

# Clinical Outcomes of Preserflo MicroShunt versus Trabeculectomy: A Retrospective 6-Month Study

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## SUMMARY

**Objective:** To characterize and compare the efficacy and safety of trabeculectomy and Preserflo microshunt (PMS) implantation in patients with open-angle glaucoma.

**Material and Methods:** This retrospective 6-month study included 100 eyes (100 patients). The 100 patients were divided into two groups of 50 patients, who were randomly assigned to either trabeculectomy or PMS implantation with mmC (0.4 mg/ml) applied using saturated sponges. The patients attended follow-up checks at 1, 8, 30, and 90 days postoperatively and at 6 months postoperatively. Endothelial cells were assessed at 3 and 6 months respectively. The main observed parameters were intraocular pressure (IOP), best corrected visual acuity (BCVA), anterior chamber depth (ACD), corneal hysteresis (CH), corneal endothelial cell density (CECD), coefficient of variation (CV), and antiglaucoma treatment.

**Results:** In patients after trabeculectomy and after PMS implantation a comparable reduction in mean IOP values of 40.2% and 45.8% respectively was recorded for both surgical approaches in comparison with the preoperative mean IOP values. In all the studied patients, regardless of the type of surgical procedure, a significant reduction of CECD values was recorded 6 months after surgery. However, PMS implantation led to a greater reduction in antiglaucoma treatment postoperatively compared to trabeculectomy. Qualified success was almost identical in the case of both operations throughout the entire course, complete success was higher in favor of PMS at the beginning of the observation, but their values converged or met from approximately day 90 to month 6.

**Conclusion:** The performed clinical evaluation of the efficacy and safety of PMS implantation compared to the classical surgical approach using trabeculectomy showed positive results related primarily to the reduction of postoperative complications, while maintaining the effectiveness of the surgical procedure. However, further clinical studies with a longer follow-up period are needed in order to provide long-term evidence of clinical efficacy.

**Key words:** glaucoma, trabeculectomy, Preserflo MicroShunt, antiglaucoma drugs

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## INTRODUCTION

Glaucoma is one of the most commonly occurring pathologies leading to blindness [1]. Untreated or insufficiently treated glaucoma represents a society-wide problem, which leads to invalidity of the patient [2]. As a result, it is essential to place a large degree of emphasis not only on the correct treatment but also on the early detection of glaucoma. Surgical solution in combination with local and if applicable also general antiglaucoma therapy can avert functional and structural changes in the visual field and on the optic nerve.

The main aim of antiglaucoma therapy is to reduce and control intraocular pressure (IOP) for the purpose of preventing the onset or worsening of damage to the optic nerve and blind spots in the visual field. Trabeculectomy as the chief representative of incisional glaucoma surgery still remains the gold standard [3], and constitutes the optimum solution for certain groups of patients with glaucoma [4]. However, in combination with surgical techniques with drainage implants it involves a higher probability of the occurrence of complications. This has led to the development of new surgical methods, the aim of which was to achieve a similar success rate in the sense of reducing

IOP, with a lower risk of occurrence of peri- and postoperative complications. These procedures are referred to as minimally invasive glaucoma surgery (MIGS) or less invasive glaucoma surgery (LIGS), and utilize physiological drainage pathways of intraocular fluid [5]. However, in most cases they require more demanding and expensive technological equipment and more time-consuming training of personnel in comparison with trabeculectomy, which is financially cost-effective and relatively undemanding with regard to surgical equipment [6], even if sometimes far more difficult in terms of accurate realization, and requires experience on the part of the surgeon.

The fundamental principle of MIGS procedures is an interminimally traumatizing micro-incision access via a very small surgical wound, which is sparing on the conjunctiva and sclera. In recent years a broad range of MIGS implants have been developed, in which the new category of minimally invasive bleb surgery (MIBS) has been established [6]. One such MIBS device is the PreserFlo MicroShunt (PMS), which is produced from thermoplastic and elastomer biomaterial (poly[styrene-block-isobutylene-block-styrene]) [7]. PMS is approved and certified in Europe, but has not yet been approved by the US Food and Drug Administration.

PMS is an ab-externo subconjunctival implant which can be used as a substitute for trabeculectomy in open-angle glaucoma. The shunt has a length of 8.5 mm and there's a rib on its body. It is implanted 4.5 mm from the proximal tip of the bevel of the MicroShunt and has a lumen of 70  $\mu\text{m}$ . It is produced from block copolymer styrene and isobutylene. It is flexible and highly biocompatible. PMS offers a new approach to glaucoma filtration surgery through a combination of a minimally invasive device with marked reduction of IOP, and requires careful dissection and placing of tissue.

A recently conducted meta-analysis compared PMS with trabeculectomy in more than 1800 patients with uncontrolled glaucoma [8]. The meta-analysis demonstrated that trabeculectomy is more effective for patients with uncontrolled glaucoma up to 2 years, especially if lower target values of IOP are under consideration. Furthermore, the analysis states a higher risk of re-intervention in the case of PMS. On the other hand, another recent meta-analysis [9] demonstrated that PMS results in a lower rate of re-intervention. With reference to this discrepancy between the performed meta-analyses it is necessary to conduct further comparative clinical trials. For this reason the aim of the presented retrospective 6-month clinical trial was to characterize the efficacy and safety of two different filtration operation procedures: trabeculectomy and implantation of PMS with the use of mitomycin C (MMC) applied with the aid of a sponge.

## MATERIAL AND METHODS

### Recruitment of patients

The surgical procedures were realized at the Eye Clinic of SZU and UNB in Bratislava on a cohort of 100 patients (100 eyes). Recruitment and monitoring of patients indi-

cated for a surgical procedure with trabeculectomy took place from January 2020 to May 2022, and of patients with an implanted PreserFlo MicroShunt from June 2022 to December 2023 at the Eye Clinic of SZU and UNB in Bratislava. The monitoring was in accordance with the principles of the Helsinki Declaration, the patients were properly instructed and signed an informed consent form before undergoing surgery. We selected the patients according to the following inclusion criteria: open-angle glaucoma, uncontrolled IOP (more than 21 mmHg), deterioration of the visual field and/or structural changes on the optic nerve papilla, no previous antiglaucoma surgical procedure, age of over 20 years and no allergy to MMC.

Patients who had undergone a previous antiglaucoma procedure or had been diagnosed with chronic or recurrent uveitis, pathological myopia or neovascularization of the iris were excluded from the study. The exclusion criteria also covered unwillingness or inability to consent to the procedure. We always included only one eye of the individual patients in the study. The patients had open-angle glaucoma, either of primary or secondary type (pseudoxfoliative and pigmentary glaucoma).

The total 100 patients were divided into two groups of 50, who underwent either trabeculectomy or PMS implantation. Because trabeculectomy represents a traditional and established surgical procedure, the first 50 eyes underwent trabeculectomy with MMC (0.4 mg/ml) applied by means of saturated sponges. The remaining 50 eyes underwent implantation of a PMS with MMC (0.4 mg/ml) applied by means of saturated sponges.

All the included patients were of Caucasian ethnicity. The demographic characteristics, the operated eye and the type of glaucoma in the patients from the individual groups are presented in Table 1.

### Preoperative examination

All the patients included in the study underwent a complete eye examination, including measurement of IOP with the aid of a Goldmann applanation tonometer (Keeler Ltd, Windsor, UK) and corneal hysteresis with the aid of the instrument Ocular Response Analyzer (ORA, Reichert Inc., NZ, USA). This was followed by an examination of best corrected visual acuity (BCVA) with the aid of ETDRS optotypes, measurement of anterior chamber depth (ACD) with the aid of Casia2 (Tomey, Germany), the number and coefficient of variability of the endothelial cells (CECD and CV) with the aid of the noncontact specular microscope Perseus (CSO, Italy). Measurement of IOP and corneal hysteresis (CH) was realized before the administration of local treatment and always at a time from 08:00 to 11:00 in order to exclude the influence of diurnal fluctuation of IOP. The number of antiglaucoma drugs the patients were using was also recorded.

Important parameters for evaluating the risk of loss of endothelial cells in antiglaucoma operations using an implant are CECD and CV, the values of which it is essential to monitor over time in order to avert the risk of endothelial decompensation. The values of these parameters are calcu-

**Table 1.** Demographic characteristics, operated eye and glaucoma type in patients according to classification into individual therapeutic groups

Demographics	Trabeculectomy	PMS
<b>Age (year)</b> mean $\pm$ SD min – max	56.1 $\pm$ 14.2 28–83	55.9 $\pm$ 17.6 22–1
<b>Gender</b> Male Female	24 (48 %) 26 (52 %)	25 (50 %) 25 (50 %)
<b>Eye</b> Right Left	25 (50 %) 25 (50 %)	27 (54 %) 23 (46 %)
<b>Glaucoma type</b> PGOU PEXG PIGM	26 (52 %) 13 (26 %) 11 (22 %)	35 (70 %) 7 (14 %) 8 (16 %)

PGOU – primary open-angle glaucoma, PEXG – pseudoexfoliation glaucoma, PIGM – pigmentary glaucoma, SD – standard deviation

lated automatically with the aid of specific software, which enables imaging of the endothelial layer of the cornea with precise specification of the shape and size of the endothelial cells. In the comparative analysis it is possible to compare the condition of the endothelial layer of the cornea of the patient after a time interval. The times set within our monitoring were at 1, 3 and 6 months after surgery.

## SURGICAL PROCEDURE

### Trabeculectomy

During the surgical procedure we used general or local paravulbar anesthesia with the aid of 2 ml 4% supracain, which is characterized by the rapid onset of its effect, with a duration of approximately 45 minutes from application. Anesthesia was applied in the superior nasal quadrant of the orbit in order to preserve the motility of the eyeball in a downward direction, and we did not need to use a tractional suture for rotation of the eyeball in a downward direction and to facilitate access to the operating field.

All the surgical procedures were performed by a single surgeon (NM). An isotonic physiological solution was used to moisten the ocular surface during the procedure, applied into an injection syringe with a blunt cannula).

After preparation and masking of the eye, limbal conjunctival peritomy was performed in the superior quadrant, followed by blunt dissection of the Tenon's capsule. In order to prevent potential hemorrhage and ensure hemostasis during the surgical procedure, the episcleral veins were coagulated with the aid of bipolar diathermy. Shallow incisions were made in order to mark the corneoscleral lamella, bordering three sides of a 5 mm square with loose ends continuing radially from the limbus. MMC (0.4 mg/ml) was applied to the bordered area by means of saturated sponges for a period of 2 minutes, which was followed by flushing with a stream of Ringer's solution. A crescent knife was used to prepare the corneoscleral lamella with a thickness of 2/3 of the sclera, followed by excision of part

of the trabecular meshwork and Schlemm's canal, thereby creating a trabecular window beneath the scleral lamella. We penetrated into the anterior chamber beneath the scleral lamella with the aid of a 30° knife.

Peripheral iridectomy was realized with the aid of Vannas scissors. This was followed by suturing of the scleral lamella with two 10-0 individual nylon sutures on the peripheral part of the square of the created lamella. The conjunctiva was sutured with a 10-0 continuous nylon suture in the direction of the limbus in order to ensure that the wound was hermetically sealed, which was confirmed at the end of the procedure by checking the tightness of the closure of the surgical wound.

### Implantation of Preserflo MicroShunt

Drainage surgery with the aid of a Preserflo implant was introduced into practice in an endeavor to develop a surgical procedure that would be safer than trabeculectomy and would at the same time achieve a similar hypotonizing effect.

After standard preparation of the operating field, the conjunctiva was dissected by the limbus, and a sufficiently wide and deep space was created by blunt dissection for the subsequent place of implantation. Hemostasis was implemented according to the standard procedures.

The ideal position for implantation is in the superior temporal or superior nasal quadrant. In order to prevent scarring, sponges with MMC (0.4 mg/ml) were applied to the scleral bed for 2 minutes behind the planned place for insertion of the implant. After removal of the sponges it was essential to rinse the area in question, as well as the surrounding tissues with a larger quantity of balanced saline solution. The place of planned incision was designated using a 3 mm marker at a distance of 3 mm behind the limbus, after which a shallow 2 mm scleral tunnel was created with the use of a 1 mm curved knife, parallel to the sclera without entry into the anterior chamber. Entry into the anterior chamber was created with the aid of a 25G curved needle, in which the direction of entry was changed upon entry to the anterior chamber on the level of the trabecular meshwork, in a parallel direction with the iris. The end of the needle was clearly visible in the anterior chamber. The implant was inserted with the aid of surgical forceps with an upward opening, with wings immersed in the scleral tunnel and the lumen visible in the anterior chamber. The implant was slid through the newly created channel in the direction of the anterior chamber, making sure that the proximal tip was kept in a sloping position. The effectiveness of filtration was checked by applying slight pressure to the cornea. If filtration is not confirmed it is necessary to rinse the implant with a cannula. At our center this is realized with the aid of application of the intracameral antibiotic cefuroxime in a dose of 0.1 ml into the anterior chamber. If the position of the implant is correct, i.e. 2–3 mm of the proximal tip of the implant is located in the central part of the depth of the anterior chamber, without touching the endothelium or iris, without obstruction, drainage of the chamber fluid must be verified. At the end of

the procedure the conjunctiva was sutured using a 10-0 continuous nylon suture, in which the distal lumen of the implant was loosely located in the sub-Tenon's space parallel to the sclera, with limitation of potential obstruction of the distal end of the implant. The Tenon's fascia could also be sutured separately. The tightness of the surgical wound was then checked. After suturing of the wound a filtration cushion began to form above the implant.

### Application of MMC

Application of MMC with the aid of a sponge represents the standard and most commonly used method of applying MMC. In the cohort of patients in this study, diluted MMC in a concentration of 0.4 mg/ml on a sponge with an exposure time of 2 minutes was applied perioperatively, with subsequent flushing with physiological solution in a quantity of at least 20 ml. In the case of application of MMC in trabeculectomy, the sponge was applied directly to the place of the future scleral lamella before it was created. By contrast, in the case of implantation of a Preserflo MicroShunt the sponge with MMC was applied to the Sub-Tenon's space in the place of the created pocket behind the planned implantation of the Preserflo MicroShunt.

### Postoperative management of patient

All the patients were administered the local antibiotic 0.5% levofloxacin and the local corticosteroid 1% prednisolone acetate in a frequency of 5x per day postoperatively. The patients were monitored at 1, 8, 30 and 90 days after surgery, and at 6 months after surgery. The endothelial cells were assessed at 3 and 6 months respectively.

Within the framework of evaluating the success of the surgical solution, "complete success" was also monitored, in which postoperative IOP was 21 mmHg or less, with a reduction of its value by at least 20% as against its original value without the use of any antiglaucoma therapy and without the need for further antiglaucoma surgery. "Qualified success" was defined similarly to complete success, but without the need for an increase of antiglaucoma therapy in comparison with the preoperative period, and without the need for further antiglaucoma surgery. "Complete failure" was defined as a condition in which further antiglaucoma surgery (with the exception of revision procedures) was required.

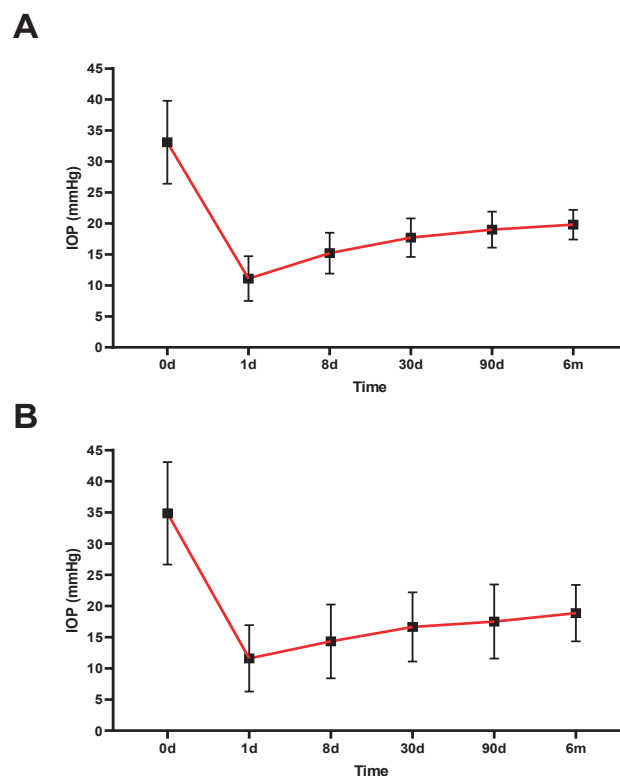
### Statistical analysis

The statistical analysis was conducted in the program language Python, and visualization of the statistical results with the aid of the program Microsoft Excel and GraphPad Prism. A Shapiro-Wilk normality test was used to determine the distribution of data. A t-test was used for normally distributed data, and a Wilcoxon paired test for data without normal distribution. In the evaluation of data a P value lower than 0.05 was considered statistically significant. A Kaplan-Meier estimator was used to evaluate the success of the operations. Fisher z-transformation was used for evaluation of the tests for the correlation coefficient, as well as a method based on t-transformation on the precondition that the correlation is equal to zero.

## RESULTS

Trabeculectomy with application of the antimetabolite MMC with the aid of a sponge ranks among the classic and most frequently performed surgical procedures for patients with glaucoma. The mean preoperative value of IOP in the cohort of 50 patients was  $33.1 \pm 6.7$  mmHg, in which the values were within a range from 24 to 51 mmHg. On the first postoperative day the mean IOP value was  $11.1 \pm 3.6$  mmHg, on the 8th day  $15.2 \pm 3.3$ , on the 90th day  $19.0 \pm 3.2$  and after 6 months  $19.8 \pm 2.4$  mmHg (reduction by 40 %) (Graph 1A). Depending on the individual types of glaucoma, the greatest reduction in IOP values was recorded in PEX glaucoma, followed by POAG and pigmentary glaucoma, but without statistically significant changes.

As with trabeculectomy, the usual method of MMC application is with the aid of a sponge. In our cohort of patients the mean preoperative value of IOP was  $34.9 \pm 8.2$  mmHg, on the first day after surgery it was  $11.6 \pm 5.3$  mmHg and after 30 days the mean IOP value was  $16.6 \pm 5.6$  mmHg. Three months after surgery the mean IOP value was  $17.5 \pm 5.9$  and 6 months after surgery the mean IOP value was  $18.9 \pm 4.5$  mmHg. The reduction of mean postoperative IOP values was statistically significant in comparison with the mean preoperative value of IOP (Graph 1B).



**Graph 1.** Graphical representation of the change in mean intraocular pressure values in patients who underwent (A) trabeculectomy or (B) implantation of the Preserflo microshunt with sponge-applied MMC. Data are expressed as mean IOP value with standard deviation

IOP – intraocular pressure, MMC – mitomycin C

Successful control of IOP was defined as attaining IOP of  $\leq 21$  mmHg without antiglaucoma drugs (complete success) or with a reduction of the number of antiglaucoma drugs (qualified success). The degree of success was determined with the aid of a Kaplan-Meier survival curve, both in patients following trabeculectomy (Graph 2A) and after implantation of a Preserflo MicroShunt (Graph 2B).

In addition to determination of IOP values, in patients after trabeculectomy selected parameters were also monitored at 6 months after the surgical procedure, which are presented in Table 2.

The number of antiglaucoma drugs used by the patients was reduced from  $3.3 \pm 0.7$  to  $1.2 \pm 0.8$  at 6 months after surgery. The mean values of the observed parameter of BCVA did not show statistically significant differences, changing from a mean preoperative value of 0.8 to a value of 0.6 postoperatively. The value of CH in the observed cohort of patients increased statistically significantly from a mean value of  $8.5 \pm 1.4$  mmHg to  $9.6 \pm 1.0$  mmHg at 6 months after surgery, which represents an increase of 10.8 %. The mean value of ACD was statistically significantly reduced from a value of  $3.4 \pm 0.4$  mm to a value of  $3.2 \pm 0.4$  mm, which represents a reduction of 0.10 mm.

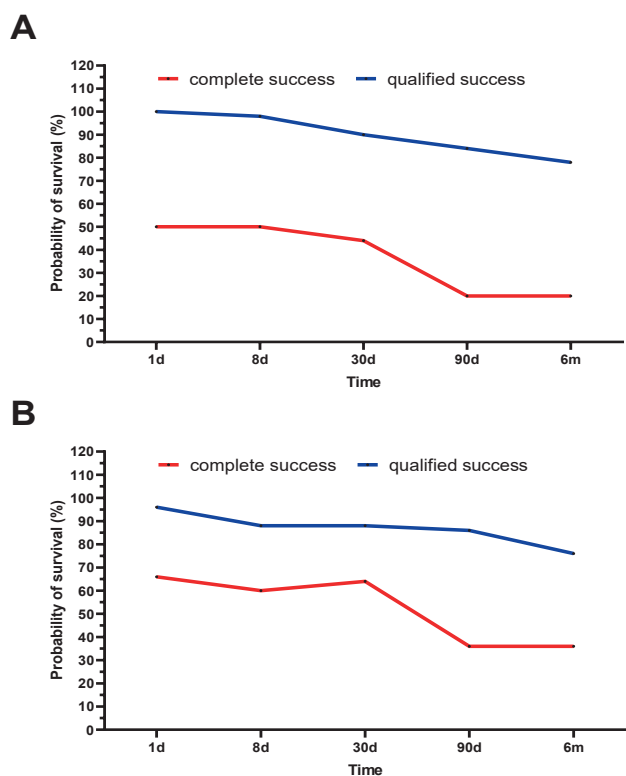
In the patients who had undergone implantation with a Preserflo MicroShunt, the increase of CH values (by approximately 25%) and the reduction of antiglaucoma therapy were

**Table 2.** Selected characteristics in patients preoperatively and after trabeculectomy with application of MMC using a sponge 6 months after surgery

Parameter	Time period		p
	Before surgery (t = 0)	Post-operative (t = 6 m)	
<b>IOP (mmHg)</b>			
Mean $\pm$ SD	$33.1 \pm 6.7$	$19.8 \pm 2.4$	$< 0.001^a$
Median (range)	31.5 (24–51)	20 (16–26)	
<b>Antiglaucoma treatment</b>			
Mean $\pm$ SD	$3.3 \pm 0.7$	$1.2 \pm 0.8$	$< 0.001^a$
Median (range)	3 (–4)	1 (0–3)	
<b>BCVA</b>			
Mean $\pm$ SD	$0.8 \pm 0.2$	$0.7 \pm 0.3$	0.27 <sup>a</sup>
Median (range)	0.8 (0.1–1.0)	0.8 (0.05–1.0)	
<b>CH (mmHg)</b>			
Mean $\pm$ SD	$8.5 \pm 1.4$	$9.6 \pm 1.0$	$< 0.001^b$
Median (range)	8.9 (4.2–11.6)	9.6 (7.3–1.2)	
<b>ACD (mm)</b>			
Mean $\pm$ SD	$3.4 \pm 0.4$	$3.2 \pm 0.4$	$< 0.001^b$
Median (range)	3.4 (2.4–4.1)	3.2 (2.3–3.9)	

MMC – mitomycin C, IOP – intraocular pressure, BCVA – best corrected visual acuity, ACD – anterior chamber depth, CH – corneal hysteresis, SD – standard deviation

<sup>a</sup> Wilcoxon's single-rank test, <sup>b</sup> paired t-test



**Graph 2.** Kaplan-Meier survival analysis of complete or qualified success of IOP control in patients after trabeculectomy with sponge-applied MMC in patients after (A) trabeculectomy or (B) implantation of the Preserflo microshunt

IOP – intraocular pressure, MMC – mitomycin C

statistically significant postoperatively (Table 3). In the case of antiglaucoma therapy the mean preoperative values of  $3.6 \pm 0.6$  were reduced to  $0.9 \pm 0.9$  at 3 and 6 months after surgery. Postoperatively as many as 66% of patients did not require and local antiglaucoma therapy, and in 38% of patients no therapy was required at 6 months after surgery. No significant change in the values of BCVA occurred postoperatively in comparison with the preoperative condition, in which the mean preoperative values were 0.66 and the postoperative values 0.72. No significant change in anterior chamber depth took place postoperatively (Table 3).

As regards types of open-angle glaucoma, the greatest effectiveness was achieved in the case of pigmentary glaucoma (reduction by 58%), followed by POAG (reduction by 45%) and PEX glaucoma (reduction by 33%).

Like all surgical procedures intervening with the anterior segment, trabeculectomy has the potential to cause damage to the cornea, and is associated with an acceleration of a loss of corneal endothelial cell density (CECD). In all patients in the cohort we recorded a significant decrease in values of CECD, from an original value of  $2338.1 \pm 554$  to  $2185.4 \pm 546.8$  (reduction by 6.54%) at 6 months after the surgical procedure. The greatest decrease of the CECD value at 6 months after surgery was recorded in the case of PEX glaucoma (by 8.4%), followed by POAG (by 6.3%) and PIGM glaucoma (by 5.4%). There was a statistically significant increase in the coefficient of variability of the endothelial cells (CV) from  $25.7 \pm 3.3$  to  $26.6 \pm 3.5$  at 6 months after surgery (Table 4).

The decrease of endothelial cells postoperatively in pa-

**Table 3.** Selected characteristics in patients preoperatively and after implantation of Preserflo microshunt with application of MMC using a sponge 6 months after surgery

Parameter	Time period		p
	Before surgery (t = 0)	Post-operative (t = 6 m)	
<b>IOT (mmHg)</b> Mean ±SD Median (range)	34.9 ±8.1 33.5 (24–60)	18.9 ±4.5 18 (12–33)	< 0.001 <sup>b</sup>
<b>Antiglaucoma treatment</b> Mean ±SD Median (range)	3.6 ±0.6 4 (2–4)	0.9 ±0.9 1 (0–4)	< 0.001 <sup>a</sup>
<b>BCVA</b> Mean ±SD Median (range)	0.7 ±0.2 0.6 (0.1–1.0)	0.7 ±0.2 0.8 (0.05–1.0)	0.009 <sup>a</sup>
<b>CH (mmHg)</b> Mean ±SD Median (range)	7.2 ±1.2 7.4 (4.3–9.7)	9.1 ±1.0 9.1 (6.9–10.7)	< 0.001 <sup>b</sup>
<b>ACD (mm)</b> Mean ±SD Median (range)	3.2 ±0.4 3.1 (2.5–4.1)	3.2 ±0.4 3.1 (2.5–4.1)	0.062 <sup>a</sup>

MMC – mitomycin C, IOP – intraocular pressure, BCVA – best corrected visual acuity, ACD – anterior chamber depth, CH – corneal hysteresis, SD – standard deviation

<sup>a</sup> Wilcoxon's single-rank test, <sup>b</sup> paired t-test

tients following implantation of a Preserflo MicroShunt was significant in all types of glaucoma, at 6 months after surgery the number had declined by approximately 6.8% in primary open-angle glaucoma, by 9.6% in pseudoexfoliative glaucoma and 8.7% in pigmentary glaucoma. We recorded the greatest decrease in pseudoexfoliative glaucoma (Table 5).

Of postoperative complications in our cohort of patients, we recorded postoperative hypotension in 24 patients (48%), shallowing of the anterior chamber by at least 1 mm in 15 patients (30%), choroidal ablation in 17 patients (34%) and hyphema in 13 patients (26%). Of latter postoperative complications (after the first month) we recorded reopening of the surgical wound in 4 patients (8%) and failure of filtration in 4 patients (8%). Graph 3A.

The complications following implantation of a Preserflo MicroShunt are presented in Graph 3B. Hypotension occurred in 12% of patients, hyphema in 10%, and reoperation was required in 8% of patients (4 patients). In two of those 4 patients revision was performed with MMC, after which filtration was restored, in one patients cyclo-

**Table 4.** Comparison of preoperative and postoperative values of CECD and CV in patients after trabeculectomy with application of MMC using a sponge with respect to glaucoma type

Parameter	Time period		p
	Before surgery (t = 0)	Post-operative (t = 6 m)	
<b>CECD (cells/mm<sup>2</sup>)</b> <b>CV (%)</b>	2338.1 ±554.0 25.7 ±3.3	2185.4 ±546.8 26.6 ±3.6	< 0.001 <sup>a</sup> < 0.001 <sup>b</sup>
<b>Typ glaukómu</b>			
<b>PGOU (n = 26)</b> <b>CECD (cells/mm<sup>2</sup>)</b> <b>CV (%)</b>	2316.5 ±509.5 26.0 ±2.8	2170.2 ±509.4 26.8 ±3.1	< 0.001 <sup>a</sup> < 0.001 <sup>b</sup>
<b>PEXG (n = 13)</b> <b>CECD (cells/mm<sup>2</sup>)</b> <b>CV (%)</b>	1983.8 ±270.9 27.7 ±2.9	1817.2 ±225.9 28.5 ±3.2	< 0.001 <sup>a</sup> 0.001 <sup>b</sup>
<b>PIGM (n = 11)</b> <b>CECD (cells/mm<sup>2</sup>)</b> <b>CV (%)</b>	2807.8 ±544.7 22.8 ±2.6	2656.4 ±550.1 23.7 ±2.9	< 0.001 <sup>a</sup> 0.003 <sup>b</sup>

MMC – mitomycin C, CECD – corneal endothelial cell density, CV – coefficient of variation, PGOU – primary open-angle glaucoma, PEXG – pseudoexfoliation glaucoma, PIGM – pigmentary glaucoma, SD – standard deviation

<sup>a</sup> paired t-test, <sup>b</sup> Wilcoxon's single-rank test

**Table 5.** Comparison of preoperative and postoperative CECD and CV values in patients after implantation of Preserflo microshunt with MMC sponge application with regard to glaucoma type

Parameter	Time period		p
	Before surgery (t = 0)	Post-operative (t = 6 m)	
<b>CECD (cells/mm<sup>2</sup>)</b> <b>CV (%)</b>	2665.4 ±470.5 25.8 ±3.1	2468.4 ±467.5 26.8 ±3.4	< 0.001 <sup>b</sup> < 0.001 <sup>a</sup>
<b>Typ glaukómu</b>			
<b>PGOU (n = 35)</b> <b>CECD (cells/mm<sup>2</sup>)</b> <b>CV (%)</b>	2749.2 ±453.3 25.6 ±3.1	2563.6 ±448.7 26.7 ±3.3	< 0.001 <sup>a</sup> < 0.001 <sup>a</sup>
<b>PEXG (n = 7)</b> <b>PEB (cells/mm<sup>2</sup>)</b> <b>CV (%)</b>	2087.7 ±257.6 25.6 ±3.1	1886.3 ±230.9 26.4 ±3.2	< 0.001 <sup>b</sup> 0.017 <sup>b</sup>
<b>PIGM (n = 8)</b> <b>CECD (cells/mm<sup>2</sup>)</b> <b>CV (%)</b>	2804.1 ±238.9 27 ±2.7	2561.4 ±257.6 27.9 ±3.5	< 0.001 <sup>b</sup> 0.23 <sup>b</sup>

MMC – mitomycin C, CECD – corneal endothelial cell density, CV – coefficient of variation, PGOU – primary open-angle glaucoma, PEXG – pseudoexfoliation glaucoma, PIGM – pigmentary glaucoma, SD – standard deviation

<sup>a</sup> Wilcoxon's single-rank test, <sup>b</sup> paired t-test

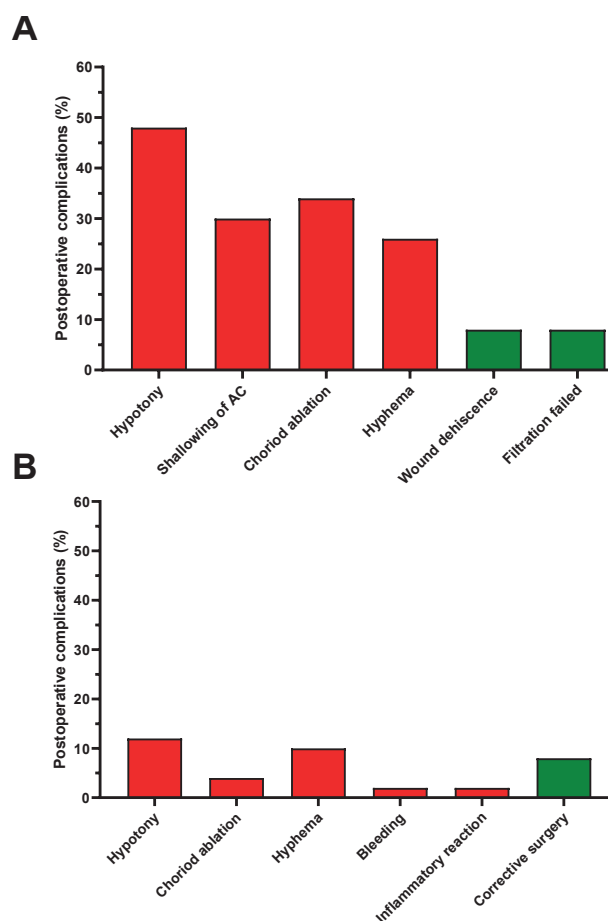
photocoagulation was required, and in the last patient a second implantation of a Preserflo MicroShunt was required. Pronounced hemorrhage occurred in a patient with a hematological disorder, in which the hemorrhage was successfully managed during hospitalization.

## DISCUSSION

The main aim of antiglaucoma therapy is to reduce and control IOP for the purpose of preventing the onset or worsening of damage to the optic nerve and blind spots in the visual field. Trabeculectomy as the chief representative of incisional glaucoma surgery still remains the gold standard [3], and constitutes the optimum solution for certain groups of patients with glaucoma [4]. However, in combination with surgical techniques with drainage implants it involves a higher probability of the occurrence of complications. This has led to the development of new surgical methods, the aim of which was a similar success rate in the sense of reducing IOP, with a lower risk of occurrence of peri- and postoperative complications. These procedures are referred to as minimally invasive glaucoma surgery (MIGS) or less invasive glaucoma surgery (LIGS), and utilize physiological drainage pathways of intraocular fluid [5]. However, in most cases they require more demanding and expensive technological equipment and more time-consuming training of personnel in comparison with trabeculectomy, which is financially cost-effective and relatively undemanding with regard to surgical equipment [6], even if sometimes far more difficult in terms of accurate realization, and requires experience on the part of the surgeon.

Despite this we must select the type of operation individually with regard to the patient and his/her target IOP, the surface of the eye and the condition of the conjunctiva. In 1968 Cairns introduced trabeculectomy, which has been successfully used since that time [10]. The principle is to create a small fistula on the corneoscleral interface, which is covered by a scleral lamella of partial depth. The scleral lamella creates resistance to the drainage of intraocular fluid. The intraocular fluid is drained with the aid of a fistula into the sub-Tenon's space, by which a filtration cushion is formed. The fluid is further drained into the circulation of the episcleral and conjunctival vessels. The scleral lamella creates resistance, and thus has the capacity to regulate the drainage of intraocular fluid through the aid of the adjustable sutures located on it [11]. The way in which the subconjunctival scar is formed in the place of the filtration cushion and how the wound heals shall influence the success of trabeculectomy [12].

An important and serious complication of trabeculectomy is its failure. In order to reduce the risk of failure and increase the success rate, antifibrotic agents are used such as MMC and 5-fluorouracil (5-FU) [13–15]. Due to its anti-proliferative effect, MMC prevents fibrosis of the filtration cushion and thereby reduces the risk of failure of filtration [16]. If MMC is used, reduction of IOP is observed even 5 years after surgery [17]. However, the risks of its use are numerous, involving the more frequent occurrence of



**Graph 3.** Incidence of postoperative complications in patients after (A) trabeculectomy or (B) implantation of the Preserflo microshunt with sponge-applied MMC. Early complications (within one month) are marked in red, late complications (more than one month) in green

MMC – mitomycin C

hyphema, avascularity of the filtration cushion, postoperative hypotonia, choroidal ablation, shallowing of the anterior chamber, failure of filtration or hyperfiltration of the surgical wound, or endophthalmitis may occur [18]. With regard to these risks, there is still no unequivocal consensus regarding the method, the concentrations and the length of exposure it is suitable to apply when using this antifibrotic agent perioperatively. The conclusions of individual authors differ with regard to the success and safety of application [19]. The conclusions of individual clinical trials differ with respect to the concentration of MMC in surgical procedures, and it is not clearly demonstrated as to whether a significant difference exists in the success and safety of operation in the case of a concentration of MMC 0.2 mg/ml and 0.4 mg/ml [19]. Kitazawa et al. in their study compared concentrations of MMC 0.2 mg/ml and 0.02 mg/ml with 5-minute exposure, in which the authors indicate that the optimal concentration could be somewhere within the range of both tested concentrations [20]. Some authors declare a higher success rate and lower IOP in the case of use of higher concentrations of MMC [19,21].

The most common method of using MMC during trabeculectomy is with the aid of a saturated sponge applied directly to the exposed sclera. In Great Britain, as well as in other countries worldwide, this method is preferred by up to 94% of surgeons [22]. The procedure also depends on the size and shape of the sponge, in which in the case of large and irregular sponges and their inaccurate placing there is a greater risk of the onset of complications such as hypotonia, infiltration and inflammation of the filtration cushion, or scarring caused by exposure to MMC [23]. A larger area of action of the sponge may cause traumatization of the conjunctiva, increasing the difficulty of any further operation in the same location [24]. Zhang et al. presented a method with the use of a sponge measuring 3.5 x 10 mm, which they placed vertically and posteriorly with the long side into the conjunctival bed beneath the scleral lamella, without coming into contact with the corneal incision [23]. This application could be minimally traumatizing for the conjunctiva, and reduces complications in connection with the filtration cushion, because it is directed more posteriorly and is more diffuse. However, the authors leave the concentration of MMC and the exposure time to the discretion of the operating surgeon.

Cases have been described in the professional literature of loss of the sponge and its leaving in the operating field, damage to the conjunctiva and the impossibility of treating a large surface of the sclera [25].

In our study we compared cohorts of patients with open-angle glaucoma, within the framework of which they were operated on using different surgical techniques, namely traditional filtration operation – trabeculectomy – and a less invasive technique forming a cushion – implantation of a Preserflo MicroShunt. In both surgical procedures the antiproliferative agent MMC was used, applied with the aid of a sponge. The patients were diagnosed with open-angle glaucoma, either POAG, PEX or pigmentary glaucoma.

Regardless of the type of surgical procedure, all patients recorded a pronounced reduction of IOP values postoperatively.

The type of surgical procedure – implantation of a Preserflo MicroShunt is suitable for use in primary open-angle glaucoma [26], and similar results were demonstrated also in the case of PEX glaucoma [27]. Furthermore, its effectiveness is being examined in other secondary types of glaucoma such as PEX and pigmentary glaucoma, or in refractory uveitic glaucoma, where it has also demonstrated a beneficial effect [28], though not with the same success rate as in POAG, PEX and pigmentary glaucoma. In secondary types of glaucoma there is a higher risk of necessary surgical revisions following its implantation [29]. An important factor is the condition of the conjunctiva before surgery, which subsequently influences the course of healing and the functionality of the implant. Storp et al. observed the success rate of the microshunt in various types of glaucoma, in which the lowest was observed in secondary types of glaucoma, where there was also the highest number of necessary revision operations [29]. For these reasons, we have so far included only three

types of open-angle glaucoma in our observed cohort – primary open-angle glaucoma, and of secondary types of glaucoma PEX and pigmentary glaucoma.

Preserflo MicroShunt is an ab-externo subconjunctival device which can be used as a substitute for trabeculectomy in open-angle glaucoma. It is produced from block copolymer styrene and isobutylene, and it is flexible and highly biocompatible. In the past this material has been used in heart stents. Restriction of flow is based on the Hagen-Poiseuille equation. According to this, at a flow speed of 2.5 µl/min the shunt should be capable of maintaining pressure at around 6.5 mmHg. The shunt in question demonstrates good postoperative hypotensive efficacy and safety. The ab-externo approach enables control of hemostasis, precise location and precise verification of flow [30].

Gubser et al. (2023) in their recent study focused on a comparison of the medium-term effectiveness of the Preserflo MicroShunt with trabeculectomy in patients with primary open-angle glaucoma, with emphasis on changes of the functional and structural parameters [31]. The authors determined that the mean value of IOP and the number of pharmaceuticals used for reducing IOP could be reduced by the implantation of a Preserflo MicroShunt, with effectiveness comparable to trabeculectomy over the course of a 2-year observation period. This study also demonstrated that structural glaucomatous damage may continue while functional glaucomatous damage remains stable after glaucoma surgery. The implantation of a Preserflo MicroShunt demonstrated potential to stabilize both functional and structural glaucomatous damage.

A recently conducted multicentric cohort study demonstrated that a higher intraoperative concentration of MMC was associated with a lower risk of failure (0.4 mg/ml as against 0.2 mg/ml of MMC) [32].

Even though Preserflo MicroShunt is a device indicated for patients with early to advanced primary open-angle glaucoma resistant to pharmacotherapy, it may also play a role in the treatment of other types of glaucoma, and also in childhood [33].

Experiences with the implantation of a Preserflo MicroShunt at new clinical centers in London have demonstrated that Preserflo MicroShunt is a safe, clinically effective and cost-effective device. The shortening of the operating time, reduction of postoperative complications and number of follow-up visits means the use of Preserflo MicroShunt was advantageous for primary filtration surgery of primary open-angle glaucoma, as well as for cases of refractory glaucoma which had already undergone unsuccessful surgery [34].

Upon a comparison of patients following trabeculectomy and implantation of a Preserflo MicroShunt, a comparable reduction of mean IOP values was recorded in both methods, but there is a difference between the reduction of antiglaucoma therapy 6 months after surgery as against the number of antiglaucoma drugs taken preoperatively, and this difference is in favor of implantation of a Preserflo MicroShunt. Implantation of a Preserflo MicroShunt therefore led to a greater reduction of antiglaucoma therapy postoperatively. Qualified success was virtually identical in

both operations throughout the entire course, while complete success at the beginning of the observation period was higher in favor of Preserflo, though their values converged or met from approximately 90 days to 6 months.

According to a study conducted by the authors Pillunat et al., reduction of IOP was similar at 6 months after both types of operations, though in the case of trabeculectomy there was a significantly higher percentage of postoperative interventions [30]. Other studies state better results in the sense of IOP values and reduction of local therapy in the case of trabeculectomy one year after surgery, though they confirm significantly fewer complications in the case of implantation of a Preserflo MicroShunt [35]. As regards the incidence of complications, a significantly lower number of complications were recorded after implantation of a Preserflo MicroShunt in comparison with trabeculectomy also in our own study. Postoperative hypotension occurred after trabeculectomy in 48% of patients. There then followed shallowing of the anterior chamber by at least 1 mm in 30% of patients, choroidal ablation in 34% and hyphema in 26%. The groups of patients after implantation of a Preserflo MicroShunt had a significantly better safety profile, in the group of patients with MMC applied with the aid of a sponge hypotension was recorded in 12% of patients and hyphema in 10%. The lower risk of complications can be explained with reference to the less invasive surgical procedure, thanks to the implant the flow of intraocular fluid into the subconjunctival space is regulated, in contrast with trabeculectomy, where postoperative adjustment of the suture is frequently necessary in order to regulate filtration according to the individual requirements of the patient.

In both groups of our patients there was a significant postoperative loss of endothelial cells. Numerous studies document a loss of endothelial cells following trabeculectomy, both with and without the use of MMC [36–39], in which a higher risk of loss was recorded in the case of PEX and uveitic glaucoma [36]. A significant loss of endothelial cells was recorded also one year after implantation of a Preserflo MicroShunt [40]. On the other hand, other authors have not recorded a significant loss of endothelial cells 17 months after implantation of a Preserflo MicroShunt [41]. Baker et al. determined a comparable decrease of the number of endothelial cells both following implantation of a Preserflo MicroShunt and after trabeculectomy [35].

Reaction to healing and incipient fibrosis are primary determinants of final intraocular pressure. Conjunctival fibrosis determines the hydraulic conductivity of the conjunctiva, which controls the flow of fluid through the tissue. IOP between 10 and 14 mmHg is associated with minimal conjunctival fibrosis and a slower deterioration of the visual field [42]. Like all healing of wounds, healing of conjunctival wounds also involves a complex interplay between growth factors, cytokines, receptors and enzymes and cross-communication between various different types of cells. The early phase of healing of conjunctival wounds following glaucoma surgery entails a loss of plasmatic proteins (fibrinogen, plasminogen and fibronectin) and blood cells (thrombocytes, polymorphonuclear neutrophils

and red blood cells) from the damaged vasculature. Conversion of fibrinogen to fibrin has the consequence of the formation of fibrin coagulations and blood clotting. During the inflammatory phase, the combination of the formation of a fibrin coagulation and the released proteins leads to a migration and attraction of neutrophils, macrophages and lymphocytes to the site of the surgical procedure [43].

Reduction of inflammation is a standard paradigm in the prevention of scarring after surgery or injury, because chronic inflammation is associated with far larger fibrosis. A better understanding of the molecular and cellular mechanisms of wound healing processes and the method and mechanism of effect of modulating agents has led to the identification and modulation of potential therapeutic targets and more effective utilization of existing agents [44].

The role of antifibrotic agents such as 5-FU and MMC in traditional filtration surgery is well known, and their use has improved the success rate of trabeculectomy in attaining target IOP. However, the increasing success rate has been accompanied by an increase of complications in association with the formation of cysts. As a consequence of this, there is currently considerable interest in the application of a more targeted approach to the modulation of wound healing. A key role in the proliferative phase of healing of surgical wounds is played by angiogenesis stimulated especially by vascular endothelial growth factor (VEGF).

Multiple studies have evaluated the use of a human recombinant monoclonal antibody against VEGF as an alternative or supplement to MMC in trabeculectomy [45–49]. The methods of administration included local, subconjunctival, intracameral and intravitreal [50]. Many of these studies demonstrated a difference in the morphology of cushions in eye treated with anti-VEGF agents. Early postoperative results showed fewer vascular and more diffuse filtration cushions in comparison with MMC. However, it appears that this effect recedes and the long-term results show greater vascularity and higher IOP when they were used as separate substances in comparison with MMC [45,48].

A recently published meta-analysis of the effectiveness of anti-VEGF and MMC on healing of wounds after glaucoma surgery out of a total number of 369 published clinical trials analyzed 7 suitable studies [51]. The meta-analysis did not detect any significant differences in the effect of anti-VEGF and MMC on healing of wounds following trabeculectomy. On the other hand, another meta-analysis focused on a comparison of the effects of trabeculectomy alone or combined with intravitreal injections of anti-VEGF agents to treat neovascular glaucoma [52]. In comparison with trabeculectomy alone, trabeculectomy with anti-VEGF recorded a lower risk of postoperative complications. The reduction of IOP was significantly greater in the group with trabeculectomy with anti-VEGF augmentation than in the group with trabeculectomy alone from the first week after surgery. According to the results of this meta-analysis, the addition of an intravitreal injection of anti-VEGF agents to trabeculectomy can improve the short-term results of patients with neovascular glaucoma.

The degree of tissue damage and the reaction of the host with regard to the severity and duration of inflammation determines the scope of conjunctival scarring. The Moorfields Safer Surgery System is a modified surgical technique which aims to minimize and modulate the effects of antimetabolites [53]. The scope of conjunctival fibrosis following glaucoma filtration surgery shall differ among individuals, because it is influenced by risk factors such as existing inflammation, duration and type of treatment with eye drops and previous anamnesis of operation [54]. Other factors of fibrosis following GFS include the suturing material, growth factors derived from the chamber fluid, mechanical transduction from the flow of aqueous humor flow, signaling molecules released from the sites of accumulation of the extracellular matrix, trans-differentiation of myofibroblasts leading to further accumulation of the matrix [54]. After trabeculectomy the system of evaluating Moorfields pads [55] is a useful instrument in predicting the long-term result of IOP. The grading system evaluates inflammation and the effective application of antimetabolites.

Simple changes in surgical techniques and application of antimetabolite therapy have markedly improved the success rate and reduced the degree of complications in glaucoma surgery, for example minimizing tissue damage and application of an adapted dose of antifibrotic agent. Modulation of healing of conjunctival wounds continues to be the subject of interest because it is the key to attaining and maintaining optimal intraocular pressure (10–14 mmHg) following glaucoma filtration surgery, with

the aim of preventing the progression of glaucoma in connection with higher pressures. New methods of treatment are based on a better understanding of tissue-specific molecular, cellular and biomechanical processes. Innovative solutions that may directly and indirectly modulate inflammatory and fibrotic processes in the optimal timing, dosing and locality bring more favorable results. Combination of treatment or sequential treatment may be more effective than a single substance, especially in individuals with a high risk of scarring. Glaucoma is increasing exponentially with the rapidly ageing population worldwide, and a plan for management that is able to cover the scope of inquiry should incorporate surgical therapy as available and successful as cataract surgery.

## CONCLUSION

In patients following trabeculectomy and following implantation of a PMS, a statistically significant reduction of IOP and use of antiglaucoma therapy was recorded, with a lower incidence of complications following implantation of a PMS. It is therefore evident that upon application of a PMS there is a lower frequency of postoperative follow-up checks, lower consumption of medications, shortening of the operating time and also a lower number of complications and demand factor for their solution. This has a significant impact on recovery of sight and on the quality of life of patients, as well as the speed of their return to regular life.

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