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Preliminary results of Preserflo Microshunt versus Preserflo Microshunt and Ologen implantation



Iraklis Vastardis^{1*} , Sofia Fili¹, Georgios Perdikakis¹, Kalliopi Kontopoulou¹, Miltos Balidis², Zisis Gatzoufas³ and Markus Kohlhaas¹

Abstract

Purpose: To report preliminary 6-month results on the use of the Preserflo Microshunt implant with and without Ologen in 50 pseudophakic eyes with moderate to advanced primary open-angle glaucoma (POAG).

Methods: Fifty pseudophakic eyes underwent ab externo Preserflo Microshunt implantation. Data was gathered retrospectively and two groups were then created, group A with application of MMC 0.2 mg/ml and group B with MMC 0.2 mg/ml and Ologen collagen matrix (OCM) implantation. Absolute success was regarded as the percentage of eyes achieving: a) $5 \leq$ intraocular pressure (IOP) \leq 13 mmHg, b) $5 \leq$ IOP \leq 16 mmHg, and c) $5 \leq$ IOP \leq 21 mmHg without additional medication or surgery and qualified success was regarded as the percentage of eyes achieving a) IOP \leq 13 mmHg, b) IOP \leq 16 mmHg, and c) IOP \leq 21 mmHg with or without medication. Evaluation was performed using a log-rank Kaplan-Meier test. A scatterplot analysis presented the treatment effect data of all eyes with a minimum of 20% IOP reduction per case. Failure was defined as requiring additional surgery, IOP greater than 21 mmHg with or without medication and failure to reach 20% IOP reduction.

Results: Mean postoperative IOP was significantly lower in both groups. IOP decreased by 49.06% in group A and by 53.01% in group B at 6 months ($P < 0.88$), respectively. Medication use was lower in both groups (Wilcoxon test, $P < 0.001$). The absolute and qualified success rates were not statistically significant between the groups (all $P > 0.05$). Cumulative IOP results per case were not statistically different in group A compared with group B. One revision surgery in group A (4% failure rate) and three in group B (12% failure rate) were performed.

Conclusions: Both groups showed equal results in terms of cumulative and mean IOP reduction, medication reduction as well as in absolute and qualified success rates. No significant difference was found in any parameters tested between Preserflo Microshunt with MMC 0.2 mg/ml and with or without OCM implantation at 6 months. Long-term follow-up is required to further evaluate this data.

Keywords: Micro invasive glaucoma surgery, Ab externo surgery, Refractory POAG, SIBS polymer, Mitomycin C

* Correspondence: vastardis.iraklis@gmail.com

¹Department of Ophthalmology, St. Johannes Academic Hospital Dortmund, Dortmund, Germany

Full list of author information is available at the end of the article



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Introduction

Glaucoma is still responsible for irreversible blindness globally [1]. Patient numbers around the world are rising and projected to reach 111.8 million soon [2]. Visual field deterioration in such patients can be prevented by lowering the intraocular pressure (IOP) which is achieved either through medication, laser treatment or surgery [3–5]. Trabeculectomy is widely performed and still regarded as the gold standard treatment. Although the method itself has been rigorously improved over the years [6], its use among surgeons is declining in favor of newer micro-invasive glaucoma surgery (MIGS) devices [7]. Surgeons appear to be favoring such alternatives due to their superior safety and efficacy profiles [8]. These glaucoma implants have been introduced as a minimally invasive surgical option to prevent further glaucoma deterioration. These devices provide an outflow pathway of the aqueous humor from the anterior chamber of the eye into the posterior subtenon space, and thus reduce IOP by mimicking the mechanism of trabeculectomy, while simultaneously conferring a standardized IOP outcome and an enhanced safety profile [9–11]. Such a device is the Preserflo™ Microshunt (Santen, Osaka, Japan) implant formerly known as the InnFocus Microshunt (Santen, Osaka, Japan). It is a minimally invasive glaucoma drainage device that forms a posterior filtration bleb under the conjunctiva and Tenon's capsule. Preserflo Microshunt consists of a polymer, the poly-styrene-block-isobutylene-block-styrene (SIBS), a stretchy material, that provokes minimal inflammation and encapsulation in comparison to other materials used in glaucoma surgery such as silicone rubber and polypropylene [12, 13]. SIBS technology was introduced in 1999 through TAXUS® (Boston Scientific's, Natick, Massachusetts, USA) as a coronary stent in surgical treatment and prevention of arterial restenosis [14]. Today, as a glaucoma micro-implant and through its unique thermo-formable features it confers multiple advantages over traditional thermoset materials such as silicone rubber [12, 13]. There are multiple clinical trials evaluating its efficacy which are currently underway in Europe, USA, Singapore, Japan and the Dominican Republic. This case series study aims to not only report preliminary 6-month results on the use of the Preserflo Microshunt in terms of mean IOP and medication reduction, but also to compare two different surgical approaches: implantation of the Preserflo Microshunt with mitomycin C (MMC, 0.2 mg/ml) treatment and implantation of the Preserflo Microshunt with MMC 0.2 mg/ml treatment and additional Ologen collagen matrix (OCM) implantation. OCM is a biodegradable

porous collagen-glycosaminoglycan copolymer matrix implant claiming wound modulation among connective and epithelial tissues. It also serves as a spacer or barrier between the sclera surface and conjunctiva [15]. Although its true benefit in glaucoma surgery is still being debated [16, 17], OCM is currently being widely utilized extending beyond glaucoma surgery [18] to other ocular pathologies, for instance in pterygium excision where it modulates the wound healing of the conjunctiva and serves as an inhibitor of recurrence [19]. In this cohort, both the late wound healing modulation of the bleb and the benefit of space creation between the Preserflo Microshunt and the Tenon's capsule were evaluated. Our null hypothesis was that the IOP should be better in the eyes that underwent additional OCM implantation in comparison with the eyes that did not, by reducing the fibrotic reaction in the bleb area. The alternative hypothesis was that the IOP was equally lowered through the Preserflo Microshunt implantation with MMC 0.2 mg/ml regardless of the additional OCM implantation. If the OCM implantation indeed reduces the fibrotic reaction in the bleb area either through its properties or by acting as a barrier or spacer, then a reduction of revision surgery, needing interventions and additional use of antimetabolites or chemotherapeutic agents such as 5-fluorouracil (5-FU) should be reported.

Material and methods

Fifty Caucasian patients and fifty eyes with treatment refractory primary open-angle glaucoma (POAG) were operated in 2020. Twenty-five eyes (group A) underwent a Preserflo Microshunt implantation with MMC (0.2 mg/ml), while the remaining 25 eyes (group B) underwent the same surgery with additional OCM implantation (Aeon Astron Europe BV, Leiden, The Netherlands). All surgeries were carried out under general anesthesia, performed by five Preserflo Microshunt certified surgeons, and took place in Saint Johannes Hospital, Ophthalmology Department, in Dortmund, Germany. All patients provided their written consent prior to surgery and the tenets of the Declaration of Helsinki were fully adhered to. The institution's ethical committee approved this retrospective case series study. The primary patient selection criterion for this study was POAG refractory to medical treatment with prior uncomplicated cataract extraction. Inclusion and exclusion criteria are listed in Table 1. The baseline examination included a complete ophthalmic history, Humphrey visual field perimetry SITA Fast, endothelial microscopy (Tomey EM 4000, Tomey GmbH Technology and Vision, Nürnberg, Germany), Scheimpflug corneal

Table 1 Inclusion and exclusion criteria of the study cohort**Inclusion Criteria**

Refractory to medical treatment POAG and moderate to advanced POAG according to HPA classification system

Prior uncomplicated cataract extraction, no prior history of glaucoma surgery or laser treatment

ACD \geq 2.7 mm, ACA \geq Schaffer 3–4°

Exclusion Criteria

Secondary glaucoma, ACG, OHT, PDG, PEXG, LTG, prior glaucoma surgery or laser treatment

Prior refractive surgery, PPV, phakic patients, corneal and retinal pathology, AMD, CME, last eye - monocular

No glaucoma medication or mono-therapy

POAG primary open-angle glaucoma; *HPA* Hodapp-Parrish-Anderson classification system; *ACD* anterior chamber depth; *ACA* anterior chamber angle; *ACG* angle-closure glaucoma; *OHT* ocular hypertension; *PDG* pigmentary dispersion glaucoma; *PEXG* pseudoexfoliation glaucoma; *LTG* low-tension glaucoma; *PPV* pars plana vitrectomy; *AMD* age-related macular degeneration; *CME* cystoid macular edema

tomography (Pentacam, OCULUS Optikgeräte GmbH, Germany), high-definition ocular coherence tomography (HD-OCT) optic disc and ganglion cell layer evaluation (Cirrus HD-OCT 500, Carl Zeiss Meditec AG, Germany), single measurement of calibrated Goldman applanation tonometry, Snellen visual acuity, slit-lamp anterior and posterior segment examination and gonioscopy with angle grading. Data was gathered again concurrently at the 1st day, 2nd week, 1st, 3rd, and 6th month including standard slit-lamp examination of the anterior and posterior segment, Goldman applanation tonometry, visual acuity testing and postoperative complications.

Surgical technique

For both groups, a 4-mm fornix based conjunctival peritomy was performed in the upper temporal or nasal quadrant in order to reveal the underlying sclera. Cauterization was performed under balanced salt solution (BSS) irrigation followed by scleral treatment with three MMC (0.2 mg/ml) soaked sponges posteriorly for three minutes. An ink marking was then placed 3 mm posterior to limbus followed by creation of an initial pocket with a 1.2-mm diamond blade. A 25-Gauge needle was then bent with the bevel up and inserted at a 90° angle into the anterior chamber, exiting at the level of the trabecular meshwork. The device was then slid through the pocket and tunnel while the fins of the device were stabilized into the scleral pocket. The aqueous humor flow chamber was tested with a sponge via observation. Finally, the device was covered from the conjunctiva and Tenon's capsule, which in turn they were separately reattached with a 10–0 nylon running suture.

For group B exclusively, the 6 mm wide and 2 mm high OCM, was additionally placed posterior to the device's fin and then tucked beneath the Tenon's capsule and conjunctiva, prior to their reattachment with the 10–0 nylon running suture. Postoperative blebs were evaluated according to the Wuerzburg bleb classification score (WBCS) [20, 21]. It is based on a score that evaluates vascularization, corkscrew vessel and encapsulation but not the height of the bleb [22]. The postoperative medication in both groups was moxifloxacin three times daily and cycloplegics two times daily for the first week combined with preservative free corticosteroid eye drops instilled six times daily. After the first week, the antibiotics and cycloplegics were discontinued and the corticosteroid regimen was tapered by reducing one drop every week for the next 6 weeks.

Statistical analysis

The mean IOP and medication reduction as well as the corrected distance visual acuity (CDVA) were evaluated with a two-way analysis of variance (two-way ANOVA) and paired samples t-test. Medication reduction between baseline and 6 months was reported using Wilcoxon test. Homoscedasticity, assumption of homogeneity, outliers assumption and the distribution of data for two-way ANOVA were also tested. Efficacy was assessed with the Kaplan-Meier survival analysis in three different postoperative IOP goals between the groups and with two different success criteria. Absolute success was regarded as the percentage of eyes that achieved a) $5 \leq \text{IOP} \leq 13$ mmHg, b) $5 \leq \text{IOP} \leq 16$ mmHg, and c) $5 \leq \text{IOP} \leq 21$ mmHg without additional medication or surgery and qualified success was regarded as the percentage of eyes that achieved a) $\text{IOP} \leq 13$ mmHg, b) $\text{IOP} \leq 16$ mmHg, and c) $\text{IOP} \leq 21$ mmHg with or without medication. We included a scatterplot analysis to present the treatment effect data of all eyes in this study that demonstrates the minimum 20% IOP reduction requirement achieved in both groups. Failure was defined as additional surgery, IOP greater than 21 mmHg with or without medication and failure to reach 20% IOP reduction. Cumulative IOP results per group were also evaluated and presented in percentages for IOP readings less or equal than 11, 13 and 15 mmHg. Intraoperative and postoperative complications as well as additional surgery rates were also evaluated as percentages. Statistical analysis was performed with MedCalc® 16.2.1 and IBM SPSS® version 22. Parametric or non-parametric tests were used according to distribution normality (Kolmogorov-Smirnov). We considered statistical significance as a *P* value < 0.05 .

Results

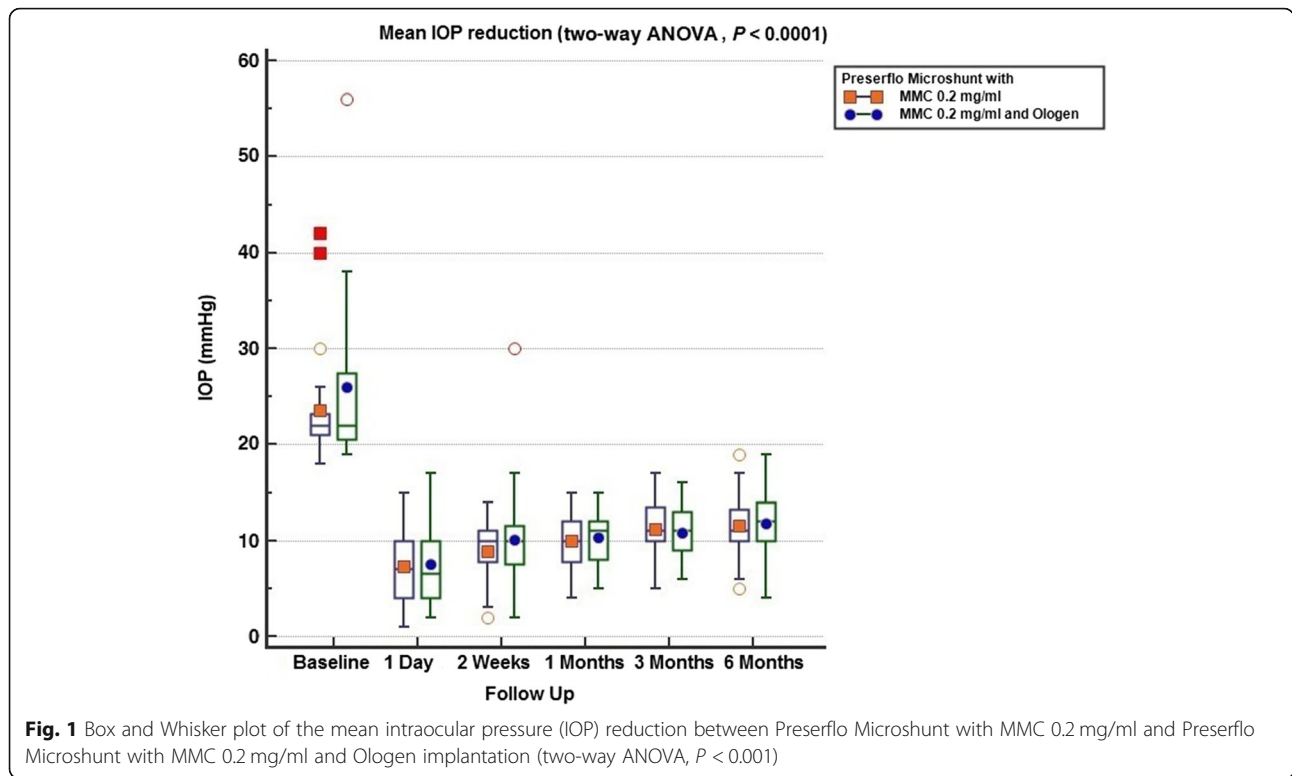
Thirty five cases were classified as advanced POAG (with a mean visual field mean deviation (MD) -20.50 ± 6.38 dB) and 15 cases as moderate (mean visual field MD -7.37 ± 0.71 dB) according to the Hodapp-Parrish-Anderson (HPA) classification system [23]. Demographics are presented in Table 2. All variables tested for the results presented between both groups A and B were comparable (Table 2). The mean postoperative IOP decreased significantly from baseline in both surgical groups. IOP in group A decreased from 23.52 ± 5.78 to 11.56 ± 3.08 mmHg (49.06% mean IOP reduction) and from 26.04 ± 8.76 to 11.75 ± 3.37 mmHg (53.01% mean IOP reduction) in group B by the 6th month (two-way ANOVA, $P < 0.001$; Fig. 1). Medication decreased in both groups compared to baseline (Table 3). Medication use in group A decreased from 2.52 ± 0.91 to 0.04 ± 0.20 (98.02% reduction, a median reduction of 2.5 medications). Medication use in group B decreased from 2.58 ± 0.82 to 0.16 ± 0.81 (94.44% reduction, a median reduction of 2.5 medications) by the 6th month (Wilcoxon test, $P < 0.001$). The Levene's equality test was statistically significant ($P < 0.001$, Table 4), and thus the data tested failed to meet the

assumption of homogeneity and outliers assumption between the groups. Regarding the power of the samples, we found that the follow-up was the only statistically significant factor ($P < 0.001$) in terms of IOP reduction with partial eta squared 0.63 (63%) and observed power of 1. No other factor or pairwise factor was significant in terms of IOP reduction (Table 4). CDVA was stable in both groups (paired samples t-test, $P = 0.95$, from baseline 0.64 ± 0.24 to the 6th month 0.66 ± 0.21 Snellen and $P = 0.33$, from baseline 0.58 ± 0.27 to the 6th month 0.61 ± 1.93 Snellen, in groups A and B, respectively). Absolute success rates in group A accounted for a) 48%, b) 64% and c) 68% in comparison to group B a) 45.8%, b) 45.8% and c) 58.3% at 6 months (Figs. 2, 3 and 4). Qualified success rate in group A accounted for a) 68%, b) 88% and c) 92% in comparison to group B a) 70.8%, b) 91.8% and c) 95.8% at 6 months (Figs. 5, 6 and 7). Log-rank Kaplan-Meier showed no statistical differences between the groups and parameters tested ($P < 0.68$, $P < 0.22$, $P < 0.48$ absolute success and $P = 0.38$, $P < 0.31$ and $P < 0.58$ qualified success, group A and group B, respectively). The scatterplot analysis verified those results (Fig. 8) by showing a 20% IOP reduction and an overall IOP reduction per

Table 2 Demographics of study participants

Demographics	n			
No. of patients	50			
No. of female patients	33			
Age (years)	76.13 ± 10.08			
No. of male patients	17			
Age (years)	79.00 ± 7.94			
No. of eyes operated total (POAG refractory to medical treatment)	50			
Baseline MD (dB) total	-13.31 ± 7.93			
Advanced POAG, Baseline MD (dB) (n = 35)	-20.50 ± 6.38			
Moderate POAG, Baseline MD (dB) (n = 15)	-7.37 ± 0.71			
		Group A	Group B	Intergroup variable comparison
		(n)	(n)	t-test, $P < 0.05$ (95% CI)
No. of eyes operated total	25	25	25	N.A
No. of pseudophakic eyes	25	25	25	N.A
Age (years)	77.58 ± 7.62	75.64 ± 12.61	75.64 ± 12.61	0.88 (-6.15 to 5.32)
Baseline MD (dB)	-13.15 ± 8.53	-13.47 ± 7.44	-13.47 ± 7.44	0.84 (-4.57 to 3.78)
Baseline average RNFL thickness (μ m)	65.04 ± 8.03	64.54 ± 10.67	64.54 ± 10.67	0.52 (-3.63 to 6.78)
Baseline IOP (mmHg)	23.52 ± 5.78	26.04 ± 8.76	26.04 ± 8.76	0.26 (-1.93 to 6.77)
Baseline antiglaucoma agents	2.52 ± 0.91	2.58 ± 0.82	2.58 ± 0.82	0.36 (-0.38 to 0.98)
Baseline DCVA (Snellen)	0.64 ± 0.24	0.58 ± 0.27	0.58 ± 0.27	0.43 (-0.23 to 0.10)

POAG primary open-angle glaucoma; IOP intraocular pressure; MD mean deviation; dB decibels; RNF retinal nerve fiber layer; CDVA corrected distance visual acuity; MMC mitomycin C; N.A not available
 Group A: Preserflo Microshunt with MMC 0.2 mg/ml
 Group B: Preserflo Microshunt with MMC 0.2 mg/ml and Ologen



case for all 50 eyes in both groups. The cumulative IOP results per group were not statistically different in group A compared to group B at 6 months (Fig. 9 and Table 4). We did not observe any severe intra-operative complications in either group. In the early postoperative follow-up, 12 eyes (24%) presented with transient hypotony (IOP < 5 mmHg) for 1 week, in which 6 of them (50%) presented a minor choroidal detachment in the retinal periphery which

resolved within 14 days, while in 1 eye (2%) the choroidal detachment persisted for over 1 month and spontaneously resolved after immediate discontinuation of the corticosteroid topical treatment. Twenty-six eyes (52%) had a normal postoperative follow-up without any interventions or complications. Four revision surgeries due to bleb fibrosis were performed at 6 months and were considered failures (8%). Three revision surgeries were

Table 3 Paired samples t-test comparison of the means in terms of medication in both groups

Follow Up	Intervention	n	Mean ± SD	Std. Error	95% Confidence interval	P
Baseline	Group A	25	2.52 ± 0.91	0.19	2.10 to 2.89	0.70
	Group B	25	2.58 ± 0.82	0.16	2.23 to 2.93	
1 Day	Group A	25	0.00 ± 0.00	0.00	0.00 to 0.00	0.00
	Group B	25	0.00 ± 0.00	0.00	0.00 to 0.00	
2 Weeks	Group A	25	0.00 ± 0.00	0.00	0.00 to 0.00	0.00
	Group B	25	0.00 ± 0.00	0.00	0.00 to 0.00	
1 Month	Group A	25	0.00 ± 0.00	0.00	0.00 to 0.00	0.00
	Group B	25	0.00 ± 0.00	0.00	0.00 to 0.00	
3 Months	Group A	25	0.00 ± 0.00	0.00	0.00 to 0.00	0.00
	Group B	25	0.00 ± 0.00	0.00	0.00 to 0.00	
6 Months	Group A	25	0.04 ± 0.20	0.04	-0.04 to 0.12	0.47
	Group B	25	0.16 ± 0.66	0.16	-0.17 to 0.51	

Group A: Preserflo Microshunt with MMC 0.2 mg/ml
 Group B: Preserflo Microshunt with MMC 0.2 mg/ml and Ologen

Table 4 Two-way ANOVA with tests of between-subjects effects for all variables tested, estimated marginal means and pairwise comparison for the IOP dependent variable and intergroup t-test comparison between Preserflo Microshunt with MMC 0.2 mg/ml and Preserflo Microshunt with MMC 0.2 mg/ml and Ologen implantation

Two-way ANOVA							
Levene's test for equality of error variances							
F	DF 1	DF 2	P				
3.9319	11	271	< 0.001				
Tests of between-subjects effects (all variables)							
Source	Sum of squares	DF	Mean square	F	Partial eta squared	Observed power^b	P
Follow up	9514.47	5	1902.89	98.70	0.639	1.0	< 0.001
Intervention	36.31	1	36.31	1.88	0.06	0.27	0.17
Follow up*Intervention	64.22	5	12.84	0.66	0.01	0.25	0.64
Residual	5224.34	271	19.27				
Estimated marginal means (IOP dependent)							
Follow up		n	Mean	Std. Error	95% Confidence interval		
Baseline		50	24.78	0.62	23.54 to 26.01		
1 Day		50	7.37	0.62	6.13 to 8.60		
2 Weeks		50	9.48	0.62	8.24 to 10.71		
1 Month		50	10.12	0.62	8.89 to 11.36		
3 Months		50	10.98	0.62	9.74 to 12.21		
6 Months		50	12.18	0.71	10.78 to 13.58		
Follow up	Intervention	n	Mean ± SD	Std. Error	t-test (P)	95% Confidence interval	
Baseline	Group A	25	23.52 ± 5.88	0.87	0.26	21.79 to 25.24	
	Group B	25	26.04 ± 8.76	0.89		24.27 to 27.80	
1 Day	Group A	25	7.24 ± 3.47	0.87	0.76	5.51 to 8.96	
	Group B	25	7.50 ± 4.23	0.89		5.73 to 9.26	
2 Weeks	Group A	25	8.88 ± 3.08	0.87	0.34	7.15 to 10.60	
	Group B	25	10.08 ± 5.48	0.89		8.31 to 11.84	
1 Month	Group A	25	9.92 ± 3.25	0.87	0.49	8.19 to 11.64	
	Group B	25	10.33 ± 2.53	0.89		8.56 to 12.09	
3 Months	Group A	25	11.20 ± 2.71	0.89	0.63	9.44 to 12.97	
	Group B	25	10.76 ± 2.78	0.87		9.03 to 12.48	
6 Months	Group A	25	12.00 ± 3.13	0.63	0.89	10.01 to 13.98	
	Group B	25	12.36 ± 3.37	0.67		10.38 to 14.35	
Pairwise comparisons (IOP dependent)			Mean difference	Std. Error	P^a	95% CI^a	
Baseline	1 Day	17.41	0.88	< 0.0001	14.78 to 20.03		
	2 Weeks	15.29	0.88	< 0.0001	12.67 to 17.92		
	1 Month	14.65	0.88	< 0.0001	12.02 to 17.28		
	3 Months	13.79	0.88	< 0.0001	11.16 to 16.42		
	6 Months	12.59	0.94	< 0.0001	9.78 to 15.40		
1 Day	Baseline	-17.41	0.88	< 0.0001	-20.03 to -14.78		
	2 Weeks	-2.11	0.88	0.27	-4.73 to 0.51		
	1 Month	-2.75	0.88	0.0314	-5.38 to -0.12		
	3 Months	-3.61	0.88	0.0009	-6.24 to -0.98		
	6 Months	-4.81	0.94	< 0.0001	-7.62 to -2.00		

Table 4 Two-way ANOVA with tests of between-subjects effects for all variables tested, estimated marginal means and pairwise comparison for the IOP dependent variable and intergroup t-test comparison between Preserflo Microshunt with MMC 0.2 mg/ml and Preserflo Microshunt with MMC 0.2 mg/ml and Ologen implantation (*Continued*)

Two-way ANOVA					
Pairwise comparisons (IOP dependent)		Mean difference	Std. Error	P ^a	95% CI ^a
2 Weeks	Baseline	-15.29	0.88	< 0.0001	-17.92 to -12.67
	1 Day	2.11	0.88	0.27	-0.51 to 4.73
	1 Month	-0.64	0.88	1.00	-3.27 to 1.98
	3 Months	-1.50	0.88	1.00	-4.13 to 1.12
	6 Months	-2.70	0.94	0.07	-5.51 to 0.10
1 Month	Baseline	-14.65	0.88	< 0.0001	-17.28 to -12.02
	1 Day	2.75	0.88	0.0314	0.12 to 5.38
	2 Weeks	0.64	0.88	1.00	-1.98 to 3.27
	3 Months	-0.85	0.88	1.00	-3.48 to 1.77
	6 Months	-2.05	0.94	0.46	-4.86 to 0.75
3 Months	Baseline	-13.79	0.88	< 0.0001	-16.42 to -11.16
	1 Day	3.61	0.88	0.0009	0.98 to 6.24
	2 Weeks	1.50	0.88	1.00	-1.12 to 4.13
	1 Month	0.85	0.88	1.00	-1.77 to 3.48
	6 Months	-1.20	0.94	1.00	-4.01 to 1.61
6 Months	Baseline	-12.59	0.94	< 0.0001	-15.40 to -9.78
	1 Day	4.81	0.94	< 0.0001	2.00 to 7.62
	2 Week	2.70	0.94	0.07	-0.10 to 5.51
	1 Month	2.05	0.94	0.46	-0.75 to 4.86
	3 Months	1.20	0.94	1.00	-1.61 to 4.01

^a Bonferroni corrected^b Computed using alpha = 0.05

Group A: Preserflo Microshunt with MMC 0.2 mg/ml

Group B: Preserflo Microshunt with MMC 0.2 mg/ml and Ologen

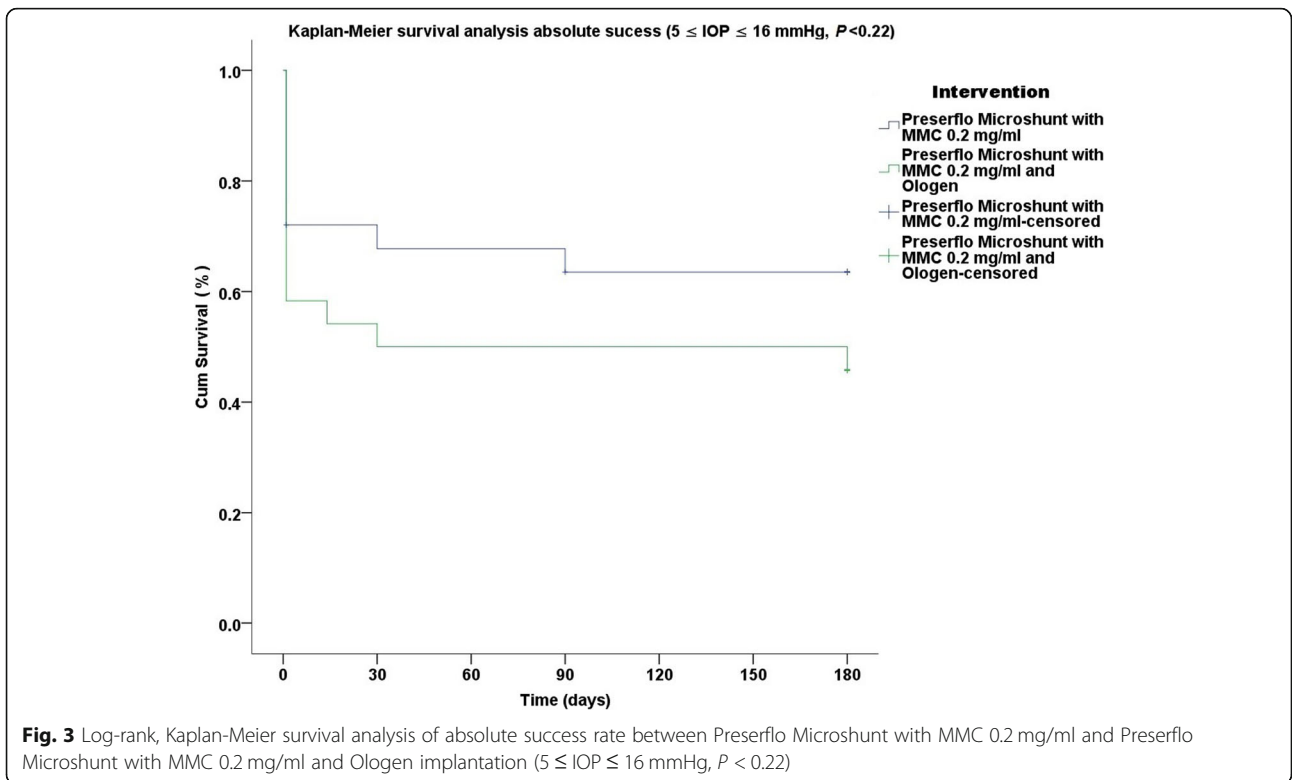
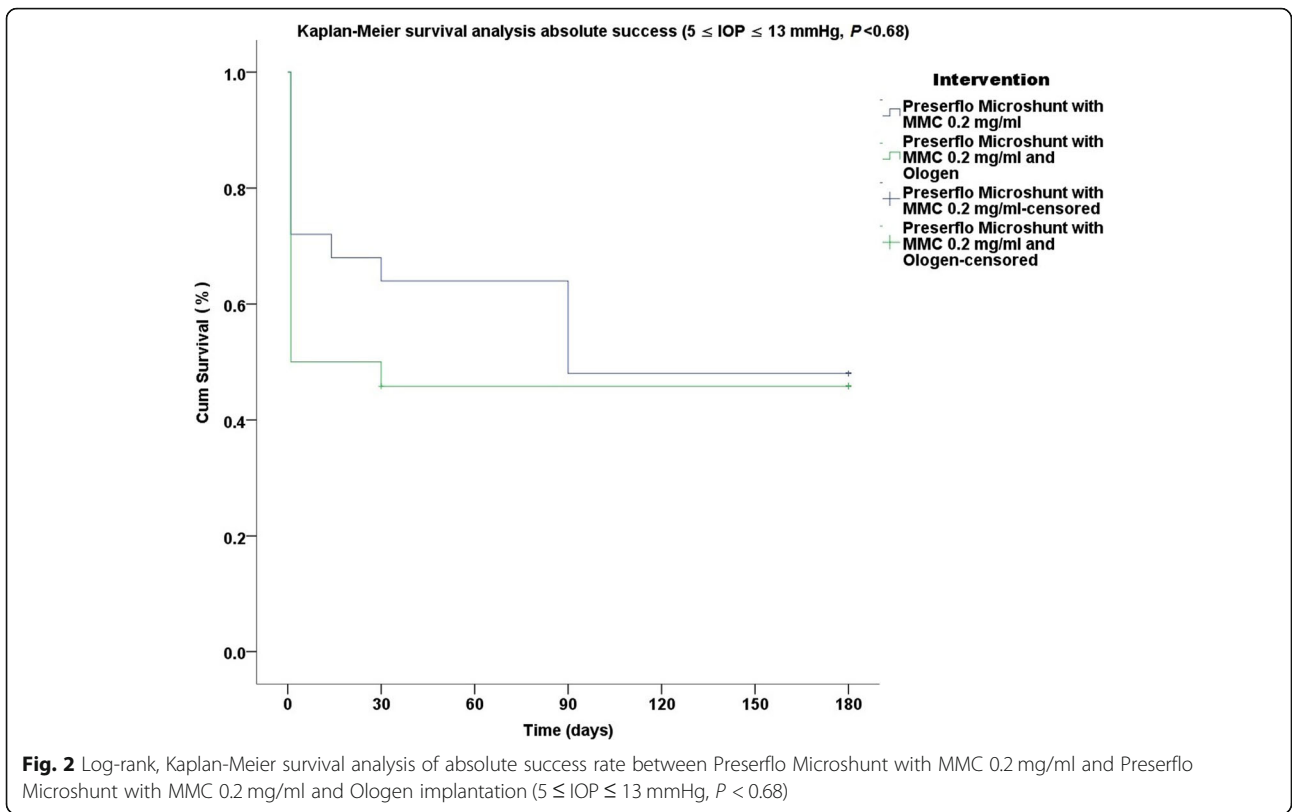
SD: standard deviation; DF: degrees of freedom; Eta: eta coefficient (An eta coefficient test is a method for determining the strength of association between a categorical variable)

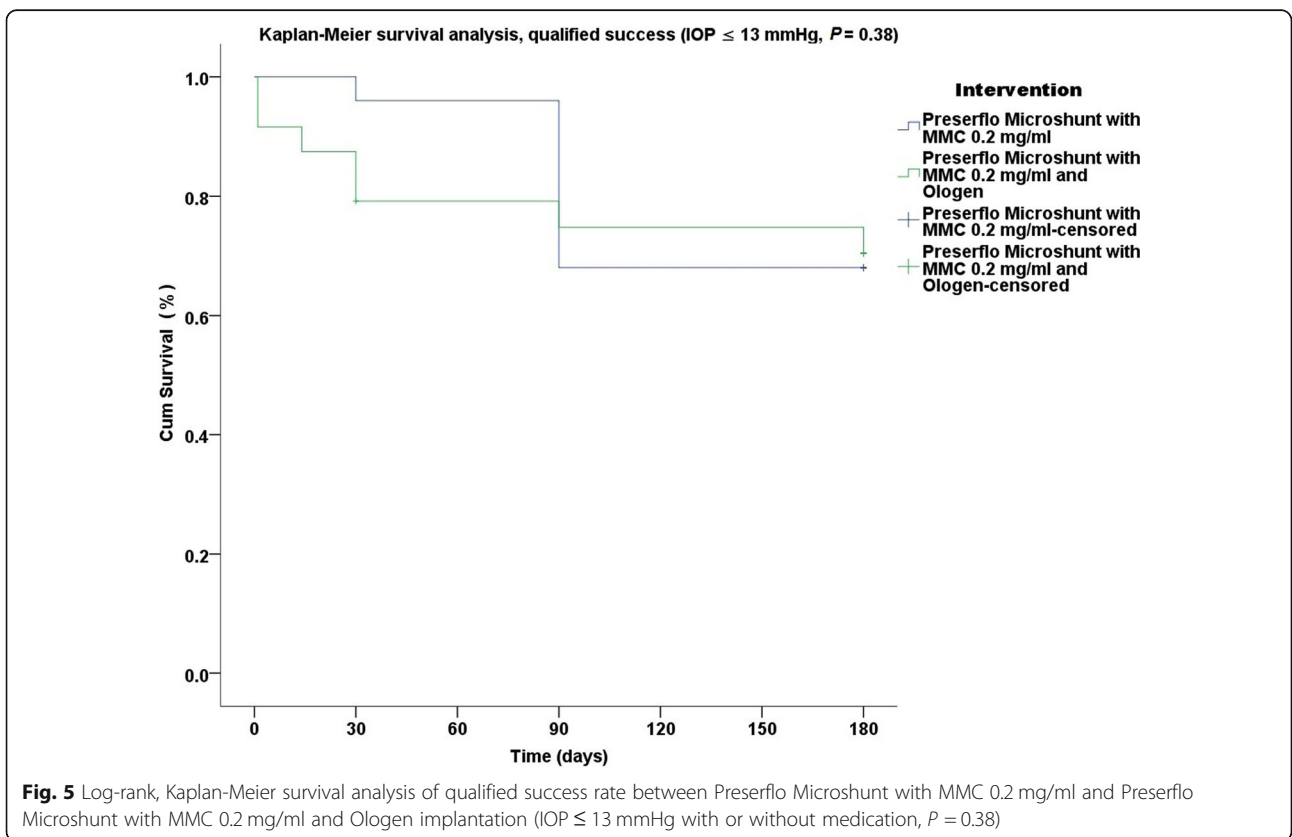
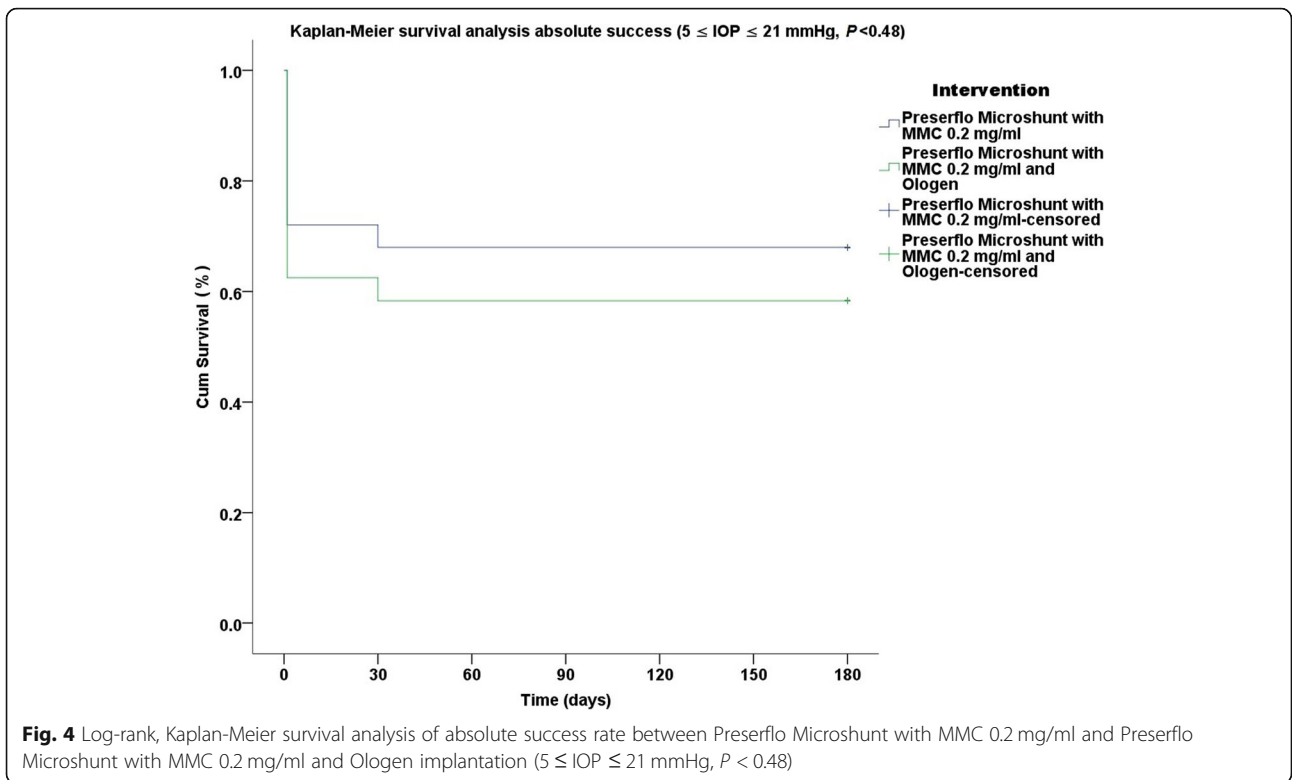
performed at 6 months in group B (12%) in comparison to one in group A (4%). Regarding bleb fibrosis, both groups shared similar characteristics in terms of age, prior surgery status and ethnicity (Table 5). All eyes were conjunctiva surgery naive prior to Preserflo Microshunt implantation and had only undergone cataract extraction. During revision surgeries, the conjunctiva, Tenon's capsule, sclera, and the Preserflo Microshunt were examined. After removal of fibrosis, the Preserflo Microshunt was checked for flow. If flow was inadequate, the tube was removed from the scleral pocket and flushed with BSS. Upon successful irrigation and adequate flow, the tube was returned back into position following scleral treatment with 0.2 mg/ml MMC for 3 min.

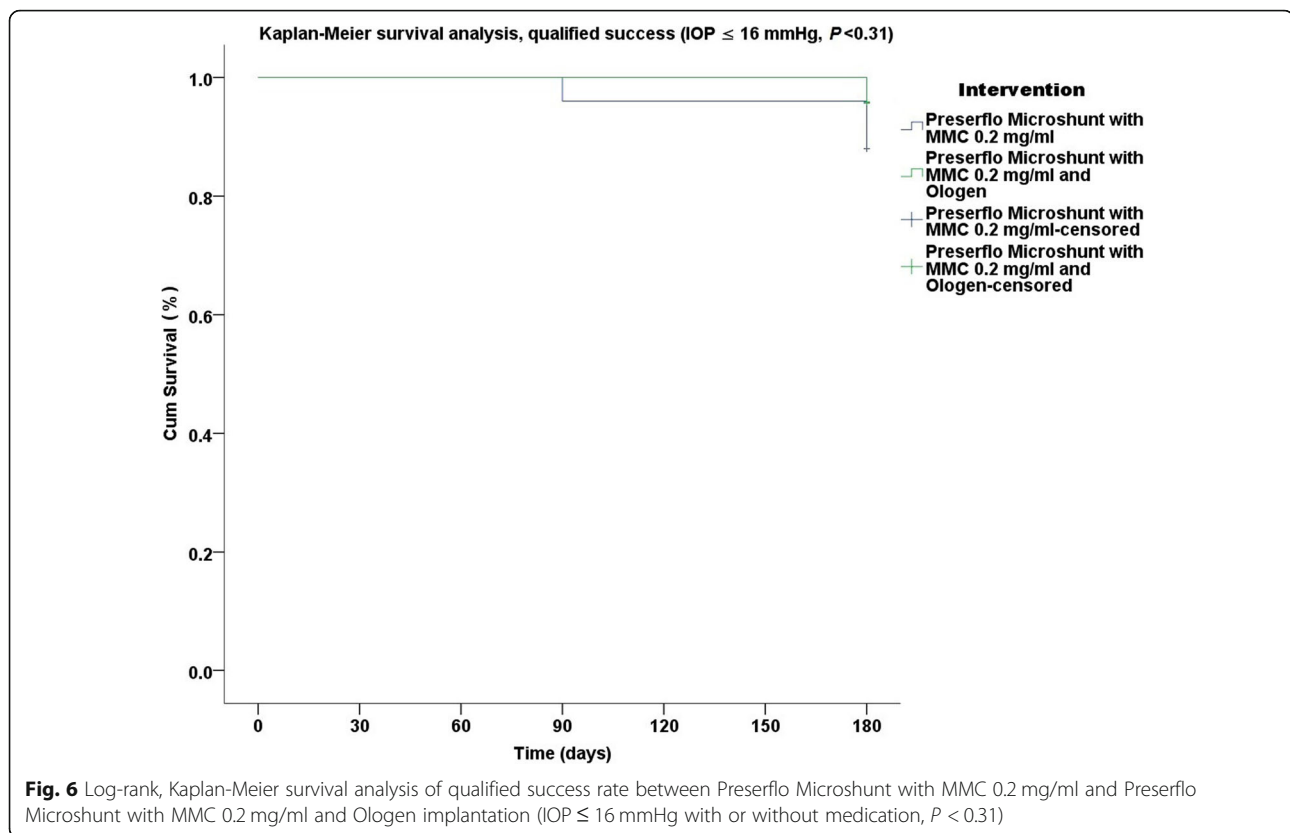
Discussion

Trabeculectomy is still regarded by many surgeons as the gold standard in surgical treatment of POAG patients [15–17, 24]. Nonetheless, its high

complication rate and demanding postoperative management have caused surgeons to seek alternative surgical approaches [25]. Such approaches include the XEN Glaucoma Gel Microstent implant (XEN-GGM, Allergan Plc., Parsippany, New Jersey), an ab interno alternative approach to trabeculectomy, which has gained vast popularity in recent years [26, 27]. XEN reduces IOP significantly and is designed to avoid postoperative hypotony which is a major advantage over the traditional trabeculectomy approach. Studies have however shown that in the long term, additional revision surgeries due to bleb fibrosis ranging from 32 to 37.7% are required to maintain a sufficient low IOP without medication [28, 29]. The Preserflo Microshunt is a relatively novel ab externo alternative to trabeculectomy. There are a few known studies to date following Preserflo Microshunt implantation outcomes [12, 30, 31, 32, 33]. Pinchuck et al. [12] first reported on a cohort of 23 successful Preserflo Microshunt implantations in 23

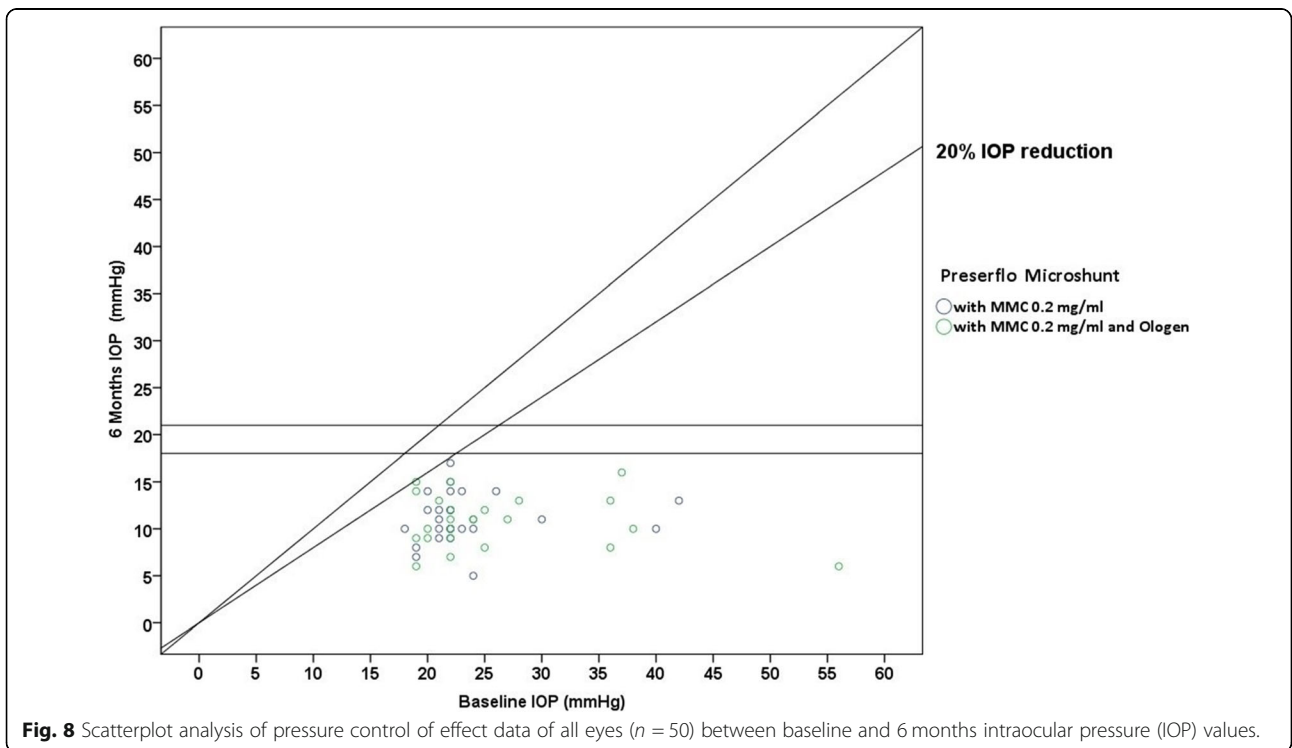
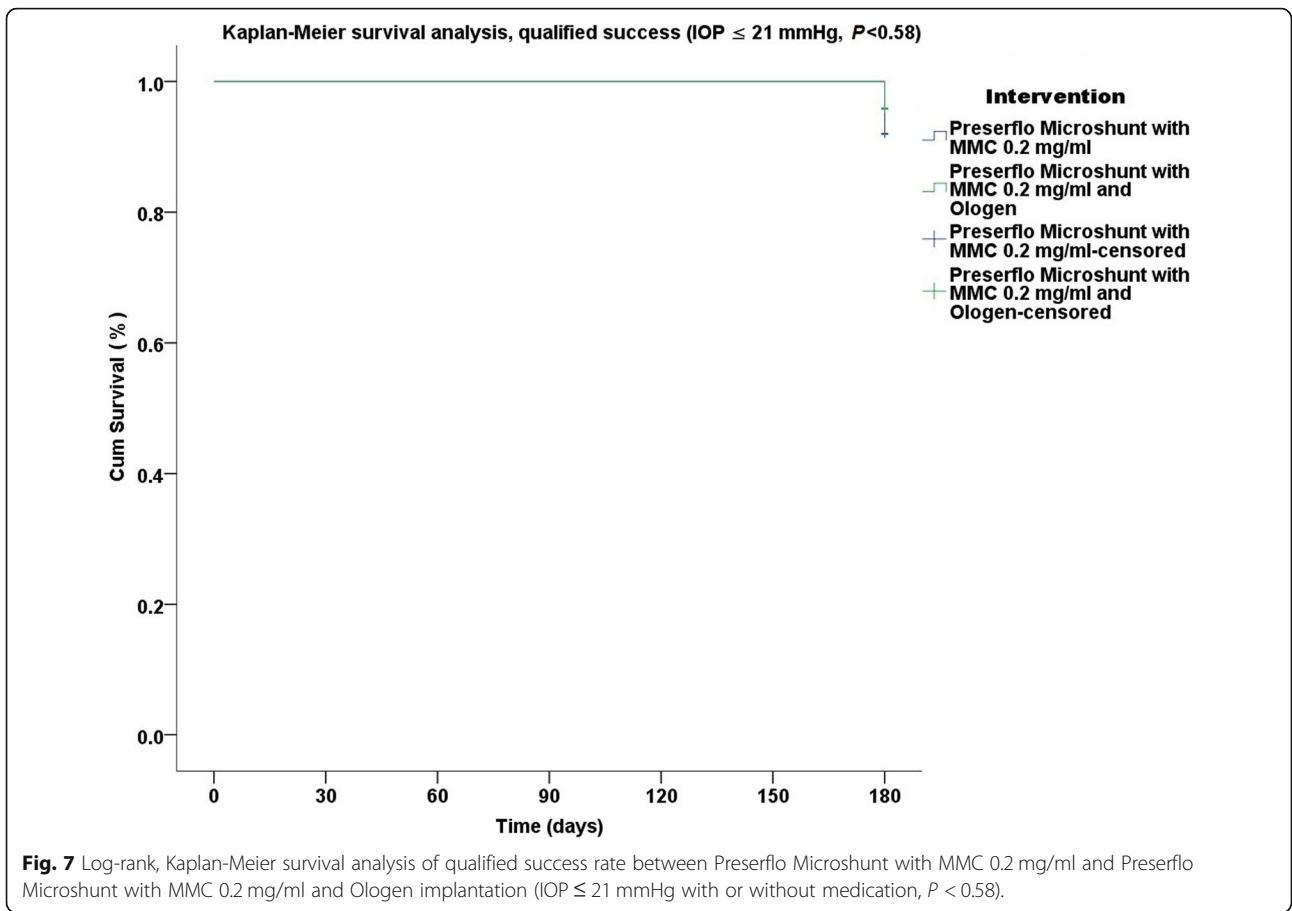






consecutive eyes. In this study, the design and features of the device as well as the steps of the surgical procedure were thoroughly described and reported. The minimal hypotony results in combination with the insignificant bleb inflammation and encapsulation results as well as the effectiveness of the procedure in lowering the IOP postoperatively provided an alternative to primary trabeculectomy. In this study, the IOP was lowered by 50 to 55% reaching a level below 14 mmHg in over 80% of patients. Similar results were reported by Riss et al. in a retrospective two-center, two-surgeon study with one-year follow-up [30]. In that observational study, the primary goal was to demonstrate the significance of different MMC concentrations, 0.4 versus 0.2 mg/ml, and different placement of an MMC sponge in anatomical locations, limbus versus deep in the pocket, in terms of IOP and medication reduction in three distinct groups. They reported a sufficient IOP and medication reduction postoperatively ranging from 38 to 55% and 72 to 85% at 12 months, respectively. The effectiveness in IOP and medication reduction following a Preserflo Microshunt implantation has been well documented in the recent years [30, 31, 32, 33]. In our current study, we found comparable results in terms of mean IOP reduction

at 6 months from 23.52 ± 5.78 to 11.56 ± 3.08 mmHg and from 26.04 ± 8.76 to 11.75 ± 3.37 mmHg in groups A and B with a 49.06% mean IOP reduction in group A and 53.01% mean IOP reduction in group B. The mean medication reduction in our study was also similar and comparable to other studies results [12, 30, 31, 32, 33] with medication reduction in group A ranging from 2.52 ± 0.91 to 0.04 ± 0.20 medications (98.02% reduction, median reduction of 2.5 medications) and in group B from 2.58 ± 0.82 to 0.16 ± 0.81 medications (94.44% reduction, median reduction of 2.5 medications) by the 6th month. In terms of absolute and qualified success, different criteria were used in all the studies so an accurate comparison is not possible. Battle et al. [32] defined qualified success as having an IOP of less than 14 mmHg and a minimum IOP reduction of 20% (IOP ≤ 14 mmHg and IOP reduction ≥ 20%). Success rate reported was 100%, 91%, and 95% for the 1st, 2nd and 3rd year, respectively. Schlenker et al. [33] defined absolute success as an IOP greater than 6 and less than 17 mmHg without hypotony ($6 < \text{IOP} < 17$ mmHg) and qualified as the same range with glaucoma medications with at least a 20% IOP reduction. Complete success was achieved in 76.9% of eyes, qualified success in 92.5%. Complete success



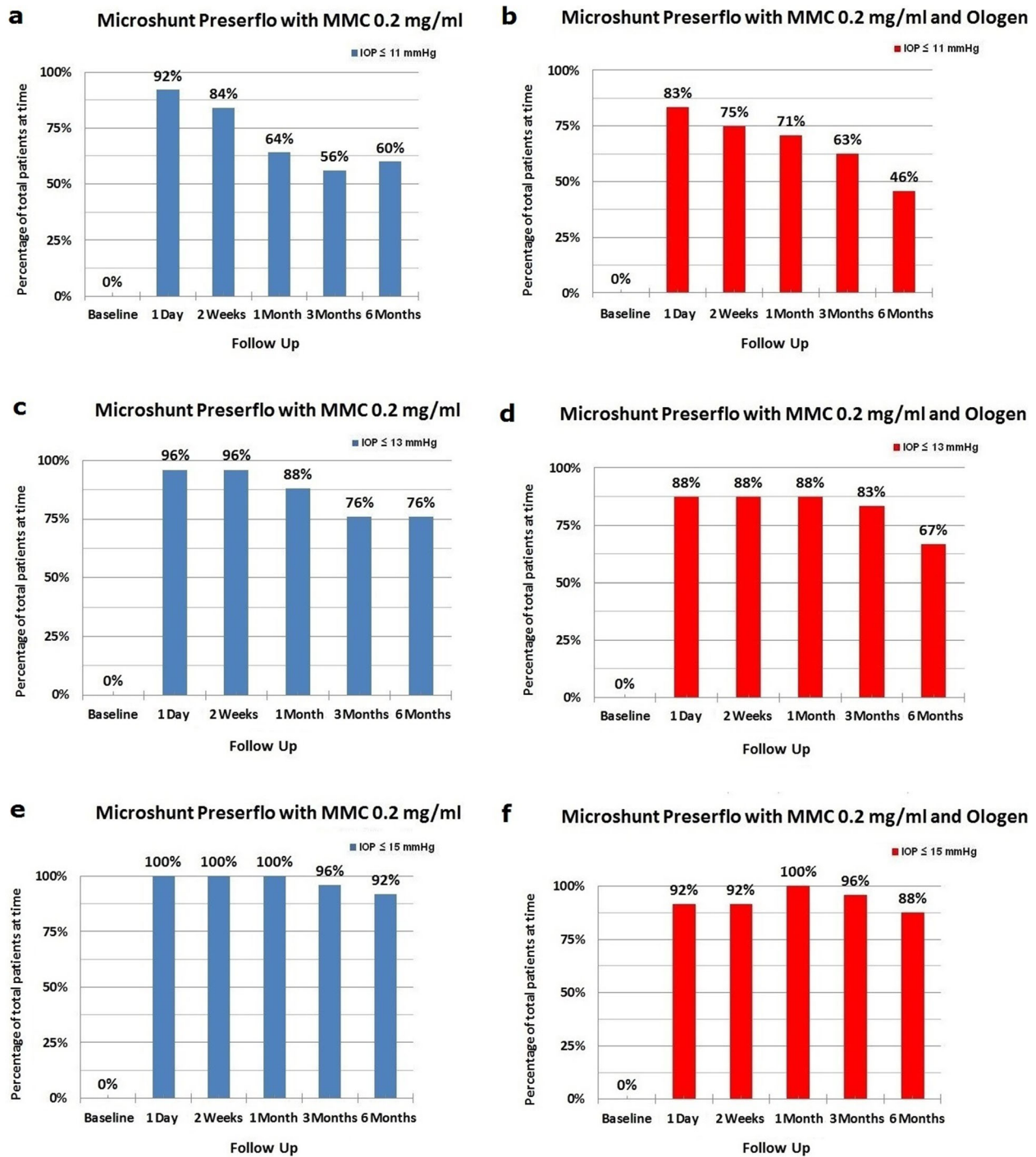


Fig. 9 Cumulative intraocular pressure (IOP) results per group (Preserflo Microshunt with MMC 0.2 mg/ml and Preserflo Microshunt with MMC 0.2 mg/ml and Ologen implantation) in percentage for IOP readings less than or equal to (a, b) 11 mmHg, (c, d) 13 mmHg and (e, f) 15 mmHg

was 75.6% for an upper IOP cut-off of 14 mmHg and 76.9% for 21 mmHg, and qualified success was 91.9 and 92.5%. Needling rate was 8.5%. Durr et al. similarly to Schlenker et al. [33] defined failure as an IOP less than 6 mmHg with vision loss, greater than 17 mmHg or less of 20% reduction in IOP without

medication. Secondary outcomes included thresholds of 6 to 14 mmHg and 6 to 21 mmHg for both complete (no medication) and qualified (with medication) success as well as qualified success for thresholds of 6 to 17 mmHg. A 61.0% complete success and 79.7% qualified success rate was reported.

Table 5 Bleb failure risk factors and failure results per group

Demographics	Group A	Group B
No. of eyes operated total	25	25
Prior ocular surgeries	Phacoemulsification	Phacoemulsification
Ethnicity of patients	Caucasian	Caucasian
No. of female patients	18	15
Age (years)	77.58 ± 7.62	75.64 ± 12.61
No. of male patients	7	10
Bleb revision surgery at 6 months (failure rate)	1 (4%)	3 (12%)

MMC mitomycin C

Group A: Preserflo Microshunt with MMC 0.2 mg/ml

Group B: Preserflo Microshunt with MMC 0.2 mg/ml and Ologen

Needling was performed in 11.8% of eyes. We reported comparable results with absolute success rate in group A reaching a) 48%, b) 64% and c) 68% in comparison to group B a) 45.8%, b) 45.8% and c) 58.3% at 6 months (Figs. 2, 3 and 4 respectively). Our qualified success rate in group A was a) 68%, b) 88% and c) 92% in comparison to group B a) 70.8%, b) 91.8% and c) 95.8% at 6 months (Figs. 5, 6 and 7 respectively). Four revision surgeries due to bleb fibrosis were performed at 6 months and were considered failures (8%). Three revision surgeries were performed at 6 months in group B (12%) in comparison to one in group A (4%). In our cohort, a concentration of MMC 0.2 mg/ml was used in all cases with placement of the soaked sponges posteriorly or deep in the pocket for 3 min. We found that the results of Riss et al. in their group C of 38% mean IOP reduction with MMC 0.4 mg/ml scleral treatment deep in the pocket at one-year follow-up were not comparable with our results. In the studies by Schlenker and Durr, [32, 33] different MMC dose of 0.2 versus 0.4–0.5 mg/ml were used in POAG versus secondary open angle glaucoma (SOAG). Our cohort included only POAG eyes with conjunctival naive patients. Other differing factors between the studies of Battle, Durr and Schlenker [31, 32, 33] and ours, were the cohorts' ethnic group, primarily Afro-Caribbean versus Caucasian, combined surgery with phacoemulsification versus standalone procedure, different MMC dose and the OCM implantation. Regarding the possible benefit provided from OCM implantation we did not find any statistical differences in terms of IOP reduction between the groups at 6 months. In group B, we performed two additional revision surgeries in comparison to group A, although both groups shared almost identical characteristics in terms of bleb failure risk (Table 5). Our current results showed no statistical difference between groups A and B. Similar results were reported

in the survival analysis (Figs. 2 and 3) and in the scatterplot analysis (Fig. 8) demonstrating equal IOP reduction among the groups. Our cumulative IOP results also did not demonstrate any statistical differences between groups A and B at 6 months (Fig. 9). In our opinion, an OCM additional implantation could have been of benefit in a cohort with mixed ethnic origin patients other than Caucasian, prior glaucoma surgery and those on long term glaucoma medication.

Conclusion

We were able to reproduce similar results to pre-existing studies [11, 29, 30, 31, 32, 33]. We did not report any adverse or severe sight-threatening complications and our revision surgery rate was 8%. Our greatest limitation is only having 6 months of data, the retrospective nature of the study and failing the assumption of homogeneity of variance. We advise caution when interpreting our results in terms of OCM evaluation and IOP or medication reduction as well as the current revision rates presented. Long-term follow-up is required to evaluate any benefit in terms of wound modulation of an additional OCM implantation following Preserflo Microshunt surgery.

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Authors' contributions

IV: Conceptualization, original draft, surgery, methodology, software, statistical analysis, writing, review and editing, supervision; SF: Surgery, methodology, statistical analysis, writing, review and editing; GP: Editing, surgery, visualization; KK: Statistical analysis, surgery; MB: Validation, methodology; ZG: Validation, methodology; MK: Conceptualization, methodology, surgery, general supervision. All authors read and approved the final manuscript.

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Availability of data and materials

Not applicable.

Declaration**Ethics approval and consent to participate**

The institution's ethical committee approved this retrospective case series study (01/2019/004_OPH_Preserflo MMC).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

¹Department of Ophthalmology, St. Johannes Academic Hospital Dortmund, Dortmund, Germany. ²Ophthalmica Eye Institute, Thessaloniki, Greece.

³Department of Ophthalmology, University Hospital Basel, Basel, Switzerland.

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