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# 3-year safety and efficacy results of PreserFlo™ Microshunt in glaucoma patients: A multicentre European cohort study

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ABSTRACT

*Purpose:* To report three-year outcomes of a multicenter cohort undergoing Preserflo Microshunt surgery (PFMS).
*Design:* Retrospective cohort study
*Methods:* Retrospective review of 100 consecutive eyes (91 patients) undergoing PFMS from four tertiary-referral glaucoma centers. Primary outcome were success rates. Secondary outcomes included: intraocular pressure (IOP), best-corrected visual acuity, medication, complications and postoperative interventions.
*Results:* 100 eyes of 91 patients were included. Qualified and complete success rates (95 % CI) were 80 % (72–87 %) and 56 % (47–65 %) for Criterion A (IOP≤21 mmHg), 75 % (67–83 %) and 55 % (46–65 %) for Criterion B (IOP≤18 mmHg), 44 % (31–50 %) and 39 % (30–49 %) for Criterion C (IOP≤15 mmHg) and 10 % (5–16 %) and 10 % (5–16 %) for Criterion D (IOP≤12 mmHg) respectively. Mean IOP decreased from 23.8 mmHg to 14.1 mmHg (reduction of 35.3 %) after 36 months with a reduction of IOP-lowering agents from 2.52 (0 – 4) to 0.69 (0 – 3). 7 eyes (7 %) needed additional glaucoma surgery. Of these, 3 eyes underwent a glaucoma drainage device and 4 eyes had a trabeculectomy.36 eyes received additional procedures after PFMS implantation. Of these, 14 eyes (14 %) underwent a surgical revision and 12 eyes (12 %) a bleb needling procedure.
The complication rate was low: 1 eye developed corneal decompensation and underwent a DMEK after 24 months. 1 eye had a conjunctival erosion requiring a revision surgery. 2 eyes developed a postoperative uveitis that was treated with topical steroids and resolved without further damage. There were no hypotony-related complications.
*Conclusions:* PFMS surgery is a safe and effective procedure for reducing IOP and pressure-lowering therapy.

## Introduction

Glaucoma is a leading cause of irreversible blindness worldwide[1]. It can initially be treated with pressure-lowering eye drops or laser treatment[2]. Minimally-invasive glaucoma surgeries (MIGS) were developed as an alternative interventional strategy for early glaucoma patients and have contributed to a more proactive approach towards performing glaucoma surgery at earlier stages[3]. The PreserFlo®-MicroShunt (PFMS) (Santen, Miami, USA) is a device that belongs to the group of less-invasive glaucoma surgeries (LIGS). LIGS are more invasive than MIGS but still less invasive than conventional trabeculectomy surgery. The PFMS, which measures 8.5 mm in length and has an internal diameter of 70 μm, is inserted via a scleral incision into the anterior chamber. It drains aqueous humor into the subconjunctival space, thus producing a filtering bleb. The PFMS has become popular for the treatment of progressing glaucoma patients, in particular those who do not need a very low target IOP. Moreover, this surgery is considered to pose less risk of postoperative hypotony compared to a traditional trabeculectomy, with the additional benefit of requiring less intensive follow-up and manipulations. The procedure's steep learning curve

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makes it easily approachable for many surgeons. A recent report of UK glaucoma surgeons showed an increased use of PFMS during the COVID-19 pandemic in order to reduce postop visits for these patients[4].

Studies on the long-term outcome of PFMS are scarce. It is necessary to have long-term data for surgical procedures in order to evaluate its efficacy since glaucoma is a chronic, lifelong disease. Two and three-year results have shown that PFMS is generally considered safe and effective in terms of lowering intraocular pressure (IOP) to the middle to low teens and maintaining this reduction in the longer term[5–8]. However, there are various potential reasons for postoperative failure, including tube obstruction and bleb scarring which may lead to the necessity of additional interventions, such as needling or revision.

The aim of this multicenter study was to determine the effectiveness and safety of PFMS surgery during a 36-months follow-up period for a real-world patient cohort.

## Materials and methods

### *Patients*

All medical records of patients who underwent PFMS surgery with MMC augmentation at four different glaucoma centers across Europe (Düsseldorf, Madrid, Pisa, Manchester) between 2015 and 2019 were reviewed. These were the same patients from our previous publication describing the one-year outcomes of this group of patients[9]. PFMS surgery was performed by four experienced glaucoma surgeons. Each center provided data for the very first 25 consecutive cases performed. There were no other specific inclusion/exclusion criteria as this was conceived as a pragmatic, real-world study. All glaucoma subtypes were included in this study, including POAG, pigmentary glaucoma, pseudoexfoliation glaucoma, and other secondary glaucoma subtypes (Table 1). We did not impose any strict inclusion/exclusion criteria to mimic how the device is used in clinical practice by glaucoma surgeons and ensure high generalizability of our results. Patients were included in the database at time of surgery and follow-up data was retrospectively collected at each postoperative visit. All patients had undergone a documented comprehensive ophthalmic examination upon presentation, including assessment of best-corrected visual acuity (BCVA) using Snellen chart (converted to logMAR for statistical evaluation), IOP measurement via Goldmann applanation tonometry, slit lamp biomicroscopy and fundus biomicroscopy. For every consecutive patient undergoing PFMS implantation, the collected pre-operative variables included sex, age, glaucoma type, BCVA, preoperative clinical features (including IOP) and detailed follow-up information consisted of BCVA, IOP, visual fields, complications and postoperative glaucoma medications as well as postoperative interventions and factors associated with failure.

### *Success criteria*

Four different success criteria were used according to IOP thresholds: 1) Criterion-A: IOP $\leq$ 21 mmHg; 2) Criterion-B: IOP $\leq$ 18 mmHg; 3) Criterion C: IOP $\leq$ 15 mmHg; 4) Criterion-D: IOP $\leq$ 12 mmHg. Success was defined as complete if reached without glaucoma medication and as qualified if reached with or without glaucoma medication. In order to compare our primary outcomes to our previously published one-year results[9] in the same patient cohort we also performed the equivalent analysis used, including IOP decrease in percentage ( %) within the success criteria (for A and B $\geq$ 20 %, for C: $\geq$25 %; for D $\geq$ 30 % from baseline). Failure was considered when the above-mentioned criteria were not fulfilled at any postoperative visit after three months or if one of the following occurred: loss of light perception, hypotony-related complications, inadequate IOP control requiring acetazolamide, surgical revision or further glaucoma surgery.

Primary outcome included success rates based on the criteria above. Secondary outcomes were mean IOP, BCVA, number of IOP-lowering drops and complications. All analyses were conducted on a de-identified data set. The study protocol conformed to the ethical guidelines of the 2000 Declaration of Helsinki as reflected in a priori approval by the institution's Human Research Committee.

**Table 1**
Demographics and clinical characteristics of patients undergoing PFMS surgery.

| | ***n* = 100 eyes, 100 pat. ( %)** |
|---|---|
| **Gender** | |
| Male / female | 53 / 39 |
| **Ethnicity** | |
| European descent | 86 (95 %) |
| African descent | 3 (3 %) |
| Asian descent | 2 (2 %) |
| **Age** | |
| Mean, Standard deviation | 67.9 / 12.1 |
| **Baseline BCVA** | |
| Median (IQR) | 0.11 (0 – 0.29) |
| **Baseline IOP** | |
| Median (IQR) | 22 (19 - 28) |
| **Number of glaucoma drops** | |
| Median (IQR) | 3 (2 – 3) |
| **Acetazolamide**, no eyes ( %) | 20 (20 %) |
| **Glaucoma subtype** | |
| Primary open-angle glaucoma | 70 (70 %) |
| Pigmentary glaucoma | 13 (13 %) |
| Normal tension glaucoma | 5 (5 %) |
| PACG | 3 (2 %) |
| Uveitic glaucoma | 2 (2 %) |
| **Lens status, no eyes ( %)** | |
| Phakic | 69 (69 %) |
| Pseudophakic | 31 (31 %) |
| **Previous LTP, no eyes ( %)** | 15 (15 %) |
| **Previous VR surgery, no eyes ( %)** | 15 (15 %) |
| **Previous Glaucoma surgery (+CEIOL), no eyes ( %)** | 5 ( %) |
| **Which surgery** | |
| Trabeculectomy | 4 (4 %) |
| Cypass | 3 (3 %) |
| XEN | 2 (2 %) |
| Viscocanalostomy | 2 (2 %) |
| Transscleral CPC | 3 (3 %) |
| Canaloplasty | 1 (1 %) |
| Istent inject | 1 (1 %) |

BCVA: best-corrected visual acuity, CEIOL: cataract extraction and intraocular lens implantation, IQR: interquartile range, IOP: intraocular pressure, LTP: laser trabeculoplasty, NTG: normal-tension glaucoma, PACG: primary angle-closure glaucoma, POAG: primary open-angle glaucoma, SD: standard deviation, VR: vitreoretinal.

### *Statistical analysis*

Statistical analysis was performed with SPSS Statistics version 27.0.0 (IBM Corporation, New York). The Kolmogorov-Smirnov test was used to verify normal distribution. Paired *t*-test ANOVA (with Bonferroni correction) was used to test differences between each pair of time points. Only 9 eyes out of 100 patients had both eyes included, that is why we chose to purposely ignore within-subject correlations. Time-dependent survival probabilities were estimated with the Kaplan-Meier method. Survival times were calculated and reported along with their 95 % confidence intervals (CIs). We considered P values $<$0.05 to be statistically significant. A Cox regression analysis was used to identify preoperative factors associated with failure. The following baseline covariates were tested: age, gender, ethnicity, glaucoma sub-type, lens status, BCVA, IOP, number of topical medications, use of acetazolamide, previous laser trabeculoplasty and previous conjunctival surgery.

## Results

100 eyes of 91 consecutive patients who underwent PFMS surgery were included in this study. The majority of patients were of European

descent (86 pat., 95 %). Detailed patient characteristics are shown in Table 1. The number of patients who completed the follow-up-time of 2 and 3 years was 96 and 88 respectively.

Primary outcomes after three-years ($n$ = 88) were related to the above-mentioned success criteria: for Criterion A, qualified and complete success rates (95 % CI) were 88 % (70–95 %) and 62 % (52–75 %) at 24 months and 80 % (72–87 %) and 56 % (47–65 %) at 36 months, respectively. For Criterion B, these were 82 % (75–88 %) and 60 % (51–70 %) at 24 months and 75 % (67–83 %) and 55 % (46–65 %) at 36 months, for Criterion C 51 % (36–56 %) and 46 % (35–54 %) at 24 months and 44 % (31–50 %) and 39 % (30–49 %) at 36 months, for Criterion D 12 % (9–20 %) and 12 % (9–20 %) at 24 months and 10 % (5–16 %) and 10 % (5–16 %) at 36 months, respectively (Fig. 1).

Taking into consideration success rates including percentages (for A and B ≥ 20 %, for C: ≥25 %; for D ≥ 30 % IOP reduction from baseline), qualified and complete success rates (95 % CI) for criterion A were 68 % (59–77 %) and 49 % (49–59 %) at 36 months respectively. For Criterion B, these were 64 % (54–73 %) and 49 % (39–59 %), for Criterion C 39 % (29–49 %) and 35 % (26–45 %) and for Criterion D 9 % (4–15 %) and 9 % (4–15 %) respectively.

7 eyes (7.95 %) failed because they needed additional glaucoma surgery. Of these, 3 eyes underwent a glaucoma drainage device (tube) and 4 eyes had a trabeculectomy. 3 eyes (3.4 %) failed because of inadequate IOP control requiring acetazolamide.

Of the 10 % of eyes that showed a complete success after 3 years for Criterion D, only one patient had previous glaucoma surgery (phacoemulsification and viscocanalostomy) and no other previous eye surgeries. None had any risk factors, such as ethnicity. All were primary-open angle glaucoma patients, two had pigmentary glaucoma.

Of the 39 % of eyes with complete success after 3 years for Criterion C, only 3 eyes had previous glaucoma surgeries (phacoemulsification and viscocanalostomy, trabeculectomy and Cypass). None had any risk factors except of one eye with diabetes. All of these were eyes with POAG with the exception of four eyes with pseudoexfoliation glaucoma and two eyes with pigmentary glaucoma. However, there were no statistically significant differences between eyes that had complete success for criterion C and D regarding age, glaucoma type and previous surgeries.

The mean preoperative IOP (range; median; interquartile range) was 23.8 mmHg (11 – 54 mmHg, 21.50 mmHg, 18.25 – 28 mmHg). The mean number of pressure lowering-agents before surgery was 2.52 agents (0 – 4; 3; 0 - 4).

IOP and medication number at any time point after surgery was significantly lower than preoperatively ($p < 0.001$) (Fig. 2).

Mean IOP decreased to 13.5 mmHg (8 – 24 mmHg; 13 mmHg; 11 – 16 mmHg) after 12 months with a mean reduction of 39.1 % (0–77.7 %; 39.6 %; 23.5 – 54.5 %), 14.0 mmHg (7 – 24 mmHg; 14 mmHg; 12 – 16 mmHg) with a mean reduction of 36.2 % (0–79.6 %; 36.3 %; 22.5 – 53.7

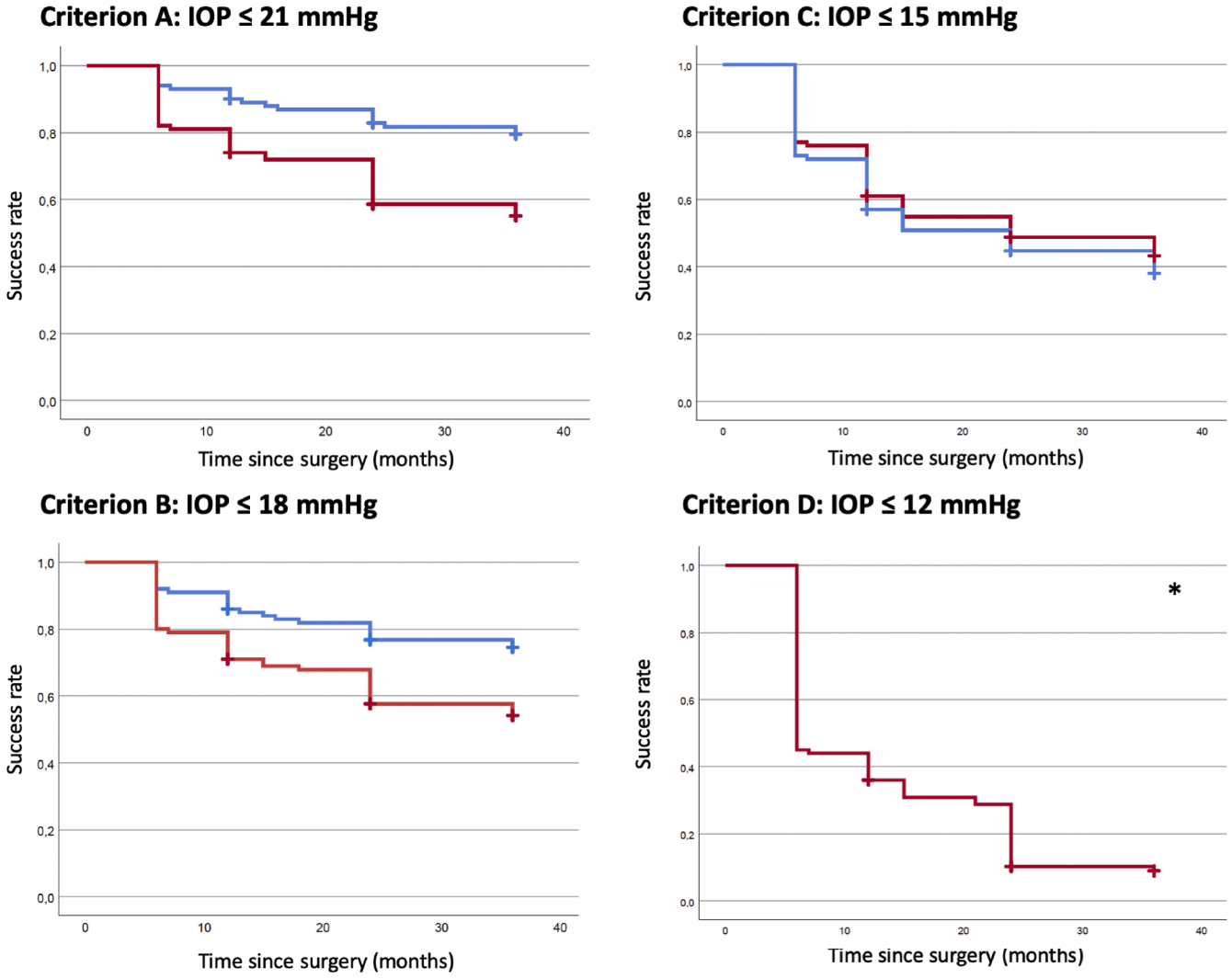


**Fig. 1.** Kaplan Meier curves: qualified (blue) and complete (red) success rates (95 % CI) 3 years after surgery. For Criterion D, qualified and complete success rates were identical (*).

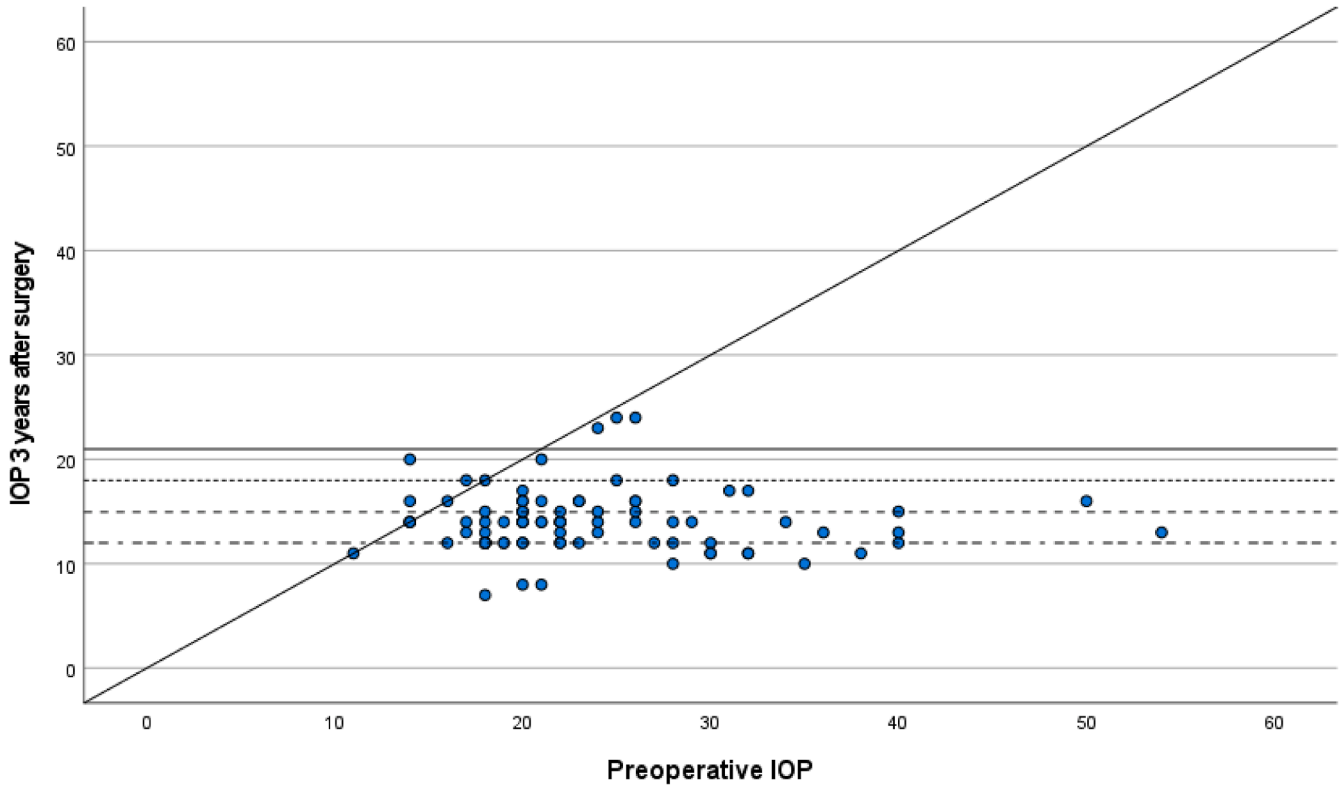


**Fig. 2.** Scatterplot of preoperative *versus* postoperative IOP values at 3 years after surgery. Dots represent eyes, horizontal lines indicate IOP used as threshold for success criteria.

%) after 24 months and 14.1 mmHg (7 - 25 mmHg; 14.0 mmHg; 12 – 16 mmHg) with a mean reduction of 35.3 % (0 –75.9 %; 35.7 %; 24.4 – 50.9 %) after 36 months (Fig. 3).

The mean number of pressure-lowering agents was significantly lower with 0.29 (0 – 3; 0; 0–0) agents after 12 months, with 0.64 (0–3; 0; 0–1) agents after 24 months and 0.69 (0 – 3; 0; 0–1) agents after 36 months (Fig. 4).

53 eyes did not have any pressure-lowering eye drops.

Mean (range) BCVA preoperatively was 0.23 logMAR (−0.28 – 2.7 logMAR; 0.11 logMAR; 0 – 0.29 logMAR) and 0.26 logMAR (−0.1 – 2.7 logMAR; 0.12 logMAR; 0.02–0.30 logMAR) after 12 months and decreased to 0.24 logMAR (0 – 2.3 logMAR; 0.20 logMAR; 0.02 – 0.27 logMAR) after 24 months and to 0.28 logMAR (−0.20 – 2.7 logMAR;

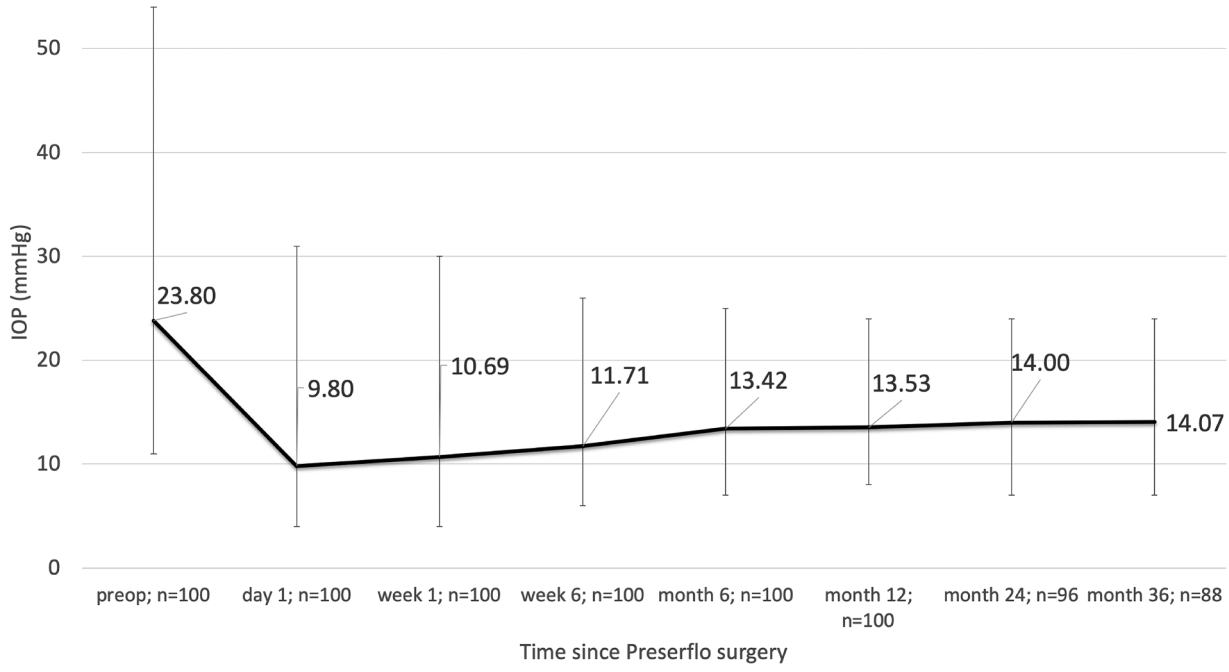


**Fig. 3.** IOP development: Mean IOP decreased from 23.8 mmHg (11 – 54 mmHg) to 14.1 mmHg (7 - 25 mmHg) (reduction of 37.3 %) after 36 months.

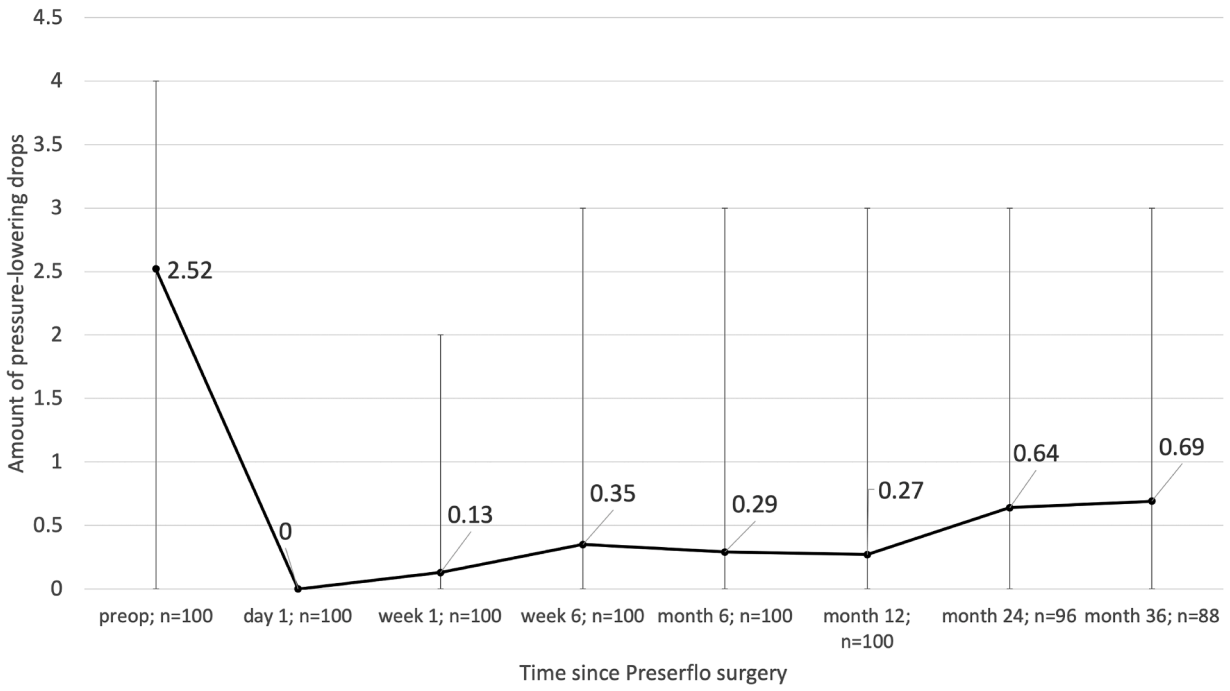


**Fig. 4.** Mean amount of pressure-lowering eye drops decreased from 2.52 (0 – 4) to 0.69 (0 – 3) after 36 months.

0.18 logMAR; 0.10 – 0.30 logMAR) after 36 months.

Postoperative complications are shown in Table 2. One patient developed corneal decompensation and underwent Descemet membrane endothelial keratoplasty (DMEK) at 24 months. One other patient had a conjunctival erosion over the implant with device exposure four weeks post-operatively requiring a revision surgery. Two patients developed a postoperative uveitis that was treated with topical steroids and resolved without further damage. There were no hypotony-related complications.

36 eyes received additional procedures after PFMS implantation. Of these, 14 eyes (15.9 %) underwent a surgical revision after a mean time interval of 16.4 months (7 – 24 months) for encapsulation, 1 eye (1.1 %) had a surgical revision for exposure and 12 eyes (13.6 %) a bleb needling procedure. Table 3 lists all postoperative procedures related to PFMS. Further procedures performed after PFMS implantation were intravitreal therapy for neovascular AMD (3 eyes, 3.4 %) and a central retinal vein occlusion (1 eye, 1.1 %) that occurred after the PFMS implantation. Five eyes (5.7 %) underwent cataract surgery by phacoemulsification.

We performed a Cox regression analysis to evaluate whether there were any preoperative factors associated with failure, but none of the factor was significantly associated with the risk of failure (age: $p = 0.38$; gender: $p = 0.18$; ethnicity: $p = 0.21$, glaucoma subtype: $p = 0.51$, preoperative drops: $p = 0.16$, preoperative acetazolamide: $p = 0.19$, previous glaucoma surgery: $p = 0.80$, lens status: $p = 0.52$, s/p vitrectomy: 0.52, preoperative IOP: 0.93, preoperative visual acuity: $p = 0.07$)

**Table 2**
Complications of PFMS surgery.

| Time Point | Complications | Eyes ( %) |
|---|---|---|
| Early (≤1 month) | Device exposure with surgical revision | 1 (1 %) |
| Late (> 1 month) | Anterior uveitis | 2 (2 %) |
| | Peripheral corneal edema | 1 (1 %) |
| | Iris incarceration | 1 (1 %) |
| | Device removal | 1 (1 %) |
| | Corneal decompensation with DMEK (descemet membrane endothelial keratoplasty) | 1 (1 %) |
| | Iris plugging PFMS → glaucoma drainage device | 1 (1 %) |

**Table 3**
Other procedures after PFMS surgery.

| Procedures | Eyes ( %) |
|---|---|
| Needling | 12 (12 %) |
| 5-FU deposit | 5 (5 %) |
| Surgical revision for encapsulation | 14 (14 %) |
| Surgical revision for exposure | 1 (1 %) |
| Device removal | 1 (1 %) |
| Flushing | 3 (3 %) |

## Discussion

PFMS is generally considered a safe and effective surgery, but studies on its long-term outcomes are scarce. Table 4 gives an overview of studies with follow-up periods of 24 and 36 months. Batlle et al. were the first to report medium-term outcomes of PFMS, presenting 3-year outcomes for 23 eyes in their study from 2016[6]. Armstrong et al. included 152 eyes from 135 patients in their study with three-year outcomes[8]. Triolo et al. reported the 36-month efficacy of PFMS in a subset of 21 eyes with refractory uveitic glaucoma[7]. Beckers et al. reported two-year outcomes of 81 patients[10], whereas Fea et al. described the outcomes of 104 patients with POAG and pseudoexfoliation glaucoma, but only at 12 months[11]. We report on a relatively large patient cohort, with a low attrition rate, with respect to the 3-year efficacy and safety of the PFMS in a multicenter retrospective study. We intentionally adopted inclusive and comprehensive study criteria to obtain pragmatic, real-world data that have high generalizability. In comparison to other studies with three-year data, our study contains outcomes of patients with mainly European descent (95 %).

Our 3-year qualified and complete PFMS success rates were 80 % (72–87 %) and 56 % (47–65 %) for Criterion A (IOP ≤ 21 mmHg), respectively ($n = 88$). Comparing IOP values and success rates across different glaucoma studies can be challenging since criteria vary among different studies. We chose success criteria that only included specific IOP thresholds, but also conducted analysis considering percentage IOP reductions (for A and $B \geq 20$ %, for C: ≥25 %; for $D \geq 30$ % from baseline). When factoring in percentage IOP reductions, qualified and complete success rates were lower with 68 % (59–77 %) and 49 %

**Table 4**
Comparison of PFMS studies with 2- or 3-year FUP data.

| Study | Number of patients included | Mean IOP | Mean IOP reduction | Glaucoma medication | Postoperative Interventions | Follow up time |
|---|---|---|---|---|---|---|
| **Armstrong et al.** | 152 eyes from 135 patients | From 20 mmHg to 36 mo: 12.4 mmHg | n/a | from 4 to 36 mo: 0 | Needling: 15 %<br>Second needling: 1 %<br>MMC injection: 6 %<br>OVD injection: 6 %<br>Revision: 7 %<br>Revision with device exchange: 6 %<br>Glaucoma drainage device: 3 % | 36 months |
| **Batlle et al.** | 23 eyes from 23 patients | From 23.8 mmHg to<br>12 mo: 10.7 mmHg<br>24 mo: 11.9 mmHg<br>36 mo: 10.7 mmHg | 12 mo: 55 %<br>24 mo: 50 %<br>36 mo: 50 % | from 2.4 to<br>12 mo: 0.3<br>24 mo: 0.4<br>36 mo: 0.7 | IOL capture and IOL reposition: 1 patient<br>Needling: 1 patient | 36 months |
| **Triolo et al.** | 21 eyes of 21 patients: uveitic glaucoma | From 26 mmHg to<br>36 mo: 15.2 mmHg | 12 mo: 26.5 %<br>24 mo: 33.5 %<br>36 mo: 30.1 % | from 4.1 to<br>36 mo: 0.9 | cystoid macular edema and intravitreal ozurdex :2 patients<br>Surgical revision: 57.1 %<br>additional glaucoma surgery: 14.3 % | 36 months |
| **Beckers et al.** | 81 eyes of 81 patients | From 21.7 mmHg to<br>12 mo: 14.5 mmHg<br>24 mo: 14.1 mmHg | 12 mo: 31.4 %<br>24 mo: 34.1 % | From 2.0 to<br>24 mo: 0.5 | Surgical revision: 8 patients<br>- Of which 2 patients with new glaucoma surgical implant<br>Additional glaucoma surgery: 3 patients<br>flap resuture: 1 patient | 24 months |
| **Scheres et al.** | 41 eyes of 33 patients | from 20.1 mmHg to<br>12 mo: 12.1 mmHg<br>24 mo: 12.1 mmHg | 12 mo: 40 %<br>24 mo: 39 % | from 2.5 to<br>12 mo: 0.6<br>24 mo: 0.7 | Bleb revision: 5 %<br>Bleb needling: 5 %<br>Additional glaucoma filtration surgery: 15 %<br>Trabecular micro-bypass stent: 2 %<br>CPC: 2 % | 24 months |
| **Our data** | 100 eyes of 91 consecutive patients | From 23.8 mmHg (Mean) to<br>12 m0: 13.5 mmHg<br>24 mo: 14.0 mmHg<br>36 mo: 14.1 mmHg | 12 mo: 39.1 %<br>24 mo: 36.2 %<br>36 mo: 35.3 % | From 2.52 to<br>12 mo: 0.27<br>24 mo: 0.64<br>36 mo: 0.69 | Needling: 12 %<br>5-FU deposit: 5 %<br>Surgical revision: 15 %<br>Device removal: 1 %<br>Flushing: 3 %<br>Additional glaucoma surgery: 7 % | 36 months |

(49–59 %) at 36 months. This discrepancy shows the difficulty in comparing success rates between different studies[12]. Armstrong et al. used three criteria for the definition of qualified and complete success: no 2 consecutive IOP > 17 mmHg (or < 6 mmHg with < 2 lines of vision loss from baseline), ≥ 20 % reduction from baseline IOP and use of glaucoma medication or using no glaucoma medications respectively[8]. Complete and qualified success was achieved in 55.6 % and 74.8 % in their study. Further, they reported on success rates using IOP cutoffs of ≥ 6 mmHg and ≤ 14, 17 and 21 mmHg without the requirement for a 20 % reduction from baseline IOP with a qualified and complete success of 77.6 % and 62.5 %, 81.6 % and 71.7 %, 84.2 % and 73 % respectively. Similar to our study, they also included success criteria without requiring a percentage IOP reduction. Scheres et al. defined success as an IOP < 18 mmHg in 2 consecutive visits after 3 months of follow-up time and reported a qualified and complete success of 79 % and 49 %, respectively after two years[5]. Fea et al. used a similar definition of success, with IOP< 18 mmHg and a reduction of more than 20 %, and reported qualified and complete success rates of 58.7 % and 26 %, respectively, at 12 months. Our results for IOP < 18 mmHg (Criterion B) were comparable to those of Scherre et al. and higher than those of Fea et al., with success rates of 75 % (67–83 %) and 55 % (46–65 %) at three years. Batlle et al. defined success as maintaining an IOP < 14 mmHg with a reduction > 20 % and reported on a qualified success rate of 95 % at three years from their single center study of 23 eyes. Durr et al. defined failure as IOP ⟨ 6 mmHg with vision loss, IOP ⟩ 17 mmHg, or <20 % reduction from IOP despite medications. They reported on a success rate of 79.7 % at 2 months[13]. These examples underscore the challenges involved in comparing success rates among the various PFMS studies.

We have previously reported the one-year results of our patient cohort. In this study, we extended the follow- up to three years for 88 of the original 100 patients. When comparing the 3-year *versus* 1-year results for Criterion A, success rates were 74 % (66–83 %) and 58 % (49–69 %) after 1 year in comparison to 68 % (59–77 %) and 49 % (49–59 %) after three years[14]. This indicates that only a small number of patients experienced a failure event for this success criterion during the two years following. This can be explained by the fact that most revisions were necessary during the first year. Once the PFMS establishes proper functionality, it appears to maintain a long-term IOP-lowering effect.

The baseline IOP of our patient cohort is comparable to many other PFMS studies: Armstrong et al. had a baseline IOP of 20 mmHg[8], Fea et al. of 25.1 mmHg[11], Triolo et al. of 26 mmHg[7], Batlle et al. of 23.8 mmHg[6]. The mean IOP in our study dropped from 23.8 mmHg preoperatively to 13.5 mmHg at 12 months, with a mean reduction of 39.1 % (0–77.7 %). This reduction remained consistent at the two- and three-year marks (14.0 mmHg (7 – 24 mmHg; mean reduction of 36.2 % (0–79.6 %)) and 14.1 mmHg (7 - 25 mmHg; mean reduction of 35.3 % (0 −75.9 %)) respectively. These values show that the IOP-lowering effect was obtained after three years with very similar values after 12, 24 and 36 months.

The IOP in our study was significantly reduced at 13.5 mmHg (8 – 24 mmHg; reduction of 39.1 %) after 12 months. This reduction aligns with other 12-month studies: Fea et al. reported an IOP of 14.1 + 3.4 mmHg[11], Durr et al. of 13 mmHg[13] and Fili et al. of 11.62 + 1.6 mmHg for combined PFMS with cataract surgery and 13.8 + 3.6 mmHg for standalone PFMS surgery[15]. Importantly, this IOP reduction was maintained at 24 months, in line with other studies with 2-year data (Our study: 14.0 mmHg, Beckers et al. 14.1 mmHg[10], Scheres et al. 12.1 mmHg[5]. The only two publications with three-year data on POAG (Armstrong et al. and Batlle et al.) reported significantly reduced IOP (12.4 mmHg and 10.7 mmHg respectively) at this time point. However, both these involved single-center data. Furthermore, the study from Batlle et al. was a specifically selected cohort which included combined procedures with phacoemulsification, had a small sample size and a high attrition rate[6]. Another PFMS study reporting 3-year outcomes was that by Triolo et al. with a mean IOP of 15.2 mmHg + 5.4 mmHg after three

years. Nonetheless, this study exclusively included uvetic patients, making the results inapplicable to the more common forms of glaucoma, such as primary open angle, pseudoexfoliative, and pigment dispersion glaucoma[7].

The mean number of pressure-lowering agents decreased from 2.52 (1 - 4) to 0.69 (0 – 3) agents after 36 months. These results are in line with the results reported by Armstrong et al. (from median 4 to median 0 after 36 months) and Battle et al. (2.4 ± 0.9 to 0.7 ± 1.1 after 36 months)[6]. The BCVA in our cohort slightly decreased from 0.23 logMAR (−0.28 – 2.7 logMAR) to 0.28 logMAR (−0.20 – 2.7 logMAR) after 36 months. This decrease was due to one patient developing retinal vein occlusion in the study eye. There were no other cases of visual deterioration after PFMS surgery.

As shown before, PFMS effectively lowers IOP and decreases the number pressure-lowering agents. Jamke et al. and Pillunat et al. compared the PFMS to trabeculectomy and showed that both procedures were equally effective and safe in lowering IOP during a follow-up period of six months and one year in patients with POAG. The rate of additionally interventions was statistically higher in the trabeculectomy group[16,17]. A comparison by Scheres et al. showed that PFMS lead to similar results in POAG as XEN stent implantation with a decrease of IOP to 12.1 mmHg (PFMS) and 13.8 mmHg (XEN) after 24 months[5].

There were very few major complications in our study. One patient from the original one-year cohort publication underwent surgical revision within the first month due to device exposure, but no similar cases occurred afterwards. Bunod et al. reported two cases of PFMS exposure and named the absence of a Tenon's flap and pre-existing ocular surface inflammation as risk factors[18,19]. Similar to our findings, stent exposure seems to occur within the first year in both these case reports. Another patient in our study developed persistent corneal decompensation needing a DMEK after 24 months. This was a patient who was known to have low endothelial cell counts and mild corneal decompensation pre-PFMS implantation as a result of previous cataract surgery. Other complications, such as anterior uveitis, were self-limiting. The safety profile of PFMS surgery is consistent with studies. Armstrong et al. described that 44 eyes (28.9 %) developed postoperative complications, of these none were significant complications. Beckers et al. reported only non-serious adverse advents (IOP requiring medication or SLT, mild-to moderate keratitis)[10]; Scheres et al. encountered mild, self-limiting complications, including hyphema in 8 % of patients, choroidal detachment in 2 %, and ptosis in 2 %[5]. Fea et al. reported hyphema and choroidal detachment in 7.7 % and 4.8 of patients, respectively[11]. Other studies reported no major complications, confirming that PFMS surgery is a safe procedure[13,15,16].

However, it is important to note that a follow-up period of 36 months might not be long enough to observe some long-term complications, such as corneal decompensation, endothelial cell loss, late leakage and bleb-related infections. Extended studies are required to assess PFMS safety beyond three years and identify potential long-term complications.

An important advantage of a PFMS is the less intensive follow-up compared to trabeculectomy surgery. In addition to shared concerns regarding post-operative bleb fibrosis, scarring and failure, and hypotony to a lesser degree, PFMS-specific issues include stent obstruction, erosion or dislocation. In our cohort, 5 eyes (5 %) received at least one post-operative 5-FU subconjunctival injection, 12 eyes (12 %) underwent bleb needling with antimetabolite, 15 eyes (15 %) surgical revision (14 eyes for encapsulation, 1 eye for exposure) and 3 eyes (3 %) stent flushing within the first three years after surgery. All needlings were performed within the first year after surgery. Surgical revisions in our one-year results were performed in only five patients (5 %)[9] whereas an additional 10 eyes underwent revision in the subsequent two years. Three eyes received the surgical revision following a needling, and 3 eyes had a needling after an initial 5-FU injection. This shows that revisions for bleb encapsulation can become necessary over time, and patients should therefore be informed in advance of this possibility. Importantly however, after needling or bleb revision, the IOP was successfully lowered without additional procedures in most patients. Only one patient who underwent bleb revision at month 24 received a trabeculectomy at month 36 with only one other undergoing a glaucoma drainage device (tube) at 18 months following a needling procedure done 6 months after initial PFMS surgery. Other studies report similar needling and revision rates. Armstrong et al. reported on a needling rate of 15.1 %, revisions occurred in 7 %[8]. Triolo et al. reported that 57.1 % of patients needing additional interventions[7]. Fea et al. showed in 18 % needling rates in their 12 month-data with 13.5 % of eyes requiring a surgical revision. Beckers et al. reported 6.2 % needling rates after 2 years,[10]. Overall, these studies confirm that the IOP-lowering effect is usually maintained after an additional 'revisional' procedure.

Only a minority of patients (7 eyes, 7 %) needed a further different glaucoma surgery within the first three years following PFMS implantation in our cohort. Of these, 3 eyes underwent glaucoma drainage device (tube) implantation, and 4 eyes underwent trabeculectomy. Armstrong et al. reported on a reoperation rate of 2.6 % (3 eyes: Baerveldt Glaucoma implant, 1 eye: Ahmed glaucoma implant)[8]. Batlle et al. small, single-centre case series reported 2 patients (8.7 %) needing additional glaucoma surgeries at 3 years: one eye received a second PFMS, while another underwent replacement of PFMS with XEN 45 gel stent (Allergan, Dublin, Ireland)[6]. Triolo et al. reported 4 eyes (19 %) needing a glaucoma drainage device implantation in their uveitic patient cohort by the end of the third post-operative year. Studies with less follow-up time also confirm that a minority (3 % to 15 %) may well need additional glaucoma surgery after PFMS implantation even within the first two years post-op.

Overall, this data shows that a considerable amount of patients (22 eyes in our study), will fail due to the need of surgical revision or additional glaucoma surgery. As described before, a higher revision rate has been described for PFMS due to bleb fibrosis and these surgical revisions already account for failure events in our study. However, in our experience, post-revision outcomes are generally very good and many of these eyes do not need repeated revisions or additional glaucoma surgery. Strzalkowska et al. have performed a study looking at IOP outcomes after open bleb revision showing that IOP was effectively and safely reduced afterwards and only a minority needed another glaucoma surgery[20]. One has to take into consideration that these eyes are considered failure due to the second surgical revision, but might still fulfill success criteria afterwards with effective IOP lowering. Rabiolo et al. identified different risk factors for PFMS failure. Pseudoexfoliation glaucoma, pigmentary glaucoma, primary angle-closure glaucoma and previous non-glaucomatous ocular surgeries were identified as risk factors[21]. Since we included all eyes irrespective of glaucoma type in our cohort, only 70 % were POAG eyes, so that the other 30 %, including pigmentary and primary angle-closure glaucoma, might have been at higher risk. Of the seven eyes needing additional glaucoma surgery, two eyes had pigmentary glaucoma and one eye primary angle-closure glaucoma. Of the other four primary-open angle glaucoma eyes with failure, two eyes had previous vitrectomy and one eye previous XEN implantation. Thus, one can conclude from these findings, that glaucoma type and previous surgeries might be important factors to identify patients at risk forfailure after PFMS surgery. Further longitudinal studies with larger patient cohorts would be useful in order to assess which glaucoma subtypes are most successful and which characteristics might account as risk factors for failure.

This study has some limitations. Firstly, a limitation of this study is its retrospective nature. We were only able to retrieve 3-year data from 88 eyes of the originally published 1-year data of 100 eyes, meaning 12 eyes were lost to follow-up, this introducing selection bias. Due to the retrospective nature of the study, we could not retrieve the exact reasons for that. Secondly, the number of data time points were limited to 24 and 36 months, with large intervals in between making the number of visits able to detect failure limited. Moreover, this was a non-comparative study, so that we were not able to provide information on how the

PFMS performs in comparison with other bleb-forming devices or other filtering surgeries. Furthermore, some variables of interest, such as endothelial cell counts, were not available since they were not routinely performed by all surgeons in this study. Additionally, we were not able to retrieve the exact data concerning MMC concentration and exposure time due to the retrospective nature of the study, so that we were not able to include this in our COX regression analysis. We did not perform a subanalysis since most patients in our cohort were POAG, and we did not have enough patients with other glaucoma subtypes to conduct robust and adequately-powered subanalysis. As a matter of fact, our cox regression models did not detect any significant different in the risk of failure among the various glaucoma subtypes. Further, we did not impose any strict inclusion or exclusion criteria and looked at the first 25 consecutive patients of every center in order to ensure high generalizability of our results.

## Conclusions

In conclusion, PFMS surgery is a safe and effective procedure leading to a sustained reduction in IOP and pressure-lowering eye drops in most cases. Success rates for low IOP values were rather modest, indicating that PFMS might not be the optimal device for patients requiring a very low target IOP. Additional interventions such as needling or revisions, while sometimes required, generally yield positive outcomes.

## Table of content

PFMS surgery is a safe and effective procedure leading to a sustained reduction in IOP and pressure-lowering eye drops in most cases. Success rates for low IOP values were rather modest, indicating that PFMS might not be the optimal device for patients requiring a very low target IOP. Additional interventions might be required during the postoperative course.

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## Data availability statement

All datasets generated during and / or analyzed during the current study are available from the corresponding author on reasonable request.

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