm$ 0.5	
Total	3.6 $\pm$ 0.5	7.1 $\pm$ 0.4	<0.0001 **
Laterality, n (%)			
Right eye	13 (45)	27 (52)	0.64
Left eye	16 (55)	25 (48)	
Glaucoma type, n (%)			
POAG	22 (76)	38 (73)	>0.99
JOAG	7 (24)	14 (27)	
BCVA, LogMAR			
Mean $\pm$ SD	−0.02 $\pm$ 0.10	0.03 $\pm$ 0.22	0.21
95% CI	−0.05, 0.01	−0.03, 0.10	
IOP, mmHg			
Mean $\pm$ SD	22.3 $\pm$ 9.0	22.1 $\pm$ 8.0	0.90
95% CI	18.9, 25.8	19.9, 24.3	
Medication score			
Mean $\pm$ SD	3.9 $\pm$ 1.1	3.6 $\pm$ 0.8	0.23
95% CI	3.5, 4.3	3.4, 3.9	
Axial length, mm			
Mean $\pm$ SD	26.1 $\pm$ 2.0	25.9 $\pm$ 1.8	0.60
95% CI	24.3, 25.0	25.4, 26.4	
AC flare, pc/ms			
Mean $\pm$ SD	9.7 $\pm$ 9.3	8.1 $\pm$ 4.6	0.31
95% CI	6.1, 13.2	6.8, 9.4	
CECD, cells/mm ²			
Mean $\pm$ SD	2601 $\pm$ 268	2572 $\pm$ 213	0.59
95% CI	2499, 2703	2512, 2631	
MD, dB			
Mean $\pm$ SD	−9.6 $\pm$ 8.2	−8.7 $\pm$ 7.3	0.61
95% CI	−6.5, −12.7	−6.6, −10.7	

p-values are determined using an unpaired *t*-test for continuous variables and Fisher's exact test for categorical variables. A ** denotes statistical significance at *p* < 0.01. Abbreviations: SD—standard deviation; CI—confidence interval; POAG—primary open-angle glaucoma; JOAG—juvenile open-angle glaucoma; BCVA—best-corrected visual acuity; IOP—intraocular pressure; AC—anterior chamber; pc/ms—photon counts per millisecond; CECD—corneal endothelial cell density; MD—mean deviation of visual field; dB—decibels.

Table 4 presents a comparison of the number of antiglaucoma medications between the unilateral and bilateral incision groups. The preoperative medication score, which was 3.9 in the unilateral group and 3.6 in the bilateral group, decreased to 2.8 (a 28% reduction) and 3.0 (a 17% reduction), respectively, at 12 months postoperatively. At postoperative day 3 and week 2, the unilateral group had a significantly lower medication score than the

bilateral group. However, at all other time points up to 12 months, no significant difference in medication scores was found between the two groups.

Table 2. Adjustment of demographic factor differences using mixed-effects regression analysis.

Parameters	F Value	p-Value
IOP		
Age	1.6	0.21
Sex	0.7	0.42
Unilateral/Bilateral	0.4	0.51
Postoperative duration	12.0	<0.0001 **
Unilateral/Bilateral × Postoperative duration	1.9	0.072
Medication score		
Age	7.0	0.011 *
Sex	1.3	0.26
Unilateral/Bilateral	1.9	0.17
Postoperative duration	23.5	<0.0001 **
Unilateral/Bilateral × Postoperative duration	4.1	0.0002 **
BCVA, LogMAR		
Age	2.5	0.12
Sex	0.4	0.52
Unilateral/Bilateral	1.0	0.33
Postoperative duration	1.0	0.41
Unilateral/Bilateral × Postoperative duration	0.2	0.98
AC flare, pc/ms		
Age	0.4	0.55
Sex	0.5	0.49
Unilateral/Bilateral	0.0	0.94
Postoperative duration	2.2	0.045 *
Unilateral/Bilateral × Postoperative duration	1.9	0.087
CECD, cells/mm ²		
Age	1.4	0.24
Sex	2.2	0.14
Unilateral/Bilateral	0.0	0.97
Postoperative duration	2.6	0.081
Unilateral/Bilateral × Postoperative duration	0.8	0.45
MD, dB		
Age	4.4	0.041 *
Sex	0.3	0.59
Unilateral/Bilateral	0.0	0.97
Postoperative duration	0.1	0.81
Unilateral/Bilateral × Postoperative duration	0.1	0.75

p-values are calculated using a mixed-effects regression model to adjust for biases arising from differences in age, sex distribution, and the inclusion of bilateral eyes from the same subject. The * and ** indicate $p < 0.05$ and $p < 0.01$, respectively. Abbreviations: IOP—intraocular pressure; BCVA—best-corrected visual acuity; LogMAR—logarithm of the minimum angle of resolution; AC—anterior chamber; pc/ms—photon counts per millisecond; CECD—corneal endothelial cell density; MD—visual field mean deviation; dB—decibels.

Table 5 presents a comparison of postoperative complications, excluding hyphema, and the required interventions between the unilateral and bilateral incision groups. There was no significant difference between the groups regarding the incidence of complications or the necessity for interventions. All eight additional glaucoma surgeries recorded in this dataset were trabeculectomies.

Table 6 provides a comparison of postoperative hyphema scores between the two groups. The overall incidence of hyphema, including cases with minimal floating RBCs in the AC, was 93% in the unilateral incision group and 96% in the bilateral incision group. The mean total RLC score was 2.6 in the unilateral incision group and 3.6 in the bilateral incision group, demonstrating a statistically significant difference ($p = 0.0017$). While the majority of cases in the unilateral incision group had a score of 3 or lower, 51% of cases in the bilateral incision group had a score of 4 or higher.

For individual components of the hyphema score, both the R and L scores were significantly higher in the bilateral incision group compared to the unilateral incision group ($p = 0.039$ and $p = 0.0013$, respectively), whereas the C score showed no significant difference between the groups. The incidence of layered hyphema (L score ≥ 1) was 28% in the unilateral incision group and 61% in the bilateral incision group.

Table 3. Comparison of preoperative and postoperative iop between the unilateral and bilateral incision groups.

Parameters	Unilateral Incision	Bilateral Incision	<i>p</i> -Value
Preoperative			
Mean $\pm$ SD, mmHg	22.3 $\pm$ 9.0	22.1 $\pm$ 8.0	0.90
95% CI	18.9, 25.8	19.9, 24.3	
POD3			
Mean $\pm$ SD	13.1 $\pm$ 9.4	15.9 $\pm$ 9.5	0.21
95% CI	9.5, 16.7	13.2, 18.5	
POW2			
Mean $\pm$ SD	18.1 $\pm$ 6.7	18.1 $\pm$ 8.3	>0.99
95% CI	15.5, 20.6	15.8, 20.4	
POM1			
Mean $\pm$ SD	17.9 $\pm$ 6.6	16.2 $\pm$ 4.9	0.20
95% CI	15.4, 20.4	14.8, 17.6	
POM3			
Mean $\pm$ SD	17.9 $\pm$ 8.4	14.7 $\pm$ 3.9	0.027 *
95% CI	14.7, 21.1	13.6, 15.8	
POM6			
Mean $\pm$ SD	16.5 $\pm$ 5.6	15.5 $\pm$ 4.1	0.38
95% CI	14.3, 18.7	14.3, 16.7	
POM9			
Mean $\pm$ SD	16.4 $\pm$ 3.3	15.3 $\pm$ 3.8	0.22
95% CI	15.0, 17.8	14.2, 16.4	
POM12			
Mean $\pm$ SD	17.1 $\pm$ 5.0	16.0 $\pm$ 3.7	0.29
95% CI	15.0, 19.2	14.9 $\pm$ 17.0	

p-values are calculated using an unpaired *t*-test. The * indicates $p < 0.05$. Abbreviations: SD—standard deviation; CI—confidence interval; POD—postoperative day; POW—postoperative week; POM—postoperative month.

Table 7 presents a comparison of BCVA between the unilateral and bilateral incision groups. The preoperative BCVA was -0.02 in the unilateral incision group and 0.03 in the bilateral incision group, remaining unchanged at -0.03 and -0.01 , respectively, at 12 months postoperatively. BCVA remained comparable between the two groups throughout the 12-month study period. The lack of changes in BCVA suggests that a visually significant cataract did not develop in most cases in either group.

Table 8 presents a comparison of AC flare between the unilateral and bilateral incision groups. The preoperative AC flare was 9.7 pc/ms in the unilateral group and 8.1 pc/ms in the bilateral group, showing minimal change at 12 months postoperatively, with values of 8.0 pc/ms and 8.5 pc/ms, respectively. AC flare remained similar between the groups throughout the study period.

Table 9 presents a comparison of CECD between the unilateral and bilateral incision groups. The preoperative CECD was 2601 cells/mm² in the unilateral group and 2572 cells/mm² in the bilateral group, with minor variations at 12 months postoperatively, measuring 2512 cells/mm² and 2553 cells/mm², respectively. CECD remained equivalent between the two groups over the 12-month period.

Table 10 presents a comparison of visual field MD between the unilateral and bilateral incision groups. The preoperative MD was -9.6 dB in the unilateral group and -8.7 dB in the bilateral group, with slight changes at 12 months postoperatively, recorded as

−9.3 dB and −9.1 dB, respectively. MD values were similar between the two groups both preoperatively and at 12 months postoperatively.

Table 4. Comparison of preoperative and postoperative medication score between the unilateral and bilateral incision groups.

Parameters	Unilateral Incision	Bilateral Incision	<i>p</i> -Value
Preoperative			
Mean ± SD	3.9 ± 1.1	3.6 ± 0.8	0.23
95% CI	3.5, 4.3	3.4, 3.9	
POD3			
Mean ± SD	2.2 ± 1.0	2.9 ± 1.0	0.0057 **
95% CI	1.8, 2.6	2.6, 3.1	
POW2			
Mean ± SD	2.3 ± 1.3	3.0 ± 1.2	0.033 *
95% CI	1.9, 2.8	2.6, 3.3	
POM1			
Mean ± SD	2.4 ± 1.2	3.0 ± 1.3	0.052
95% CI	2.0, 2.9	2.7, 3.4	
POM3			
Mean ± SD	2.7 ± 1.2	2.8 ± 0.8	0.70
95% CI	2.2, 3.2	2.5, 3.0	
POM6			
Mean ± SD	2.6 ± 0.9	2.9 ± 0.9	0.29
95% CI	2.3, 3.0	2.6, 3.1	
POM9			
Mean ± SD	2.7 ± 0.8	3.0 ± 0.8	0.17
95% CI	2.4, 3.1	2.8, 3.2	
POM12			
Mean ± SD	2.8 ± 0.9	3.0 ± 0.8	0.20
95% CI	2.4, 3.1	2.8, 3.3	

p-values are calculated using an unpaired *t*-test. The * and ** indicate $p < 0.05$ and $p < 0.01$, respectively. Abbreviations: SD—standard deviation; CI—confidence interval; POD—postoperative day; POW—postoperative week; POM—postoperative month.

Table 5. Postoperative complications (except for hyphema) and interventions.

Parameters	Unilateral Incision	Bilateral Incision	<i>p</i> -Value
IOP spike (>30 mmHg)	3 (10)	11 (21)	0.18
Fibrin formation	0 (0)	3 (6)	0.55
Additional glaucoma surgery	5 (17)	3 (6)	0.13
Hyphema washout	1 (3)	3 (6)	>0.99
AC paracentesis	0 (0)	1 (2)	>0.99

p-values are calculated using Fisher's exact probability test. Abbreviations: IOP—intraocular pressure; AC—anterior chamber.

Figure 1 displays the Kaplan–Meier survival curves for successful IOP control in both the unilateral and bilateral incision groups. Failure was defined using three criteria: IOP exceeding 18 mmHg (Criterion A), 15 mmHg (Criterion B), or 12 mmHg (Criterion C), in combination with an IOP reduction of less than 20% from the preoperative level. At 12 months postoperatively, the cumulative survival rates for successful IOP control were 24.1% in the unilateral incision group and 26.9% in the bilateral incision group based on Criterion A; 13.8% and 17.3%, respectively, based on Criterion B; and 3.4% and 5.8%, respectively, based on Criterion C. The log-rank test yielded *p*-values of 0.41 for Criterion A, 0.24 for Criterion B, and 0.08 for Criterion C, indicating no significant differences in survival rates between the unilateral and bilateral incision groups.

Unlike filtering surgeries, where a reduction of less than 20% in IOP may be a meaningful indicator of failure, applying this criterion to trabeculotomy might be overly stringent [28]. Therefore, an additional analysis was conducted using alternative failure criteria,

where failure was defined as IOP exceeding 18 mmHg (Criterion D), 15 mmHg (Criterion E), or 12 mmHg (Criterion F), along with any postoperative IOP exceeding the preoperative level. Under these criteria, at 12 months postoperatively, the cumulative survival rates for successful IOP control were 41.4% in the unilateral incision group and 53.9% in the bilateral incision group based on Criterion D, 20.7% and 26.9%, respectively, based on Criterion E, and 3.4% and 5.8%, respectively, based on Criterion F. The log-rank test yielded *p*-values of 0.37 for Criterion D, 0.46 for Criterion E, and 0.08 for Criterion F, again showing no significant differences in survival rates between the unilateral and bilateral incision groups.

Table 6. Postoperative hyphema severity scored by SU-RLC scoring system.

Parameters	Unilateral Incision	Bilateral Incision	<i>p</i> -Value
Any hyphema, n (%)	27 (93)	50 (96)	0.61
Total RLC score			
Mean $\pm$ SD	2.6 $\pm$ 1.5	3.6 $\pm$ 1.9	0.017 *
95% CI	2.0, 3.1	3.0, 4.1	
0, n (%)	2 (7)	2 (4)	0.017 *
1	5 (17)	6 (12)	
2	8 (28)	10 (19)	
3	9 (31)	8 (15)	
4	1 (3)	8 (15)	
5	2 (7)	7 (13)	
6	2 (7)	8 (15)	
7	0 (0)	3 (6)	
R score			
0, n (%)	3 (10)	2 (4)	0.039 *
1	12 (41)	16 (31)	
2	9 (31)	14 (27)	
3	5 (17)	20 (38)	
L score			
0, n (%)	21 (72)	19 (39)	0.0013 **
1	6 (21)	17 (33)	
2	2 (7)	13 (25)	
3	0 (0)	3 (6)	
C score			
0, n (%)	10 (34)	22 (42)	0.49
1	19 (66)	30 (58)	

p-values are calculated using an unpaired *t*-test for continuous data and the Cochran–Armitage trend test for ordinal data. The * and ** indicate *p* < 0.05 and *p* < 0.01, respectively. Abbreviations: SU-RLC—Shimane University postoperative hyphema scoring system; R score—score for floating red blood cell density in the anterior chamber; L score—score for layered hyphema; C score—score for blood clot in the anterior chamber; SD—standard deviation; CI—confidence interval.

Finally, Table 11 presents the results of the Cox proportional hazards model analysis, which evaluated factors potentially influencing IOP control based on each of the six failure criteria (A–F). In a model adjusted for age, sex, glaucoma type, preoperative IOP, preoperative medication score, and the presence of surgical complications, the incision extent was not identified as a significant factor under any of the criteria.

For Criterion D, the presence of surgical complications showed a borderline significant association with surgical success (*p* = 0.048). For Criterion E, a higher preoperative IOP was significantly associated with surgical failure (*p* = 0.0028).

Table 7. Comparison of preoperative and postoperative BCVA between the unilateral and bilateral incision groups.

Parameters	Unilateral Incision	Bilateral Incision	<i>p</i> -Value
Preoperative			
Mean $\pm$ SD, LogMAR	−0.02 $\pm$ 0.10	0.03 $\pm$ 0.22	0.21
95% CI	−0.05, 0.01	−0.03, 0.10	
POW2			
Mean $\pm$ SD	−0.00 $\pm$ 0.11	0.05 $\pm$ 0.27	0.29
95% CI	−0.04, 0.04	−0.02, 0.13	

Table 7. *Cont.*

Parameters	Unilateral Incision	Bilateral Incision	<i>p</i> -Value
POM1			
Mean $\pm$ SD	-0.03 ± 0.08	0.02 ± 0.17	0.21
95% CI	$-0.06, 0.01$	$-0.03, 0.06$	
POM3			
Mean $\pm$ SD	-0.03 ± 0.08	-0.00 ± 0.12	0.40
95% CI	$-0.06, 0.01$	$-0.04, 0.03$	
POM6			
Mean $\pm$ SD	-0.02 ± 0.08	-0.01 ± 0.13	0.57
95% CI	$-0.06, 0.01$	$-0.05, 0.03$	
POM9			
Mean $\pm$ SD	-0.03 ± 0.09	0.00 ± 0.15	0.31
95% CI	$-0.07, 0.01$	$-0.04, 0.04$	
POM12			
Mean $\pm$ SD	-0.03 ± 0.07	-0.01 ± 0.13	0.37
95% CI	$-0.06, -0.00$	$-0.04, 0.03$	

p-values are calculated using an unpaired *t*-test. Abbreviations: BCVA—best-corrected visual acuity; LogMAR—logarithm of the minimum angle of resolution; SD—standard deviation; CI—confidence interval; POW—postoperative week; POM—postoperative month.

Table 8. Comparison of preoperative and postoperative ac flare between the unilateral and bilateral incision groups.

Parameters	Unilateral Incision	Bilateral Incision	<i>p</i> -Value
Preoperative			
Mean $\pm$ SD, pc/ms	9.7 ± 9.3	8.1 ± 4.6	0.31
95% CI	6.1, 13.2	6.8, 9.4	
POW2			
Mean $\pm$ SD	9.7 ± 5.3	13.8 ± 19.6	0.28
95% CI	7.7, 11.7	8.2, 19.3	
POM1			
Mean $\pm$ SD	9.2 ± 5.2	10.3 ± 5.7	0.37
95% CI	7.2, 11.1	8.7, 11.9	
POM3			
Mean $\pm$ SD	7.6 ± 2.8	9.5 ± 5.4	0.072
95% CI	6.5, 8.6	8.0, 11.0	
POM6			
Mean $\pm$ SD	7.5 ± 2.4	7.8 ± 2.7	0.61
95% CI	6.5, 8.4	7.0, 8.5	
POM9			
Mean $\pm$ SD	7.7 ± 2.2	8.7 ± 3.3	0.15
95% CI	6.8, 8.6	7.8, 9.7	
POM12			
Mean $\pm$ SD	8.0 ± 2.1	8.5 ± 3.7	0.52
95% CI	7.1, 8.9	7.5, 8.9	

p-values are calculated using an unpaired *t*-test. Abbreviations: AC—anterior chamber; pc/ms—photon counts per millisecond; SD—standard deviation; CI—confidence interval; POW—postoperative week; POM—postoperative month.

Table 9. Comparison of preoperative and postoperative CECD between the unilateral and bilateral incision groups.

Parameters	Unilateral Incision	Bilateral Incision	<i>p</i> -Value
Preoperative			
Mean $\pm$ SD, cells/mm ²	2601 ± 268	2572 ± 213	0.59
95% CI	2499, 2703	2512, 2631	
POM6			
Mean $\pm$ SD	2548 ± 181	2550 ± 214	0.97
95% CI	2476, 2619	2489, 2610	

Table 9. Cont.

Parameters	Unilateral Incision	Bilateral Incision	<i>p</i> -Value
POM12			
Mean $\pm$ SD	2512 $\pm$ 185	2553 $\pm$ 229	0.44
95% CI	2434, 2590	2487, 2619	

p-values are calculated using an unpaired *t*-test. Abbreviations: CECD—corneal endothelial cell density; SD—standard deviation; CI—confidence interval; POM—postoperative month.

Table 10. Comparison of preoperative and postoperative MD between the unilateral and bilateral incision groups.

Parameters	Unilateral Incision	Bilateral Incision	<i>p</i> -Value
Preoperative			
Mean $\pm$ SD, dB	−9.6 $\pm$ 8.2	−8.7 $\pm$ 7.3	0.61
95% CI	−6.5, −12.7	−6.6, −10.7	
POM12			
Mean $\pm$ SD	−9.3 $\pm$ 7.3	−9.1 $\pm$ 6.9	0.94
95% CI	−12.4, −6.2	−11.1, −7.1	

p-values are calculated using an unpaired *t*-test. Abbreviations: MD—mean deviation; dB—decibel; SD—standard deviation; CI—confidence interval; POM—postoperative month.

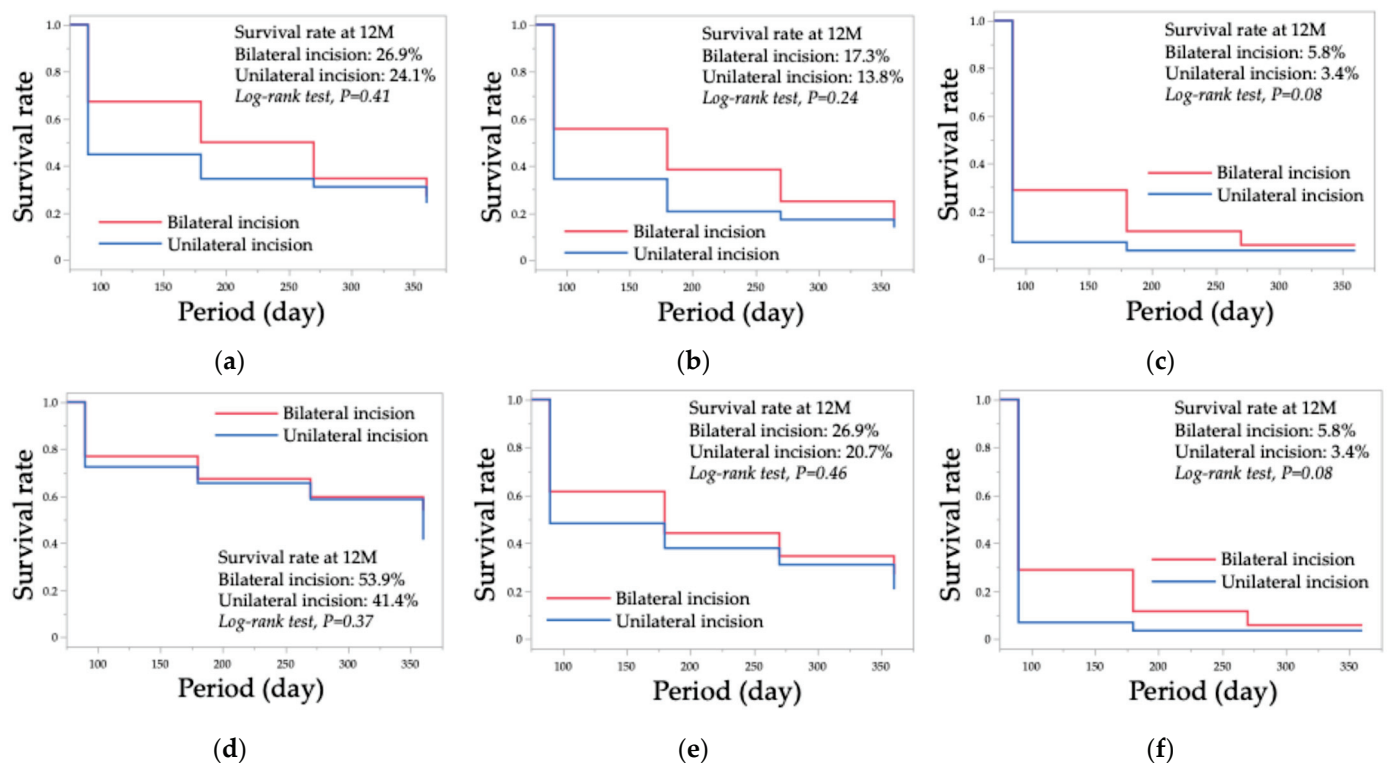


Figure 1. Kaplan–Meier survival curves illustrate IOP control outcomes for the unilateral and bilateral incision groups based on six failure criteria. Criterion A (a) defines failure as an IOP reduction of less than 20% from preoperative levels and/or an IOP exceeding 18 mmHg. Criterion B (b) applies the same percentage reduction threshold but with an upper IOP limit of 15 mmHg, while Criterion C (c) further lowers this threshold to 12 mmHg. Criterion D (d) considers failure to have occurred when the IOP reduction is less than 0% from preoperative levels and/or exceeds 18 mmHg. Similarly, Criterion E (e) sets this limit at 15 mmHg, and Criterion F (f) at 12 mmHg. Additionally, patients who required further glaucoma surgery or lost light perception were classified as failures.

Table 11. Possible factors associated with IOP control rate.

Parameters	HR	95% CI Range	p-Value
Criteria A (Success: ≤ 18 mmHg and $\geq 20\%$ reduction)			
Age,/yr	0.99	0.97, 1.02	0.59
Sex, F/M	1.57	0.92, 2.69	0.098
JOAG/POAG	1.19	0.60, 2.38	0.62
Unilateral/Bilateral	0.98	0.53, 1.80	0.95
Preoperative IOP,/mmHg	0.98	0.94, 1.02	0.39
Preoperative Medication,/medication	1.12	0.85, 1.50	0.42
Surgical complication, y/n	0.73	0.42, 1.28	0.28
Criteria B (Success: ≤ 15 mmHg and $\geq 20\%$ reduction)			
Age,/yr	1.00	0.97, 1.02	0.93
Sex, F/M	1.61	0.97, 2.67	0.066
JOAG/POAG	1.00	0.53, 1.88	>0.99
Unilateral/Bilateral	1.02	0.57, 1.82	0.95
Preoperative IOP,/mmHg	1.02	0.98, 1.05	0.27
Preoperative Medication,/medication	1.22	0.94, 1.61	0.14
Surgical complication, y/n	0.76	0.45, 1.31	0.33
Criteria C (Success: ≤ 12 mmHg and $\geq 20\%$ reduction)			
Age,/yr	1.00	0.98, 1.03	0.74
Sex, F/M	1.14	0.71, 1.84	0.58
JOAG/POAG	0.83	0.47, 1.47	0.52
Unilateral/Bilateral	1.13	0.66, 1.94	0.65
Preoperative IOP,/mmHg	1.01	0.98, 1.04	0.51
Preoperative Medication,/medication	0.96	0.75, 1.25	0.78
Surgical complication, y/n	0.83	0.47, 1.47	0.46
Criteria D (Success: ≤ 18 mmHg and $\geq 0\%$ reduction)			
Age,/yr	0.97	0.94, 1.01	0.12
Sex, F/M	1.66	0.84, 3.27	0.14
JOAG/POAG	1.13	0.53, 2.39	0.75
Unilateral/Bilateral	0.87	0.43, 1.78	0.70
Preoperative IOP,/mmHg	1.02	0.98, 1.06	0.28
Preoperative Medication,/medication	0.99	0.72, 1.39	0.96
Surgical complication, y/n	0.50	0.25, 0.99	0.048 *
Criteria E (Success: ≤ 15 mmHg and $\geq 0\%$ reduction)			
Age,/yr	0.99	0.97, 1.02	0.46
Sex, F/M	1.60	0.93, 2.75	0.089
JOAG/POAG	0.83	0.43, 1.58	0.56
Unilateral/Bilateral	0.90	0.50, 1.64	0.74
Preoperative IOP,/mmHg	1.04	1.00, 1.07	0.028 *
Preoperative Medication,/medication	1.10	0.84, 1.45	0.49
Surgical complication, y/n	0.67	0.38, 1.17	0.16
Criteria F (Success: ≤ 12 mmHg and $\geq 0\%$ reduction)			
Age,/yr	1.00	0.98, 1.03	0.74
Sex, F/M	1.14	0.71, 1.84	0.58
JOAG/POAG	0.83	0.47, 1.47	0.52
Unilateral/Bilateral	1.13	0.66, 1.94	0.65
Preoperative IOP,/mmHg	1.01	0.98, 1.04	0.51
Preoperative Medication,/medication	0.96	0.75, 1.25	0.78
Surgical complication, y/n	0.83	0.50, 1.37	0.46

p-values are calculated using the Cox hazard model based on six failure criteria. Criterion A defines failure as an IOP reduction of less than 20% from preoperative levels and/or an IOP exceeding 18 mmHg, while Criterion B applies the same percentage reduction threshold with an upper IOP limit of 15 mmHg, and Criterion C lowers this threshold to 12 mmHg. Criterion D considers failure to have occurred when the IOP reduction is less than 0% from preoperative levels and/or exceeds 18 mmHg, with Criterion E setting this limit at 15 mmHg and Criterion F at 12 mmHg. Patients who required additional glaucoma surgery or experienced a loss of light perception were also classified as failures. The * indicates $p < 0.05$. Abbreviations: HR—hazard ratio; F—female; M—male; JOAG—juvenile open-angle glaucoma; POAG—primary open-angle glaucoma; IOP—intraocular pressure.

4. Discussion

This study is a retrospective observational study comparing the surgical efficacy and safety of standalone TMH between the unilateral TM incision group and the bilateral TM

incision group. Regarding surgical efficacy parameters, including IOP, medication score, visual field MD, and survival analysis, no significant differences were observed between the two groups, except for a few instances. Additionally, safety evaluation parameters, including BCVA, AC flare, and CECD, showed no differences between the groups. The only clinically remarkable difference observed was in postoperative hyphema, where the bilateral group had a significantly higher hyphema score than the unilateral group.

A study using perfused autopsy eyes suggested that the extent of trabeculotomy may influence IOP reduction [7]. Investigating the impact of incisions on one or both sides and examining the correlation between incision extent and IOP reduction following goniotomy or trabeculotomy may provide further insights. Previous studies have compared the surgical effects of different incision extents in trabeculotomy/goniotomy; however, these studies included cases with simultaneous cataract surgery, pseudophakic eyes, or both [11,14,16,20]. As a result, the pure effect of MIGS could not be fully assessed. A key strength of our study is that we focused on patients with phakic POAG, including adult-onset JOAG, who had no prior ocular surgeries, allowing us to compare different incision extents in TMH more directly.

In this study, univariate analysis showed that at three months postoperatively, IOP was significantly lower in the bilateral group (Table 3). However, three days and three months postoperatively, the medication score was significantly lower in the unilateral group (Table 4). Additionally, survival analysis revealed no significant differences between the two groups (Figure 1). In multivariate analysis, no significant differences in IOP or medication score were found between the groups, but duration was a significant factor (Table 2). These findings indicate that both groups experienced significant postoperative reductions in IOP and medication scores regardless of incision extent. A previous study compared nasal and bilateral TMH incisions combined with cataract surgery in patients with open-angle glaucoma and found no significant differences in IOP or medication score between the groups throughout the study period [20]. Similarly, other studies on TMH reported no significant differences in IOP reduction, medication score, or success rates between 1-quadrant and 2-quadrant TMH procedures [14]. In studies on other trabeculotomy/goniotomy techniques, including Trabectome surgery with 0- to 160-degree incisions [29] and gonioscopy-assisted transluminal trabeculotomy (GATT) with 150- to 320-degree incisions [11], no significant differences in surgical outcomes were observed. A multicenter study also found no significant differences in IOP reduction, medication number, or cumulative survival probability for complete and qualified success rates among 120-, 240-, and 360-degree standalone goniotomy procedures, as well as when these were combined with cataract surgery [16]. Given these findings, along with our current results, unilateral trabeculotomy may be sufficient for most cases of open-angle glaucoma. However, individual variability may exist, highlighting the need for further research to determine specific cases where a more extensive trabecular meshwork incision could be more beneficial.

Regarding postoperative complications and additional procedures, no significant differences were found between the unilateral and bilateral groups. However, postoperative hyphema was notably more severe in the bilateral group. This finding aligns with our previous analysis of TMH combined with cataract surgery [20]. A greater incidence of postoperative layered hyphema was reported in GATT with a 360-degree incision compared to a 180-degree incision [12]. Similarly, goniotomy with a 360-degree incision resulted in more frequent hyphema than that with a 120-degree incision [15,16]. Previous research also demonstrated that early postoperative hyphema scores were higher in eyes undergoing TMH compared to those receiving first- and second-generation iStent implants [27,30]. These findings suggest that hyphema severity correlates with incision width in angle

surgeries. Furthermore, clot formation following trabeculotomy has been identified as a significant factor contributing to elevated IOP one week postoperatively [31]. Another study indicated that a two-quadrant TMH procedure had a significantly higher proportion of transient postoperative IOP elevation [14]. In the present study, multivariate analysis revealed a significant interaction between medication score, duration, and incision width (Table 1), with a lower early postoperative medication score in the unilateral group compared to the bilateral group (Table 4). Therefore, differences in the degree of anterior chamber bleeding may explain the variations in early postoperative medication scores. However, despite early postoperative differences in hyphema scores, no significant impact was observed on other safety parameters or final visual function, though these differences may have influenced early visual recovery. Given that IOP reduction was comparable between the two groups, the unilateral incision approach, which may facilitate a faster visual recovery, could be clinically more advantageous than the bilateral incision method.

The study had several limitations, including its retrospective design, differences in sample size between the groups, relatively small cohort, and the inclusion of both eyes from some subjects. However, the use of mixed regression analysis likely mitigated some biases. Additionally, the lack of information regarding anticoagulant and antiplatelet agent use was a limitation. Another limitation was the relatively short follow-up period. Nonetheless, the study had strengths, including a comprehensive assessment of patient clinical characteristics and the inclusion of only patients without a history of intraocular surgery.

5. Conclusions

In conclusion, our study demonstrated that the extent of IOP and medication number reductions achieved with standalone TMH were equivalent regardless of incision width. While the overall safety profiles were similar, procedures with a wider incision width resulted in increased hyphema severity in the early postoperative period. When performing TMH on phakic eyes with POAG/JOAG without a history of prior surgery, a trabecular meshwork incision of approximately one-third of the circumference results in the maximum clinical effect.

Author Contributions: Conceptualization, K.S. and M.T.; methodology, K.S. and M.T.; investigation, K.S., C.I., H.O. and M.T.; data curation, K.S., C.I., H.O. and M.T.; writing—original draft preparation, K.S. and M.T.; writing—review and editing, C.I. and H.O. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study adhered to the tenets of the Declaration of Helsinki; the institutional review board (IRB) of Shimane University Hospital reviewed and approved the research (IRB No. 20200517-1; 22 July 2024).

Informed Consent Statement: Preoperatively, all participants provided written informed consent for surgery; however, the IRB approval did not require that each patient provide written informed consent for publication; instead, the study protocol was posted at the study institutions to notify participants about the study.

Data Availability Statement: Data are fully available upon reasonable request to the corresponding author.

Acknowledgments: The English grammar and wording were edited using Chat GPT 4o.

Conflicts of Interest: The microhooks used were co-developed by Masaki Tanito and Inami & Co., Ltd. (Tokyo, Japan). Tanito receives royalties from Inami & Co., Ltd. The company had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the

manuscript, or in the decision to publish the results. Other authors report no conflict of interest in this work.

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Article

Clinical Outcomes of Gonioscopy-Assisted Transluminal Trabeculotomy in Eyes After Failed Trabeculectomy

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Abstract

Background: This study aims to present the clinical outcomes, safety profile, and mid-term results of gonioscopy-assisted transluminal trabeculotomy (GATT) in eyes with failed trabeculectomy. **Methods:** The studied group consisted of 62 patients after failed trabeculectomy. All patients underwent GATT, as a standalone procedure or in combination with cataract surgery (Phaco-GATT), between 2021 and 2023 and had at least 12 months of follow-up. The patients were examined at 1 day, 7 days, 1 month, 3 months, 6 months, and 12 months after surgery, with evaluation of visual acuity, intraocular pressure (IOP), number of antiglaucoma drops, and possible surgical complications. **Results:** The mean IOP before surgery was 37.22 ± 9.07 mmHg, and after the GATT procedure, it significantly decreased to 15.91 ± 5.28 mmHg at the 12-month follow-up. A comparison of patients with one or more previous antiglaucoma procedures showed no differences. A comparison of the degrees of successful canulating and deroofting of Schlemm's canal revealed no statistical significance concerning IOP values or the number of medications. When comparing the IOP between the patients after standalone GATT and Phaco-GATT, a tendency for higher IOP values in the latter group was observed. In 21 (33.3%) patients, hyphema affecting visual acuity was observed early after surgery, which resolved spontaneously. Six patients (9.7%) needed additional surgery to obtain the target pressure. **Conclusions:** GATT is an effective and safe IOP-lowering surgical option in open-angle glaucoma patients with failed trabeculectomy.

Keywords: GATT; MIGS; glaucoma surgery; failed trabeculectomy

1. Introduction

Glaucoma is a group of conditions leading to irreversible sight loss and characterised by progressive loss of retinal ganglion cells [1]. It is one of the most common diseases causing blindness worldwide. In 2020, glaucoma affected over 76 million people, and by 2040, it is expected to be diagnosed in 111.8 million [2]. Although not always elevated, intraocular pressure (IOP) is the only modifiable risk factor in glaucoma treatment that can influence the disease course, as demonstrated by large clinical trials [1]. Moreover, many studies have shown that the successful treatment of glaucoma is based on lowering IOP [3,4] to the target IOP level, which sufficiently decreases the glaucoma progression rate to an acceptable level. The target pressure can be obtained using medical, laser, or surgical treatment.

Trabeculectomy, a golden standard in glaucoma surgery, is an incisional antiglaucoma procedure introduced by Cairns in 1968 [5]. During the surgery, an additional path is created

for aqueous humour to leave the eye's anterior chamber, omitting the natural outflow pathways. Since its introduction, trabeculectomy has been modified with releasable sutures and the additive use of antimetabolites to make the procedure more efficient and safer, with a longer-lasting IOP-lowering effect [6]. Trabeculectomy can obtain IOP in low teen values, which is usually enough to slow glaucoma progression [7]. However, its high efficacy is contrasted by the risk of complications, some of which, usually related to hypotony, are potentially sight-threatening [8]. The final success of trabeculectomy depends not only on the perfect surgical technique but also on the ability to effectively control postoperative healing processes [9]. The late failure of trabeculectomy usually results from scarring within the area of newly created outflow [10]. In cases of primary trabeculectomy failure, revision procedures are usually performed to restore bleb outflow [11]. However, its efficacy is lower compared to primary procedures because each subsequent procedure affecting the conjunctiva and sclera causes excessive scarring, resulting in unrestrained healing [12].

Although trabeculectomy is very effective in decreasing IOP, its safety profile is not always satisfactory. Thus, new surgical procedures have been introduced, focusing on minimising side effects. The techniques in antiglaucoma surgery that are grouped as minimally invasive glaucoma surgery (MIGS) include procedures that spare the conjunctiva and sclera; some of them improve the natural aqueous humour outflow pathways via Schlemm's canal (SC). Gonioscopy-assisted transluminal trabeculotomy (GATT), proposed by Groover et al. [13], is a bleb-independent ab interno intervention, where the inner Schlemm's canal wall is removed and the conventional pathway of aqueous humour is promoted by decreasing outflow resistance. Previously published studies have proved that GATT is a primary antiglaucoma procedure effective in lowering IOP in different types of open-angle glaucoma, juvenile open-angle glaucoma, and childhood glaucoma [13–17].

MIGS techniques are usually offered to glaucoma patients as a first-line surgical treatment in cases with mild to moderate stages of the disease. The aim of this study is to evaluate the efficacy and safety of GATT in patients with prior failed primary trabeculectomy.

2. Materials and Methods

2.1. Studied Group

The studied group consisted of 62 patients after trabeculectomy at the Department of Diagnostics and Microsurgery of Glaucoma, Medical University of Lublin, Poland. All patients who met the inclusion criteria were prospectively included. This study was designed with the approval of the Local Ethics Committee and the Resolution of the Bioethics Committee and performed in accordance with the standards set by the Declaration of Helsinki.

The inclusion criteria were as follows:

- Previously performed failed trabeculectomy;
- Target IOP not obtained after the previous surgical procedures and maximal tolerated antiglaucoma drops;
- Open-angle glaucoma;
- Age over 18 years;
- Written consent agreement to the surgery and to inclusion in this study.

Patients with normal-tension glaucoma were not included in the study group.

At the qualification, the patients underwent detailed anterior and posterior eye segment evaluation with measurement of best-corrected visual acuity, IOP, gonioscopy, and 24-2 perimetry (if BCVA was better than 0.1).

All the patients underwent GATT as a standalone procedure or in combination with cataract phacoemulsification by two experienced surgeons between 2021 and 2023 and had at least 12 months of follow-up. The combined procedure with cataract surgery was

performed in 18 eyes (29%), and GATT alone was performed in 44 eyes (71%). Forty patients were diagnosed with primary open-angle glaucoma (POAG) and twenty-two with pseudoexfoliative glaucoma (PEXG). The detailed demographic characteristics of the studied group are shown in Table 1.

Table 1. Demographic features of the studied group.

Number of Patients	62
Age	72 ± 12.46 years
Gender	29 F/33 M
Type of glaucoma	POAG 40 PEXG 22
IOP	37.22 ± 9.07 mmHg
MD	−16.63 ± 10.27 dB
Number of medications	2.48 ± 1.06
Mean number of previous surgeries	1.59 ± 0.67
Time from the last incisional surgery	27.82 ± 21.32 months

The patients were examined 1 day (1 D), 7 days (7 D), 1 month (1 M), 3 months (3 M), 6 months (6 M), and 12 months (12 M) after the surgery. At each visit, slit-lamp examination, IOP (Goldmann applanation tonometry), BCVA (Snellen decimal scale), and binocular ophthalmoscopy were performed. After the surgery, all antiglaucoma medications were withdrawn, and the patients received topical ofloxacin and dexamethasone 5 times a day up to the 10 D visit, when the treatment was gradually reduced up to 1 M, when all postoperative medications were stopped. In cases of hyphema, the patients additionally received 1% tropicamide for 10 days. Surgical success was recorded according to the previously established criteria, and the possible complications were noted. If the success criteria were not met, antiglaucoma drops were introduced, starting with a single medication. The early spike of IOP was considered when IOP extended the success criteria 1 D after surgery; the increase in IOP at 10 D was classified as surgical failure.

Two criteria were established to assess the success of the surgery:

- S1 A 30% decrease in IOP as compared to the value measured at the last visit before surgery;
- S2 $IOP \leq 18$ mm Hg.

Both criteria were reported as a total success (“S1” or “S2”) when they were met without antiglaucoma drops. Qualified success (“QS1” or “QS2”) was noted when the criteria were fulfilled with additional medical treatment. In cases where additional surgical treatment was needed to reach a target IOP level, the procedure was considered a failure.

2.2. Surgical Procedure

At the temporal side of the eye, a 1.6 mm clear corneal incision was performed. Cohesive viscoelastic was injected to fill the anterior chamber. Around 1 to 2 clock hours later, goniotomy was performed at the opposite site of the angle. One end of a Prolene 6/0 suture was blunted with cautery and gently inserted into the goniotomy. Along 360 degrees, the Schlemm’s canal was then cannulated. If cannulation in one direction did not fully encircle the Schlemm’s canal’s circumference, from the same goniotomy, cannulation in the other direction was attempted. By pulling both ends of the suture, the inner wall of the Schlemm’s canal was peeled off, causing canal unroofing. The extent of Schlemm’s canal deroofing was noted; the surgery aimed to achieve the maximal possible opening. This was followed by anterior chamber irrigation to wash out the viscoelastic, and intracameral cefuroxime was injected.

In 18 eyes, GATT surgery was combined with phacoemulsification. A standard 2.2 mm clear corneal incision cataract surgery was performed at the temporal side of the eye before GATT. After implanting the posterior chamber intraocular lens, a solution of miochol was injected to constrict the pupil. All steps of GATT were subsequently performed as previously described. Cataract surgeries were performed by AČH, and GATT procedures were performed by EKJ.

Statistical evaluation of the data was performed using Statistica 13.1 (Polish version, Statsoft Poland, Kraków, Poland). The results were reported mainly as mean $\pm$ SD or percentage values. A *p*-value lower than 0.05 was considered statistically significant.

3. Results

In the studied group, the mean IOP before surgery was 37.22 ± 9.07 mmHg, and after the GATT procedure, it significantly decreased to 15.91 ± 5.28 mmHg at the 12-month follow-up. When comparing all the postoperative values to the preoperative values, statistical significance was found at all points. Table 2 shows all the postoperative IOP measurements. Moreover, IOP was stable after the procedure at the time of the study (IOP 1 D vs. 12 M; *p* = 0.6095). According to the established criteria of success in 12 M, the success rate was 88.8% for S1 and 90.3% for S2; however, approximately half of the patients needed antiglaucoma medication to fulfil the criteria. At 12 M, observation failures were more frequent in the early postoperative period, with stabilisation after 1 M. The detailed success rate results are presented in Tables 3 and 4.

Table 2. Mean IOP at each follow-up.

Preoperative	37.22 $\pm$ 9.07 mmHg
1 D	15.27 $\pm$ 5.45 mmHg *
10 D	18.83 $\pm$ 9.00 mmHg *
1 M	19.24 $\pm$ 6.27 mmHg *
3 M	18.05 $\pm$ 12.54 mmHg *
6 M	15.82 $\pm$ 4.88 mmHg *
12 M	15.91 $\pm$ 5.28 mmHg *

* At all postoperative visits, IOP was significantly lower compared to the preoperative values, *p* < 0.0001.

Table 3. Success criteria: 30% IOP decrease.

30% IOP Decrease	1 D	10 D	1 M	3 M	6 M	12 M
S	79.0%	56.4%	46.7%	51.6%	54.8%	54.8%
QS	79.0%	61.3%	77.3%	88.8%	91.9%	88.8%
F	21.0%	38.7%	22.7%	11.2%	8.1%	11.2%

Table 4. Success criteria: IOP lower than 18 mmHg.

IOP Lower than 18 mmHg	1 D	10 D	1 M	3 M	6 M	12 M
S	88.7%	75.8%	50.0%	51.6%	51.6%	50%
QS	88.7%	80.6%	77.4%	90.3%	93.5%	90.3%
F	11.2%	19.4%	22.6%	9.7%	6.5%	9.7%

A statistically insignificant decrease in BCVA was noted on day 1 after surgery. It was caused by hyphema, which spontaneously resolved in all cases at the 10 D visit. The details of the BCVA changes are presented in Table 5. Preoperatively, the mean MD was -16.63 ± 10.27 dB and did not change during the follow-up period (at 12 M MD

-14.38 ± 9.64 dB; $p = 0.3571$). The mean number of antiglaucoma medications taken daily decreased significantly after the surgery at 12 M (2.48 ± 1.06 and 1.45 ± 1.21 , respectively; $p = 0.0002$). However, an increase in medications between 1 D and 12 M was noted (Table 6).

Table 5. Best-corrected visual acuity during the study.

Best-Corrected Visual Acuity		<i>p</i> -Value Compared to Preoperative
Before the surgery	0.48 ± 0.37	x
1 D	0.32 ± 0.31	$p = 0.008$
10 D	0.40 ± 0.3	$p = 0.0420$
1 M	0.46 ± 0.31	$p = 0.3482$
3 M	0.54 ± 0.34	$p = 0.6896$
6 M	0.53 ± 0.33	$p = 0.8072$
12 M	0.47 ± 0.37	$p = 0.5563$

Table 6. Number of antiglaucoma medications taken by the patients during the study.

Number of Antiglaucoma Medications	
Before the surgery	2.48 ± 1.06
1 D	0.25 ± 0.74 *
10 D	0.44 ± 0.97 *
1 M	0.84 ± 1.16 *
3 M	1.11 ± 1.18 *
6 M	1.25 ± 1.25 *
12 M	1.45 ± 1.21 *

* At all postoperative visits, the number of antiglaucoma drops was significantly lower compared to the preoperative values, $p < 0.0001$.

In 32 patients, only trabeculectomy was performed before the GATT procedure. Thirty patients had more than one procedure (including trabeculectomy with one or two bleb revisions). Analysis of IOP decrease between these two groups revealed no statistical significance after 12 months (12 M 15.08 ± 5.82 vs. 16.85 ± 4.78 $p = 0.4519$), and the percentage decrease values were 56.6% and 58.0%, respectively. There was also no statistical significance in the number of medications taken daily after 12 months (1.58 ± 1.31 in group one vs. 1.33 ± 1.15 in group two; $p = 0.6250$).

According to the extent of the opening of Schlemm's canal, patients were divided into two groups: one with an opening of 180 degrees or less and one with an opening of more than 190 degrees. Comparison of the degrees of successful Schlemm's canal cannulation and deroofing revealed no statistical significance concerning the IOP values or the number of medications at any follow-up point. The IOP comparison results are shown in Table 7. Additionally, the number of previous antiglaucoma surgeries did not influence the IOP results (Table 8).

Table 7. Comparison of IOP values depending on the extent of Schlemm's canal deroofing.

	90–180 Degrees	190–360 Degrees	<i>p</i> -Value
Number of patients	24	38	
Before surgery	37.31 ± 9.02	37.94 ± 10.17	$p = 0.8146$
Day 1	15.87 ± 5.95	13.47 ± 3.55	$p = 0.1235$
Day 10	18.19 ± 6.93	20.82 ± 13.73	$p = 0.3190$
1 M	19.76 ± 6.75	18.56 ± 5.34	$p = 0.5232$
3 M	18.68 ± 14.43	16.64 ± 5.58	$p = 0.6105$
6 M	16.06 ± 5.27	14.66 ± 3.64	$p = 0.4630$
12 M	15.31 ± 5.16	18.2 ± 5.67	$p = 0.2871$

Table 8. Comparison of mean IOP depending on the number of previous antiglaucoma surgeries.

	One Glaucoma Surgery Before GATT	More than One Glaucoma Surgery Before GATT	<i>p</i> -Value
Number of patients	32	30	
Before surgery	34.78 ± 7.97	40.12 ± 9.56	<i>p</i> = 0.0144
Day 1	14.40 ± 4.18	16.32 ± 6.05	<i>p</i> = 0.1504
Day 10	18.91 ± 5.66	18.73 ± 12.03	<i>p</i> = 0.9339
1 M	18.59 ± 6.5	20.03 ± 5.99	<i>p</i> = 0.3535
3 M	16.60 ± 5.39	19.68 ± 17.4	<i>p</i> = 0.3783
6 M	15.94 ± 4.51	15.62 ± 5.52	<i>p</i> = 0.8381
12 M	15.08 ± 5.82	16.85 ± 4.78	<i>p</i> = 0.4519

Comparing the IOP values between the patients after standalone GATT and Phaco-GATT revealed a tendency for higher IOP values in the latter group at 10 D and 6 M. The detailed results of the comparison are shown in Table 9.

Table 9. Comparison of IOP values between the GATT and Phaco-GATT groups.

	GATT	Phaco-GATT	<i>p</i> -Value
number of patients	44	18	
IOP preoperatively	37.0 ± 9.28	37.88 ± 8.63	<i>p</i> = 0.7313
Day 1	15.41 ± 5.76	14.88 ± 4.52	<i>p</i> = 0.7318
Day 10	17.66 ± 6.02	22.29 ± 14.36	<i>p</i> = 0.0664
1 M	19.46 ± 5.95	18.58 ± 7.25	<i>p</i> = 0.6213
3 M	18.76 ± 14.5	16.26 ± 4.83	<i>p</i> = 0.5190
6 M	15.07 ± 3.57	17.5 ± 6.92	<i>p</i> = 0.1551
12 M	16.52 ± 5.81	14.42 ± 3.64	<i>p</i> = 0.3877

In 21 (33.3%) patients, hyphema affecting visual acuity was observed at 1 D, which spontaneously resolved at the 10 D visit without additional treatment. Six patients (9.7%) required additional surgery to reach the target pressure: two patients required an Ahmed valve; two patients required cyclophotocoagulation of the ciliary body; one patient required needling revision; and one patient required trabeculectomy.

4. Discussion

Late failure of trabeculectomy with increased IOP is caused by excessive scarring. In our department, in cases of unsuccessful trabeculectomy, needling revision is typically performed. The technique is carried out with a bent 5G needle to disrupt formed synechiae at the level of conjunctiva, Tenon's capsule, and intrascleral; additionally, the needle is introduced into the anterior chamber via a fistula [12]. However, such intervention subsequently activates the healing processes, finally leading to the renewal of inflammatory scarring at the level of the conjunctiva and Tenon's capsule. A longer period between primary trabeculectomy and revision can lead to better IOP-lowering results for the latter, probably due to the superior attenuation of inflammation. However, clinically successful IOP lowering is not always obtained with a revision procedure, and it is best to plan the next surgery based on the different mechanisms of IOP-lowering action.

The main site of outflow resistance for aqueous humour from the eye's anterior chamber in conventional outflow pathways is thought to be located in the region of the inner wall of SC and the juxtacanalicular tissue (JCT) [18]. The high IOP in POAG is caused by an increase in the outflow resistance at this level. However, on the other hand, elevated IOP during the course of glaucoma also causes multiple changes within

SC [19,20]: studies evaluating POAG patients showed decreased SC cross-sectional area, perimeter, and length [21–23]. Histopathologic studies revealed increased collapse and narrowing of collector channels (CCs) and intrascleral veins, adhesion of SC endothelium to CC orifice walls, and herniation of JCT with blockage of CC orifices [24]. Additionally, a decrease in SC size after trabeculectomy was described and attributed to a decline in meshwork perfusion and extracellular material accumulation, leading to increased outflow resistance [25]. Considering the mentioned SC changes during the course of glaucoma, SC-based surgeries are believed to lose efficacy in advanced stages of glaucoma. Moreover, it was long thought that SC-based procedures are not effective in chronic adult glaucoma, especially in cases of previous surgery omitting natural outflow pathways, such as trabeculectomy. However, some studies show GATT IOP-lowering efficacy in advanced glaucoma [16,26,27], and, on the other hand, the expansion of SC after trabeculectomy is reported [28].

GATT is based on removing the inner wall of Schlemm's canal and, as a result, decreasing outflow resistance. Its efficacy depends on the proper function of distal outflow pathways, which, unfortunately, cannot be plausibly evaluated before the surgery. Only a few studies have evaluated the efficacy of GATT in patients after incisional, bleb-forming surgeries. Grover et al. [29] described 35 patients who underwent GATT after primary incisional surgery and found that the procedure was safe and successful in treating 60% to 70% of open-angle patients with prior incisional glaucoma surgery. Cubuk et al. [30] reported a case series study that included 26 eyes of patients who underwent GATT using the 5/0 Prolene suture to treat medically uncontrolled moderate to advanced glaucoma despite a previous trabeculectomy surgery. In this group, the average baseline IOP was 25.3 ± 5.4 (16–45) mmHg, which significantly declined after the procedure to IOP values that were lower in PEXG than in POAG patients (13.4 mmHg vs. 17.1 mmHg). To obtain such an IOP, most patients needed antiglaucoma medication, but the GATT procedure enabled a significant reduction in their numbers. Wang et al. [31] described 44 eyes of 35 patients (21 with juvenile-onset open-angle glaucoma and 14 with adult-onset POAG). Of the patients, 79.5% underwent one previous incisional surgery and 20.5% underwent two prior surgeries. In the case series, IOP decreased from 27.4 ± 8.8 mm Hg on 3.6 ± 0.7 medications preoperatively to 15.3 ± 2.7 mm Hg on 0.5 ± 0.9 medications at the 24-month visit. The complete and qualified success rates were 60.9% and 84.1%, respectively. Siddhartha et al. [32] studied 27 eyes after a failed trabeculectomy and 3 eyes after a failed glaucoma drainage device, which underwent GATT (21 eyes) or Phaco-GATT (9 eyes). In this group post-GATT, the IOP decreased from 27.1 ± 7 mmHg to 16.9 ± 6 mmHg at the end of 15 months. At postoperative 1 year, the probability of complete success was 20% for an IOP criterion of both 21 and 16 mm Hg, but the qualified success probability at 1 year was 82% for an IOP of 21 mmHg and 57% for an IOP of 16 mmHg.

The mean IOP value in our patients at the 12 M visit was 15.91 mmHg, which was significantly lower than the preoperative values. The rates of success for precluded criteria were about 90%; however, almost half of the patients needed medical treatment to obtain them. Only six patients needed additional surgery. In the case of GATT, as a minimally invasive procedure, the IOP-lowering results are encouraging. Additionally, the results of our study seem to be more favourable than the previous reports. We believe that the higher rate of success in our group is related to two possible reasons. The first is the high baseline IOP, which makes it easier to obtain a 30% decrease in IOP, which is usually difficult with SC surgery in cases with IOP lower than 20 mmHg. The second possible reason may be the midterm follow-up. On the other hand, most surgical failures after GATT are observed within 3 months after the surgery and are probably related to permanent distal outflow impairment.

In our group of patients, high preoperative IOP with a mean value of more than 37 mmHg on maximal tolerated medical therapy drew attention. It was originally believed that in patients with such high IOP values, SC and natural outflow pathways are not to be preserved, and the results of MIGS are unsatisfactory. Our previous study [33], similar to this one, shows that despite high preoperative IOP, the 12 M IOP is about 15 mmHg, not worse than the results typically obtained with this technique. Additionally, we divided the patients into two groups: one group with one failed trabeculectomy and a second group with patients after trabeculectomy with additional IOP-lowering interventions. Although the preoperative IOP was significantly higher in the latter group, there was no difference in the postoperative IOP values. These results show that the GATT technique may be effectively applied in quite a broad spectrum of open-angle glaucoma patients, and high IOP values are not a bad prognostic factor.

Our study is the first to show that in GATT after trabeculectomy, the limited removal of the SC inner wall is also sufficient to successfully decrease IOP. The localisation of collector channels is not obvious and predictable in patients before the surgery. Studies of the pig eye showed that the main localisation of the outflow is the nasal-inferior quadrant. However, in humans, the localisation of the outflow is more variable and differs not only between subjects but also between the two eyes of one patient. Additionally, in the human eye, low-flow regions could become high-flow, and vice versa, based on need [34]. This suggests that as the opening of Schlemm's canal is increased, a lower IOP may be obtained. This was not confirmed in previous studies evaluating GATT as primary surgery, which surprisingly showed that results of GATT and hemiGATT were similar [35–38]. Moreover, hemiGATT performed in superior or inferior hemispheres did not differ in postoperative IOP [39]. Our results also confirm this for refractory glaucoma: the 180-degree deroofing of Schlemm's canal allowed us to obtain a 12 M IOP similar to total Schlemm's canal deroofing. The other argument for hemiGATT is that it causes less hyphema and accelerates eye recovery compared to 360 GATT. The exception is congenital glaucoma, where the maximal Schlemm's canal opening is related to a lower IOP [40].

Previous trabeculectomy poses the risk that advancing the catheter in SC might be difficult or even impossible in the sclerostomy area; the advancement of the catheter may also be prematurely terminated with its appearance in the anterior chamber. However, GATT surgery is usually possible by changing the direction of the suture or making other adjustments to the technique. Depending on the position of the sclerotomy against SC, we usually choose the direction of the first catheter implementation to be opposite to the localisation of the sclerotomy to obtain the maximal part of the circumference catheterised at the first attempt.

In our group of patients, in cases of lens opacification, GATT surgery was combined with cataract surgery. In the case of many MIGS surgeries, adding cataract removal enables lower postoperative IOP. However, few studies compare GATT and Phaco-GATT. Zhang et al. [41] compared postoperative IOP reduction between a GATT alone group and a GATT combined with cataract extraction group. The number of postoperative glaucoma medications was higher in the GATT alone group, and the reoperation rate was also higher in the GATT group. In a retrospective analysis of 64 eyes, Yozgat et al. [42] also confirmed that Phaco-GATT and standalone GATT demonstrated comparable efficacy and safety over a two-year period. On the other hand, Bozkurt et al. [43] showed that GATT alone has a superior lowering effect on IOP than combined surgery, but there was no difference in the final IOP values. A possible explanation for the worse results of Phaco-GATT is the more inflammatory reaction caused by the combined procedure. A similar tendency for the inferior IOP-lowering effect of the combined procedure was also observed in our study, but a further evaluation of a larger patient group is required.

Moreover, cataract surgery has a different influence on glaucoma patients depending on the history of trabeculectomy. Teckan et al. [44] analysed the effect of uneventful cataract surgery on IOP in PEX glaucoma with and without previous trabeculectomy with adjacent MMC. In the trabeculectomised eyes, an increase in IOP and the mean number of medications was significant. In our group of patients, mitomycin was typically applied on sponges during primary trabeculectomy and injected during the revision procedure. In this study, during GATTs combined with cataract surgeries, no injections of antimetabolite or anti-VEGF were applied to protect the bleb. The further decrease in bleb function caused by cataract surgery may be the reason that the IOP-lowering results were slightly worse in the Phaco-GATT group. The potential influence of adjunctive therapies during Phaco-GATT requires further evaluation.

GATT surgery is a safe procedure. One of its very common complications is hyphema, which is usually self-limiting and transient. In this case series, hyphema spontaneously resolving within 10 D after surgery without IOP spikes was observed in 33% of the patients. Macrohyphema was described as a negative prognostic factor for GATT success [45]. Our studies show that hyphema after GATT is rarely combined with high IOP, and even if it requires surgical removal, IOP remains stable and low. In our group of patients, we did not notice early IOP spikes after the surgery. One possible reason is the maximal removal of viscoelastics before the end of the surgery. This decreases the incidence of IOP spikes but increases the risk of prominent hyphema. However, in our group of advanced glaucoma patients, IOP safety was crucial, and a possible decrease in BCVA was discussed with the patients before surgery. The possible complications reported by other authors, such as Descemet detachment, irydodialysis, ciliochoroidal detachment, corneal oedema, vitreous haemorrhage, malignant glaucoma [46,47], or cystoid macular oedema, were not observed in our studied group.

This study has some limitations. The evaluation of surgical success was performed according to established criteria across all patients. However, in clinical practice, individual values of target IOP are set to monitor each patient. GATT typically allows for lowering IOP to a mid-teen value, which was also shown in this study. This value is not always enough to stabilise glaucoma progression, especially in advanced cases. In our study, we attempted to open SC to the maximal extent; however, this was not always possible. For statistical reasons, the studied group was divided into two groups according to tear extent: more and less than 180 degrees. It is possible that the lower extent of the procedure, especially below 120 degrees, may cause a lower IOP decrease. However, the number of patients with an SC opening extent below one-third of its circumference was too small to conclude. Additionally, in our group, the time between trabeculectomy and GATT was not reported because our study group was heterogeneous regarding the number of procedures. Some patients had undergone additional revision procedures, which may influence the inflammatory status of the anterior chamber and, finally, the GATT results.

To conclude, our study shows that GATT is an effective and safe IOP-lowering procedure applied in open-angle glaucoma patients after unsuccessful trabeculectomy.

Author Contributions: Conceptualisation, A.Ć.-H. and E.K.-J.; methodology, A.Ć.-H. and E.K.-J.; software, D.W.-D.; formal analysis, D.W.-D. and E.K.-J.; investigation, A.Ć.-H. and E.K.-J.; data curation, D.W.-D. and E.K.-J.; writing—original draft preparation, A.Ć.-H. and E.K.-J.; visualisation, D.W.-D. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki. It was approved by the local ethical committee at the Medical University of Lublin (approval number KE-0254/27/2022) on 25 March 2022 and by the Resolution of the Bioethics Committee (approval number KE-0254/149/2018) on 24 May 2018.

Informed Consent Statement: Informed consent was obtained from all subjects involved in this study.

Data Availability Statement: The data are available on request from the corresponding author.

Conflicts of Interest: The authors declare no conflicts of interest.

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Article

Comparison of Surgical Times for Gonio Lenses and Viewing Systems in iStent Inject[®] W Surgery

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Abstract

Background/Objectives: The aim of the study was to investigate the difference in operative times for iStent inject[®] W (iStent) implantation based on variations in the gonio lens and with use of a surgical microscope or the NGENUITY[®] 1.5 (Alcon Laboratories, Inc. Fort Worth, TX, USA) which is a digitally assisted surgery system). **Methods:** This retrospective study included patients who underwent iStent implantation performed by the same surgeon at Juntendo University Urayasu Hospital between January 2021 and December 2022. Participants were divided into Group M, which utilized a disposable gonio lens (Ocular Instruments, Washington, DC, USA) and the surgical microscope; Group A, which used Ahmed's DVX Surgical Gonio lens[®] (Ocular Instruments) and the surgical microscope; and Group D, which employed the disposable gonio lens and the NGENUITY[®] system. The preparation and recovery times were retrospectively compared as the primary outcome across the three groups. **Results:** Preparation and recovery times were significantly shorter in Group A than those in the other two groups (both $p < 0.01$). There were no significant differences in preparation ($p = 0.968$) and recovery times ($p = 0.841$) between groups M and D. **Conclusions:** In iStent surgery, preparation and recovery times for angle observation were shorter with the Ahmed gonio lens than with the disposable gonio lens. No difference was observed between the surgical microscope and digitally assisted surgery methods. The Ahmed gonio lens is useful for surgeons who perform cataract surgery through an upper incision.

Keywords: surgical time comparison; iStent implantation; gonio lens systems

1. Introduction

Glaucoma is the leading cause of blindness in Japan. The Tajimi Study reported a 3.9% prevalence rate of primary open-angle glaucoma [1]. Although it is standard practice to initially reduce intraocular pressure (IOP) using glaucoma eye drop therapy, when the eye drops are insufficient to produce this effect, surgical intervention is considered. Recently, compared to trabeculectomy, minimally invasive glaucoma surgery (MIGS) has become more widely used because of its scar-sparing approach. The iStent[®] (Glaukos Corporation, Laguna Hills, CA, USA) was one of the first MIGS devices, introduced by Spiegel et al. in 2007 [2]. In 2012, it was approved by the U.S. Food and Drug Administration for use in surgery simultaneously with cataract surgery in patients with early to intermediate-stage open-angle glaucoma treated with eye drops. In Japan, the guidelines for using intraocular drainage with cataract surgery were established in 2016, with a second edition released in 2019, and the criteria for iStent[®] use were significantly expanded

in the second edition [3]. Following this expansion, iStent[®] is now used during cataract surgery in cases of early- and intermediate-stage glaucoma and cataract progression.

Implantation of the iStent[®] requires placing a gonio lens on the cornea for angle observation, with an inclination of approximately 70° to the visual axis. For direct gonioscopy that requires the surgeon to tilt the microscope or the patient's head, the Swan–Jacob gonio lens (Ocular Instruments, Washington, DA, USA) or the disposable hands-free surgical gonio lens (Ocular Instruments, Washington, DA, USA) (hereafter referred to as the “disposable gonio lens”) can be used. Double-mirror gonio lenses that allow observation of the angle without tilting the microscope include the Mori gonio lens (Ocular Instruments, Washington, DA, USA) (hereafter referred to as “Mori gonio lens”) and Ahmed's DVX Surgical Gonio lens[®] (Ocular Instruments, Washington, DA, USA) (hereafter referred to as “Ahmed gonio lens”) (reprinted from R.E. Medical Corporation, “Surgical Lens Catalog”, which compares typical gonio lenses, as shown in Figure 1 and Table 1). The Mori goniotomy lens has a magnification of 0.8× and a 110° field of view, enabling angled observation with a direct view under the surgical microscope [4]. Ahmed gonio lens[®] has a magnification of 1.3× and a 120° field of view, superior to those of the disposable and the Mori gonio lens, enabling angle observation under a microscope with a frontal view. Few reports exist on the use of the Ahmed gonio lens. The only study on its use for dissecting angle adhesions in patients with primary angle-closure glaucoma was published by Lei et al. in 2022 [5].



Figure 1. Cont.



(c)



(d)

Figure 1. Typical surgical gonio lenses. (a) Swan–Jacob lens; (b) disposable hands-free surgical gonio lens; (c) Ahmed DVX surgical gonio lens; (d) Mori goniotomy lens.

Table 1. Comparison of typical surgical gonio lenses.

	Swan–Jacob	Disposable	Ahmed DVX	Mori
Microscope tilt	70°	70°	Unnecessary	Unnecessary
Magnification	1.2×	1.2×	1.3×	0.8×
View angle (°)	90	90	120	110
Eyepiece (mm)	9.5	15.5	10.0	11.5
Handle	With	Without	With	Without
Cost ^{※1}	USD 650.00	USD 30.00/unit ^{※2}	USD 1050.00	USD 850.00

^{※1} The cost of each gonio lens from R.E. Medical Corporation was accurate at May 16 2025. ^{※2} The disposable gonio lens is sold in a carton of 10.

Digital surgery, also known as “heads-up surgery” or “digitally assisted surgery (DAS)”, is performed by viewing the surgical field projected onto a 3D monitor. In DAS, the surgeon does not need to look through the surgical microscope; therefore, the microscope and the surgeon’s line of sight do not need to align. DAS can also be used in NGENUITY® digital surgery to process images of the surgical field, enhancing the observation of the angle during the MIGS procedure, as with the iStent. Despite the increasing use of MIGS, there is limited information on the impact of varying gonio lenses and observation systems on the operating time and outcomes.

Therefore, we aimed to address this gap by investigating the difference in operative times for iStent inject® W (hereafter referred to as “iStent”) implantation with varying gonio lenses and viewing systems.

2. Materials and Methods

2.1. Case Background

This study was approved by the Ethics Committee of Juntendo University Urayasu Hospital and conducted following the principles of the Declaration of Helsinki. Informed consent was obtained from all patients.

In this retrospective study, we included cases of iStent implantation performed by the same surgeon (Y.S.) at Juntendo University Urayasu Hospital between January 2021 and December 2022. The cases were divided into three groups: Group M, which used the disposable gonio lens and microscope oculars; Group A, which used the Ahmed gonio lens and lens barrel; and Group D, the DAS group, which used the disposable gonio lens and NGENUITY® 1.5 (Alcon Laboratories, Inc. Fort Worth, TX, USA). The study included 24 eyes from 24 patients in Group M (mean age: 74.4 ± 6.4 years), 25 eyes from 25 patients in Group D (mean age: 71.4 ± 10.7 years), and 19 eyes from 19 patients in Group A (mean age: 73.0 ± 6.6 years). Preparation and recovery times were evaluated from the surgical videos and compared retrospectively.

We reprinted the “Surgical Lens Catalog” from R.E. Medical Corporation, comparing typical gonio lenses in Figure 1 and Table 1.

2.2. Surgical Method

A 1.00 mm side port was created in all three groups, the anterior chamber was formed using the DisCoVisc 1.0® (Nihon Alcon K.K. Tokyo, Japan) viscoelastic agent, and a 2.40 mm main upper incision was made. The anterior capsule was then incised, and phacoemulsification and cortical aspiration were performed, followed by intraocular lens implantation. After injecting the viscoelastic substance and forming the anterior chamber, the iStent was implanted in each group: in Group M, after injecting the viscoelastic substance into the anterior chamber, the surgeon moved to the patient’s ear side, adjusted the microscope barrel tilt, changed the patient’s head position, and repositioned the microscope in the XYZ direction. The disposable gonio lens was then placed to visualize the angle, the iStent was inserted with both hands through the side port on the ear side, and the anterior chamber was washed. In Group A, after injecting the viscoelastic material into the anterior chamber, the Ahmed gonio lens was used to visualize the angle, and the iStent was inserted with one hand, followed by anterior chamber irrigation. In Group D, after injecting the viscoelastic substance into the anterior chamber, the microscope oculars were rotated toward the ear, the microscope oculars’ tilt was adjusted, and the patient’s head position and microscope alignment in the XYZ direction were modified. The disposable gonio lens was placed to visualize the angle, the iStent was inserted with both hands through the side port on the ear side, and the anterior chamber was washed.

The preparation time was defined as the interval from the end of cataract surgery (when the viscoelastic injection needle was removed from the eye) to the moment the anterior chamber angle could be visualized under the microscope. The recovery time was defined as the interval from completing iStent implantation (when the injector was removed from the anterior chamber) to when the anterior chamber was visible under the microscope. Preparation and recovery times were the primary outcomes, and other metrics (e.g., safety, complications) were not evaluated in this study. The procedures for preparation and recovery in each group are presented in Tables 2 and 3.

Table 2. Procedures for preparing each group.

	Group M	Group A	Group D
Removal of viscoelastic material injection needle from inside the eye	○	○	○
The surgeon moves to the temporal side	○		
Tilt the microscope	○		○
Change in patient's head position	○		○
Adjusting the position of the microscope	○		○
Put the gonio lens on the cornea	○	○	○
Observe the angle	○	○	○

○ The procedure is necessary.

Table 3. Procedures for recovery in each group.

	Group M	Group A	Group D
Removal of iStent inject W [®] from the anterior chamber	○	○	○
The surgeon moves upward	○		
Change in patient's head position	○		○
Restore the tilt of the microscope	○		○
Adjusting the position of the microscope	○		○
Observe the anterior chamber	○	○	○

○ The procedure is necessary.

2.3. Statistics

Continuous variables in the case backgrounds were analyzed using the Kruskal–Wallis test, while binary nominal variables were analyzed using Fisher's exact test. The Bonferroni correction was used when comparing preparation and recovery times. Statistical significance was set at $p < 0.05$, and the analysis was performed using IBM SPSS (v26 [for Mac]) (IBM Corp., Armonk, NY, USA).

3. Results

A total of 68 patients (24 in Group M, 19 in Group A, and 25 in Group D) were included in the study. The demographic characteristics of each group are presented in Table 4. The mean age of the patients was 74.4 ± 6.4 years in Group M, 73.0 ± 6.6 years in Group A, and 71.4 ± 10.7 years in Group D, with no significant difference between the groups. There was no significant difference in the sex distribution among the study groups. There was no significant difference in the number of right and left eyes among all groups.

Table 4. Patient background.

	Group M	Group A	Group D	<i>p</i> -Value
No. (eye)	24	19	25	
Age (years)	74.4 ± 6.4	73.0 ± 6.6	71.4 ± 10.7	0.62
Male: Female	11:13	8:11	17:8	0.17
Right: Left (eyes)	13:11	9:10	12:13	0.91

Kruskal–Wallis test with Bonferroni correction.

The preparation and recovery times for each group are shown in Table 5. The preparation time was 54.5 ± 18.2 s in Group M, 20.9 ± 5.6 s in Group A, and 51.6 ± 14.1 s in Group D. The recovery time was 19.5 ± 5.9 s in Group M, 9.6 ± 4.6 s in Group A, and 20.0 ± 5.3 s in Group D. In all cases, Group A had significantly shorter preparation ($p < 0.01$) and recovery ($p < 0.01$) times than groups M and D. There were no significant differences between groups M and D in the preparation ($p = 0.968$) and recovery ($p = 0.841$) times.

Table 5. Preparation and recovery times for each group.

	Group M	Group A	Group D	<i>p</i> -Value
Preparation time (seconds)	54.5 ± 18.2	20.9 ± 5.6	51.6 ± 14.1	<0.01
Recovery time (seconds)	19.5 ± 5.9	9.6 ± 4.6	20.0 ± 5.3	<0.01

Kruskal–Wallis test with Bonferroni correction.

4. Discussion

In this study, we examined the difference in preparation and recovery times between iStent implantation using a gonio lens and viewing system. We found that preparation and recovery times were shorter with the Ahmed gonio lens than with the disposable gonio lens and DAS. In iStent implantation, using a disposable gonio lens requires the surgeon to move to the patient's ear side and reposition the patient's head. In contrast, with the Ahmed gonio lens, these steps are not needed, allowing for a shorter procedure time. There was no significant difference in preparation and recovery times between when NGENUITY® was used with a disposable gonio lens and when a surgical microscope was used with a gonio lens. However, the preparation and recovery times were significantly shorter in the group using the Ahmed gonio lens.

Double-mirror-type gonio lenses, such as the Ahmed gonio lens, have reduced resolution and a narrower field of view owing to double image reflection. However, the Ahmed gonio lens surpasses the Mori gonio lens [3] in magnification and field of view. Clear angle observation is essential for iStent surgery and other angle-related MIGS procedures [6]. This study suggests that the Ahmed gonio lens may reduce iStent implantation times, even for surgeons performing phacoemulsification through an upper incision without switching to a lateral position. Similar to the Mori gonio lens' usefulness for trabeculectomy and other angle surgeries [4], the Ahmed gonio lens is considered beneficial for iStent® surgery and other angle procedures.

DAS performed using NGENUITY® has been reported in vitreous surgery, cataract surgery, and trabeculectomy [7–9]. The advantages of digital surgery with NGENUITY® include natural image reproduction with a high dynamic range, a wide depth of field, lower intraocular illumination levels than conventional microscopes [10], and enhanced visibility through image processing of the surgical field. In MIGS procedures for the trabecular meshwork, such as iStent, improved visualization enhances the contrast between the trabecular meshwork and the surrounding tissue. With a disposable gonio lens, the surgeon must move to the ear side; however, with NGENUITY®, the surgeon can insert

the iStent by simply rotating the telescope while remaining in the upper position. In this study, there was no significant difference in preparation or recovery times between when NGENUITY[®] was used with a disposable gonio lens and when a surgical microscope was used with a gonio lens. However, in canal-based MIGS, NGENUITY[®] offers an advantage in terms of angle visualization and digital image enhancement [11].

When using the Ahmed gonio lens for angle observation, the gonio lens must be held in the left hand. The iStent injector is held in the right hand for the right eye and in the left hand for the left eye. Training is essential to master the operation. In 2003, Ayaki et al. studied the learning curve for performing phacoemulsification and aspiration with a lateral incision in five ophthalmologists. They examined the learning curve for making a lateral corneal incision, performing phacoemulsification and aspiration, and inserting the intraocular lens, using the right hand for the right eye and the left hand for the left eye [12]. For first-time left-hand surgery, experience with other surgical techniques using the right hand seemed difficult to apply. This trend in the learning curve for the left hand seemed to align with the progress of beginners. The iStent inject is designed to enhance procedural efficiency and ease the learning curve for successful implantation [13]. However, if a surgeon struggles to perform iStent implantation stably with one hand, using a disposable gonio lens that allows angle observation without needing the other hand may be an option. Over time, one-handed implantation could become feasible as the surgeon gains proficiency.

This study has some limitations. We only examined surgeries involving an upper incision and did not assess the impact of different angle lenses on operating time using a lateral incision. Additionally, the time required for iStent implantation was not considered, and further investigation into this aspect will be necessary. Moreover, this was a retrospective study with a small sample size. In addition, the surgeon's proficiency with the gonio lens and viewing system may have affected the results.

5. Conclusions

Using the Ahmed gonio lens in iStent implantation reduced the preparation and recovery times for angle observation when compared with those using disposable gonio lenses. The Ahmed gonio lens is useful for surgeons who perform cataract surgery using an upper incision.

Author Contributions: Conceptualization, T.F.; methodology, Y.S.; software, S.M.; validation, T.F.; formal analysis, Y.S.; investigation, T.F.; resources, S.M.; data curation, T.F.; writing—original draft preparation, T.F.; writing—review and editing, N.E.; visualization, Y.S.; supervision, N.E.; project administration, Y.S.; funding acquisition, Y.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Juntendo University Urayasu Hospital (protocol code E21-0058-U01). Approval Date: 20 August 2021.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The raw data supporting the conclusions of this article will be made available by the authors on request.

Acknowledgments: We would like to express our gratitude to all the staff of the Ophthalmology of Juntendo University Urayasu Hospital for their support and cooperation.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

SPSS	Statistical Package for the Social Sciences
PEA	Phacoemulsification and Aspiration
IOP	Intraocular Pressure
MIGS	Minimally Invasive Glaucoma Surgery
DAS	Digitally Assisted Surgery

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Article

Visualization of the Postoperative Position of the Hydrus[®] Microstent Using Automatic 360° Gonioscopy

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Abstract: Introduction: Glaucoma, one leading cause of irreversible vision loss worldwide, is primarily caused by elevated intraocular pressure (IOP). Recently, minimally invasive glaucoma surgeries (MIGSs) have become popular due to their shorter surgical times, tissue-sparing nature, and faster recovery. One such MIGS, the Hydrus[®] nickel–titanium alloy Microstent, helps lower IOP by improving aqueous humor outflow. The NIDEK GS-1 automated 360° gonioscope provides advanced imaging of the chamber angle for evaluation and documentation. The aim of this study was to test automated 360° gonioscopy for the detection of postoperative positional variations after Hydrus[®] Microstent implantation. This study is the largest to date to evaluate post-op positioning of the Hydrus[®] Microstent using the NIDEK GS-1. **Materials and Methods:** This study analyzed postoperative outcomes and stent location in eyes diagnosed with mild to moderate glaucoma that underwent Hydrus[®] Microstent implantation with or without phacoemulsification. Patients with prior IOP-lowering surgery or vitrectomy were excluded. Analyses of the postoperative Hydrus[®] Microstent position were based on the evaluation of automated 360° gonioscopy images. **Results:** Twenty-three eyes were included in the study, and all showed a reduction in IOP and a decrease in antiglaucomatous drop use postoperatively. Postoperative gonioscopic images showed variations in implant position. In all cases, the proximal inlet was clearly visible in the anterior chamber. The degree of protrusion into the anterior chamber was variable. The distal tip of the stent was visible behind the trabecular meshwork in Schlemm’s canal in five cases, in the anterior chamber in one case, and not visible in seven cases. In no case did postoperative alterations in the position of the implant lead to explantation. **Conclusions:** This study demonstrated that the Hydrus[®] Microstent can effectively lower IOP even in the presence of postoperative positional variations. Automated 360° gonioscopy was found to be a useful tool to verify and document the postoperative position of the implant. Positional changes did not require device explantation in any of the cases evaluated.

Keywords: minimally invasive glaucoma surgery; glaucoma; Hydrus Microstent; Gonioscopy; imaging

1. Introduction

Glaucoma is one of the leading causes of irreversible vision loss worldwide. The disease can eventually cause blindness. The main risk factor for the progression of the disease is elevated intraocular pressure (IOP). Pathophysiologically, the progressive loss of retinal ganglion cells results in optic nerve damage and visual field loss. The most effective strategy to influence the progression of glaucoma is to lower IOP. The first line of treatment includes IOP-lowering eye drops and laser surgery [1–3]. If these approaches are not sufficient, several surgical procedures are available to correct the imbalance between aqueous humor production and outflow. The epithelium of the ciliary body is responsible for the production of aqueous humor, which drains mainly through the trabecular meshwork and Schlemm’s canal into the episcleral veins [1,2].

In recent years, there has been a trend in glaucoma surgery towards minimally invasive glaucoma surgery (MIGS) to lower intraocular pressure (IOP). These procedures are an alternative to traditional methods such as trabeculectomy, with the goal of achieving similar postoperative IOP reduction. These procedures are particularly suitable for individuals with mild or moderate primary open-angle glaucoma. The goals of MIGS are shorter surgical times, tissue-sparing procedures, ease of use, and shorter rehabilitation times. MIGS is often combined with cataract surgery, but is also available as a stand-alone treatment option [4–7].

The Hydrus[®] Microstent (Ivantis Inc., Irvine, CA, USA) is one such ab-interno trabecular micro-bypass implant that is inserted through the trabecular meshwork into Schlemm's canal. The microstent is made of nitinol, a metal alloy of nickel and titanium. The device is 8 mm long (major/minor axes: 292 μ m/185 μ m) [5].

The implant improves aqueous humor outflow through four laser-cut windows by bypassing the trabecular meshwork and dilating Schlemm's canal by approximately 90°. The Hydrus[®] Microstent is approved for use in conjunction with phacoemulsification [5].

Randomized controlled trials have demonstrated the efficacy of the Hydrus[®] Microstent: clinical studies have shown a significant reduction in IOP after the implantation of the Hydrus[®] Microstent compared to phacoemulsification alone [8].

Gonioscopy, the examination of the anterior chamber angle, plays an important role in the assessment of aqueous outflow facility. This examination helps to differentiate between open and closed angles and to assess their pigmentation as well as iris configuration [9]. Especially in glaucoma patients, gonioscopy is used to select patients for MIGS implantation based on anatomical conditions. Conventional gonioscopy methods often provide a limited view of the angle without visual documentation. The NIDEK GS-1 Gonioscope was the first device to automatically provide 360° color imaging of the anterior chamber angle with a 16x mirrored facet lens [10–12].

Gonioscopy is commonly used to assess the postoperative positioning of chamber angle-based MIGS devices. The purpose of this study was to evaluate automated 360° gonioscopy for the detection and documentation of postoperative positional variation after Hydrus[®] Microstent implantation. To our knowledge, this is the largest study of its kind.

2. Materials and Methods

The present study was conducted in accordance with the ethical standards of the Ethics Committee of the Medical Association of Westphalia-Lippe and the University of Münster. It adhered to the tenets of the Declaration of Helsinki. Informed consent and ethical approval were waived by the Ethics Committee of the University of Münster, North Rhine-Westphalia, Germany, due to the retrospective nature of this study in accordance with Section 6 of the Health Data Protection Act of North Rhine-Westphalia (GDStG NRW). This study was conducted at the Department of Ophthalmology, University Hospital Münster, Münster, Germany.

The study design is illustrated in Figure 1.

For this study, we analyzed electronic medical records (FIDUS, Arztservice Wente GmbH, Darmstadt, Germany) of patients with primary open-angle glaucoma (POAG) and pseudoexfoliative glaucoma (PEX-G) who underwent Hydrus[®] Microstent implantation combined with phacoemulsification or alone.

The inclusion criteria for Hydrus[®] Microstent implantation was the presence of mild to moderate glaucoma with an open angle (open-angle glaucoma/pseudoexfoliation glaucoma). Patients with angle closure, traumatic, malignant, uveitic, and neovascular glaucoma, and those with chamber angle anomalies were excluded.

Patients had to have available data on postoperative IOP, information on postoperative antiglaucomatous medications, and any additional IOP-lowering procedures and ocular adverse events following Hydrus[®] Microstent implantation. Patients who had previously undergone IOP-lowering procedures with filtering and cyclodestructive methods and those who had undergone vitrectomy were excluded.

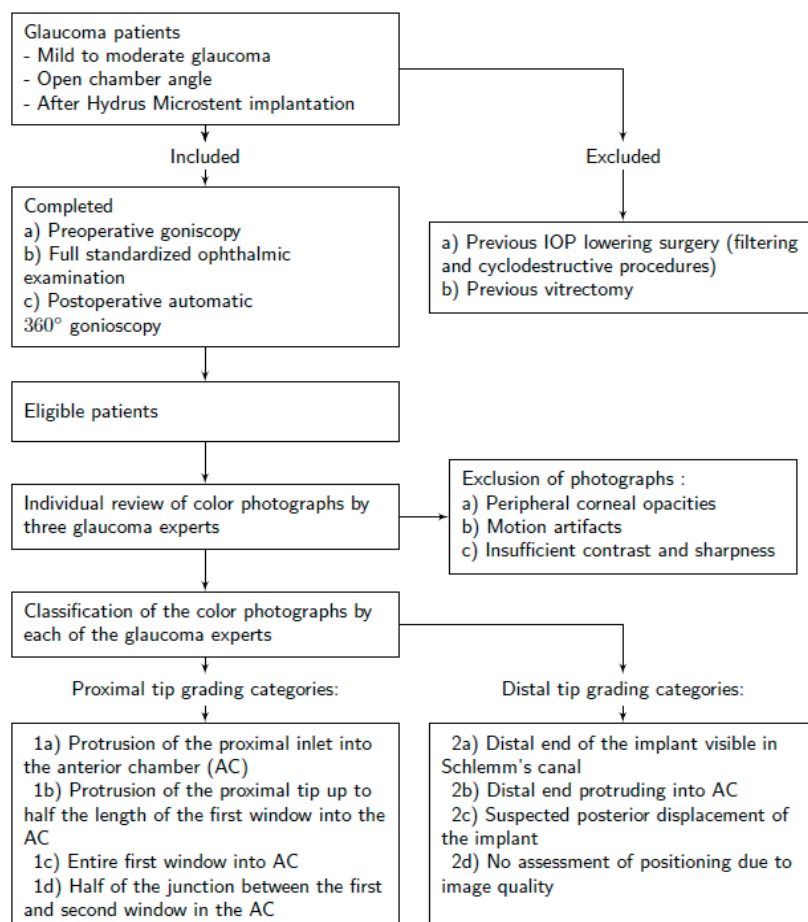


Figure 1. Study design.

All patients underwent a standardized ophthalmic examination including refractive and anterior segment examination, funduscopy, Goldmann applanation tonometry, and perimetry. Perimetry was performed with the standard 30-2 Swedish Interactive Threshold Algorithm (SITA fast) program using the automated Humphrey Visual Field Analyzer II (HFA II, model 750, manufactured by Carl Zeiss Meditec AG, Jena, Germany).

Preoperative gonioscopy was performed to rule out angle abnormalities (synechiae, rubeosis, angle closure), which was necessary to ensure eligibility for Hydrus[®] Microstent implantation. The procedures were performed by three glaucoma surgeons using either a combined cataract and MIGS procedure or a single MIGS implant in cases of previous cataract surgery and resulting pseudophakia. In the case of cataract surgery, phacoemulsification was performed through a clear corneal incision. A detailed description of the procedure can be found in the freely available manual. During implantation, a gonioscope (Alcon, Fort Worth, Texas, USA) was used to visualize the anterior chamber angle. Miosis facilitates implantation. Implantation is performed with a hand-held delivery system after the cannula is inserted through the clear corneal incision into the anterior chamber. The microstent can be advanced through the trabecular meshwork into Schlemm's canal using a tracking wheel on the cannula. The implant passes through Schlemm's canal during implantation. At the end of implantation, only the inlet of the implant should be visible in the anterior chamber. If properly positioned, the stent will appear opaque through the trabecular meshwork in the canal. A shiny stent is anterior to the trabecular meshwork. It is recommended that the inlet be positioned in the anterior chamber.

If the stent is not visible during implantation, it may be posterior to Schlemm's canal. In this case, repositioning is recommended.

Postoperatively, patients underwent automated 360° gonioscopy to visualize the postoperative positioning of the Hydrus[®] Microstent (Figures 2–4). The examination was

performed by two experienced glaucoma specialists. Immediately after the examination, they reviewed the individual images from the 16 image directions. In addition to the individual images, 360° images of the chamber angle were obtained. Implant position was independently assessed by three experienced glaucoma specialists using the single images and the 360° composites. The postoperative position of the implant was described according to the following staging: 1a describes a protrusion of the proximal inlet into the anterior chamber. The proximal inlet (Figure 3, 1a) of the implant continues uninterrupted into a first recess, referred to here as the “first window”. This was followed by three more apertures (windows 2–4). Stage 1b describes a protrusion of the proximal end of the implant up to half the length of the first window into the anterior chamber. In Stage 1c, the entire first window is in the anterior chamber, and in Stage 1d, half of the connection (“spine”) between the first and second windows is also in the anterior chamber.

The assessment of the distal tip was divided into categories 2a–d. In Stage 2a, the distal end of the implant is visible in Schlemm’s canal; in Stage 2b, it protruded into the anterior chamber. In Stage 2c, the entire chamber angle is clearly visible on gonioscopy, but the distal tip of the implant could not be visualized, suggesting the posterior displacement of the implant out of Schlemm’s canal. Stage 2d contains all cases in which the image quality does not allow assessment of the distal position. Images that could not be classified as class 1 or 2 due to anatomic conditions such as peripheral corneal opacities or motion artifacts were excluded from the analysis. Only images with sufficient contrast and sharpness to visualize the structures of Schlemm’s canal were included.

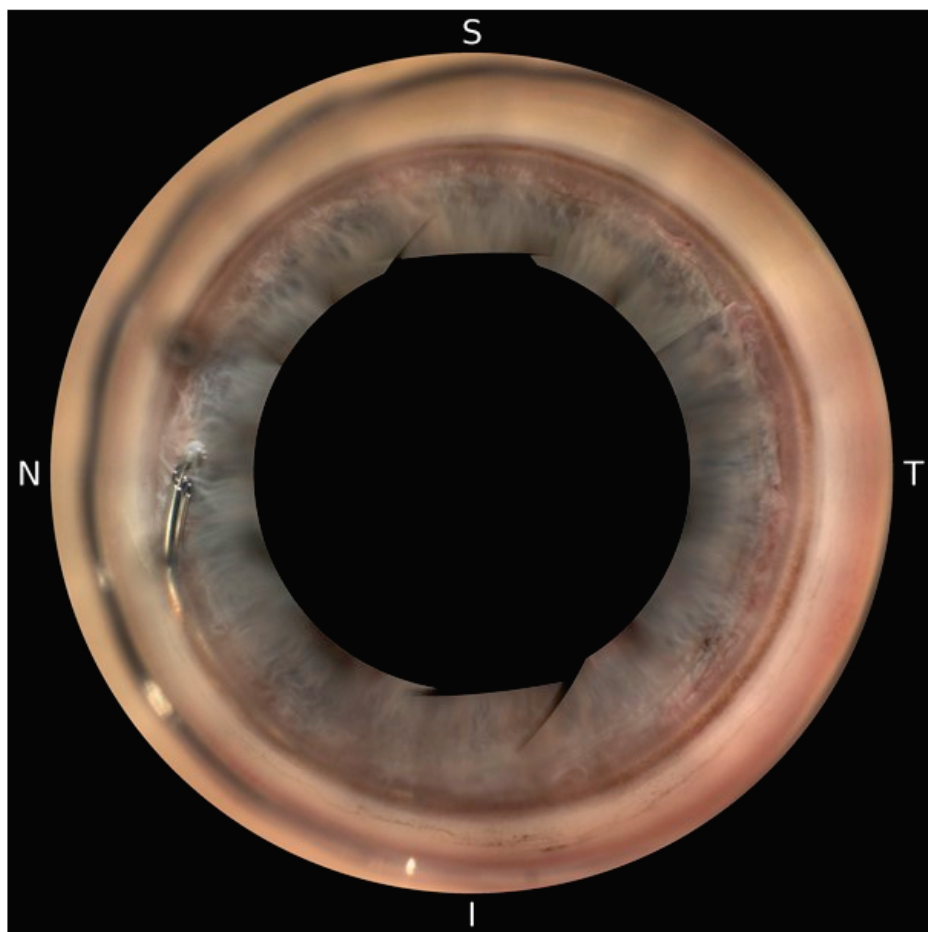


Figure 2. Hydrus® Microstent visualized with NIDEK GS-1 Gonioscope.

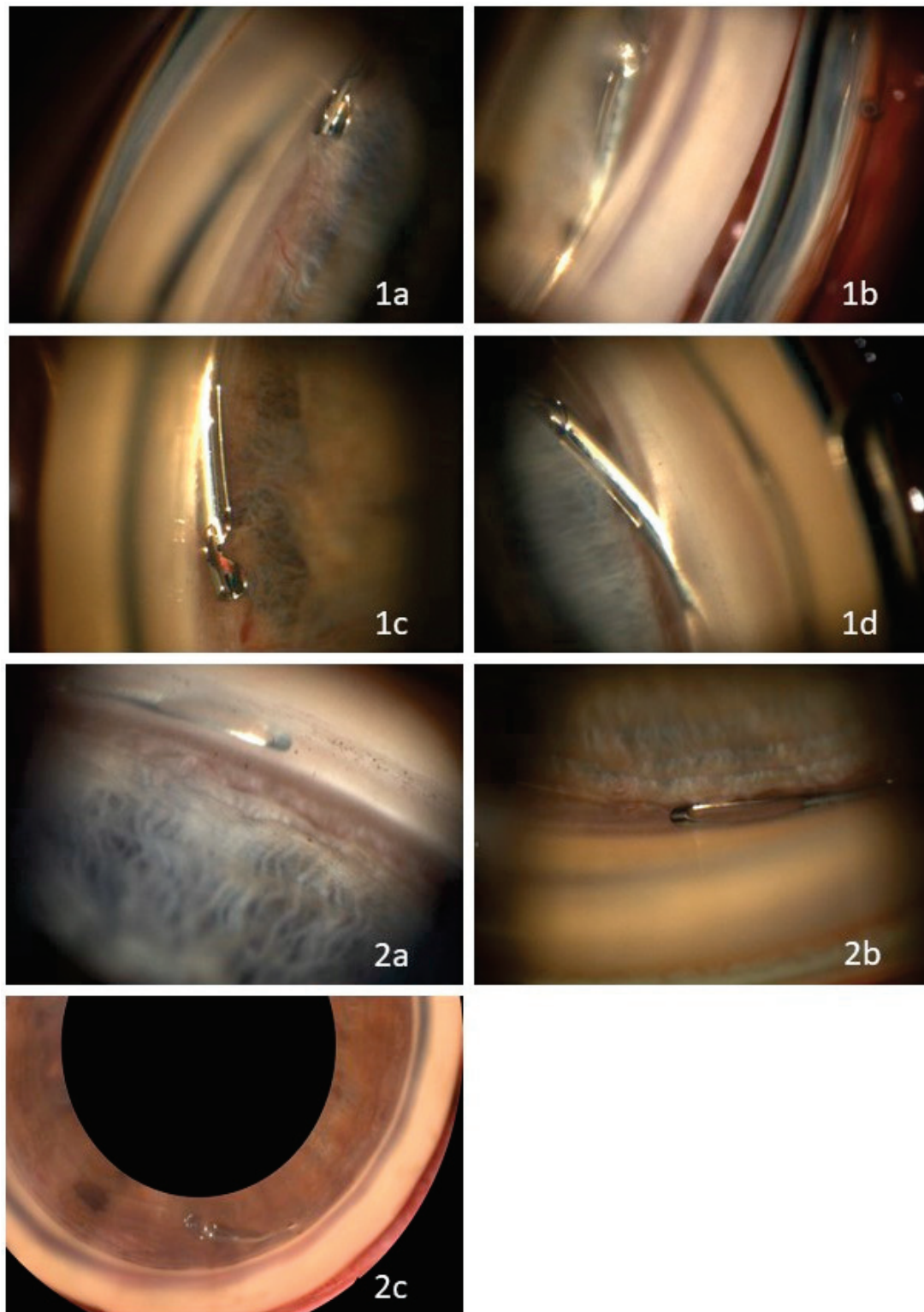


Figure 3. Visualization of the postoperative position of the proximal and distal tips of the Hydrus® Microstent using automated 360° gonioscopy. Only the proximal tip is visible in the anterior chamber (1a). Half of the first window of the stent (viewed from the proximal end with the inlet in the anterior chamber) protrudes into the anterior chamber (1b). The entire first window is in the anterior chamber (1c). At least half of the bridge, called the spine, between the first and second windows is in the anterior chamber (1d). The distal rounded tip is clearly visible behind the trabecular meshwork within Schlemm's canal (2a). The distal tip protrudes into the anterior chamber (2b). The distal stent is not visible through the trabecular meshwork, suggesting a posterior location (2c).

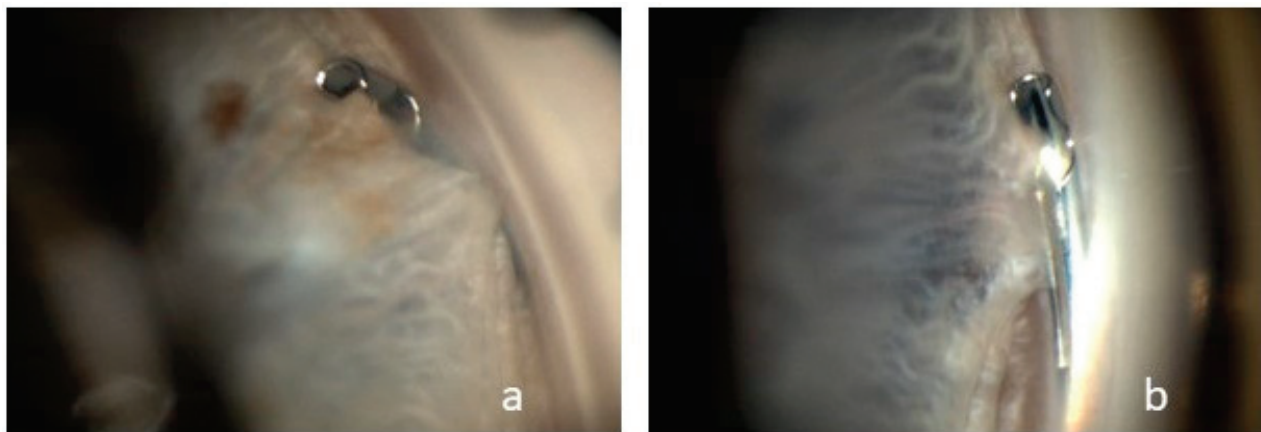


Figure 4. Visualization of two cases (a,b) of peripheral synechiae between the iris and the proximal tip of the Hydrus® Microstent.

3. Statistical Analysis

Statistical analysis was performed using GraphPad Prism 10 (GraphPad Software, Boston, MA, USA) with data extracted from the electronic patient record (FIDUS, Arzt-service Wente GmbH, Darmstadt, Germany). Normal distribution was tested using the Shapiro–Wilk test. The Wilcoxon matched-pairs signed rank test was used to analyze IOP and the number of drops used over time (nonparametric, dependent samples). Statistical significance was defined as a *p*-value less than 0.05.

4. Results

A total of 23 eyes were included in the study. The demographics of the study cohort are shown in Table 1. In six cases, the Hydrus® Microstent was implanted as a stand-alone procedure. All eyes showed a reduction in IOP and a reduction in the number of antiglaucomatous eye drops compared to preoperative values (Table 2). In the subgroup analysis of Stage 2c patients, there was also a statistically significant reduction in IOP one month after surgery. There was no difference between eyes treated with a combination of cataract surgery and Hydrus® Microstent implantation compared to stand-alone Hydrus® Microstent implantation.

Table 1. Study cohort demographics and baseline characteristics. Continuous variable data are reported as mean ($\pm$ standard deviation) or median (25th percentile; 75th percentile), depending on data distribution.

Patients/Eyes (n)	17/23
Diagnosis	
POA-Glaucoma	20/23 (87.0%)
PEX-Glaucoma	3/23 (13.0%)
Age (years)	69.5 $\pm$ 7.8
Sex (m/f)	3 (17.6%)/14 (82.4%)
Visual field MD (db)	−5.0 [−10.6; −2.8]
Baseline IOP (mmHg)	20.0 [16.0; 24.0]
Number of antiglaucoma eye drops at baseline	2 [1; 3]

POA-glaucoma, primary open-angle glaucoma; PEX-glaucoma, Pseudoexfoliative glaucoma; m, male; f, female; IOP, intraocular pressure; MD, mean deviation.

Table 2. IOP and antiglaucomatous eye drops in the observation period. Data on continuous variables are reported as the median (25th percentile; 75th percentile) based on the data distribution.

IOP in mmHg	Baseline vs.	20.0 [16.0; 24.0]	<i>p</i> -value
	1 month	14.0 [11.0; 15.0]	<0.0001
	6 months	14.0 [11.5; 16.5]	0.0234
	12 months	14.0 [12.25; 18.5]	0.1172
Daily antiglaucomatous eye drops (n)	Baseline vs.	2 [1; 3]	
	1 month	1 [1; 2]	0.0156
	6 months	1 [1; 2]	0.1562
	12 months	2 [1.25; 2]	0.6562

IOP, intraocular pressure.

Analysis of the postoperative 360° gonoscopic images revealed the following findings: Interobserver variability in image interpretation and classification did not differ, as the structures defined for grading were clearly definable, except for the definition of distal dislocation. The final grading of the postoperative positions was in full agreement among all three subviewers. The distribution of the different implant positions is shown in Table 3. Figure 3 shows the different types of positions of the proximal and distal tip. In four implants only, the inlet was in the anterior chamber (1a). In 14 cases, approximately half of the first window of the stent (viewed from the proximal end with the inlet in the anterior chamber) protruded into the anterior chamber (1b). In three cases, the entire first window was in the anterior chamber (1c). In two cases, at least half of the bridge, called the spine, was visible between the first and second windows in the anterior chamber (1d). In no case was the second window (viewed from the proximal end with the entrance in the anterior chamber) visible in the anterior chamber.

Table 3. Assessment of the position of the Hydrus® Microstent in the chamber angle.

Position Assessment	Eyes (n)
Position of the proximal tip	
1a	4/23 (17.4%)
1b	14/23 (60.9%)
1c	3/23 (13.0%)
1d	2/23 (8.7%)
Position of the distal tip	
2a	5/23 (21.7%)
2b	1/23 (4.3%)
2c	7/23 (30.4%)
2d	10/23 (43.5%)

n, number.

In five cases, the distal rounded tip was clearly visible behind the trabecular meshwork within Schlemm's canal (2a). In one case (2b), the distal tip was in the anterior chamber. In seven cases, the distal stent was not visible through the trabecular meshwork, suggesting a posterior location (2c). In 10 cases, the distal course could not be assessed (2d).

A subgroup analysis of groups 1a and 1b (*n* = 18) showed a statistically significant reduction in IOP at one and six months postoperatively compared to the baseline IOP. In this group, the number of antiglaucomatous eye drops was statistically significantly reduced at one month compared to the baseline. In the 1c and 1d groups (*n* = 5), there was no statistical reduction in IOP or the number of antiglaucomatous drops. Among implants with a presumed posteriorly displaced posterior end (2c, *n* = 7), two cases had only associated proximal inlets in the anterior chamber (1a). In five other cases, a grade 1b situation was found proximally. In all cases with grade 2c involvement (*n* = 7), there was

a statistically significant reduction in IOP at one month postoperatively compared to the baseline.

Of the three PEX-glaucoma eyes, one eye belonged to group 1a and two to group 1b. Distally, the stent was visibly located in Schlemm's canal in two eyes (2a); in one case, the distal position could not be assessed (2d). All three showed a reduction in IOP and a reduction in the number of antiglaucomatous eye drops over the observation period.

Intraoperative and postoperative Adverse Events.

In none of the cases in our cohort did any of the intraoperative events detailed in the instructions for use occur.

Postoperatively, hypertensive IOP occurred in four eyes. In all cases, IOP was well controlled with local and systemic IOP-lowering therapy. In none of the cases could a malposition of the stent explain the IOP elevation. In one patient, IOP elevation was suspected as a reaction to the administration of topical steroids. Only in one of the four cases could the IOP not be lowered to the target range and, therefore, a filtering glaucoma surgery was planned. Postoperative hypotension below 6 mmHg for one month was not observed in any of the cases.

Peripheral synechiae between the iris and the implant without obstruction was observed in four cases (Figure 3).

5. Discussion

The goal of minimally invasive glaucoma surgery (MIGS) devices is to lower intraocular pressure sufficiently. They are particularly suitable for patients with mild or moderate open-angle glaucoma and promise a lower risk profile compared to conventional methods such as trabeculectomy [4].

MIGS devices can be categorized by the mechanism by which they reduce IOP. In addition to the devices that drain aqueous humor suprachoroidally and those that filter under the conjunctiva and form a filtering bleb, there are also angle-based implants. Besides the Kahook Dual Blade, the ISTENT[®] family of implants are prominent representatives of angle-based MIGS implants [13]. ISTENT inject[®] and ISTENT inject[®] W (Glaukos Corporation, Laguna Hills, CA, USA) are second and third generation angle-based bypass systems. The implants improve aqueous humor outflow through the trabecular meshwork into Schlemm's canal. Postoperative IOP reduction, the reduction of antiglaucoma medications, and the safety of the product have been demonstrated in studies [14–18]. In their analysis of the postoperative positioning of ISTENT inject[®] microstents, Gillmann et al. presented anterior segment optical coherence tomography (AS-OCT) as an evaluation method in addition to gonioscopy. In their postoperative analysis, more implants were visible with AS-OCT than with gonioscopy. They also examined the postoperative diameter of Schlemm's canal and found that it was enlarged in patients after ISTENT[®] implantation compared to the control group ($308.7 \pm 197.4 \mu\text{m}$ versus $126.9 \pm 60.3 \mu\text{m}$) [15,19]. In a previous study, we evaluated the postoperative visualization of ISTENT inject[®] using automated gonioscopy. Only 14.3% of the implants could not be visualized [20]. In addition to automated gonioscopy, we believe that AS-OCT is a very interesting method to analyze the postoperative positioning of the Hydrus[®] Microstent, especially for devices that cannot be visualized by gonioscopy due to a presumed posterior dislocation. Due to its long course in Schlemm's canal, we assume good visualization and dilation of the canal.

The Hydrus[®] Microstent is a MIGS implant approved for the treatment of mild to moderate primary open-angle glaucoma in adults in combination with cataract surgery to lower intraocular pressure.

The randomized, controlled, multicenter HORIZON study compared cataract surgery with cataract surgery combined with Hydrus[®] Microstent implantation over five years [5,8].

A total of 187 eyes underwent cataract surgery and 369 eyes underwent combined surgery. At five years, there were significantly more eyes in the combination group with IOP reduction to 18 mmHg without medication or less than in the control group. The combination group was also more likely to achieve an IOP reduction of 20% or more

without medication [8]. In our cohort, a reduction in IOP and a reduction in the use of IOP-lowering medications were also achieved over the observation period.

Gonioscopy is used for the visualization and examination of the iridocorneal angle. It is part of a complete eye examination, especially in glaucoma patients, and has both diagnostic and therapeutic implications [9]. The performance and the results of the gonioscopy are dependent on the examiner. It takes a lot of practice and training to master manual gonioscopy [21]. Only a portion of the corneal angle can be examined at a time.

Because different examiners may perceive and evaluate angle structures differently, the interpretation of the findings obtained during the examination is subjective. A joint assessment of the chamber angle is almost impossible because the gonioscopy is performed by only one person at a time. Important treatment decisions depend on this assessment. The fact that the chamber angle is photodocumented by automated gonioscopy means that a joint assessment can be performed by multiple health care professionals. The time of the assessment is independent of the time of the examination. Another advantage is that structures in the anterior chamber that are located in different planes can be visualized by different focusing [10–12].

However, in our experience, even with automated gonioscopy, training is necessary to obtain reliable results. In addition, the use of automated gonioscopy is still dependent on patient cooperation. As with the use of handheld devices, a clear view of the anterior chamber is necessary to obtain meaningful images. Motion artifacts also play a role, resulting in the shifting of the individual images that make up a 360° image. Corneal opacity, whether postoperative due to edema or other changes, complicates the assessment of the anterior chamber angle, as evidenced by the number of our patients in whom the anterior chamber angle implant could not be fully assessed.

A number of intra- and postoperative complications have been described. The Horizon study defined adverse events related to stent implantation. These included postprocedural malapposition, peripheral anterior synechiae with partial or complete device occlusion, and device removal. The cumulative number of events for the occurrence of postprocedural malapposition was 1.4 at two-, three-, four-, and five-years postprocedure.

Peripheral anterior synechiae with device occlusion was reported as a cumulative event in 3.5 cases at two years and 5.4 cases at five years. As in the prospective, randomized study by Pfeiffer et al. and in the COMPARE study by Ahmed et al., we were able to demonstrate the formation of focal peripheral anterior synechiae, which is also listed in the Hydrus® Manual as the most frequent complication of combined MIGS and cataract surgery with a prevalence of 40% [5,22,23]. Pfeiffer et al. followed their patients for 2 years and reported synechiae in 12% of their patients in the first year, increasing to 18.8% in the second year [22]. In our study with a shorter follow-up, there were four cases in which we observed peripheral synechiae in the proximal inlet area. The patients in our study cohort in whom synechiae formation was visualized were examined by 360-degree gonioscopy at a mean interval of 278.25 days, suggesting that synechiae formation may increase in the postoperative course. In addition to synechiae formation, Ahmed et al. described tissue adhesions to the iris as a postoperative side effect, which in one patient had to be removed by yttrium–aluminum–garnet laser treatment. In none of these cases did the IOP evolution indicate implant occlusion [8]. None of the eyes included in our study required secondary surgical intervention.

In the IVANTIS instructions for use, malposition was defined as an adverse event if the position required a follow-up procedure for repositioning or explantation. This included corneal endothelial contact, central endothelial cell loss >30%, device obstruction, or chronic inflammation or irritation [5,8]. Based on this definition of malposition as an adverse event, no such event was identified in our cohort. The Hydrus® Microstent instructions for use lists intraoperative adverse events. In the HORIZON study, an adverse event occurred in 3.8% of the cases. The most common of these was a hyphaema resulting in decreased vision during the procedure (1.1%). Device malposition, Descemet's membrane detachment,

iris prolapse, and wound incarceration were also reported. In our cohort, there were no intraoperative adverse events in significantly fewer cases.

In addition, the proximal end of the Hydrus[®] Microstent is less parallel to the chamber angle in all cases in our study compared to the 24-month images in the Horizon study but extends slightly further into the anterior chamber. In only one case did the most distal end protrude into the anterior chamber (Figure 3; Table 3).

The microstent is made of nitinol, an alloy of nickel and titanium. According to the manufacturer, the material offers flexibility, strength, and biocompatibility. In addition, the material is elastic enough to be inserted into and support Schlemm's canal. During the manufacturing process, the microstent is heat-set to match the curvature of Schlemm's canal. During implantation, the proximal inlet is placed in the anterior chamber to ensure aqueous humor drainage through the windows of the implant.

Laroche et al. suggest a postoperative change in stent configuration as a possible explanation. They describe that the curvature of the stent corresponds to a circle with a diameter of 12 mm, while the mean diameter of the cornea is 11.74 mm. The nitinol used is a flexible material that, according to the manufacturer, has both shape memory and flexibility [5].

As described by Laroche et al. in their case series, it can be assumed that a greater curvature of the Hydrus[®] Microstent compared to the course of Schlemm's canal into which it regresses causes the distal end to protrude into the anterior chamber in the cases described in our study [24]. Assuming that the distal end was still in the canal intraoperatively, an increase in curvature in the postoperative course would be expected. This may also explain a slight incision of the chamber angle as a subtle goniotomy through the proximal end, especially in cases where the proximal tip protrudes into the anterior chamber (grade 1c + d) (Figure 3).

The patients in our study had an axial length between 22.35 mm and 25.42 mm. We did not find a correlation between increased axial length and postoperative change in stent position.

Across all groups, there was a statistically significant reduction in postoperative IOP as well as a reduction in the number of daily antiglaucomatous eye drops. The question of the relationship between IOP reduction and drop reduction and the postoperative position of the implant in the chamber angle is very interesting in addition to the general assessment of the position by automated gonioscopy. A larger number of cases in all defined classes is necessary to provide a sufficient answer and is currently being planned. Patients with POAG were also included in the pivotal studies. The three patients with PEX-glaucoma included in this study also showed a clinical reduction in IOP and a reduction in the number of postoperative eye drops. In the future, it would be desirable to study more patients with PEX-glaucoma to obtain statistically verifiable evaluations of IOL positioning and postoperative outcomes. This is particularly interesting because the included eyes with PEX-glaucoma showed IOP reduction in the study but were not included in the pivotal trials.

Contraindications to implantation include changes in the iridocorneal angle. These include angle closure glaucoma and post-traumatic conditions, the presence of neovascularization, and congenital changes in the angle.

None of these baseline findings were present in the patient cohort. However, anatomical changes in Schlemm's canal that cannot be assessed preoperatively may lead to changes in implant position. Although no intraoperative resistance was observed during implantation, subtle adhesions and herniations in Schlemm's canal cannot be excluded.

Although this is the largest cohort studied after Hydrus[®] implantation using automated gonioscopy, a limitation of the study is the relatively small number of eyes included. After completion of this feasibility study, a larger number of eyes would be useful to create subgroups. These could be grouped according to the location and type of glaucoma.

Another limitation is the retrospective design of the study, as gonioscopy was performed at different times after surgery. In order to standardize variables in the future,

prospective studies are desirable. As this is both a relatively new surgical technique and a new imaging modality, future follow-up studies with longer observation periods are desirable and planned.

6. Conclusions

The study results show a reduction in IOP after Hydrus[®] Microstent implantation. Automated 360° gonioscopy proved to be a useful tool to verify and document the postoperative position of the implant.

We have demonstrated variations in the postoperative position of the Hydrus[®] Microstent. Attempts to explain this have focused on anatomic conditions, stent configuration, and the interaction between the two. This study demonstrated that the Hydrus[®] Microstent can effectively lower IOP even in the presence of post-op positional alterations. Positional changes did not require device explantation in any of the cases evaluated.

Follow-up studies with a larger number of patients and a longer follow-up period are currently being planned to track changes in position beyond the 12th month after implantation.

Author Contributions: Conceptualization, J.A.Z. and V.C.B.; methodology, J.A.Z. and V.C.B.; validation, J.A.Z., S.K. and R.-L.M.; formal analysis, J.A.Z. and S.K.; investigation, J.A.Z. and S.K.; resources, R.-L.M., N.E. and V.C.B.; data curation, J.A.Z. and S.K.; writing—original draft preparation, J.A.Z. and S.K.; writing—review and editing, J.J.S., C.W., R.-L.M., N.E. and V.C.B.; visualization, J.A.Z. and S.K.; supervision, R.-L.M., V.C.B. and N.E. All authors have read and agreed to the published version of the manuscript.

Funding: We acknowledge support from the Open Access Publication Fund of the University of Muenster.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and adhered to the ethical standards issued by the ethics committee of the Westphalian Wilhelms-University of Münster, Germany. Ethical review and approval were waived for this study due to its retrospective nature.

Informed Consent Statement: Patient consent was waived due to the retrospective nature of this study.

Data Availability Statement: The data that support the findings of this study are available on request.

Conflicts of Interest: The authors declare no conflicts of interest.

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Article

Comparison of XEN45 Gel Stent Outcomes in Glaucoma: Ab Externo Open-Conjunctiva Approach with Ologen vs. Ab Interno Closed-Conjunctiva Approach

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Abstract

Background/Objectives: This study evaluated the efficacy and safety of the ab externo open-conjunctiva (AEO) approach with adjunctive Ologen collagen matrix (OCM) compared to ab interno closed-conjunctiva (AIC) techniques for XEN45 gel stent implantation in patients with refractory open-angle glaucoma. The goal was to determine whether the AEO with OCM approach offers advantages in intraocular pressure (IOP) control and postoperative outcomes. **Methods:** A retrospective, comparative case series was conducted on 76 eyes from 76 patients with open-angle glaucoma who underwent XEN45 implantation between 2017 and 2022 at a single tertiary center. The patients were divided into Group 1 (AEO with OCM, n = 47) and Group 2 (AIC, n = 29). Postoperative IOP, the number of glaucoma medications, surgical complications, bleb revisions, and failure rates were recorded over 12 months. The AEO technique, supported by OCM, was assessed for its potential to reduce postoperative fibrosis and improve long-term outcomes. **Results:** Both groups experienced significant IOP reductions over time compared to baseline. However, Group 1 had superior outcomes, requiring fewer glaucoma medications postoperatively ($p < 0.05$), and demonstrated lower rates of complications (10.6% vs. 31.0%, $p = 0.026$) and bleb revisions (8.5% vs. 34.5%, $p = 0.005$). Kaplan–Meier survival analysis showed significantly greater cumulative surgical success in Group 1 compared to Group 2 ($p < 0.001$). **Conclusions:** The AEO with OCM approach to XEN45 implantation may provide improved safety and efficacy compared to the AIC approach. It appears to be beneficial in minimizing postoperative fibrosis, reducing the medication burden, and lowering complication and failure rates. Prospective randomized trials are needed to validate these findings.

Keywords: XEN45 gel stent; ab externo; ab interno; Ologen collagen matrix; Minimally invasive glaucoma surgery (MIGS); glaucoma surgery

1. Introduction

Glaucoma, an optic neuropathy, remains a significant contributor to irreversible vision loss and blindness globally [1]. Elevated intraocular pressure (IOP) stands as the sole modifiable risk factor among the myriad factors implicated in optic nerve damage [2]. Primary treatment methods include IOP-lowering medications, laser procedures, and surgery. Trabeculectomy, established in 1968, remains the gold-standard incisional surgical procedure for glaucoma treatment; however, it carries a notable complication rate of up to 57%, including hypotony, bleb leaks, choroidal effusion, endophthalmitis, and bleb-related infections [3,4].

In recent years, minimally invasive glaucoma surgery (MIGS) has emerged as a promising alternative to traditional incisional procedures [5]. One such innovation is the XEN45 gel stent (XGS), designed to provide a safer and less invasive means of lowering IOP [6,7]. The XGS, a 6 mm hydrophilic tube, facilitates aqueous humor drainage to the subconjunctival space, offering comparable efficacy and reduced complications compared to trabeculectomy within the first year post-surgery [8]. Its introduction has sparked interest in exploring different surgical techniques for optimal implantation, including ab interno closed-conjunctiva (AIC), ab interno open-conjunctiva (AIO), ab externo closed-conjunctiva (AEC), and ab externo open-conjunctiva (AEO) techniques [9]. AIC is currently the only Food and Drug Administration (FDA)-approved approach, requiring corneal incisions to insert the XGS.

A debate revolves around the optimal method for XGS implantation. The ab externo approach, particularly the open-conjunctiva technique, has garnered attention due to its potential benefits, including easier teaching, lower procedural costs due to reduced reliance on specialized instrumentation and reduced operating time, improved visualization during surgery, better control over bleb morphology and aqueous outflow, avoidance of corneal incisions, and overall improved prospects for long-term IOP control [10–14]. Conversely, the closed-conjunctiva approach offers simplicity and familiarity but may lack the advantages of the open approach. A recent study demonstrated that AEO led to significantly lower postoperative IOP compared with AIC, which was the first time a significant difference in IOP reduction was observed between these two procedures [15]. However, another study found no statistical difference in outcomes when comparing the AEO and AIC approaches, although both approaches were shown to be safe and efficacious [16].

Amid the gaps in knowledge and the variability in the findings, our study aimed to assess the efficacy of the ab externo open-conjunctiva approach, specifically when enhanced with adjunctive Ologen collagen matrix (OCM), compared to the FDA-approved AIC approach to XGS implantation. OCM, placed between the conjunctiva and the episcleral space, serves to prevent postoperative fibrosis and acts as a reservoir by absorbing aqueous humor into its porous structure [17,18]. While several studies have analyzed the effects of Ologen in other glaucoma surgeries, the utilization of Ologen for XGS implantation is still controversial considering the paucity of studies and the inconsistent results. Specifically, one study reported significant decreases in IOP and medication usage, alongside improved management of conjunctival fibrosis and a reduced need for postoperative interventions, with OCM augmentation [19]. However, another study utilizing an ab externo technique found no significant differences in surgical outcomes between XGS implantation with and without OCM augmentation [20].

To our knowledge, no study has directly compared the efficacy of AEO enhanced with OCM and the AIC approach to XGS implantation. We hypothesized that augmenting the AEO technique with OCM would result in more significant decreases in IOP, medication usage, and complication rates compared to the AIC approach. Ultimately, by evaluating the potential clinical advantages of the AEO approach enhanced with OCM over AIC, we

aimed to inform surgical decision-making and enhance the efficacy and safety of glaucoma interventions.

2. Materials and Methods

2.1. Design

This study was a single-center, retrospective, comparative case series of 76 patients who underwent XEN45 gel stent placement between 2017 and 2022, with follow-ups ranging from 1 to 12 months, at the Walter Reed National Military Medical Center (WRNMMC). The study protocol was reviewed and deemed exempt by the WRNMMC Institutional Review Board (WRNMMC-EDO-2020-0546), and it complied with all Health Insurance Portability and Accountability Act (HIPAA) requirements.

The patients were identified in a surgical database, and their data were retrieved from their electronic medical records. The inclusion criteria encompassed all adult patients (≥ 18 years) who underwent XEN45 gel stent implantation with AIC or AEO with OCM during the study period. Pediatric patients were excluded. Additional exclusion criteria included insufficient follow-up, defined as fewer than two postoperative visits with documented IOP and medication statuses. The recorded patient information included demographic variables such as age, gender, diagnosis, and the laterality of the eye undergoing surgery. The preoperative data encompassed visual acuity, IOP, the number of glaucoma medications, the extent of visual field loss, the pretreatment maximum IOP, and prior glaucoma procedures. The postoperative data included IOP, the medication burden, complications, revisions, surgical failures, and any additional glaucoma interventions. To assess the medication burden, each active IOP-lowering agent was counted as one medication, whether delivered as a single drop or as part of a fixed combination. For example, timolol–dorzolamide was counted as two medications. Oral agents such as acetazolamide were counted as one medication.

The primary outcomes were IOP reduction, the number of IOP-lowering medications, and cumulative success probabilities derived from Kaplan–Meier (KM) analyses. Secondary outcomes included postoperative complications, revisions, and surgical failure. For the KM survival analysis, surgical failure was defined as (1) having an IOP ≤ 5 mmHg or > 18 mmHg on two consecutive visits after baseline or (2) the number of IOP-lowering medications being > 0 at any point during the follow-up visits. Postoperative complications included intraocular pressure (IOP) elevation > 30 mmHg, hyphema, iris obstruction of the stent, rebound iritis, wound leak, choroidal effusions, hypotony maculopathy, corneal decompensation, symptomatic bleb extension, cystoid macular edema, and corneal abrasion. Revisions were defined as transconjunctival bleb needling procedures. To account for the prior surgical status, surgical eyes were defined as those that had undergone at least one prior incisional glaucoma surgery, including trabeculectomy, installing glaucoma drainage devices, or microinvasive glaucoma surgery procedures such as the iStent or a prior XEN45 implantation. Eyes that had only undergone non-incisional procedures—such as laser peripheral iridotomy, selective laser trabeculoplasty, argon laser trabeculoplasty, or cataract extraction without concurrent glaucoma surgery—were not considered to have undergone a prior surgery.

Data points were recorded at specific intervals: postoperative day 1, week 1, weeks 2 to 3, months 1 to 2, months 3 to 4, months 5 to 8, and months 9 to 12.

2.2. Surgical Techniques

The surgeries were conducted by a single surgeon (W.I.K.) and were carried out using topical anesthesia. Group 1 consisted of patients who underwent AEO implantation of an XGS. Group 2 comprised patients who underwent one of two ab interno closed-conjunctiva

techniques: (1) the standard ab interno closed technique and (2) an ab interno technique with pneumo-dissection and visco-expansion. The two AIC groups were combined for analysis based on a methodological precedent established by Ruda et al. in 2023, as well as considerations of the limited sample size [21]. The specific surgical techniques utilized are outlined below.

Group 1: Ab externo open-conjunctival technique (AEO) (n = 47): Tetracaine was applied for topical anesthesia. A 6 mm, fornix-based conjunctival flap was created, followed by infusion of 2% lidocaine into the sub-Tenon's space for anesthesia. The XGS was implanted via an ab externo approach, entering the sclera 2 mm posterior to the limbus. A 12 mm by 1 mm disk of Ologen collagen matrix was folded in half and placed into the subconjunctival sub-Tenon's space. The folded Ologen sheet was placed under and over the XGS to envelop it. The conjunctival peritomy was closed using an 8-0 Vicryl suture. Then, 0.1 to 0.15 mL of mitomycin C, with a concentration ranging from 0.2 to 0.4 mg/mL, was injected into the superior subconjunctival space.

Group 2: Standard ab interno closed-conjunctiva technique (n = 18): Mitomycin C, with a concentration ranging from 0.2 to 0.4 mg/mL, was injected superiorly into the subconjunctival space using a 30-gauge needle. A paracentesis port was created nasally with a sideport blade, followed by an injection of Methylparaben-free (MPF) 1% lidocaine and Miochol into the anterior chamber. The anterior chamber was filled with an ophthalmic viscoelastic device, and a 1.8 mm clear corneal incision was made inferotemporally. The XGS was implanted via an ab interno approach through the corneal incision under gonioscopic visualization. Residual viscoelastic material was irrigated out, and the anterior chamber was reformed with a balanced salt solution before suturing the clear corneal wound with a single 10-0 nylon interrupted suture.

Group 2: Ab interno closed-conjunctival pneumo-dissection and visco-expansion technique (n = 11): This technique was similar to the standard technique described above, except that air was introduced into the subconjunctival space via a 30-gauge needle approximately 6 mm posterior to the limbus. Subsequently, the pneumo-dissected space was further expanded with an ophthalmic viscoelastic device. The XGS was then delivered as described above into the supra-Tenon capsule space created by the pneumo-dissection and the viscoelastic device, allowing for separation of the conjunctiva and the Tenon capsule to form a supra-Tenon capsule pocket for stent implantation.

2.3. Statistical Analysis

Data analysis was conducted using commonly available software (Microsoft Excel and IBM SPSS Version 29). All tests were two-tailed, with statistical significance set at $p < 0.05$. Continuous variables were summarized as means with standard deviations or 95% confidence intervals, while categorical variables were expressed as frequencies and percentages.

Demographic variables were compared between the groups using the chi-square test. To analyze the trajectory of IOP over time and the effect of prior surgery, a linear mixed model was employed. This model was chosen to account for missing data at later postoperative time points and to allow pairwise comparisons between baseline and postoperative IOPs. The reported means are model-adjusted estimates.

Postoperative glaucoma medication use was analyzed using non-parametric methods due to the zero-inflated distribution of the data. The Mann–Whitney U test was used to compare the number of medications between the surgical groups at each time point, while the Wilcoxon signed-rank test was used for within-group comparisons between the baseline and postoperative values. These results are presented as medians, interquartile ranges (IQRs), and observed minimums (min) and maximums (max).

The complication rates and bleb revisions were compared between the groups using the chi-square test. Kaplan–Meier survival analysis was performed to estimate the time to surgical failure, defined as an intraocular pressure (IOP) ≤ 5 mmHg or >18 mmHg without the use of IOP-lowering medications on two consecutive follow-up visits or loss of light perception. The patients were censored at the time of failure, the last available follow-up, or at 12 months. The survival distributions were compared between the groups using the log-rank (Mantel–Cox) test.

3. Results

3.1. Baseline Clinical Data

This study included 76 eyes of 76 patients who underwent XEN45 gel stent implantation. Table 1 displays the preoperative clinical data and demographic characteristics of the study cohort. All patients had some form of open-angle glaucoma. At baseline, Group 1 had a mean visual field loss of -13.67 ± 7.81 dB and a mean preoperative IOP of 24.91 ± 6.75 mmHg on a median of 4.00 (min–max: 2–8) medications. Group 2 had a mean visual field loss of -12.46 ± 9.71 dB and a mean preoperative IOP of 22.76 ± 7.48 mmHg on a median of 4.00 (2–5) medications.

Table 1. Baseline characteristics.

Parameter	AEO with OCM (Group 1) n = 47	AIC (Group 2) n = 29	p-Value
Age at surgery, mean (SD) [years]	68.66 (19.04)	68.97 (10.48)	0.93
Female sex, n (%)	28 (60%)	12 (41%)	0.12
Race, n (%)			0.11
African American	26 (55%)	22 (76%)	
Caucasian	15 (32%)	5 (17%)	
Asian	6 (13%)	1 (3%)	
Hispanic or Latino	0 (0%)	1 (3.4%)	
Glaucoma characteristics			
Preoperative HVF MD, mean (SD)	-13.67 (7.81)	-12.46 (9.71)	0.72
Preoperative IOP, mean (SD)	24.91 (6.75)	22.76 (7.48)	0.20
Preoperative number of glaucoma medications, median (min–max)	4.00 (2–8)	4.00 (2–5)	0.16
Prior surgery, n (%)	14 (30%)	5 (17%)	.22
Glaucoma type, n (%)			0.13
Primary open angle	37 (79%)	28 (97%)	
Mixed mechanism	1 (2%)	0 (0%)	
Pseudoexfoliation	2 (4%)	0 (0%)	
Pigment dispersion	0 (0%)	0 (0%)	
Posner–Schlossman	0 (0%)	1 (3.4%)	
Uveitic	4 (9%)	0 (0%)	
Traumatic open angle	3 (6%)	0 (0%)	

Abbreviations: IOP = intraocular pressure; HVF MD = Humphrey Visual Field Mean Deviation; SD = standard deviation.

In total, 14 patients in Group 1 (30%) and 5 patients in Group 2 (17%) had a history of prior incisional glaucoma surgery, with no statistically significant difference between the

groups. Previous surgeries were noted as follows: CyPass, iStent, trabeculectomy, Trabectome, gonioscopy-assisted transluminal trabeculotomy, Kahook Dual Blade, endoscopic cyclophotocoagulation, Baerveldt glaucoma implant, Ahmed glaucoma valve, and prior XEN45 gel stent implantation.

3.2. Follow-Up Data

Outcomes were recorded at each follow-up visit from postoperative day 1 to 12 months. The sample sizes of the patients at each postoperative time point are presented in Table S1 in the Supplementary Materials.

For Group 1, the mean preoperative IOP of 24.91 ± 6.75 mmHg dropped to 12.67 ± 4.05 mmHg on 0.61 ± 1.02 medications at the last follow-up. For Group 2, the mean preoperative IOP of 24.18 ± 7.75 mmHg decreased to 12.05 ± 2.46 mmHg on 1.91 ± 1.54 medications at the last follow-up. The IOP was significantly lower after XGS implantation in both Group 1 and 2 at all postoperative time points compared with the preoperative levels in all eyes ($p < 0.001$; Table 2). There were no postoperative time points after XGS implantation at which the IOPs were significantly different between the two groups (Table 2). However, the mean number of medications was significantly lower compared with baseline at each postoperative time point for both groups ($p < 0.001$). Group 1 (AEO with OCM) showed a significantly lower median medication requirement compared to Group 2 (AIC) at specific time points: at 1 week (median: 0.0 [min 0, max 3, IQR 0] vs. 0.0 [min 0, max 3, IQR 0], $p = 0.04$), at 2–3 weeks (median: 0.0 [min 0, max 2, IQR 0] vs. 0.0 [min 0, max 4, IQR 2], $p < 0.001$), at 1–2 months (median: 0.0 [min 0, max 3, IQR 0] vs. 1.0 [min 0, max 4, IQR 2], $p < 0.001$), at 3–4 months (median: 0.0 [min 0, max 4, IQR 0] vs. 1.0 [min 0, max 4, IQR 1], $p < 0.001$), and at 9–12 months (median: 1.0 [min 0, max 3, IQR 2] vs. 2.0 [min 0, max 5, IQR 2], $p = 0.01$) (Table 1).

Table 2. Comparison of mean intraocular pressures and median medication counts at baseline and postoperative intervals across surgical groups.

		AEO, Group 1 (n = 47)		AIC, Group 2 (n = 29)		P (Among Groups)	
		IOP (mmHg)	Meds	IOP (mmHg)	Meds	IOP (mmHg)	Meds
Pre-op		24.92 (23.47–26.36)	4 (2)	22.76 (20.92–24.60)	4 (1)	0.07	0.41
Day 1							
	Mean (95% CI)	8.04 (6.57–9.51)	0 (0)	7.40 (5.53–9.26)	0 (0)	0.59	0.21
	P (compared with baseline)	<0.001		<0.001		-	-
Week 1							
	Mean (95% CI)	9.71 (8.18–11.23)	0 (0)	10.68 (8.79–12.58)	0 (0)	0.43	0.04
	P (compared with baseline)	<0.001		<0.001		-	-
Weeks 2–3							
	Mean (95% CI)	12.01 (10.36–13.67)	0 (0)	12.54 (10.67–14.40)	0 (2)	0.68	<0.001
	P (compared with baseline)	<0.001		<0.001		-	-

Table 2. Cont.

	AEO, Group 1 (n = 47)		AIC, Group 2 (n = 29)		P (Among Groups)	
	IOP (mmHg)	Meds	IOP (mmHg)	Meds	IOP (mmHg)	Meds
Months 1–2						
Mean (95% CI)	12.91 (10.66–13.72)	0 (0)	10.32 (8.43–12.22)	1 (2)	0.13	<0.001
P (compared with baseline)	<0.001		<0.001		-	-
Months 3–4						
Mean (95% CI)	13.24 (11.54–14.94)	0 (0)	11.80 (9.84–13.76)	1 (1)	0.28	<0.001
P (compared with baseline)	<0.001		<0.001		-	-
Months 5–8						
Mean (95% CI)	12.48 (10.55–14.41)	0.5 (2)	11.68 (9.57–13.78)	2 (2)	0.58	0.08
P (compared with baseline)	<0.001		<0.001		-	-
Months 9–12						
Mean (95% CI)	13.87 (11.67–16.07)	1 (2)	12.75 (10.50–15.00)	2 (2)	0.48	0.01
P (compared with baseline)	<0.001		<0.001		-	-

Note: Medication description written as median (IQR). Abbreviations: AEO = ab externo open, AIC = ab interno closed, CI = confidence interval, IOP = intraocular pressure, meds = medications, pre-op = preoperative.

3.3. Rates of Complications and Revisions

Postoperative complications included intraocular pressure (IOP) elevation > 30 mmHg, hyphema, iris obstruction of the stent, rebound iritis, wound leak, choroidal effusions, hypotony maculopathy, corneal decompensation, symptomatic bleb extension, cystoid macular edema, and corneal abrasion. All IOP spikes occurred within the first postoperative month. Complications were observed in 5 of 47 patients (10.6%) in Group 1, which was significantly lower than in Group 2, where 9 of 29 patients (31.0%) experienced complications ($p = 0.026$). Revisions were defined as transconjunctival bleb needling procedures. Bleb needling was performed in 4 of 47 patients (8.5%) in Group 1, compared to 10 of 29 patients (34.5%) in Group 2 ($p = 0.005$).

3.4. Kaplan–Meier Survival Analysis

Kaplan–Meier analysis demonstrated significantly higher cumulative surgical success in Group 1 (AEO with OCM) compared to Group 2 (AIC) (log-rank test, $\chi^2 = 27.150$, $df = 1$, $p < 0.001$) (Figure 1). The mean survival time was 206.5 ± 21.3 days (95% CI: 164.8–248.2) in Group 1 versus 50.4 ± 16.5 days (95% CI: 18.5–83.4) in Group 2. The median survival times were 180 days for Group 1 (95% CI: 98.3–261.7) and 14 days for Group 2 (95% CI: 8.1–19.9). Censoring occurred primarily after 200 days in Group 1 and before 100 days in Group 2. The survival curves showed a pronounced early drop in the closed group, reflecting earlier surgical failure.

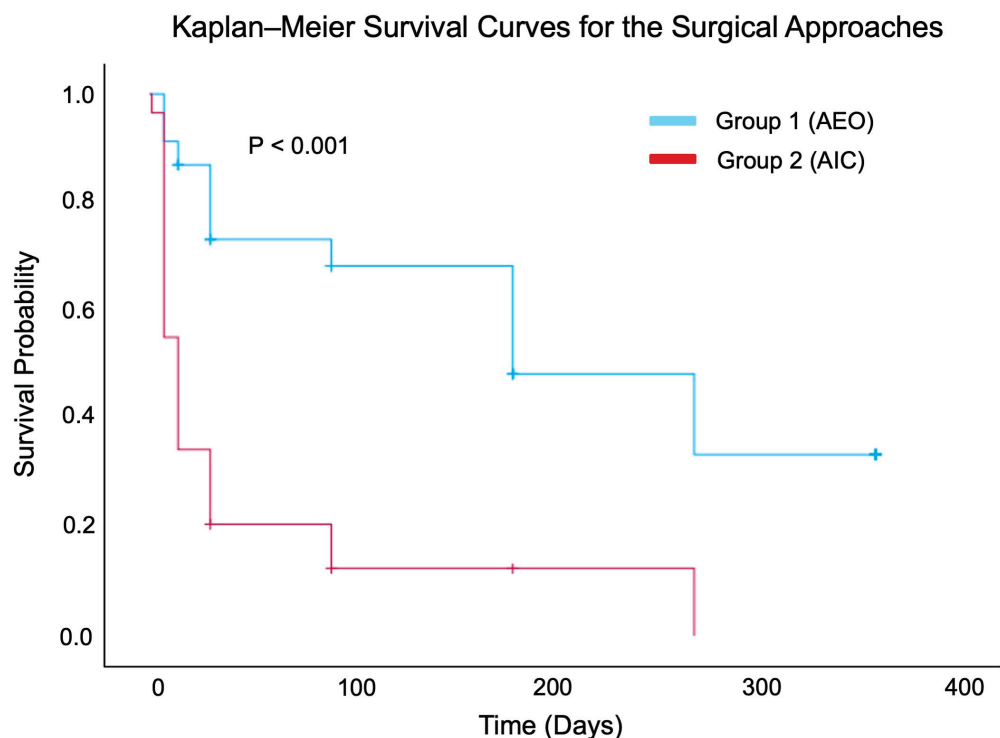


Figure 1. Kaplan–Meier survival curves depicting the time to surgical failure following XEN45 implantation via the AEO and AIC conjunctival approaches. Surgical failure was defined as (1) having an IOP ≤ 5 mmHg or >18 mmHg on two consecutive visits after baseline or (2) the number of IOP-lowering medications being > 0 at any point during the follow-up visits. Censored cases are marked with tick marks. Abbreviations: AEO = ab externo open, AIC = ab interno closed.

4. Discussion

In this retrospective case series of patients with refractory open-angle glaucoma, we compared outcomes following XEN45 gel stent implantation using an AEO approach with adjunctive Ologen collagen matrix (Group 1) versus an AIC conjunctival approach (Group 2). Both groups demonstrated meaningful reductions in intraocular pressure (IOP), with no significant differences in IOP reductions between them. However, Group 1 consistently required fewer glaucoma medications at multiple postoperative time points. Additionally, Group 1 demonstrated significantly lower rates of postoperative complications—including IOP spikes and hyphema—as well as fewer surgical revisions. Notably, Kaplan–Meier survival analysis revealed significantly greater cumulative surgical success in the AEO group compared to the AIC group. These findings underscore the safety and efficacy of XGS implantation using the AEO with OCM technique, which was noninferior for IOP control and superior in terms of medication reduction, complication rates, and overall surgical success.

While our study aligns with a similar retrospective study by Tan et al. [16], which did not find a significant difference in IOP reduction between AEO and AIC groups, our results diverge from a recently published study by El Helwe et al. that reported significant differences in postoperative IOP levels, favoring the AEO group [15]. Notably, the discrepancy between our results and those of El Helwe et al. might be attributed to differences in the patient populations. El Helwe et al. included a substantial proportion of mixed-mechanism glaucoma patients in the AEO group, whereas our study primarily focused on open-angle glaucoma cases. This divergence underscores the importance of considering the heterogeneity of glaucoma presentations when evaluating the efficacy of different surgical approaches. Our study further indicates that incorporating OCM into

XGS implantation via the AEO approach did not confer superior outcomes in terms of IOP reduction, nor did it enhance the efficacy of this approach. These findings align with those of Park et al., who similarly observed no enhancement in the efficacy of the AEO technique with OCM augmentation for XGS implantation [20].

However, it is noteworthy that although we did not observe a significantly superior reduction in IOP, the AEO with OCM technique resulted in significant medication reductions at multiple time points over the 12-month period. This aligns with our Kaplan–Meier survival analysis, in which surgical failure was defined not only by an IOP outside the target range (≤ 5 mmHg or > 18 mmHg on two consecutive visits) but also by the need for any IOP-lowering medications. Accordingly, the significant survival advantage observed in the AEO group reflects its greater ability to maintain the target IOP without pharmacologic support, despite similar mean IOP values between the groups. These findings are consistent with a study that found a significantly greater medication reduction at 1 year in a group treated using the open-conjunctiva approach regardless of whether the approach was ab externo or ab interno [22]. However, our findings contrast with those of Tan et al., where medication usage was comparable between open and closed techniques. The significant reduction in the number of IOP-lowering medications associated with the open approach in our study could be attributed to several factors. The open approach may facilitate the formation of larger and more functional blebs compared to the closed approach. A well-functioning bleb is essential for maintaining adequate aqueous humor drainage and optimal IOP control. Therefore, patients treated using the open approach may require fewer medications to achieve and maintain target IOP levels. Overall, while the AEO with OCM approach may not have achieved significantly lower IOP levels, it did lead to a reduction in the medication usage required to maintain IOP levels comparable to those in the closed-conjunctiva group. This suggests that the AEO with OCM approach could be more effective than the AIC approach.

Moreover, our study demonstrated the superior performance of the AEO with OCM technique, with significantly lower complication and revision rates as well as greater cumulative surgical success, as shown by the Kaplan–Meier survival analysis. These results are consistent with the findings of Do et al., who demonstrated a comparable success rate and a lower needling rate in an open-conjunctiva group compared to a closed-conjunctiva group [22]. The increased incidences of bleb revisions and stent exposure associated with the closed-conjunctiva approach may be attributed to the technical challenge of consistently and precisely placing the injector needle in the subconjunctival space. Additionally, the higher rate of proximal occlusion of the shunt by the iris observed in closed techniques may stem from the inability to make micro-adjustments once the stent has been deployed. Furthermore, when placing the stent via a closed approach, maintaining the anterior chamber with a cohesive viscoelastic device may artificially widen the angle if the chamber is overfilled or hyperinflated, potentially leading to posterior delivery of the device and subsequent stent obstruction.

However, our findings diverge from those of El Helwe et al., who observed a trend towards a higher rate of postoperative complications in the AEO group, albeit just shy of statistical significance ($p = 0.06$) [15]. Furthermore, they reported a significantly elevated incidence of early hypotony and inflammation in the ab externo open-conjunctiva group compared to the ab externo closed-conjunctiva group, attributing it to increased tissue disruption and the higher likelihood of subclinical microfluidic leaks associated with conjunctival opening. OCM represents one proposed approach to address this issue [23]. Hence, our utilization of OCM may explain the disparity in our findings compared to those of El Helwe et al. Ologen was specifically developed to mechanically prevent conjunctival and episcleral adhesions, thereby reducing bleb fibrosis [17,18]. Our findings suggest that

OCM augmentation in the AEO approach may contribute to reduced complication, revision, and failure rates.

This study has several limitations. Firstly, its retrospective design and small sample size may limit the generalizability of the findings. Moreover, the relatively short follow-up period of 12 months, coupled with some patients being lost to follow-up or having irregular follow-up visits, may have introduced potential biases. Additionally, this study's reliance on outcomes from a single surgeon may not have fully captured variations in surgical technique and expertise across different surgeons. The decision to perform needling at various postoperative time points was left to the discretion of the surgeon, potentially introducing variability in treatment protocols. Further, the inclusion of two different closed-conjunctival techniques in Group 2, namely the standard AIC conjunctiva technique and AIC conjunctiva pneumo-dissection and visco-expansion, may have introduced variability. Due to the small sample size, our study followed the methodology of a prior study that combined these techniques into one group [21]. However, future studies with larger sample sizes should consider analyzing long-term outcomes based on specific surgical techniques.

While a recent study with a substantial sample size reported sustained intraocular pressure reductions and confirmed the long-term safety of XEN45 implantation over a 3-year period, it did not differentiate between the surgical approaches used for stent placement [24]. This highlights the need for further studies comparing outcomes across specific techniques. Additionally, although the overall comparison across all four racial groups did not yield a statistically significant difference ($p = 0.11$), we observed a higher proportion of African American patients in the AIC cohort (76%) compared to the AEO group (55%). This difference, while not statistically significant, may still have clinical relevance. Our study was not powered to evaluate the influence of race on surgical outcomes; however, this observation highlights the need for future studies with larger, more diverse populations to explore potential racial or genetic factors that may impact surgical efficacy. Lastly, while our study utilized an ab externo approach for XGS implantation, it is noteworthy that XGS was originally developed for use with an ab interno approach, necessitating cautious interpretation of our results in this context.

In conclusion, we advocate for the open-conjunctival ab externo technique for XEN45 gel stent implantation with Ologen collagen augmentation. The results of this study indicate a promising trend towards achieving greater rates of complete and qualified surgical success, reduced medication dependency, a lower needling frequency, fewer postoperative complications, and decreased failure rates with this approach. However, to validate these findings and facilitate wider adoption, prospective randomized controlled studies are essential. We envision that this study will catalyze further prospective analyses aimed at enhancing postoperative outcomes for patients with glaucoma, ultimately advancing this field and improving patient care.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/jcm14134426/s1>, Table S1: Sample size of patients at each post-operative time point by surgical group.

Author Contributions: W.I.K. designed and implemented this study. S.J.J., S.Y.K., J.T., and S.R. conducted the statistical analysis of the data and drafted the manuscript. J.T., H.S.R., M.O.O.-O., and W.I.K. contributed to revisions and reviews and provided insights. W.I.K. provided oversight from inception to final review. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki, and the study protocol was approved by the institutional review board at Walter Reed National Military Medical Center (WRNMMC-EDO-2020-0546) on 20 July 2020. No animal subjects were used in this study.

Informed Consent Statement: Human subjects were included in this study. All participants provided informed consent.

Data Availability Statement: The datasets presented in this article are not readily available due to U.S. Department of Defense (DoD) restrictions related to research conducted at a military medical center. Requests for data access may be directed to Dr. Won Kim (email: wonkim74@gmail.com) and will be reviewed in accordance with institutional and DoD data sharing policies.

Conflicts of Interest: The authors declare no conflicts of interest.

Disclaimers: The views expressed herein are those of the authors and do not reflect the official policy or position of the Uniformed Services University of the Health Sciences, Walter Reed National Military Medical Center, San Antonio Military Medical Center, the Department of Defense, or any other agency of the U.S. Government. The identification of specific products or scientific instrumentation is considered an integral part of the scientific endeavor and does not constitute endorsement or implied endorsement on the part of the authors, the DoD, or any component agency. The authors have no proprietary or commercial interests in any materials discussed in this article.

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Article

Postoperative Outcomes of PreserFlo MicroShunt in Patients with Exfoliation Glaucoma

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Abstract: **Objectives:** This study aimed to evaluate the postoperative outcomes of the PreserFlo MicroShunt in Asian patients with exfoliation glaucoma. **Methods:** We used the Kaplan–Meier method to analyze 29 eyes of 29 patients with exfoliation glaucoma (mean age: 80.7 ± 8.3 years; 16 males; 24 eyes with intraocular lens implants; preoperative intraocular pressure [IOP]: 32.5 ± 9.3 mmHg; preoperative antiglaucoma medications: 3.4 ± 1.0 ; Asian ethnicity: 100%) who underwent PreserFlo MicroShunt surgery alone at Saneikai Tsukazaki Hospital from November 2022 to November 2023. The criteria for survival were a reduction in IOP of $\geq 20\%$, no additional glaucoma surgery, and IOP of 5–21 mmHg (condition 1), 5–18 mmHg (condition 2), and 5–15 mmHg (condition 3). Needling and glaucoma eye drops were considered qualified successes. **Results:** The mean follow-up period was 27.9 weeks, with a reoperation rate of 31% (9 cases). The complete and qualified success survival rates at 24 weeks were 56%, 52%, and 49%, and 67%, 59%, and 53% for conditions 1–3, respectively. The complete and qualified success survival rates at 48 weeks were 47%, 43%, and 45%, and 52%, 46%, and 48% for conditions 1–3, respectively. **Conclusions:** The postoperative outcomes of the PreserFlo MicroShunt in Asian patients with exfoliation glaucoma demonstrated an approximate 50% success rate at both 24 and 48 weeks, with a reoperation rate of approximately 30%. Caution is warranted when performing PreserFlo MicroShunt in patients with exfoliation glaucoma.

Keywords: glaucoma surgery; innfocus; preserflo; microshunt; exfoliation glaucoma; pseudoexfoliation glaucoma; subconjunctival filtration surgery; open-angle glaucoma

1. Introduction

Glaucoma is a disease that causes permanent visual field defects and is the second leading cause of irreversible blindness globally [1,2]. Reducing intraocular pressure (IOP), which slows the progression of visual field loss, is the only evidence-based treatment available [3]. Glaucoma is categorized into several types, including primary open-angle glaucoma (POAG), primary angle closure glaucoma, and exfoliation glaucoma [4]. In exfoliation glaucoma, microfibril deposits produced throughout ocular tissue, typically observed at the pupillary border and the anterior lens capsule, are the exfoliation material [5]. Exfoliation glaucoma presents a risk of higher IOP and a more rapid progression of visual field defects [6].

Eye drops, laser therapy, and surgery are current glaucoma treatments. Surgery is generally considered when more conservative treatments fail to preserve the visual field. Trabeculectomy is still the gold standard among glaucoma surgeries; however, it has a perseverant learning curve for surgeons, with several complications, including hypotony [7,8].

PreserFlo (Santen, Osaka, Japan) MicroShunt is a novel glaucoma implant device, with a length of 8.5 mm and an inner diameter of 70 μm , which is inserted subconjunctivally via an ab externo approach [9]. The device's tube length and lumen diameter were selected to

accommodate sloughed endothelial cells (40–50 μm) while providing sufficient resistance to limit pressure reduction and minimize the risk of hypotony [10]. Postoperative hypotony is less prevalent with the PreserFlo MicroShunt than with trabeculectomy [9]. In cases involving the PreserFlo MicroShunt, postoperative hypotony occurred in 30.9% of patients, with only 3.8% developing persistent hypotony. In contrast, hypotony occurred in 51.1% of patients following trabeculectomy, with 15.8% experiencing persistent hypotony [9]. These findings suggest that hypotony associated with the PreserFlo MicroShunt is typically transient and resolves over time.

In POAG, the PreserFlo MicroShunt provided considerable IOP reduction, but its IOP-lowering effect was less than that of trabeculectomy [9]. Previous studies on the use of PreserFlo MicroShunt for exfoliation glaucoma, although limited and retrospective, have reported reduced postoperative IOP and decreased number of glaucoma eye drops required [11–13]. However, the reported success rates of PreserFlo MicroShunt differ widely, from 26% to 90% [11–13].

Exfoliation glaucoma is a condition often associated with elevated IOP [6]. Previous studies revealed preoperative IOP levels of approximately 20 mmHg [11–13]. The postoperative outcomes of PreserFlo MicroShunt for exfoliation glaucoma with high preoperative IOP remain unclear. Additionally, the effectiveness of PreserFlo MicroShunt for exfoliation glaucoma remains debatable. Furthermore, the surgical success rate of the PreserFlo MicroShunt for POAG and refractory uveitic glaucoma has been reported to vary significantly across different ethnicities [14,15]. However, the success rate for exfoliation glaucoma in Asian patients remains unknown. Therefore, this study aimed to investigate the postoperative outcomes of PreserFlo MicroShunt in Asian patients with exfoliation glaucoma.

2. Materials and Methods

2.1. Study Design

This single-center, retrospective observational study was reviewed by the ethics committee in accordance with the Declaration of Helsinki (IRB No: 2404001). All patients provided written informed consent. The study included all patients with exfoliation glaucoma who underwent standalone PreserFlo MicroShunt surgery at Saneikai Tsukazaki Hospital between November 2022 and November 2023.

2.2. Inclusion and Exclusion Criteria

All patients with exfoliation glaucoma who underwent standalone PreserFlo MicroShunt surgery were included. Only the first operated eye was included for patients who underwent bilateral surgeries. This study excluded patients who underwent simultaneous PreserFlo MicroShunt and cataract surgery. Previous glaucoma surgeries, including filtration surgeries, were not considered exclusion criteria. Additionally, patients under 18 years of age were excluded from the study.

2.3. Baseline Measurements

Baseline measurements were collected at the time surgery was indicated. No washout of glaucoma medication was performed. Information regarding the glaucoma diagnosis, age, sex, lens status, laterality, IOP measured by Goldmann applanation tonometry, best-corrected visual acuity, and the number of antiglaucoma medications (both topical and oral) was recorded on the day surgery was deemed necessary.

2.4. Diagnosis and Surgical Indication

All patients underwent slit-lamp microscopy preoperatively, where the pupillary margin or anterior lens capsule exhibited that exfoliation material. Additionally, gonioscopy confirmed the presence of the scleral spur and trabecular meshwork, and the absence of angle closure, leading to a diagnosis of exfoliation glaucoma. All patients had un-

controlled IOP despite maximum conservative treatment and were considered to require surgical intervention.

2.5. Preoperative Management

Patients were instructed to follow preoperative preparations, which included discontinuing all topical antiglaucoma medications in the eye to be operated on three days prior to surgery. Instead, dexamethasone 0.1% eye drops were prescribed to be used four times a day.

2.6. Surgical Method

A 7-0 silk traction suture was placed on the cornea, and 2% lidocaine was administered for sub-Tenon anesthesia. The conjunctiva was incised 7 mm along the limbus at the superior or inferior temporal quadrant. The subconjunctival and Tenon's capsules were dissected to expose the sclera, and bleeding areas were coagulated. Mitomycin C 0.04% was applied for 3 min using neurosurgical sponges and then irrigated with saline of 50 cc. A 1.0-mm side port was established, and a double-step knife was used to puncture the anterior chamber 3.5 mm from the limbus. The PreserFlo MicroShunt was inserted until the fins were positioned within the sclera. The PreserFlo MicroShunt was confirmed to be parallel to the iris within the anterior chamber. Balanced salt solution (BSS) was injected through the side port to validate aqueous humor outflow from the tip of the PreserFlo MicroShunt. The Tenon's capsule and conjunctiva were draped over the PreserFlo MicroShunt and sutured at the limbus with 8-0 Vicryl to prevent BSS leakage from the conjunctival suture sites.

2.7. Postoperative Management

All patients discontinued glaucoma eye drops postoperatively and were prescribed fluoroquinolone and dexamethasone eye drops four times daily, continuing for one to several months at the surgeon's discretion. The surgeon was responsible for making decisions about needling (including slit-lamp needling), antiglaucoma medication, and reoperation.

2.8. Patients

A total of 29 eyes from 29 patients were included in this study. Table 1 presents the demographic data for the included eyes. The preoperative number of antiglaucoma medications was 3.4 (± 1.0), and the mean IOP was 32.6 mmHg. The PreserFlo MicroShunt was inserted from the superior temporal quadrant in 13 eyes and from the inferior temporal quadrant in 16 eyes.

Table 1. Patient Demographics and Clinical Characteristics.

Characteristics	Value
Study Demographics:	
Number of cases (patients, eyes)	29 (29)
Age (y, mean $\pm$ SD)	80.7 $\pm$ 8.3
Number of males (%)	16 (55)
Number of right eyes (%)	16 (55)
Ethnicity:	
Number of Asian (%)	29 (100)
Number of White (%)	0 (0)
Number of Black (%)	0 (0)
Preoperative Clinical Characteristics:	
IOP (mmHg, mean $\pm$ SD)	32.6 $\pm$ 9.1
Number of antiglaucoma medications, (mean $\pm$ SD)	3.4 $\pm$ 1.0
Previous ocular surgery:	
Number of filtration surgeries (%)	6 (20)
Number of other glaucoma surgeries (%)	7 (24)
Number of cataract surgeries (%)	24 (83)
Number of pars plana vitrectomies (%)	5 (17)

Table 1. *Cont.*

Characteristics	Value
Insertion site:	
Number of superior temporal insertions (%)	13 (46)
Number of inferior temporal insertions (%)	16 (53)
Follow-up and Outcomes:	
Follow-up period (weeks, mean $\pm$ SD)	27.9 $\pm$ 20.6
Final visit IOP (mmHg, mean $\pm$ SD)	16.9 $\pm$ 10.5
Final follow-up period (weeks, mean $\pm$ SD)	46.1 $\pm$ 20.9

SD = standard deviation; y = years.

2.9. Insertion Site

This study included 13 patients who had the PreserFlo MicroShunt inserted in the superotemporal quadrant and 16 patients who had it inserted from the inferotemporal quadrant. The inferotemporal approach was chosen not only for cases where conjunctival scarring was present in the superior conjunctiva due to previous glaucoma or other surgeries, but also to preserve the superior conjunctiva for potential future glaucoma surgeries, even in the absence of scarring. Additionally, patients with prostaglandin-associated periorbital syndrome [16] presented challenges with superonasal insertion of the PreserFlo MicroShunt. There was no difference in the surgical procedure between superotemporal and inferotemporal insertions, except for the variation in the surgical site. Due to the structural characteristics of the PreserFlo MicroShunt, which creates blebs away from the limbus, the formation of avascular blebs was considered to be rare. As a result, the decision to use the inferotemporal insertion approach was made relatively frequently.

2.10. Analysis Methods

The primary outcome was the cumulative rate of surgical success at 24 weeks. The Kaplan–Meier method was used to analyze postoperative IOP. Kaplan–Meier survival criteria included an IOP reduction of $\geq 20\%$ from preoperative IOP and postoperative IOP within specified ranges (condition 1: 5–21 mmHg; condition 2: 5–18 mmHg; condition 3: 5–15 mmHg). Failure was considered the requirement for additional glaucoma surgery other than needling. IOP that did not meet the criteria on two consecutive visits was considered a failure on the first day. Survival rates were calculated under two conditions—complete success and qualified success—for each IOP criterion. Complete success was defined as achieving the IOP criteria without the use of additional antiglaucoma medication or needling, whereas qualified success was defined as achieving the criteria with the use of either. The failure rate and 95% confidence intervals (CI) for each condition at 24 weeks and 48 weeks were calculated.

The secondary outcome includes the hazard ratio for the survival criteria. Hazard analysis was conducted using a Cox proportional hazards model with factors, including age, sex, preoperative IOP, lens status, history of glaucoma surgery, and direction of PreserFlo MicroShunt insertion (superior or inferior temporal quadrant). The hazard ratios and 95% CI were calculated for each factor.

The Python lifelines package (version 0.28.0) was used for Kaplan–Meier and Cox hazard model analyses.

3. Results

3.1. Kaplan–Meier Curve

The Kaplan–Meier survival rates and their 95% CI for each condition are shown in Figure 1. The complete and qualified success survival rates at 24 weeks were 56% (95% CI: 36–72%), 52% (32–69%), and 49% (30–66%), and 67% (45–81%), 59% (38–75%), and 53% (33–69%) for conditions 1–3, respectively, indicating that approximately half of the cases met the criteria for complete success under each condition. The complete success and qualified survival rates at 48 weeks were 47% (28–66%), 43% (24–61%), and 45% (26–62%), and 52% (31–70%), 46% (25–64%), and 48% (28–65%) for conditions 1–3, respectively.

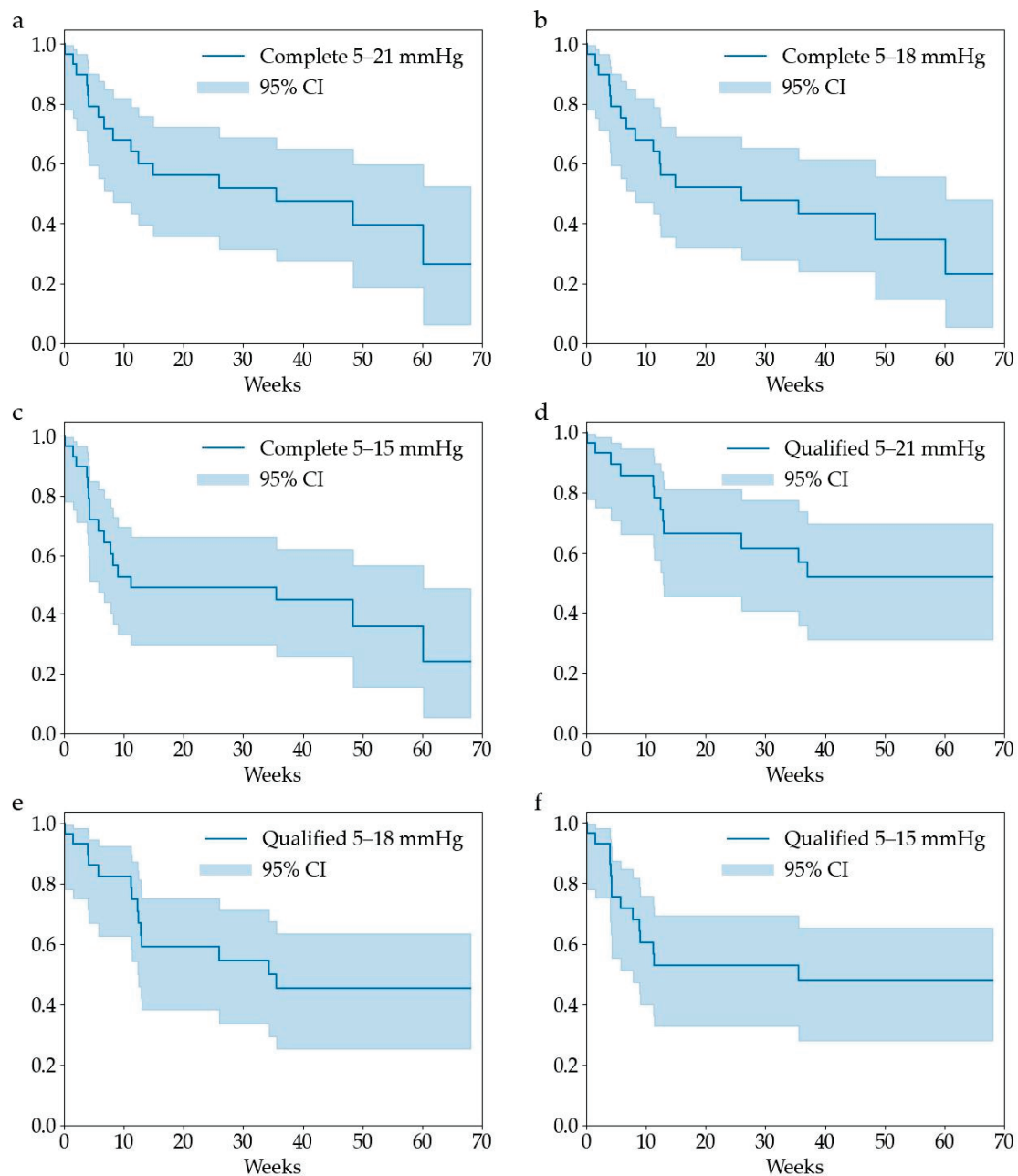


Figure 1. Kaplan–Meier survival curves of each condition. (a) complete success, condition 1; (b) complete success, condition 2; (c) complete success, condition 3; (d) qualified success, condition 1, (e) qualified success, condition 2; (f) qualified success, condition 3.

3.2. IOP

IOP and the number of antiglaucoma medications were significantly reduced from $32.6 (\pm 9.1)$ mmHg and $3.4 (\pm 1.0)$ to $16.9 (\pm 10.5)$ mmHg and $1.0 (\pm 1.3)$, respectively, at the final visit. Hypotony, defined as an IOP below 5 mmHg, was observed in five cases (17%). Four of these cases recovered with conservative treatment, while one developed choroidal detachment, requiring anterior chamber reformation using a viscoelastic substance. In cases of ocular hypertension, needling or antiglaucoma medications were utilized. No subconjunctival injections of antimetabolites were administered.

3.3. Reoperation

Reoperation was performed when needling and antiglaucoma medications failed to sufficiently lower IOP. A total of nine cases (31%) required reoperation due to ocular

hypertension. Eight of these cases involved bleb reconstruction, while one case experienced loss of the anterior chamber and ocular hypertension, necessitating anterior chamber reformation surgery 11 days postoperatively. The average IOP at the time of reoperation was 29 mmHg, and the average number of antiglaucoma medications was 3.3. The median time to reoperation was 98 days (range: 11 to 420 days). Details of the cases requiring reoperation are provided in Supplementary Table S1. During reoperation, encapsulated and adherent blebs were frequently observed, and in one case, PreserFlo MicroShunt obstruction was noted.

3.4. Cox Proportional Hazard Model

In the Cox hazard model, hazard ratios were calculated for age, sex, lens status, preoperative IOP, history of glaucoma surgery, and inferior insertion of the PreserFlo MicroShunt. The hazard ratios for the complete success under condition 2 were 1.01, 1.00, 1.00, 0.98, 1.00, and 0.52, respectively, with none showing statistical significance. The details of the hazard ratios and confidence intervals for other conditions are provided in Supplementary Table S2.

3.5. Bleb Morphology

Mostly diffuse vascular blebs formed in the fornix area. However, avascular blebs were observed in three cases: one with superotemporal insertion and two with inferotemporal insertion. In all three cases, the avascular blebs formed away from the limbus and were localized rather than diffuse. No cases of tube exposure were observed, and no signs of infection were present at the time of evaluation. Furthermore, no significant association was found between the formation of avascular blebs and the insertion site ($p = 1.0$, Fisher's exact test).

4. Discussion

Exfoliation glaucoma is a glaucoma subtype with a high risk of progression [5,6]. It is characterized by significant diurnal variations in IOP and a rapid progression of glaucomatous neuropathy and visual field loss [17]. Frequently, glaucoma surgery is required to achieve lower IOP [18]. The postoperative outcomes of trabeculectomy in exfoliation glaucoma have been inferior [19–21], similar, or superior [22–25] to those in POAG, depending on the study. Trabeculectomy for exfoliation glaucoma may be less effective than for POAG in Asian populations [18]. This study retrospectively assessed the outcomes of PreserFlo MicroShunt in exfoliation glaucoma at a single institution. The preoperative IOP in this study was high, at 32.6 mmHg, and the success rate at 48 weeks was 43–52%.

Studies have reported on the effectiveness of PreserFlo MicroShunt in POAG. Scheres et al. treated 41 eyes with POAG, revealing an IOP reduction from 20.1 mmHg to 12.1 mmHg at 2 years postoperatively, with a complete success rate of 58% at 1 year [26]. Riss et al. performed InnFocus MicroShunt (PreserFlo MicroShunt) surgery on 87 eyes with POAG, demonstrating an IOP reduction from 23.8 mmHg to 10.7 mmHg [27]. Battle et al. conducted a prospective study on 23 eyes with POAG, reporting a success rate of 91% at 1 year postoperatively, with only one case requiring needling or considered a surgical failure [28].

Reports on the postoperative outcomes of PreserFlo MicroShunt in exfoliation glaucoma are limited. Fea et al. conducted a multicenter study that included 81 eyes with POAG and 23 eyes with exfoliation glaucoma treated with PreserFlo MicroShunt. They revealed a success rate of 26% for complete success (no glaucoma eye drops) and 58.7% for qualified success (with glaucoma eye drops) at 12 months postoperatively, with IOP of ≤ 18 mmHg, and no significant difference in the postoperative success rates between exfoliation glaucoma and POAG [12]. Nobl et al. treated 31 eyes with exfoliation glaucoma with a baseline IOP of 20.8 mmHg using PreserFlo MicroShunt and reported an average IOP of 12.8 mmHg, a complete success rate of 83.9%, a qualified success rate of 90.3%

at 12 months postoperatively, and postoperative hypotony in 45% of cases [11]. Wagner et al. studied 26 eyes with POAG and nine eyes with exfoliation glaucoma, reporting a preoperative IOP of 18.0 mmHg and a complete success rate of 54.8% at 6 months postoperatively [13]. Although the handling of hypotony and needling in criteria differs, the outcomes of PreserFlo MicroShunt in exfoliation glaucoma are still under debate. In previous studies, preoperative IOP in exfoliation glaucoma was similar to that in POAG [12]. However, our study revealed a higher preoperative IOP of 32.6 mmHg. In this study, the success rate was similar to that reported by Wagner et al., slightly better than that reported by Fea et al., and lower than that reported by Nobl et al. [11–13]. The hazard ratio for preoperative IOP did not reach statistical significance in this study, indicating no significant effect of preoperative IOP on postoperative outcomes (Supplementary Table S2).

Previously reported factors affecting the postoperative outcomes of the PreserFlo MicroShunt include the location and concentration of MMC application, ethnicity, glaucoma subtype, and baseline IOP. Riss et al. reported that, for the InnFocus MicroShunt, a 0.04% MMC concentration yielded better results than a 0.02% concentration, and that applying MMC near the limbus may be superior to application deep in the pocket [27]. Additionally, Bhayani et al. found that non-Caucasian ethnicity was consistently associated with an increased risk of failure [14]. Bhayani et al. conducted a multicenter retrospective cohort study analyzing the results of the PreserFlo MicroShunt in 100 eyes, 70% of which were from patients with POAG, and reported up to an 8-fold difference in the hazard ratio between Caucasian and non-Caucasian patients based on postoperative IOP criteria [14]. Triolo et al. performed PreserFlo MicroShunt surgery on 21 eyes of patients with refractory uveitic glaucoma and reported a 45-fold difference in cumulative surgical success between White British and non-White British ethnicities [15]. These ethnic differences may be more pronounced in eyes with inflammation. Another potential factor is the glaucoma subtype. Balas et al. summarized that POAG had better outcomes compared to secondary open-angle glaucoma [29]. Ibarz et al., in a study of 54 patients, reported that higher baseline IOP was associated with better postoperative outcomes [30]. Ibarz et al. also noted that successful PreserFlo MicroShunt postoperative patients had thicker bleb walls and a larger filtration bleb surface area [30]. In this study, MMC was applied at a concentration of 0.04%, extending from the limbus to deep in the pocket. The baseline IOP was relatively high compared to other studies, and all cases involved Asian patients with exfoliation glaucoma. Asian ethnicity and exfoliation glaucoma may have contributed to poorer postoperative outcomes.

Several factors could contribute to the lower postoperative outcomes of PreserFlo MicroShunt in exfoliation glaucoma. One factor is the presence of transforming growth factor beta (TGF β) in exfoliation glaucoma. TGF β is a major modulator of the extracellular matrix in exfoliation syndrome [31] and is considered a key modulator in the wound healing process [32]. Exfoliation glaucoma is associated with high TGF β 1 levels in aqueous humor [33], indicating a different wound healing process in the filtering bleb compared to POAG [32]. Another factor is the effect of ethnicity. This study focused on Japanese patients. The outcomes of trabeculectomy for exfoliation glaucoma are inferior to those for POAG in Asian patients [18], and the LOXL1 gene variant associated with exfoliation glaucoma differs between Asians and Caucasians [34]. PreserFlo MicroShunt surgery guides aqueous humor to the filtering bleb; thus, similar to trabeculectomy, postoperative outcomes may vary by ethnicity. A third factor is the potential tube occlusion or adhesion by fibrous material in exfoliation glaucoma. Exfoliation material is produced in various anterior segment tissues [5,35], and the aqueous humor contains a high level of protein [35], increasing its viscosity. One of the major complications of glaucoma implant surgery is tube occlusion [36]. Potentially, the PreserFlo MicroShunt may be more prone to occlusion among glaucoma devices with an internal diameter of 70 μ m and a long tube length. Exfoliation material adheres to the zonules, causing zonular weakness [36]. The prolapse of the vitreous into the anterior chamber causes PreserFlo MicroShunt occlusion in exfoliation glaucoma. In this study, the reoperation rate was 31% (nine cases) (Supplementary Table S1). The

methods for reconstructing the filtering bleb after PreserFlo MicroShunt surgery warrant future investigation.

The association between the PreserFlo MicroShunt insertion site and postoperative outcomes remains unknown. PreserFlo MicroShunt inferior insertion has the advantage of preserving the superior conjunctiva for potential future trabeculectomy. Additionally, there did not appear to be a clear difference in bleb morphology between inferior and superior insertions. In this study, there was a tendency to form diffuse and relatively low blebs. No significant differences in bleb morphology based on the insertion site were observed. Avascular blebs have been associated with bleb-related infections [37], and careful follow-up is required to monitor for such complications in the future. Further studies are required to evaluate the safety and efficacy of PreserFlo MicroShunt inferior insertion.

Another factor that may have influenced the results is the effect of postoperative hypotony. In this study, five cases (17%) experienced hypotony with IOP below 5 mmHg; however, four of these cases subsequently showed favorable outcomes with well-controlled IOP. Similarly, Nobl et al. reported that 45% of patients experienced postoperative hypotony, but 86% eventually achieved good IOP control [11]. Since postoperative hypotony might be transient, it might be preferable to establish some form of a “sanctuary period” specifically for hypotony-related failure when calculating the cumulative survival rate. In this study, we followed the precedent set by Fea et al. and defined two consecutive occurrences of hypotony as failure. Further research is needed to determine the appropriate duration of such a sanctuary period if it were to be introduced. Two potential causes of postoperative hypotony are the suppression of aqueous humor production and excessive filtration. Hypotony due to reduced aqueous humor production may lead to poor bleb formation, whereas hypotony caused by excessive filtration is often followed by a favorable course. The relationship between transient postoperative hypotony and subsequent surgical outcomes warrants further investigation.

This study has several limitations. First, this was a retrospective study conducted at a single center. We included all cases of standalone PreserFlo MicroShunt surgery for exfoliation glaucoma to minimize bias, but some bias remains inevitable. Multicenter prospective studies are required. Second, the mean follow-up period was relatively short at 27.9 weeks. Long-term follow up is crucial for evaluating the outcomes of glaucoma surgery. Additionally, this study did not compare outcomes with other glaucoma types. We limited our report to exfoliation glaucoma. Third, this study only included Asian patients. There may be significant differences in the postoperative outcomes of the PreserFlo MicroShunt between Asian, Caucasian, and other ethnic groups; however, it is important to note that this report focuses solely on Asian patients, specifically Japanese. Ethnic differences have been identified in POAG and uveitic glaucoma [14,15], but the impact of ethnicity in exfoliation glaucoma remains unknown, warranting further investigation. Fourth, transient hypotony was considered a surgical failure in this study. In PreserFlo MicroShunt cases, transient hypotony tends to resolve over time [9]. Previous studies have shown that transient hypotony occurs in about 45% of cases [11], but it rarely results in persistent hypotony. However, in the current cumulative survival rate calculation using the Kaplan–Meier method, surgery was deemed a failure if hypotony occurred twice consecutively. In this study, four out of five patients who experienced transient hypotony eventually had favorable outcomes, but these were still classified as surgical failures in the analysis. Future studies may need to refine the cumulative survival rate calculation method, such as excluding hypotony within a specific postoperative period from being considered a surgical failure. Fifth, this study does not address the success rates of needling and bleb revision surgery following the insertion of a PreserFlo MicroShunt. In this study, needling and bleb revision surgery were performed to manage postoperative elevated IOP, but the small number of cases prevented further evaluation of their success rates. Many aspects, such as the success rates of needling and bleb revision surgery methods following the placement of a PreserFlo MicroShunt, remain unknown. Sixth, postoperative management, particularly the initiation of eye drops and needling, is not standardized and is left to the

surgeon's discretion. The variability in target IOP between patients results in differences in decision-making regarding when to start eye drops, which likely affects the success rate. Seventh, the sample size was limited to 29 eyes, which may have influenced the results. A study with a larger sample size might yield different outcomes. Eighth, the comparison between inferior and superior insertion cases was also limited by the small sample size, making a detailed comparison difficult. There were 13 superior insertion cases and 16 inferior insertion cases, and no significant differences were observed in bleb morphology or hazard ratios. With a larger sample size, some differences might become apparent. Ninth, the study did not exclude eyes with a history of filtration surgery. This decision was made to align this study's conditions with those of previous studies by Fea et al. [12] and Nobl et al. [11], both of which did not exclude such cases, and also to avoid reducing the sample size. However, the proportion of eyes with a history of filtration surgery in our study was six cases (20%), which is higher than the 3.8% reported by Fea et al. [12], and this may have influenced the results.

5. Conclusions

The postoperative outcomes of PreserFlo MicroShunt in exfoliation glaucoma revealed an approximate 50% success rate at 24 weeks and a reoperation rate of approximately 30%. Caution is warranted when performing PreserFlo MicroShunt in Asian patients with exfoliation glaucoma.

Supplementary Materials: The following supporting information can be downloaded at <https://www.mdpi.com/article/10.3390/jcm13206132/s1>: Table S1: Details of reoperation cases; Table S2: Results of the Cox proportional hazard model.

Author Contributions: Conceptualization, S.N. and H.W.; Methodology, S.N. and R.A.; Software, H.W.; Validation, H.W. and S.N.; Formal Analysis, H.W.; Investigation, H.W.; Resources, S.N. and R.A.; Data Curation, H.W.; Writing—Original Draft Preparation, H.W.; Writing—Review and Editing, S.N. and R.A.; Visualization, H.W.; Supervision, S.N.; Project Administration, S.N. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of Saneikai Tsukazaki Hospital (IRB NO: 2404001 and date of approval: 16 April 2024).

Informed Consent Statement: Written informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Acknowledgments: The author thanks his coworkers Etsuko Terao, Yasuko Fujisawa, Kanae Ueda, Yuki Nagata, Saki Dote, and Satomi Oogi for obtaining data.

Conflicts of Interest: The authors declare no conflicts of interest.

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Article

Comparing Corneal Biomechanic Changes between Solo Cataract Surgery and Microhook Ab Interno Trabeculotomy

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Abstract: Background/Objectives: This study aimed to examine the postoperative changes in the corneal biomechanical properties between solo cataract surgery and solo microhook ab interno trabeculotomy (LOT). **Methods:** This retrospective case–control study included 37 eyes belonging to 26 patients who underwent solo cataract surgery and 37 eyes belonging to 31 patients who underwent solo μ LOT. These two groups were matched according to their preoperative intraocular pressure (IOP), axial length (AL), and age. Corneal Visualization Scheimpflug Technology (Corvis ST) was used to obtain four biomechanical parameters representing the corneal stiffness or corneal deformation at the highest concavity, including stiffness parameter A1 (SP-A1), stress–strain index (SSI), peak distance (PD), and deflection amplitude max (DefAmpMax). These parameters were compared preoperatively and 6 months postoperatively, and between the two surgical groups. **Results:** Preoperatively, the patients' IOP, age, and AL, as well as their results in four Corvis ST parameters, were similar between the two groups ($p > 0.05$). No significant difference was observed in SP-A1; however, PD and DefAmpMax were significantly larger, and SSI was significantly smaller postoperatively in the LOT group than in the cataract group. **Conclusions:** Corneal stiffness was reduced, and the cornea was more deformed with LOT than cataract surgery.

Keywords: cataract; trabeculotomy; glaucoma; Corvis ST; Ocular Response Analyzer

1. Introduction

Glaucoma is one of the leading causes of irreversible blindness in the world. Intraocular pressure (IOP) is the only established modifiable factor for halting the progression of glaucoma. Currently, minimally invasive glaucoma surgery (MIGS) has greatly expanded the surgical treatment options in glaucoma to reduce IOP. Cataract surgery is often performed in aged patients, and many studies have reported a decrease in IOP after cataract surgery. However, one recent study indicated that this “IOP reduction” was not associated with preventing disease progression [1]. This may be due to biomechanical changes in the eye following cataract surgery [2]. Indeed, the biomechanical properties of the eye are also important in the disease because they affect IOP measurement [3,4]. Moreover, they play an important role in the pathogenesis of glaucoma [5]. Due to advancements in biometric techniques in recent decades, the biomechanical features of an eye can be measured directly. Corneal Visualization Scheimpflug Technology (Corvis ST; Oculus GmbH,

Wetzlar, Germany) visualizes and records corneal deformation through the application of an air jet using an ultra-high-speed Scheimpflug camera in detail and provides data on biomechanical parameters. These Corvis ST parameters are associated with the severity [6] and visual field progression [7] of glaucoma.

We recently reported a considerable difference in the postoperative changes in biomechanical corneal properties between LOT combined with cataract surgery and solo cataract surgery. However, a more detailed investigation could not be conducted because LOT was combined with cataract surgery, and preoperative IOP was not matched between the two groups [8]. Thus, in this study, we compare the changes in corneal stiffness and maximum corneal deformation measured with Corvis ST between solo LOT and solo cataract surgeries, where background factors, such as preoperative IOP, age, and axial length, are matched.

2. Materials and Methods

The Research Ethics Committee of Seirei Hamamatsu General Hospital approved this retrospective study (#4027, approved on 3 August 2022) that was conducted following the tenets of the Declaration of Helsinki. All participants signed a written informed consent form permitting us to store and use their clinical information in the hospital database for research.

2.1. Participants

This study included glaucomatous patients who received solo LOT surgery and non-glaucomatous eyes that received solo cataract surgery. To avoid the interference of possible effects of these variables on the cornea's biomechanical properties, preoperative IOP, age, and axial length were matched between the two groups. The inclusion criteria for the LOT group were as follows: (1) wide open angle with gonioscopy; (2) typical glaucomatous changes in the optic nerve head (e.g., rim notch with a rim width ≤ 0.1 disk diameter, a vertical cup-to-disk ratio > 0.7 , or a retinal nerve fiber layer defect); and (3) glaucomatous VF defects compatible with the optic nerve head changes meeting the Anderson–Patella criteria [9] on two consecutive examinations. In the present study, we only included those with a preoperative IOP < 22 mmHg, so that a group matched with the cataract group could be created.

The solo cataract group included participants without any abnormal eye-related findings, except for cataracts on biomicroscopy, gonioscopy, and fundoscopy. Those with any history of ocular diseases, such as diabetic retinopathy or age-related macular degeneration, were excluded.

The exclusion criteria for the two groups excluded patients with any corneal abnormality that could affect the Corvis ST measurement, such as keratoconus, and contact lens wearers. Also, patients with conditions such as neurological disorders, cranial trauma, or neoplasms, as well as patients who used chloroquine medication that could result in the development of a VF loss, were excluded.

2.2. Surgical Technique

All procedures were performed at the Seirei Hamamatsu General Hospital between June 2020 and March 2023 by a single surgeon (R.A.). All surgeries were conducted under topical anesthesia. In the cataract group, a clear corneal incision of 2.4 mm in length was made and phacoemulsification with intraocular lens implantation in the posterior chamber was performed. Postoperatively, patients could receive topical anti-inflammatory, topical steroid, and topical antibiotic medications for up to 3 months, 6 weeks, and 6 weeks, respectively. In the LOT group, a trabeculotomy microhook was used to incise the trabecular meshwork through two quadrants. Postoperatively, the patients could receive topical steroids, topical antibiotics, and topical pilocarpine for up to 6 weeks, 6 weeks, and 6 months, respectively. In the LOT group, all antiglaucoma medications prescribed

preoperatively were discontinued postoperatively; however, they were resumed at the discretion of the attending physician.

2.3. Clinical Data Acquisition

We collected background demographic data at baseline, such as preoperative IOP, age, sex, and axial length, from the medical charts. Axial length was measured preoperatively using the IOL Master ver. 5.02 (Carl Zeiss Meditec, Dublin, CA, USA). Corvis ST and Goldmann applanation tonometer (GAT) IOP measurements were performed preoperatively and 6 months postoperatively. Corvis ST was measured randomly at 15 min intervals. Eye drop score accounted for 1 point for a component of topical antiglaucomatous medication or a tablet of oral acetazolamide.

2.4. Corvis ST

The principles of Corvis ST measurements have been described in detail in other papers [8,10]. In brief, a high-speed Scheimpflug camera records 140 images of corneal deformation for 30 ms after the injection of an air pulse emitted from the device. Subsequently, the cornea experiences the first applanation during inward corneal movement (A1), at the highest concavity (HC), when the cornea is most significantly depressed, and the second applanation during outward corneal movement (A2). Using the recorded images, the Corvis ST device yields various parameters, such as corneal stiffness or deformation at the HC. In this study, all parameters were calculated using the latest version of the Corvis ST software (version 1.6r2223). More intuitive Corvis ST parameters were also calculated from raw parameters. For instance, “stiffness parameter A1” (SP-A1) and the “stress–strain index” (SSI) were also obtained as Corvis ST parameters related to corneal stiffness. SP-A1 is the ratio of the loading on the cornea to its deformation at the first applanation, calculated as follows:

$$\text{SP-A1} = \frac{\text{adjAP1} - \text{bIOP}}{\text{A1DefAmp}}$$

where adjAP1 is the adjusted air pressure on the cornea at the first applanation, bIOP is the Corvis ST-derived biomechanical IOP, and A1DefAmp represents corneal apex displacement at the first applanation. A higher SP-A1 value indicates a stiffer cornea, as more loading is required to flatten the cornea [11]. Thus, SP-A1 shows a secant elastic modulus at a single state of the cornea, and the nonlinear relationship between IOP, corneal morphology, and elastic properties of the cornea was excluded in the formula [12], enabling the independence of SP-A1 on IOP and corneal geometry (e.g., CCT). In contrast, the SSI measures the nonlinearity of the stress–strain relationship of the eye; the SSI was developed using finite-element methods to represent corneal stiffness as materially independent from the IOP and corneal geometry [13]. The SSI is indicated on a normalized scale, where the average value for 50-year-old eyes is 1. Higher SSI values indicate stiffer and less deformable corneas. PD is the distance between nondeformed peaks at the HC, and DefAmpMax is the maximum displacement of the corneal apex compared to the baseline.

Each Corvis ST parameter was measured thrice, and the mean values were used for the analysis. Only reliable Corvis ST measurements were used, as suggested by the “OK” quality indicator displayed on the instrument monitor.

2.5. Statistical Analysis

The mean values of baseline clinical factors and Corvis ST parameters were compared between the LOT and cataract groups with linear mixed models, where the random effect was the patient, because of the inclusion of either one or two eyes. In addition, changes in SP-A1, SSI, PD, and DefAmpMax between pre- and postoperative values (dSP-A1, dSSI, dPD, and dDefAmpMax, respectively) were calculated, and their association with the GAT IOP change (dGAT IOP) was investigated using the linear mixed model. The marginal R^2 value for the linear mixed model was calculated based on the method reported by Nakagawa et al. [14].

We used the statistical programming language R 4.4.1 (The R Foundation for Statistical Computing, Vienna, Austria) for the data processing and analyses.

3. Results

We included 37 eyes from 31 patients with glaucoma who underwent LOT and 37 eyes from 26 patients who underwent solo cataract surgery. In the LOT group, 30 eyes had primary open-angle glaucoma, 2 eyes had exfoliation glaucoma, 2 eyes had chronic angle closure glaucoma, 2 eyes had secondary open-angle glaucoma, and 1 eye had developmental glaucoma. Moreover, 16 eyes were phakic and the remaining 21 eyes were pseudophakic. The mean and SD of the mean deviation (MD) value measured with the Humphrey Field Analyzer (Carl Zeiss Meditec, Dublin, CA, USA) were -12.7 and 7.0 dB in the remaining 29 eyes. Such measurements were not conducted in the remaining eight eyes for various reasons, such as poor vision.

Table 1 and Figure 1 show the preoperative basic characteristics in each group. Preoperatively, the age, axial length, CCT, and GAT IOP score were similar between the two groups (all $p > 0.05$, linear mixed model). Additionally, PD, DefAmpMax, SP-A1, and SSI values were not significantly different between the two groups ($p > 0.05$, linear mixed model, adjusted for age, AL, and GAT IOP).

Table 1 and Figure 1 show the comparisons of each variable's pre- and postoperative values within each group. GAT IOP was not significantly different when comparing the pre- and postoperative scores in both groups (all $p > 0.05$, linear mixed model). The pre- and postoperative eye drop scores were not significantly different within the LOT group.

Table 1 and Figure 1 also show the postoperative characteristics in each group. The GAT IOP was not significantly different between the two groups. In contrast, the LOT group had significantly larger PD and DefAmpMax values and a significantly smaller SSI compared with the cataract group ($p < 0.001$, linear mixed model, adjusted for age, AL, and GAT IOP). SP-A1 was not significantly different between both groups ($p = 0.29$).

Table 2 shows the associations between dSP-A1, dSSI, dPD, and dDefAmpMax and dGAT IOP. All associations were significant in the LOT group ($p < 0.001$, linear mixed model), and this was similar in the Cat group, except for dPD. However, the Cat group's mR^2 values were much lower compared with those in the LOT group.

Table 1. Basic characteristics and biomechanical parameters at baseline.

Parameters	LOT Group		Cat Group		p -Value *	p -Value **	p -Value †	p -Value ††
	Pre	Post	Pre	Post				
Age (years)	75.3 ± 8.2 (52–88)		74.5 ± 7.7 (60–90)		-	-	0.71	-
Axial length (mm)	25.2 ± 2.2 [21.4–30.9]		24.0 ± 2.4 [21.2–33.1]		-	-	0.19	-
Eye drop score	2.4 ± 1.6 [0 to 5]	2.6 ± 1.2 [0 to 5]	-	-	-	-	-	-
GAT IOP (mmHg)	17.0 ± 3.1 [8.0–21.0]	14.2 ± 4.5 [6.0–29.0]	15.9 ± 2.5 [8.0–21.0]	13.4 ± 2.7 [9.0–23.0]	<0.001	<0.001	0.071	0.55
CCT (μm)	528.5 ± 37.0 [456.0–608.0]	526.6 ± 37.6 [452.0–606.0]	541.8 ± 27.0 [490.0–590.0]	544.2 ± 28.3 [490.0–606.0]	0.32	0.33	0.063	0.023
Peak Distance (mm)	5.1 ± 0.36 [4.2–5.8]	5.3 ± 0.38 [4.5–6.1]	5.0 ± 0.29 [4.1–5.7]	5.1 ± 0.32 [4.1–5.8]	<0.001	0.24	0.62	<0.001
Maximum deflection amplitude (mm)	0.97 ± 0.14 [0.72–1.3]	1.08 ± 0.17 [0.76–1.4]	0.93 ± 0.11 [0.69–1.2]	0.98 ± 0.12 [0.67–1.2]	<0.001	<0.001	0.31	<0.001
SP-A1 (mmHg/mm)	105.4 ± 22.7 [67.5–150.4]	95.3 ± 26.9 [55.4–153.5]	105.0 ± 15.0 [82.0–137.1]	94.2 ± 17.9 [64.3–136.4]	<0.001	0.0015	0.98	0.29
SSI	1.19 ± 0.29 [0.66–1.87]	1.04 ± 0.24 [0.64–1.60]	1.28 ± 0.24 [0.77–1.79]	1.21 ± 0.25 [0.73–1.73]	<0.001	0.068	0.55	<0.001

LOT, solo trabeculotomy; Cat, solo cataract surgery; CCT, central corneal thickness; GAT, Goldmann applanation tonometry; SP-A1, stiffness parameter upon first applanation; SSI, stress–strain index. p -values according to linear mixed model: * between pre- and postoperative values (LOT group); ** between pre- and postoperative values (Cat group); †, between LOT and Cat groups (pre operation); ††, between LOT and Cat groups (post operation).

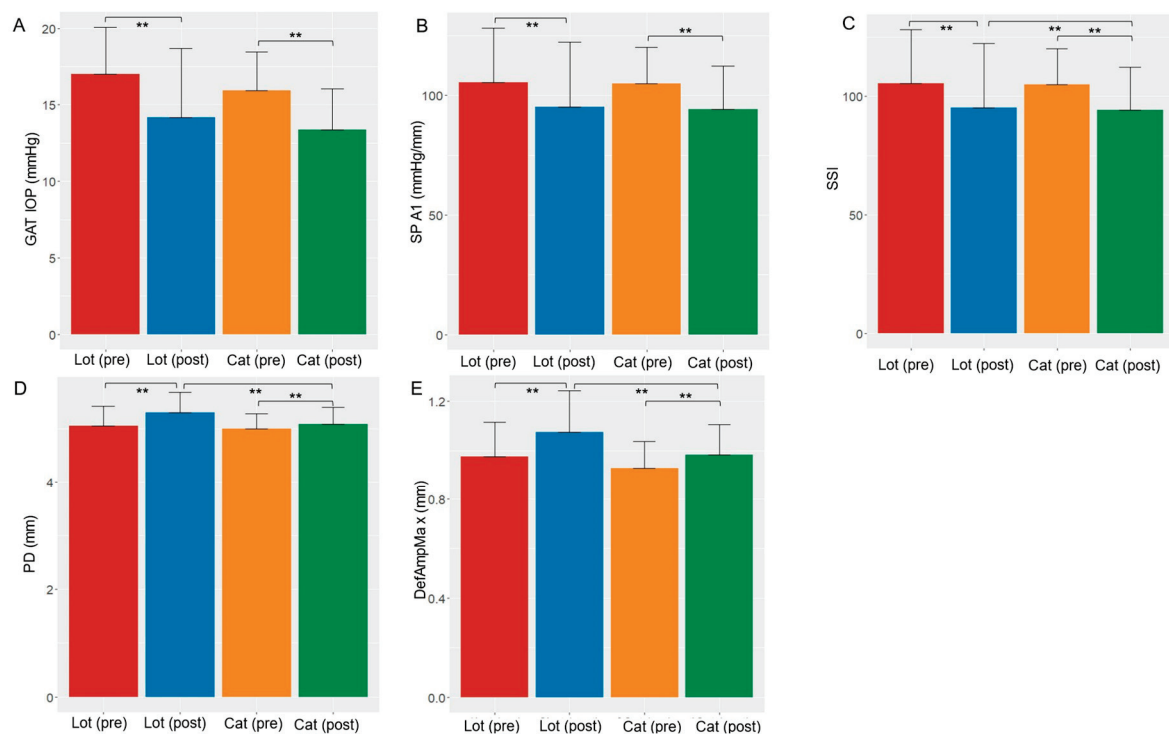


Figure 1. Comparisons of each variable between pre- and postoperative values and between each group: (A) GAT IOP, (B) SP-A1, (C) SSI, (D) PD, (E) DefAmpMax. GAT, Goldmann applanation tonometry; IOP, intraocular pressure; SP-A1, stiffness parameter upon first applanation; SSI, stress–strain index; PD, peak distance; DefAmpMax, maximum deformation amplitude. **: $p < 0.01$.

Table 2. Associations between Corvis ST parameters and GAT IOP changes.

	LOT Group				Cat Group			
	Partial Regression Coefficient	SE	<i>p</i> -Value	mR ²	Partial Regression Coefficient	SE	<i>p</i> -Value	mR ²
Change in peak distance (mm)	−0.044	0.0086	<0.001	0.42	−0.023	0.012	0.065	0.11
Change in maximum deflection amplitude (mm)	−0.022	0.0035	<0.001	0.52	−0.018	0.0048	<0.001	0.31
Change in SP-A1 (mmHg/mm)	2.33	0.46	<0.001	0.39	2.72	0.87	0.0039	0.25
Change in SSI	0.029	0.0069	<0.001	0.32	0.035	0.011	0.0035	0.25

LOT, solo trabeculotomy; Cat, solo cataract surgery; SE, standard error; GAT, Goldmann applanation tonometry; SP-A1, stiffness parameter upon first applanation; SSI, stress–strain index.

4. Discussion

Our study examined Corvis ST-measured postoperative changes in the corneal biomechanical properties in age-, AL-, and IOP-matched patients, namely in 37 glaucomatous eyes that received solo LOT and 37 eyes without glaucoma that received solo cataract surgery. Consequently, both groups showed a postoperative decrease in IOP. In addition, we found decreased corneal stiffness (as suggested by decreased SP-A1 and SSI) and corneal deformation (as suggested by increased PD and DefAmpMax) after LOT surgery, whereas only SP-A1 and DefAmpMax were changed in the Cat group. The SSI, PD, and DefAmpMax values showed a significantly greater change in the LOT group than in the Cat group.

Cataract surgery can reduce IOP by 3.4–1.5 mmHg [15–18]. Our findings showed a reduction in IOP by 2.50 mmHg in the cataract group (Table 1 and Figure 1). The IOP reduction following cataract surgery may be explained by several mechanisms. First, the posterior traction on the scleral spur by the anterior lens zonules becomes weak as the lens thickens, which results in a decrease in the outflow facility [18,19]. However, cataract surgery would resolve this condition. Particularly in eyes with a narrow angle, the reduction in lens volume results in angle widening and facilitates aqueous outflow [15]. Second, the outflow facility is increased due to the metalloproteinase production induced by the stress from high IOP or ultrasonic vibrations during phacoemulsification or the remodeling of the trabecular endothelium [20,21]. In addition, the cornea being more deformable would be another reason for “true” IOP reduction [4,22,23].

Previous studies have shown that IOP was reduced between 5 and 19.9 mmHg after LOT [24]. In the current study, the IOP reduction was 2.8 mmHg on average (Table 1 and Figure 1). This difference could be attributed to the difference in preoperative IOP values. Previous studies have shown that postoperative IOP after LOT is largely dependent on the preoperative IOP [24]. In contrast, our study only included those with a preoperative IOP < 22 mmHg in the analysis, resulting in the creation of a group matched with the cataract group.

Despite similar pre- and postoperative GAT IOP and preoperative Corvis parameters between both groups, the Corvis parameters were significantly different postoperatively (Table 1 and Figure 1). First, the SSI was reduced postoperatively in both groups, but it was greatly reduced significantly in the LOT group compared with the cataract group. The SSI is a parameter that was developed based on the findings obtained in a finite-element model experiment wherein biomechanical eye responses were analyzed at different IOP levels, and it is a parameter of corneal stiffness arising from material status, which is independent of IOP [13]. This implies that the reduced SSI in the cataract group could be attributed to the effect of the incision during the cataract surgery, whereas the incision in LOT surgery was very small, and its effect on corneal stiffness would be negligible. In eyes with glaucoma, the trabecular meshwork is stiff and resistant to external stress [25]. LOT removes this resistance, and even the pectinate ligament is incised. Our findings indicated that the effect of the incision in the trabecular meshwork and the pectinate ligament on SSI was significantly larger than that of the incision in cataract surgery. Although SP-A1 was significantly lower postoperatively than preoperatively in both groups, SP-A1 did not differ postoperatively between both groups. SP-A1 is dependent on the IOP; however, this cannot explain this finding because the pre- and postoperative IOP values were not significantly different between both groups (Table 1 and Figure 1). This result would indicate that the effects of the incision in cataract surgery and the pectinate ligament in LOT surgery on corneal stiffness are almost identical at the A1 time point (no significant difference in SP-A1). However, the latter was significantly larger after that time point (significant difference in SSI). The cornea being more deformable at the HC, as suggested by the larger PD and DefAmpMax values in the LOT group compared to the cataract group, would support this. Similarly, the changes in PD, DefAmpMax, SP-A1, and SSI were more closely related to the change in IOP in the LOT group than they were in the cataract group (Table 2).

Previous studies have suggested that IOP decreases after cataract surgery; however, the rate of visual field progression is not altered after this surgery [26,27]. Furthermore, in Kim et al.’s research, it was reported that visual field progression is actually even accelerated after cataract surgery compared to its preoperative level [1]. The mechanism for this result is unclear; however, a postoperative reduction in the measured IOP may not entirely be a true IOP reduction but may also occur due to postoperative biomechanical changes, such as corneal softening [2]. The cornea is similarly soft after LOT, but the biomechanical properties are also largely changed with this surgery.

Antiglaucoma medications have significant influences on not only IOP but also other biomechanical properties of the ocular tissue, such as corneal thinning [28–30] and soft-

ening [31,32]. We discontinued all topical antiglaucoma medications postoperatively, including prostaglandin analogs, but they were resumed at the discretion of the attending physician in the postoperative follow-up period. Thus, the eye drop score was not significantly different before and after LOT surgery, implying that this effect is only negligible.

The present study has limitations. The sample size was relatively small, and further validation of the current results in a larger dataset is required. Another limitation is the retrospective nature of this study: this study's data are limited to a period of 6 months after the operation. Extended follow-up evaluation would be advantageous in comprehending the enduring biomechanical alterations and their consequences on visual outcomes and the advancement of diseases. Finally, although this study considered the effects of antiglaucoma drugs, their possible influence on corneal biomechanics could not be thoroughly investigated because of the relatively small sample size. Thus, our findings should be considered as initial findings that necessitate additional ongoing research in order to validate the conclusions. Moreover, eyes with relatively low IOP were selected in the LOT group. This consideration was needed in our selection of glaucoma patients, because biomechanical corneal properties are closely associated with IOP, and postoperative changes in the biomechanical corneal properties cannot be compared between the two surgeries unless the pre- and postoperative IOP values are matched.

In conclusion, the results of the present study suggest that the cornea becomes softer and more deformable after LOT and cataract surgeries, but this effect was more pronounced in the LOT group.

Author Contributions: R.A.: conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing—original draft preparation, and writing—review and editing. S.A., Y.F., S.N., H.M. and Y.K.: methodology, resources, and writing—review and editing. All authors have read and agreed to the published version of the manuscript.

Funding: This study was supported by grants (numbers 19H01114, 18KK0253, 20K09784, and 20K18337) from the Ministry of Education, Culture, Sports, Science and Technology of Japan and the Research Funding for Longevity Sciences (22–25) from the National Center for Geriatrics and Gerontology (NCGG), Japan.

Institutional Review Board Statement: The Research Ethics Committee of Seirei Hamamatsu General Hospital approved this retrospective study (#10619) that was conducted following the tenets of the Declaration of Helsinki.

Informed Consent Statement: All participants signed a written informed consent form permitting the storage of their clinical information in the hospital database and its use for research.

Data Availability Statement: All data can be made available if a request is made to the corresponding author.

Conflicts of Interest: The authors declare no conflicts of interest.

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ISBN 978-3-7258-8574-9