Early Clinical Outcomes of the Preserflo Microshunt Device

Resultados Clínicos Iniciais do Dispositivo Preserflo Microshunt

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ABSTRACT

INTRODUCTION: The purpose of this study was to assess the efficacy and safety profile of the Preserflo® Microshunt device, which is an *ab externo* sub-Tenon's aqueous shunt approved for the surgical treatment of glaucoma,

METHODS: Retrospective single-center observational study. Patients who underwent standalone or combined phacoemulsification-Preserflo® Microshunt implantation with a minimum of 3 months of post-operative follow-up were included. Primary outcome measures included surgical success defined as a ≥ 30% decrease in IOP from baseline and unmedicated IOP ≤18 mmHg. Secondary outcomes included number of hypotensive drops and adverse effects.

RESULTS: Ninety-two (92) eyes from 77 patients (mean±SD age 68±18 years) were included, most of which underwent standalone surgery (n=74 eyes; 80%). Average post-operative follow-up time was 9±6 months, with over three quarters of eyes (n=70; 76%) completing at least 6 months of follow-up and a third (n=30; 33%) with at least 12 months. Mean IOP was significantly reduced from a baseline measurement of 22±5.8 mmHg throughout follow-up, with a 12-month IOP of 13.9±4.8 mmHg (p<0.0001). Mean number of medications was reduced from 2.8±0.9 to 0.5±0.9 at last follow-up (p<0.0001), with 75% of eyes remaining drop-free throughout follow-up. Absolute success at 12 months was 46% and 64% if medication was allowed (qualified). Complications included self-limited intra-operative bleeding or post-operative hyphema (total n=9; 10%), and shallow anterior chamber (n=4; 4%). No major or sight-threatening complication was recorded.

CONCLUSION: Early audit of real-world data from Preserflo® use suggests this to be a safe and effective surgical option for the treatment of medically uncontrolled glaucoma.

KEYWORDS: Glaucoma/surgery; Glaucoma Drainage Implants; Filtering Surgery; Intraocular Pressure.

RESUMO

INTRODUÇÃO: O objectivo deste estudo foi analisar a eficácia e perfil de segurança do Preserflo® Microshunt, um dispositivo de filtração subtenoniana *ab externo* aprovado para tratamento

cirúrgico do glaucoma.

MÉTODOS: Estudo observacional retrospectivo. Foram incluídos doentes implantados com Preserflo® Microshunt isoladamente ou em combinação com facoemulsificação com um mínimo de 3 meses de seguimento. O *outcome* primário foi o sucesso cirúrgico definido como uma redução mínima de 30% da pressão intraocular (PIO) basal e uma PIO não medicada ≤18 mmHg. *Outcomes* secundários incluíram o número de medicações hipotensivas e efeitos adversos.

RESULTADOS: Foram incluídos 92 olhos de 77 doentes (idade média ± DP 68±18 anos), a maioria dos quais submetidos a cirurgia isolada (n=74 olhos; 80%). O tempo médio de seguimento pós-operatório foi de 9±6 meses, tendo mais de três quartos (n=70; 76%) completado pelo menos 6 meses de seguimento e um terço (n=30; 33%) com o mínimo de 12 meses. A PIO média foi significativamente reduzida em todos os pontos de análise face à PIO basal de 22±5,8 mmHg até 13,9±4,8 aos 12 meses (p<0,0001). O número médio de medicações hipotensivas desceu 2,8±0,9 para 0,5±0,9 na última observação (p<0,0001), com 75% dos olhos sem medicação durante todo o seguimento. O sucesso absoluto aos 12 meses foi de 46%, e 64% contando com medicação (qualificado). As complicações incluíram hemorragia angular intra-operatória ou hifema pós-operatório (n total=9; 10%), e câmara anterior baixa (n=4; 4%), com resolução espontânea. Não se registaram quaisquer complicações graves ou com necessidade de intervenção cirúrgica.

CONCLUSÃO: A análise inicial do Preserflo® Microshunt em contexto clínico sugere que é uma cirurgia segura e eficaz no tratamento do glaucoma não controlado medicamente.

PALAVRAS-CHAVE: Cirurgia Filtrante; Glaucoma/cirurgia; Implantes de Drenagem de Glaucoma; Pressão Intraocular.

INTRODUCTION

Glaucoma is the leading cause of irreversible blindness globally and prevalence is expected to rise over the next decades.[1,2] Conventional glaucoma surgery such as trabeculectomy and tube shunts are still the most widespread techniques for intraocular pressure (IOP) control.[3,4] However, both tubes and trabeculectomies have a significant rate of reoperations and adverse effects, mainly hypotony and its related complications.[5–7] Moreover, both surgeries often require additional post-operative interventions such as intraluminal stent removal (in the case of valveless tubes) and suture lysis or releasable suture removal (in the case of trabeculectomies).[6] In order to simplify surgical technique, reduce operating room time and decrease the burden of post-operative visits and interventions, while potentially offering a better safety profile, several alternative surgical devices and procedures, collectively called MIGS (minimally invasive glaucoma surgery), have been introduced in the past decade and have risen in popularity.[3,4,8] However, most MIGS procedures are not capable of providing adequate long-term IOP control in moderate-to-advanced glaucoma.[9] The definition of MIGS has recently been changed to only include *ab-interno* non-bleb forming procedures,[10] thereby excluding devices such as the XEN gel stent (Allergan, Dublin, Ireland) and the Preserflo® Microshunt (previously known as Innfocus Microshunt; PMS, Santen Pharmaceutical Co. Ltd., Osaka, Japan). The Preserflo® Microshunt is an *ab externo* bleb-forming device with a 70µm lumen made from a highly biocompatible material [poly(styrene-*block*-isobutylene-*block*-styrene, or SIBS], approved for surgical treatment of medically uncontrolled primary open-angle glaucoma. This device was designed to approach the clinical performance of trabeculectomy, while being easier to implant and reducing persistent hypotony rates and the need for post-operative interventions.[11,12] Published series report variable success rates of 53.9% up to 92.5% at 12 months of follow-up and a favourable safety profile.[13–18] Most of these however were calculated using heterogenous criteria and below standard when compared to the World Glaucoma Association (WGA) Guidelines.[19] In fact, most resorted to IOP lowering of 20% or setting up the threshold criteria at 21 mmHg, which may be unsuitable in real life care of glaucoma patients. Nevertheless, early head-to-head comparison of the Preserflo® Microshunt with trabeculectomy showed similar IOP control and medication burden reduction but lower probability of success at 12 months, with a higher proportion of post-operative visits and interventions in trabeculectomy patients.[18,20] Most commonly reported adverse effects included transient hypotony, shallow anterior chamber, bleb encapsulation and wound leakage.[13–17] Sight-threatening complications are rare with the Preserflo® but have been reported, including hemorrhagic choroidal detachment and malignant glaucoma.[18,21,22] The majority of evidence so far has come from strict prospective clinical trial conditions, with carefully selected patients, which may not adequately represent a surgeon's patient population, thus reducing the relevance of published results. Evidence stemming from real-world clinical settings may often be more useful for clinicians because it translates more closely to clinical practice and wider patient populations, with varying glaucoma diag

nosis, and may better prepare surgeons and patients for their expected outcomes, both in terms of surgical success and possible complications.[23] Therefore, the purpose of this study was to analyse early efficacy and safety outcomes of the Preserflo® Microshunt in a real-world setting using standard, clinically acceptable success criteria.

MATERIAL AND METHODS

DESIGN AND PATIENT SELECTION

Retrospective single-center observational study conducted in a tertiary hospital. Our study adhered to tenets of the Declaration of Helsinki, was approved by the local Ethics Committee and informed consent was obtained from all participants. Our study was registered with the ISRCTN registry (96192007), as per GDPR recommendations. Consecutive patients with medically uncontrolled glaucoma and/or intolerance to medication warranting glaucoma surgery who were implanted with a Preserflo® Microshunt between June 2019 and May 2021 were included in this study. The surgical decision was made at the surgeon's discretion, according to patient compliance, IOP control and medication-related adverse reactions. Patients previously with diagnosed angle closure glaucoma who had resolved their angle closure after cataract surgery were included, as were those with appositional angle closure glaucoma who underwent combined surgery with phacoemulsification. Phakic patients with angle closure were not eligible for Preserflo® implantation. Patients with a post-operative follow-up < 3 months were excluded.

SURGICAL TECHNIQUE

All patients underwent the same surgical protocol and were operated on by an experienced glaucoma subspecialist. In summary, a sub-Tenon's block was administered, followed by placement of a superior peripheral corneal traction suture for upper quadrant exposure. A 4-mm fornix-based conjunctival peritomy was fashioned to access and dissect a deep pocket within the sub-Tenon's space between the superior and lateral rectus muscles. Wet-field bipolar cautery was used to achieve adequate hemostasis of the scleral bed, followed by placement of 3 LASIK shields (EYETEC, Antwerp, Belgium) saturated with 0.4 mg/mL mitomycin-C during 2 minutes. After copious balanced-salt solution (BSS) lavage, the implantation site was marked with 3-mm scleral marker (Fig. 1A) and 1-mm wide and 1-2-mm long superficial scleral pocket was created with a triangular knife. A needle tract was fashioned by passing a 25-gauge needle into the anterior chamber, approximately between the cornea and iris (Fig. 1B). The microshunt was then rinsed with BSS and carefully inserted into the tract ensuring the shunt's posterior fin was adequately wedged in the scleral pocket (Fig. 1C). Prior to tucking the device under the Tenon's and conjunctiva, aqueous flow was checked at its distal end (Fig. 1D). Both Tenon's and conjunctiva were closed using 7-0 vicryl. In cases combined with phacoemulsification, cataract extraction was performed immediately after mitomycin-C application and before creating the scleral pocket. Patients were instructed to suspend all hypotensive medication and were started on tobramycin and dexamethasone drops 4 times a day for 6 weeks, with slow tapering.

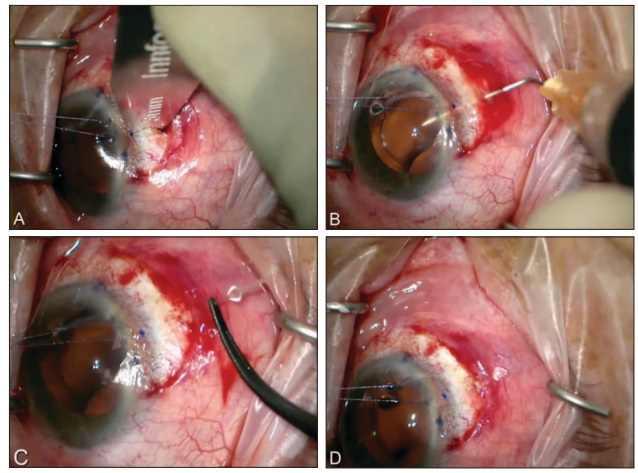

Figure 1. Operating room microscope pictures of different steps of the Preserflo® Microshunt implantation. 1A, marking the implantation site with 3-mm scleral marker; 1B, threading a 25-gauge needle through the tract; 1C, careful implantation of the microshunt using forceps; 1D, checking aqueous humour flow at the distal end of the device prior to conjunctival closure.

STUDY VISITS AND DATA COLLECTION

Data was retrospectively retrieved from patient files from last pre-operative visit (1 month prior to surgery at the most), surgical report, day 1, day 7, months 1, 3, 6, 12, 18 and 24, whenever applicable. Variables collected included demographic and clinical characteristics, medication, IOP measurements using Goldmann applanation tonometry (GAT), slit-lamp examination, fundoscopic findings, adverse effects and reoperations.

OUTCOMES AND DEFINITIONS

The primary outcome was surgical success. This was defined as IOP ≤ 18 mmHg plus ≥ 30% IOP reduction from baseline. Success was considered absolute if unmedicated or qualified if otherwise. Criteria for failure included prolonged hypotony (IOP < 5 mmHg on two consecutive visits), loss of light perception, additional glaucoma surgery or surgery to address post-operative complications, with the exception of bleb revision or needling procedures. Secondary outcomes included IOP, mean number of hypotensive medications, adverse effects and reoperation rates. Outcomes were defined in accordance to trial design recommendations by the WGA.[19]

STATISTICAL ANALYSIS

Statistical analysis was performed with Prism 8 (GraphPad Software; San Diego, CA, USA). Distribution normality

was assessed with the Shapiro-Wilk test. Continuous variables were expressed as mean±SD and tested using 2-sided Student t-test or Kolmogorov-Smirnov test according to normality, while categorical variables were tested with Fisher exact test or Chi-square test when appropriate. Success survival rates were tested using Kaplan–Meier curves and were compared using a log-rank test. Spearman correlation coefficient was used to test correlations between categorical variables. A *p*-value of 0.05 was considered for statistical significance.

RESULTS

Ninety-two eyes from 77 patients were included in this study. Mean age at time of surgery was 68±18 years with primary or secondary forms of open-angle glaucoma constituting the majority of cases (n=84, 91%). Microshunt was a primary intervention in most patients (n=72; 78%). Twenty eyes (22%) had a history of previous glaucoma surgery, mostly with trabeculectomy (n=8, 9%) and XEN gel stent (n=7, 8%). No patient had history of laser therapy for glaucoma. For detailed baseline demographic information, glaucoma diagnosis and previous surgical history see Table 1. Mean post-operative follow-up time was 9±6 months, with 70 eyes (76%) having completed 6 months of follow-up and a third at least 12 months. Most patients underwent standalone surgery (n=74; 80%), with the remaining patients having undergone uncomplicated standard phacoemulsification combined with microshunt implantation. The combined surgery subgroup had a significantly lower follow-up time versus the standalone subgroup (5.2±1.7 *vs* 9.7±6.4 months, respectively; *p*=0.01).

Both IOP and number of medications were significantly reduced from baseline values of 22±5.8 mmHg and 2.8±0.9 at all timepoints (*p*<0.001). Mean IOP and number of medications at 12 months were 13.9±4.8 and 0.8±1.1, respectively (Fig. 2 and Table 2). The mean IOP percentage reduction from baseline was 39%. Moreover, at months 3, 6 and 12, the proportion of eyes with IOP ≤ 18 mmHg at were 93%, 93% and 83%, and drop-free eyes accounted for 89%, 83% and 60% of our sample at the same timepoints, respectively, with 75% of eyes remaining drop-free throughout their respective follow-up. Absolute success rates at months 3, 6 and 12 was 77%, 69% and 46%, while qualified success was 86%, 79% and 64%, respectively (Fig. 3). Standalone and combined surgery subgroups showed comparable progression of IOP profiles, despite higher recorded IOP in the combined surgery group during the first month (13.5±4.5 *vs* 10.6±4.1 at month 1, respectively; *p*=0.02; Fig. 4).

We recorded 23 cases of failure during follow-up. All cases failed due to inadequate IOP control despite medical therapy (n=23) with 3 eyes needing additional glaucoma surgery (2 cases had a Preserflo® Microshunt replacement and 1 case had a posterior drainage device implanted).

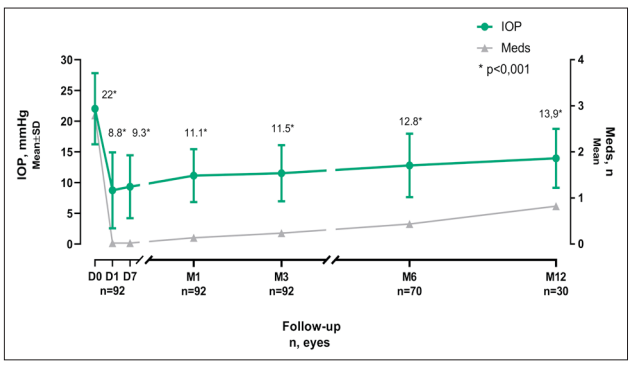

Figure 2. Graphical representation of mean IOP and number of medications over time.

Table 1. Baseline sample demographic and clinical characteristics.

Characteristics	
Age (years, mean±SD)	68±18
Ethnicity (patients, N (%))	
Caucasian	73 (95)
African descent	3 (4)
Hispanic	1 (1)
Female gender (patients, N, (%))	37 (48)
Diagnosis (eyes, N (%))	
POAG	44 (48)
SOAG	40 (43)
Pseudoexfoliative	30 (33)
Uveitic[a]	6 (7)
Steroid-induced	2 (2)
Pigmentary	1 (1)
Due to previous ocular surgery[b]	1 (1)
PCAG[c]	6 (7)
PCG[d]	2 (2)
Previous glaucoma surgery (eyes, N (%))	20 (22)
Trabeculectomy	8 (9)
XEN gel stent	7 (8)
Posterior drainage device	2 (2)
Baerveldt-XEN	1 (1)
Ultrasound circular cyclocoagulation	1 (1)
Endocyclophotocoagulation	1 (1)

PCAG, primary closed-angle glaucoma; PCG, primary congenital glaucoma; POAG, primary open-angle glaucoma; N, number; SOAG, secondary open-angle glaucoma; SD, standard deviation

[a] All uveitic patients had gonioscopically documented open angles without significant peripheral anterior synechiae.

[b] One patient with glaucoma following penetrating keratoplasty had gonioscopically documented open angle without significant peripheral anterior synechiae.

[c] All patients with previous PCAG diagnosis who underwent standalone surgery had resolved their angle closure following previous cataract surgery. One phakic PCAG patient underwent combined surgery.

[d] Two older patients with remote PCG diagnosis had gonioscopically documented open angles.

Table 2. IOP measurements and medication during follow-up.

	Baseline	D1	D7	M1	M3	M6	M12	*p*-value baseline *vs* each timepoint
Eyes, N	92	92	92	92	92	70	30	n/a
IOP, mmHg (m±SD)	22±5.8	8.8±6.2	9.3±5.1	11.1±4.3	11.5±4.6	12.8±5.2	13.9±4.8	<0.001
IOP reduction from baseline, % (m±SD)	n/a	57±35	55±26	46±24	45±24	42±25	39±23	n/a
Topical medication, N (m±SD)	2.8±0.9	0.0±0.2	0.0±0.2	0.1±0.5	0.2±0.7	0.4±0.9	0.8±1.1	<0.001
Oral CAI, N of patients	6	0	0	0	0	0	0	n/a

CAI, carbonic anhydrase inhibitor; D, day; IOP, intraocular pressure; M, month m±SD, mean±standard deviation; N, number of; n/a, not applicable.

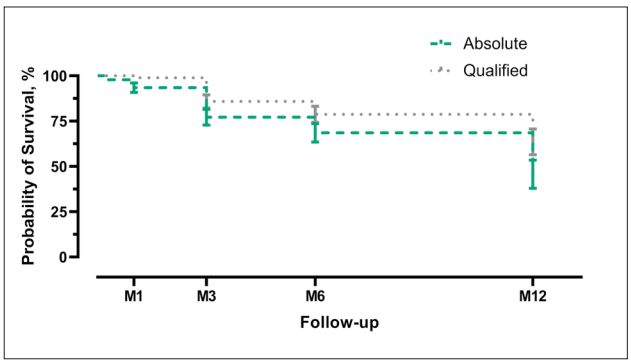

Figure 3. Kaplan-Meier survival curves for surgical success.

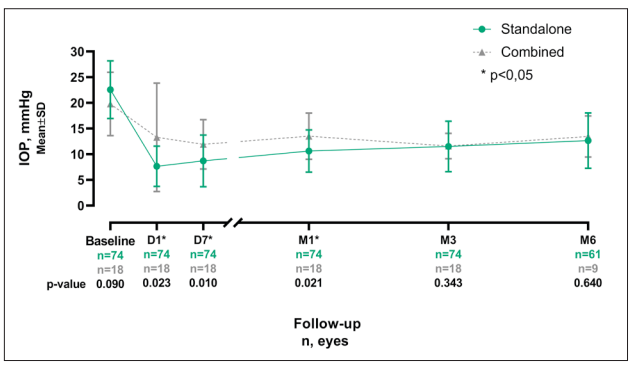

Figure 4. IOP profile comparing standalone and combined surgery groups.

There were no failures due to complications. There were 15 recorded post-operative complications, all occurring within the first month of surgery (some eyes experienced more than one complication). Most complications were hemorrhagic in nature (4 eyes with intra-operative angular bleeding and 5 cases of hyphema on day 1). There were also 4 cases of shallow anterior chambers (not flat, without iridocorneal contact), 1 eye had a wound leakage and another eye suffered from a choroidal effusion. All early complications resolved within one week with medical therapy. Two eyes developed bleb encapsulation and underwent mitomycin-C-augmented bleb revision in one case and needling in the other one. There was no record of serious adverse effects, reinterventions (other than reoperations) or slit-lamp procedures during follow-up. Moreover, we found no correlation between recorded complications and patient lens status, surgery subgroup, glaucoma subtype or history of previous glaucoma surgery (p>0.05).

DISCUSSION

In this study we retrospectively analysed early clinical and safety outcomes with the Preserflo® Microshunt in a real-life setting. This is an *ab externo* microshunt ideally aimed at the treatment of moderate to advanced OAG while mitigating post-operative complications and interventions associated with trabeculectomy and posterior drainage devices.[11,27] Despite early promising results, with good IOP control approaching that of trabeculectomy, evidence from real-life data is scarce. Fea *et al* conducted a real-life assessment with POAG and PXG patients and reported post-operative 1-year IOP of 14.1±3.4 mmHg and absolute and qualified success rates of 26% and 58.7%, respectively.[14] Another study by Martinez de la Casa with OAG patients who underwent standalone or combined surgery reported 1-year IOP of 14.6±3.5 mmHg and 62.1% of absolute success.[17] Our results months showed a favourable IOP profile in the mid-to-low teens throughout follow-up (IOP at 12 months of 13.9±4.8 mmHg), with a mean reduction in IOP of 39% and 83% of patients registering an IOP ≤ 18 mmHg at 12 months. Survival analysis showed that almost two-thirds of patients (64%) had fulfilled qualified success criteria at 12 months and nearly half (46%) did so without medication (absolute). These results are comparable to those in previously published studies in the same timeframe.[13–18]

It should be noted that these published results have varied significantly, from qualified success rates over 90% at 3 years to 53.9% at 12 months. Variability in reported results may be partly explained by differences in study protocol and methodology, mitomycin-C exposure time and concentration, surgeon experience with the device, baseline sample characteristics, among others. Additionally, the majority of this literature employed less strict success criteria, most authors opting either for a higher IOP threshold (e.g. 21 mmHg) or a lower reduction from baseline (20%). Our stricter success definitions (IOP ≤ 18 mmHg plus 30% decrease from baseline) are in keeping with recommendations from the WGA

on trial design[19] and we believe these are more appropriate when testing surgical options for moderate-to-advanced glaucoma and are similar to the outcomes used when testing trabeculectomy results. On the other hand, these composite success outcomes do not fully illustrate all patients' requirements when undergoing surgery. Several patients in our sample had appropriate pre-operative IOP control but either had significant adverse effects from topical medication or had trouble with drop administration. In these cases, although the purpose of surgery was to reduce medications burden while maintaining roughly the same IOP as in the pre-operative period, they were often considered failures for not having attained a 30% IOP drop, despite having reached their clinical goal. In fact, 75% of eyes remained drop-free throughout their respective follow-up.

Our results also show a very favourable safety profile, with no sight-threatening adverse effects or the need for reinterventions due to complications. Most adverse effects were mild and self-limited, such as anterior chamber bleeding and shallow anterior chamber in the immediate post-operative period. We recorded no cases of slit-lamp interventions during follow-up. This may be partly because no restrictive sutures or stents are used with the Preserflo® Microshunt. This contrasts with trabeculectomy literature and our own centre's experience, with most trabeculectomy patients undergoing some form of suture-related intervention (such as suture lysis or release of releasable suture) or early reinterventions to address complications (such as anterior chamber refill due to hypotony).[6,18,20] Quality-of-life and cost-effectiveness studies would be invaluable to determine if this perceived clinical advantage of Preserflo® Microshunt over traditional incisional surgery has an impact on clinical practice and patient outcomes.

Exploratory analysis comparing standalone and combined surgery subgroups was limited by the difference in sample size and follow-up time. However, we did note higher IOP measurements within the first month of surgery in the combined subgroup, which may be of clinical relevance. This effect has also been observed with other phaco-glaucoma surgery combinations such as trabeculectomy[24] or XEN gel stent[25] and may be due to increased anterior chamber inflammation after cataract surgery.[26]

Since the Preserflo® Microshunt is approved for use in primary open-angle glaucoma, most samples published to date have included only POAG and pseudoexfoliative glaucoma (PXG) patients.[13–18] However, its use in other forms of secondary open angle glaucomas has been proposed by experts, as well as in angle-closure cases when combined with cataract surgery or in pseudophakic patients.[27] Our sample included mostly POAG and PXG patients but also other forms of OAG such as uveitic, steroid-induced and some patients with previously diagnosed PCAG, either pseudophakic or undergoing combined surgery. This off-label use was left to the surgeon's discretion, and we believe that inclusion of these patients is in keeping with the real-life data proposal of this study. It is unclear if this had any impact on overall success or safety outcomes due to the small number of patients with these diagnoses.

The Preserflo® Microshunt shares some features with both trabeculectomy and posterior drainage devices since it is an *ab externo* posterior bleb-forming microtubular device, and thus not a MIGS procedure. Therefore, comparing it with trabeculectomy may help adequately position this device in the current glaucoma surgical arsenal. Trabeculectomy is typically found to achieve 2-year IOP in the low-teens and success rates over 70%-80%.[6,28] Our qualified success at 12 months was 64%, and most published series on the Preserflo® also disclose slightly inferior success rates to those in trabeculectomy studies.[13–16] Moreover, a recently published direct comparison of Preserflo® with trabeculectomy showed a lower success rate (53.9% *vs* 72.7%) and higher final IOP (14.3±4.3 *vs* 11.1±4.3 mmHg)[18] at 1-year in the Preserflo® group. This body of evidence suggests that, while the Preserflo® Microshunt is an adequate choice for moderate-to-advanced glaucoma patients, capable of achieving final IOPs in the low-to-mid-teens, trabeculectomy is still the gold standard, success-wise. However, since Preserflo® surgery seems to require fewer post-operative visits, slit-lamp interventions, with a lower rate of hypotony and complications requiring surgical intervention, it may be more advantageous for those patients at a higher risk for complications or less likely to adhere to a more burdensome visitation post-operative period, while still achieving good IOP control and significant reduction of medication burden.[13–18,20]

Our study has some limitations inherent to its retrospective design. Also, the presence of a heterogeneous follow-up time and control group should be noted as limitations. However, we consider the inclusion of diagnosis other than POAG and PXG and of eyes with history of previous glaucoma surgery to strengthen our results in accordance with a real-life data setting.

In conclusion, our study showed that the Preserflo® Microshunt was able to achieve IOP control in the mid-teens and significant reduction of medication burden as far as 12 months in different forms of glaucoma, while showing a favourable safety profile with no major complications recorded in our patient sample. Furthermore, combination with phacoemulsification and history of previous glaucoma surgery did not seem negatively impact success outcomes in the short term. Further studies are warranted to determine long term outcomes of this device, both in trial setting and with real-life data. Moreover, quality-of-life and cost-effectiveness studies should help address the purported advantages of this surgical option regarding post-operative interventions and burden of consultations in clinical practice.

CONTRIBUTORSHIPS TATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

RB, AB and LAP: Study and protocol design
RB, PG and RP: Data collection
RB, PJ and DM: Analysis and interpretation of results
AB and RP: Statistical review and support

RB, LAP: Manuscript preparation and supervision

All authors critical appraisal of the manuscript and approved the final version

RESPONSABILIDADES ÉTICAS

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

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Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pela Comissão de Ética responsável e de acordo com a Declaração de Helsínquia revista em 2013 e da Associação Médica Mundial.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

ETHICAL DISCLOSURES

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Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2013).

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REFERENCES

1. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: A systematic review and meta-analysis. Ophthalmology. 2014;121:2081-90. doi:10.1016/j.ophtha.2014.05.013
2. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. Lancet Glob Heal. 2021;9:e144-e160. doi:10.1016/S2214-109X(20)30489-7
3. Vinod K, Gedde SJ, Feuer WJ, Panarelli JF, Chang TC, Chen PP, et al. Practice Preferences for Glaucoma Surgery. J Glaucoma. 2017;26:687-693. doi:10.1097/IJG.0000000000000720
4. Rathi S, Andrews CA, Greenfield DS, Stein JD. Trends in Glaucoma Surgeries Performed by Glaucoma Subspecialists versus Nonsubspecialists on Medicare Beneficiaries from 2008 through 2016. Ophthalmology. 2021;128:30-8. doi:10.1016/j.ophtha.2020.06.051
5. Gedde SJ, Schiffman JC, Feuer WJ, Herndon LW, Brandt JD, Budenz DL. Treatment Outcomes in the Tube Versus Trabeculectomy (TVT) Study After Five Years of Follow-up. Am J Ophthalmol. 2012;153:789-803.e2. doi:10.1016/j.ajo.2011.10.026
6. Gedde SJ, Feuer WJ, Lim KS, Barton K, Goyal S, Ahmed IK, et al. Treatment Outcomes in the Primary Tube Versus Trabeculectomy Study after 3 Years of Follow-up. Ophthalmology. 2020;127:333-45. doi: 10.1016/j.ophtha.2019.10.002.
7. Chu C, Liebmann JM, Ciof GA, Blumberg DM, Al-aswad LA. Reoperations for Complications Within 90 Days After Glaucoma Surgery. J Glaucoma. 2020;29:344-6. doi:10.1097/IJG.0000000000001484
8. Conlon R, Saheb H, Ahmed IIK. Glaucoma treatment trends: a review. Can J Ophthalmol. 2017;52:114-24. doi:10.1016/j.jcjo.2016.07.013
9. Coleman AL, Richter G. Minimally invasive glaucoma surgery: current status and future prospects. Clin Ophthalmol. 2016:189. doi:10.2147/OPTH.S80490
10. European Glaucoma Society. Terminology and Guidelines for Glaucoma. 5th ed. Amsterdam: Publicomm; 2020.
11. Pinchuk L, Riss I, Batlle JF, Kato YP, Martin JB, Arrieta E, et al. The use of poly(styrene-block-isobutyleneblock- styrene) as a microshunt to treat glaucoma. Regen Biomater. 2016;3:137-42. doi:10.1093/RB/RBW005
12. Batlle JF, Fantes F, Riss I, Pinchuk L, Alburquerque R, Kato YP, et al. Three-year follow-up of a novel aqueous humor microshunt. J Glaucoma. 2016;25:e58-e65. doi:10.1097/IJG.0000000000000368
13. Shaarawy TM, Aptel F, Beckers HJ. 12-month interim results of a multicentre open-label study of the InnFocus MicroShunt® Glaucoma Drainage System in patients with primary open-angle glaucoma. Invest Ophthalmol Vis Sci. 2018;59:3457.
14. Fea AM, Laffi GL, Martini E, Economou MA, Caselgrandi P, Sacchi M, et al. Effectiveness of MicroShunt in Patients with Primary Open-Angle and Pseudoexfoliative Glaucoma: A Retrospective European Multicenter Study. Ophthalmol Glaucoma. 2022;5:210-8. doi: 10.1016/j.ogla.2021.08.005.
15. Schlenker MB, Durr GM, Michaelov E, Ahmed IK. Intermediate Outcomes of a Novel Standalone Ab Externo SIBS Microshunt With Mitomycin C. Am J Ophthalmol. 2020;215:141-53. doi:10.1016/j.ajo.2020.02.020
16. Beckers HJ, Aptel F, Webers CA, Bluwol E, Martínez-de-la-Casa JM, García-Feijoó J, et al. Safety and Effectiveness of the PRESERFLO® MicroShunt in Primary Open-Angle Glaucoma: Results from a 2-Year Multicenter Study. Ophthalmol Glaucoma. 2022;5:195-209. doi: 10.1016/j.ogla.2021.07.008.
17. Martínez-de-la-Casa JM, Saenz-Francés F, Morales-Fernandez L, et al. Clinical outcomes of combined Preserflo Microshunt implantation and cataract surgery in open-angle glaucoma patients. Sci Rep. 2021;11:1-8. doi:10.1038/s41598-021-95217-x
18. Baker ND, Barnebey HS, Moster MR, Stiles MC, Vold SD, Khatana AK, et al. Ab-Externo MicroShunt versus Trabeculectomy in Primary Open-Angle Glaucoma: One-Year Results from a 2-Year Randomized, Multicenter Study. Ophthalmology. 2021;128:1710-21. doi: 10.1016/j.ophtha.2021.05.023.
19. Shaarawy TM, Sherwood MB, Grehn F, editors. Guidelines on Design and Reporting of Surgical Trials - World Glaucoma Association. Philadelphia: Kugler Publications; 209.
20. Pillunat KR, Herber R, Haase MA, Jamke M, Jasper CS, Pillunat LE. PRESERFLO™ MicroShunt versus trabeculec-

tomy: first results on efficacy and safety. Acta Ophthalmol. 2022;100:e779-e790. doi: 10.1111/aos.14968.
21. Gizzi C, Costa G, Servadei R, Abed E, Ning B, Sharma A, et al. A case of malignant glaucoma following insertion of Preserflo™ MicroShunt. Eur J Ophthalmol. 2022;32:NP115-9. doi: 10.1177/11206721211003492.
22. Micheletti E, Riva I, Bruttini C, Quaranta L. A Case of Delayed-onset Hemorrhagic Choroidal Detachment after PreserFlo Microshunt Implantation in a Glaucoma Patient under Anticoagulant Therapy. J Glaucoma. 2020;29:E87-E90. doi:10.1097/IJG.0000000000001584
23. Agrawal P, Bradshaw SE. Systematic Literature Review of Clinical and Economic Outcomes of Micro-Invasive Glaucoma Surgery (MIGS) in Primary Open-Angle Glaucoma. Ophthalmol Ther. 2018;7:49-73. doi:10.1007/s40123-018-0131-0
24. Derick RJ, Evans J, Baker ND. Combined phacoemulsification and trabeculectomy versus trabeculectomy alone: a comparison study using mitomycin-C. Ophthalmic Surg Lasers. 1998;29:707-13.
25. Marcos Parra MT, Salinas López JA, López Grau NS, Ceausescu AM, Pérez Santonja JJ. XEN implant device versus trabeculectomy, either alone or in combination with phacoemulsification, in open-angle glaucoma patients. Graefe's Arch Clin Exp Ophthalmol. 2019;257:1741-50. doi: 10.1007/s00417-019-04341-y.
26. Siriwardena D, Kotecha A, Minassian D, Dart JK, Khaw PT. Anterior chamber flare after trabeculectomy and after phacoemulsification. Br J Ophthalmol. 2000;84:1056-7. doi:10.1136/bjo.84.9.1056
27. Kerr NM, Ahmed IIK, Pinchuk L, Sadruddin O, Palmberg PF. PRESERFLO MicroShunt. In: Minimally Invasive Glaucoma Surgery. Berlin: Springer; 2021. p.91-103.
28. Kirwan JF, Lockwood AJ, Shah P, et al. Trabeculectomy in the 21st century: A multicenter analysis. Ophthalmology. 2013;120:2532-9. doi:10.1016/j.ophtha.2013.07.049

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