E-PTFE (Gore-Tex®) implant with or without low-dosage mitomycin-C as an adjuvant in penetrating glaucoma surgery: 2 year randomized clinical trial

Salvatore Cillino,[1] Lucio Zeppa,[2] Francesco Di Pace,[1] Alessandra Casuccio,[1] Daniele Morreale,[1] Fabio Bocchetta[1] and Gaetano Lodato[1]

[1]Department of Clinical Neuroscience, Section of Ophthalmology, University of Palermo, Italy
[2]Ocular Surgery Unit, Public Hospital 'S. Giuseppe Moscati', Avellino, Italy

ABSTRACT.

Purpose: **To test the expanded polytetrafluoroethylene (ePTFE) as a new adjuvant in trabeculectomy.**

Methods: **Consecutive glaucoma surgical inpatients were observed at the Department of Ophthalmology of Palermo University. Sixty patients (60 eyes) were randomly assigned to undergo trabeculectomy (T), trabeculectomy with mitomycin-C (TMMC), with ePTFE (TG) or with mitomycin-C and ePTFE (TGMMC). Postoperative visits were scheduled at 24 hr, 7 days, 1, 3, 6, 12, 18 and 24 months. Complete success and qualified success were assessed at two target intraocular pressure (IOP) levels – ≤21 and ≤17 mmHg – by Kaplan–Meier curves.**

Results: **The postoperative IOP reduction was significant ($P < 0.01$) at the endpoint in all groups, with a mean IOP of 16.9 (±2.9), 16.2 (±2.7), 15.3 (±3.4) and 15.2 (±4.3) mmHg in T, TMMC, TG and TGMMC eyes, respectively. No intergroup difference was found at either IOP targets. The Kaplan–Meier curves relating to either the ≤21 mmHg or the ≤17 mmHg target IOP did not show significant intergroup differences for complete and qualified success rate. When ePTFE was used, a trend favouring the medium-term survival rate was noted. No adverse reaction to the ePTFE was present, and no membrane extrusion or conjuctival erosion were noted in any cases. Hypotony was significantly more frequent ($P = 0.035$) in groups without ePTFE. Moreover, the late MMC-related complications were more frequent when MMC was applied.**

Conclusion: **Expanded polytetrafluoroethylene implant in trabeculectomy is well tolerated and could act as a filtration modulating device. Therefore, it is useful in reducing early hypotony-related complications and contributes to attaining medium-term IOP control that is comparable to the low-dosage MMC.**

Key words: adjuvants – e-PTFE – glaucoma surgery – mitomycin-C – trabeculectomy

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Introduction

Progressive loss of efficacy after glaucoma surgery remains an unsolved problem.

Many adjunctive procedures, such as the use of antimetabolites, implants, bleb needling, suture lysis and amniotic membrane transplantation (Melamed et al.1990; Kitazawa et al. 1991; Skuta et al. 1992; Kolker et al. 1994; Smith et al. 1997; Meyer et al. 1997; Tezel et al. 1998; Fujishima et al. 1998; Membrey et al. 2000; Singh et al. 2000; Yue et al. 2003; Feyi-Waboso & Ejere 2004; Ambresin et al. 2002; Moreno-Lopez & Perez-Alvarez 2006), have been proposed to enhance and maintain the hypotensive effect of trabeculectomy or deep sclerectomy. Evidence-based data indicate that the use of mytomicin-C (MMC) during trabeculectomy has a significant positive effect on postoperative intraocular pressure (IOP) (Jampel et al. 2002; Wilkins et al. 2005). In our experience, MMC can be regarded as an enhancement of the deep sclerectomy IOP-lowering effect without evidence of antimetabolite-related complications (Cillino et al. 2005). On the other hand, MMC-augmented glaucoma surgery can be associated with a significantly higher frequency of late bleb leaks (Anand & Atherley 2005; Anand et al. 2006).

A detailed database search (Medline and PubMed) failed to show any report on the use of synthetic implant materials as adjuvants in penetrating glaucoma surgery (Jampel et al. 2002; Wilkins et al. 2005).

Since 1978, expanded polytetrafluoroethylene (ePTFE: Gore-Tex® or Zytex®) has been widely used in cardiac and gynaecological surgery and soft-tissue augmentation with minimal complications, being regarded as one of the most chemically inert and biocompatible materials known (Sakamoto et al. 1978; Meus et al. 1983; Monk et al. 1998; Giovanni et al. 1999). Expanded polytetrafluoroethylene is made up of a number of solid nodes inter-connected by a matrix of thin fibrils. The peculiarity of this non-reabsorbable material is microporosity, watertightness at low pressure, gas and water vapour permeability and the ability to minimize tissue attachment to the material in reconstructive procedures. The usefulness of ePTFE substitutes in providing a clear plane of dissection and minimizing adhesions has also been documented in both experimental investigations and clinical studies (Sterling 2002; Kawaguchi et al. 2003).

In particular, the PRECLUDE® pericardial ePTFE membrane, a pericardial substitute, allows control of adhesions between tissues and artificial surfaces by modulation of the size of interstices. The membrane thickness is 0.1 mm with a pore size of < 1 μm. This small pore size excludes tissue ingrowth, limiting attachment between the membrane and adjacent structures. The explanted PRECLUDE® ePTFE membranes that were examined histologically showed loosely adherent cells at the tissue–membrane interface and no evidence of collagen or cellular infiltration. PRECLUDE® pericardial membrane is a white, opaque material, but after implantation the material becomes wet with proteinaceous, aqueous fluids and turns translucent. This is because of its microporous nature and the thinness of the material; this usually occurs within 2–6 weeks (Minale et al. 1988; Leprince et al. 2001).

Expanded polytetrafluoroethylene has also been used in the ophthalmological field in experimental reports, as a substitute of silicone sponge in scleral buckling procedure, as a reinforcement material over the tubes of glaucoma drainage implants or as an artificial meshwork wick in rabbit eyes (Tawakol et al. 1989; Helies et al. 1998; Jacob et al. 2001). Moreover, Gore-Tex® patches have been clinically used in Mooren's ulcer, necrotizing scleritis and rheumatic corneal ulcer (Huang et al. 1994; Amm & Nolle 2002).

Recently, a tube implant made of ePTFE membrane (Gore-Tex®) has been successfully used to treat refractory glaucoma patients on a long-term basis (Kim et al. 2003).

In this paper, we report our experience in the use of a thin membrane of expanded polytetrafluoroethylene (PRECLUDE® pericardial ePTFE membrane) as a new adjuvant in trabeculectomy.

In particular, we carried out a randomized clinical trial with the aim of verifying the safety and efficacy of an ePTFE membrane patch as an adjuvant in trabeculectomy (alone or combined with low-dosage MMC) compared to simple trabeculectomy (with or without low-dosage MMC) in maintaining the fistula in penetrating glaucoma surgery.

We tested the possibility that the ePTFE membrane, placed beneath the scleral flap, could allow a better and longer lasting IOP reduction. This effect could derive from a reduction of the cicatricial sealing area between the scleral flap and the scleral bed because of the ability of the interposed ePTFE membrane to minimize tissue attachment, as mentioned earlier. Moreover, the interposed membrane could act as a modulating barrier against excessive filtration in the early and/or late postoperative period. Practically, we verified whether the Preclude® ePTFE membrane, especially in association with MMC, could represent a viable tool to obtain a low target IOP with fewer postoperative side-effects.

Materials and Methods

Study design

This study was a randomized, parallel four-group clinical trial.

Randomization was determined just before surgery. Sixty patients – 15 for each surgical technique – were randomly assigned based on a surgical chart number to undergo a trabeculectomy (T) (which served as surgical control group), a trabeculectomy with mitomycin-C (TMMC), a trabeculectomy with GORE PRECLUDE® pericardial implant (TG) or a trabeculectomy with mitomycin-C and GORE PRECLUDE® pericardial implant (TGMMC).

Patients

Consecutive Caucasian glaucoma surgical patients observed at the Department of Ophthalmology of the University of Palermo between 1 September 2003 and 31 August 2004 were selected. Ethical committee approval for ePTFE clinical use was obtained (No. 8/03). Sixty patients (60 eyes) were enrolled (considering an alpha error of 0.05 and beta error of 0.20) according to the inclusion and exclusion criteria. Inclusion criteria were: age 18 or older, diagnosis of primary open-angle glaucoma (POAG) or pseudoexfoliation glaucoma (PEXG), inadequate IOP control (IOP > 21 mmHg) and/or progressive visual field deterioration under maximum tolerated medical therapy. Other required inclusion criteria were availability, willingness and sufficient cognitive awareness to comply with examination procedures. Exclusion criteria were: concurrent participation during the last 30 days in any other clinical trial, use of systemic or ocular medications that may affect vision, acute or chronic disease or illness that would increase the operative risk or confound the outcomes of the study (e.g. immunodeficiency, connective tissue disease, diabetes, etc.), uncontrolled systemic or ocular disease other than glaucoma, clinically significant cataract where combined surgery was indicated, history of ocular trauma or prior ocular surgery.

Patients were thoroughly informed about the procedures, and written informed consent was obtained.

Eligible patients were admitted to hospital and underwent a complete preoperative ophthalmological examination the day before surgery to record the baseline values of study variables.

The preoperative visit collected the following data for each patient: age, gender, medical history including presence of ocular pathology, number and

type of antiglaucomatous drugs used, applanation tonometry performed 24 hr before surgery under maximum tolerated topical therapy, slit-lamp examination, visual field testing by Humphrey visual field.

Surgical techniques

Patients underwent surgery during the second day of hospitalization. All operations were carried out, under peribulbar anaesthesia, by two surgeons (S.C. and L.Z.) who were well trained and experienced in the procedures. During a previous training curve, five glaucomatous volunteers with uncontrolled IOP greater than 21 mmHg had undergone trabeculectomy with PRECLUDE® ePTFE implant. One case experienced a partial membrane extrusion 1 month postoperatively, because of unstable insertion, after which the ePTFE patch was secured to the scleral bed by one nylon 10-0 suture in all cases.

The technique included superior rectus muscle grasping with a 4-0 traction silk suture in all cases. After creating a superior fornix-based conjunctival/tenonian flap, the sclera was exposed and lightly cauterized to avoid any retraction after the scleral flap was obtained. A 5.0×4.0 mm wide and about 300μm thick scleral flap was dissected using a precalibrated round blade (Sharpoint, Surgical Specialities Corporation, Reading, PA, USA) or diamond knife (Meyco, Janache S.n.l., Como, Italy) and a bevel-up crescent knife (Alcon, Milan, Italy) at 12 o'clock position. When an ePTFE membrane implant was scheduled, two intrascleral pockets were dissected with a bevel-up crescent knife, continuing the scleral bed under the flap at its two vertical edges, with an extension of at least 0.5 mm. When MMC use was scheduled, a fluid-retaining sponge (such as a Weck-cell sponge), fashioned to be approximately 7×3 mm in length and width and about 0.5 mm in depth, was soaked with MMC in a concentration of 0.2 mg/ml and placed on the scleral bed under the scleral flap, as described in a previous study (Cillino et al. 2005). The sponge was left in position for 2 min, with the conjunctival flap pulled over the scleral flap in order to make the Tenon's-capsule side of the conjunctiva get in contact with the MMC. The sponge was removed with a forceps and the eye irrigated with 15 ml of balanced salt solution. A temporal paracentesis was performed and the anterior chamber was irrigated with a 1% acetylcholine solution (Myochol, Novartis Pharmastein AG, Stein, Switzerland). An ophthalmic viscoelastic device (Healon, AMO Inc., Santa Ana, CA, USA; Ophthalin, Ioltech SAS, La Rochelle and Carl Zeiss Meditec Le Pecq, France) was injected at the paracentesis site to increase the iris–cornea distance, and thereafter a block of corneoscleral wall, with an area of about 1 mm^2, was amputated with a 30° disposable blade and Vannas scissors until a pigmented trabecular line was observed on the specimen. After performing iridectomy, a 0.1 mm thick ePTFE membrane (GORE® PRECLUDE® pericardial W.L. Gore and Associates Inc., Flagstaff, AZ, USA) was inserted, when scheduled, over the trabeculectomy area into the two intrascleral pockets previously dissected. In particular, a rectangular 6×3 mm ePTFE patch was fashioned by straight Vannas scissors, trimming the four angles to obtain an octagonal figure. This patch was then repeatedly perforated on its surface with a corneal 1×2 teeth microsurgical forceps creating multiple parallel arrows and inserted by the short sides into the pockets (Fig. 1). The patch was secured to the scleral bed with one nylon 10-0 suture to avoid early postoperative dislocation. The holes should guarantee aqueous filtration, avoiding early closure of the fistula by the watertight membrane, and facilitate the proliferation of late fibrovascular bridges to anchor this no-stick patch to the surrounding scleral environment.

The scleral flap was closed with two nylon 10-0 sutures at each corner, avoiding excessive tension. The conjunctival flap was sutured with 10-0 nylon sutures. The filtration was assessed by balanced salt solution injected via the paracentesis.

Postoperatively, all groups were treated by topical steroid/antibiotic drops four times daily for 15 days, then two times daily for 15 days. Instillation of 1% atropine drops was added during the first few days. Atropine was continued up to 2 weeks in cases with hypotonus-related complications.

Main outcome measures

Postoperative visits were scheduled at 24 ± 4 hr, then at 7 ± 1 days, 2 and 3 weeks, 1, 2, 3, 6, 12, 18 and 24 months. Unscheduled visits were allowed according to the patients' needs or the examiners' judgment and were recorded carefully. Two and 3 week data have not been included in the statistical analysis. All patients completed the 24 month follow-up period.

IOP was the primary outcome measure. The baseline IOP value was the IOP measured at the preoperative visit 24 hr before surgery. In case of postoperative IOP measurements higher than 21 mmHg after topical steroid withdrawal, IOP-lowering medication

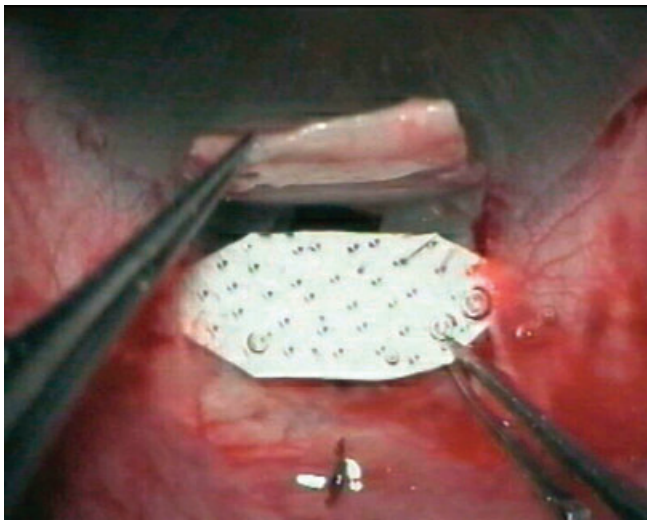

Fig. 1. Trabeculectomy with expanded polytetrafluoroethylene (ePTFE) membrane implant: perforated ePTFE patch insertion.

was added. We decided not to perform suturelysis or needling in any case, to avoid bias because of the use of further adjuvant procedures besides ePTFE or MMC.

Postoperative IOP level, number of antiglaucoma medications and early or late postoperative complications were checked at each control, to evaluate indirectly (as stated earlier) the degree of cicatricial failure and/or excessive outflow in ePTFE-augmented trabeculectomy versus ePTFE plus MMC-augmented, MMC-augmented or simple trabeculectomy. Moreover, bleb avascularity, transconjunctival oozing, delayed bleb leaks and hypotonus maculopathy were evaluated as signs of MMC-related complications.

Complete success was defined as a normal endpoint IOP without antiglaucoma medications, while qualified success was defined as a normal endpoint IOP with or without medications. These categories were assessed at two target IOP levels – ≤21 and ≤17 mmHg – in all four groups.

Statistical analysis

The sample size was chosen to assure a power of 90% or more in detecting at least a 3 mmHg difference among groups and a standard deviation (SD) of 3 mmHg, with a two-sided alpha error of 5% and beta error of 20%. Randomization was determined just before surgery by sealed-envelope technique. Demographic variables and other baseline variables were tabulated and checked for homogeneity among the four treatment groups. Parametric and non-parametric variables were compared by univariate analysis of variance (ANOVA) and Kruskal Wallis statistic test, respectively, to evaluate surgical intergroup differences; discrete variables were analysed using the chi-square test. The paired Wilcoxon signed-rank test and the paired samples Student's *t*-test were used for non-parametric and parametric analysis, respectively, to evaluate intragroup differences at different time periods. The proportion of surgical failures and adverse events in each treatment group was compared. All statistical tests were two-tailed and were applied at the 5% significance level. Success was evaluated on the basis of Kaplan–Meier cumulative probability (log rank test). Data were analysed with Epi Info software, version 3.2.2 (Centers for Disease Control and Prevention, Atlanta, Georgia, USA) and the SPSS Software (version 14.0; SPSS Inc., Chicago, Illinois, USA).

Results

Patients in the four treatment groups did not significantly differ for age, sex, type of glaucoma, mean number of preoperative medications and duration of the preoperative topical antiglaucoma therapy (Table 1). The mean preoperative IOP (±SD) was 28.6 (±5.2) in T eyes, 30.9 (±6.1) in TMMC eyes, 35.3 (±5.1) mmHg in TG eyes and 30.6 (±4.8) in TGMMC eyes, without significant intergroup difference. One day postoperatively, the IOP dropped at 8.4 (±2.1), 8.7 (±4.5), 10.6 (±6.7) and 10.4 (±3.7) mmHg, respectively (Table 2), without significant intergroup difference but with a significant difference ($P < 0.01$) relating to the preoperative value in each group. The postoperative IOP reduction was still significant at the endpoint in all groups with respect to the preoperative value ($P < 0.01$), with a mean IOP of 16.9 (±2.9), 16.2 (±2.7), 15.3 (±3.4) and 15.2 (±4.3) mmHg in T, TMMC, TG and TGMMC eyes, respectively (Table 2). The first day and first week IOP was significantly lower when compared to the first month IOP value in T and TMMC cases ($P < 0.05$ and $P < 0.01$, respectively) (Table 2).

No intergroup difference was present at any scheduled postoperative observation time (Table 2, Fig. 2).

The mean number of antiglaucoma medications was significantly reduced ($P < 0.001$) at the endpoint in all groups: from 2.6 (±0.2) to 0.7 (±0.2), from 2.7 (±0.1) to 0.6 (±0.2), from 2.5 (±0.6) to 0.7 (±0.1) and from 2.5 (±0.4) to 0.5 (±0.4) in T, TMMC, TG and TGMMC, respectively, without significant intergroup differences.

The success rates in the study groups are reported in Table 3. In particular, when a ≤21 mmHg target IOP without medications (complete success) was considered, it was achieved in eight eyes (53.3%) in the T group, eight eyes (53.3%) in the TMMC group, 10 eyes (66.7%) in the TG group and nine eyes (60%) in the TGMMC group, without significant difference. When a ≤21 mmHg target IOP with or without medications (qualified success) was considered, 13 (86.7%) eyes in the T group and 14 (93.3%) eyes in each of the remaining groups were respectively found, again without significant intergroup difference. When a ≤17 mmHg target IOP without medications (complete success) was considered, five eyes (33.3%), seven eyes (46.7%), 10 eyes (66.7%) and nine eyes (60%) were found in the T, TMMC, TG and TGMMC groups, respectively. As for a ≤17 mmHg target IOP with or without medications (qualified success), 11 eyes (73.3%) in the T group, 10 eyes (66.7%) in the TMMC group and 12 eyes (80%) in both the ePTFE-patch-augmented (TG and TGMMC) groups were found, respectively, without statistically significant difference. The Kaplan–Meier cumulative survival curves relating either the ≤21 mmHg target IOP or ≤17 mmHg target IOP (Figs 3 and 4) did not show significant intergroup differences as for complete and qualified success

Table 1. Characteristics of the glaucoma patients.

	T	TMMC	TG	TGMMC	*P*
Eyes	15	15	15	15	–
Male/female	8/7	9/6	7/8	6/9	0.721*
Age (mean ±SD), years	71.1 (4.1)	68.1 (6.1)	67.2 (9.0)	65.3 (7.6)	0.194†
POAG/PEXG diagnosis	9/6	10/5	10/5	11/4	0.896*
Mean preoperative IOP (±SD), mmHg	28.6 (5.2)	30.9 (6.1)	35.3 (5.1)	30.6 (4.8)	0.395†
Preoperative drugs, mean (±SD)	2.6 (0.2)	2.7 (0.1)	2.5 (0.6)	2.5 (0.4)	0.900†
Mean time (months) from the initial topical therapy to surgery (±SD)	30.3 (15.8)	31.5 (16.2)	33.4 (18.9)	32.3 (16.4)	0.648†

T, trabeculectomy; TMMC, trabeculectomy with mitomycin-C; TG, trabeculectomy with ePTFE; TGMMC, trabeculectomy with mitomycin-C and ePTFE; POAG, primary open-angle glaucoma; PEXG, pseudoexfoliation glaucoma; IOP, intraocular pressure; SD, standard deviation.
*Chi-square test.
†ANOVA.

Table 2. Pre- and postoperative IOP in the surgical groups.

	T		TMMC		TG		TGMMC		
	IOP	P^*	IOP	P^*	IOP	P^*	IOP	P^*	$P^\dagger$
Preoperative	28.6 (5.2)	–	30.9 (6.1)	–	35.3 (5.1)	–	30.6 (4.8)	–	0.395
Postoperative									
1st day	8.4 (2.1)	$<0.01^{\ddagger}$	8.7 (4.5)	$<0.01^{\ddagger}$	10.6 (6.7)	$<0.01^{\ddagger}$	10.4 (3.7)	$<0.01^{\ddagger}$	0.486
1st week	9.4 (2.8)	$<0.01^{\ddagger}$ $<0.05^{\S}$	10.5 (5.1)	$<0.01^{\ddagger}$ $<0.05^{\S}$	12.2 (3.8)	$<0.01^{\ddagger}$	12.0 (3.7)	$<0.01^{\ddagger}$	0.331
1st month	14.7 (3.7)	$<0.01^{\ddagger\S\P}$	15.1 (3.5)	$<0.01^{\ddagger\S\P}$	12.4 (2.6)	$<0.01^{\ddagger}$	14.1 (3.3)	$<0.01^{\ddagger}$	0.206
3rd month	15.2 (3.8)	$<0.01^{\ddagger}$	15.3 (3.3)	$<0.01^{\ddagger}$	16.7 (3.0)	$<0.01^{\ddagger}$	15.4 (2.4)	$<0.01^{\ddagger}$	0.854
6th month	16.4 (3.2)	$<0.01^{\ddagger}$	14.8 (3.0)	$<0.01^{\ddagger}$	15.8 (4.0)	$<0.01^{\ddagger}$	16.5 (2.6)	$<0.01^{\ddagger}$	0.428
9th month	16.1 (2.8)	$<0.01^{\ddagger}$	15.1 (2.3)	$<0.01^{\ddagger}$	15.6 (2.9)	$<0.01^{\ddagger}$	15.8 (2.4)	$<0.01^{\ddagger}$	0.549
12th month	17.4 (2.7)	$<0.01^{\ddagger}$	16.4 (2.4)	$<0.01^{\ddagger}$	16.1 (3.2)	$<0.01^{\ddagger}$	16.5 (2.3)	$<0.01^{\ddagger}$	0.610
18th month	16.6 (2.5)	$<0.01^{\ddagger}$	16.6 (2.5)	$<0.01^{\ddagger}$	14.8 (3.5)	$<0.01^{\ddagger}$	15.4 (4.4)	$<0.01^{\ddagger}$	0.584
24th month	16.9 (2.9)	$<0.01^{\ddagger}$	16.2 (2.7)	$<0.01^{\ddagger}$	15.3 (3.4)	$<0.01^{\ddagger}$	15.2 (4.3)	$<0.01^{\ddagger}$	0.576

T, trabeculectomy; TMMC, trabeculectomy with mitomycin-C; TG, trabeculectomy with ePTFE; TGMMC, trabeculectomy with mitomycin-C and ePTFE; IOP, intraocular pressure.
Values for IOP are expressed as mean (±SD).
*Intragroup analysis (paired samples *t*-test).
†Intergroup analysis (ANOVA).
‡Versus preoperative IOP.
§Versus 1 day.
¶Versus 1 week.

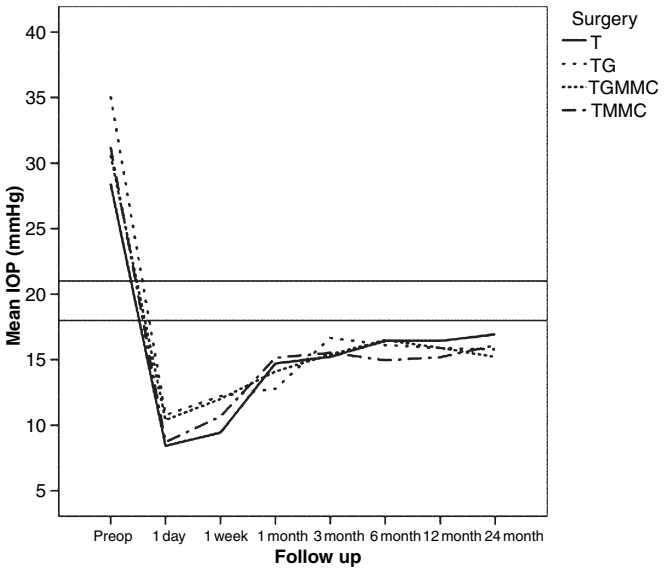

Fig. 2. Intraocular pressure (IOP) variation over time in the four surgical treatment groups.

Table 3. Success rates (%) in the study groups at two target IOP levels.

	T	TMMC	TG	TGMMC	P^*
≤21 mmHg					
Complete success	8/15 (53.3)	8/15 (53.3)	10/15 (66.7)	9/15 (60.0)	0.860
Qualified success	13/15 (86.7)	14/15 (93.3)	14/15 (93.3)	14/15 (93.3)	0.884
≤17 mmHg					
Complete success	5/15 (33.3)	7/15 (46.7)	10/15 (66.7)	9/15 (60.0)	0.268
Qualified success	11/15 (73.3)	10/15 (66.7)	12/15 (80.0)	12/15 (80.0)	0.807

T, trabeculectomy; TMMC, trabeculectomy with mitomycin-C; TG, trabeculectomy with ePTFE; TGMMC, trabeculectomy with mitomycin-C and ePTFE.
*Pearson's chi-square test.

rate (log rank $P = 0.235$ and log rank $P = 0.814$, respectively) even when ePTFE is used; a trend favouring the medium-term survival rate can be noted. This is more evident regarding the complete success cases.

Over a 2 month period, the white ePTFE patch, when implanted, could be observed under the filtration bleb area (Fig. 5); it then disappeared because of complete discoloration of the patch in all cases.

The frequency of postoperative complications – i.e. hyphaema, anterior chamber inflammation with fibrinous reaction, early hypotony (defined as an IOP <8 mmHg or <10 mmHg with choroidal detachment or shallow anterior chamber), shallow or flat anterior chamber, choroidal detachment – is shown in Table 4. No adverse reaction to the ePTFE material was present in the TG and TGMMC groups, and in no cases were membrane extrusion or conjuctival erosion noted. No significant intergroup difference was found in terms of hyphaema and inflammation. Hypotony was significantly more frequent ($P = 0.035$) in groups without the ePTFE patch (i.e. T and TMMC) compared to the other two groups. Moreover, Table 4 indicates the late MMC-related complications: cystic-avascular blebs are more (but not significantly) frequent when MMC (with or without ePTFE) is applied.

Discussion

The postoperative behaviour in the four glaucoma surgery groups is quite similar. As stated earlier, all groups were matched with regard to factors determining success of filtering surgery

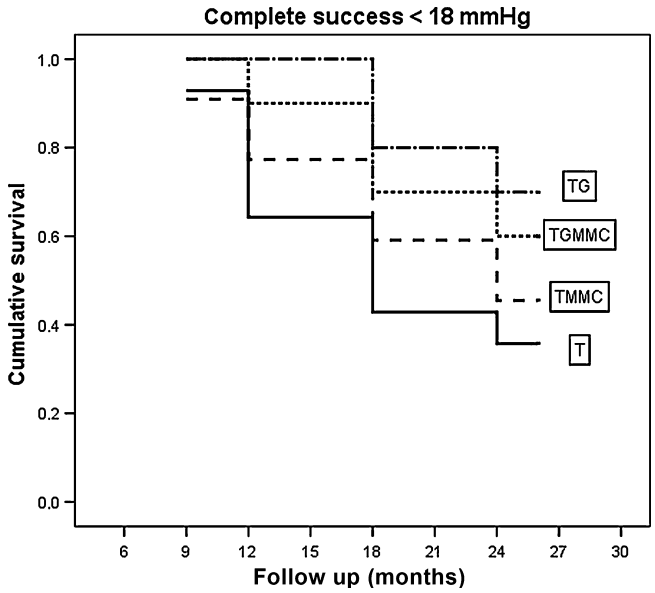

Fig. 3. Kaplan–Meier cumulative probability curve of complete success (without medication) for intraocular pressure (IOP) < 18 mmHg.

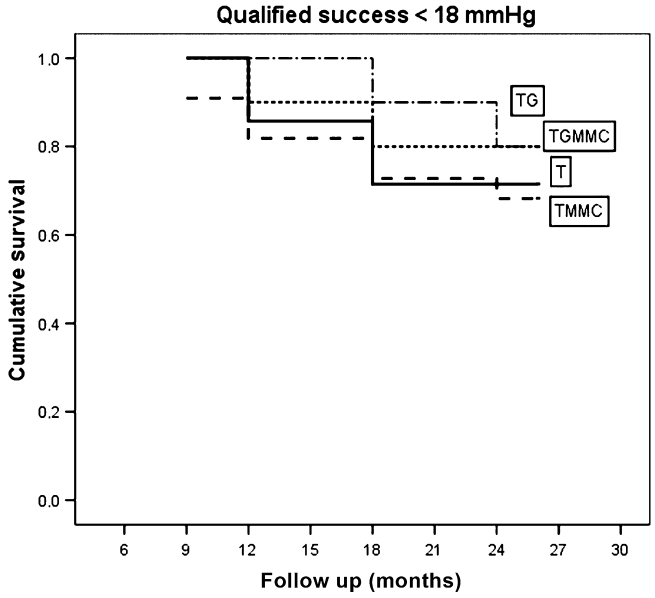

Fig. 4. Kaplan–Meier cumulative probability curve of qualified success (with or without medication) for intraocular pressure (IOP) < 18 mmHg.

such as race, age, type of glaucoma, duration of topical treatment, absence of any previous ocular surgery, etc. The endpoint degree of IOP lowering in the T group does not significantly differ from that found in the groups where the adjuvants (MMC, ePTFE or both) were used. As stated in the Materials and Methods section, we chose not to perform other adjunctive procedures such as adjustable/releasable sutures or needling to avoid bias and because of some contradictory data. In fact, even if some authors report favourable outcomes, other data seem to indicate that releasable sutures cannot exclude the risk of hypotony during the first postoperative days; they do not seem of great utility in phakic eyes when used after 10 postoperative days (Stalmans et al. 2006; Kapetansky 2003; Ralli et al. 2006; Fontana et al. 2006). Needling does not seem significantly better than medical therapy after trabeculectomy (Feyi-Waboso & Ejere 2004).

During the 2 year follow-up, the mean IOP was below target values in all four groups. Indeed, no intergroup difference is present at any follow-up time. This finding is in contrast with the evidence-based data of a positive adjuvant effect of intraoperative MMC in trabeculectomy (Jampel et al. 2002; Wilkins et al. 2005).

On the other hand, reports indicating no statistically significant difference in the overall outcome of phacotrabeculectomy between control and MMC groups of non-selected patients with POAG, or no significant difference in the cumulative success probability of MMC-augmented trabeculectomy compared to trabeculectomy alone, are not infrequent (Shin et al. 1996; Tsai et al. 2003).

Moreover, the large (5.0×4.0 mm) 300μm thick scleral flap we established to provide protection against excessive outflow reduces the direct contact area between the underlying MMC sponge and the overlying conjunctiva, probably decreasing the antifibrotic effect. Also, the relatively small sample size could enhance the lack of homogeneity with respect to the postoperative parameters in our groups.

The postoperative IOP behaviour from the first day to the first month appears to be more stable in the groups where ePTFE was used i.e. (TG and TGMMC) than in the T and TMMC groups, as indicated by the lack of significant difference between the first day, first week and the first month IOP levels in the two former groups. This finding could indicate a sort of modulation of the aqueous outflow provided by the ePTFE barrier, through its small holes and along its surface, as postulated in the Introduction. This barrier effect could be of benefit, because a heavy early IOP reduction is correlated with more hypotony-related complications, and has been shown to be very poorly correlated to 1 year IOP control in antimetabolite-augmented trabeculectomy (Polikoff et al. 2005).

Even when comparing the TG and TGMMC groups, no difference in IOP behaviour because of the adding of MMC to the ePTFE patch can be demonstrated in our sample.

We believe that the similar degree of early hypotony in both the T and TMMC groups is related to the procedure (i.e. flaps fashioning, suturing technique, etc.) because the antimetabolite effect is not significant in the early postoperative period.

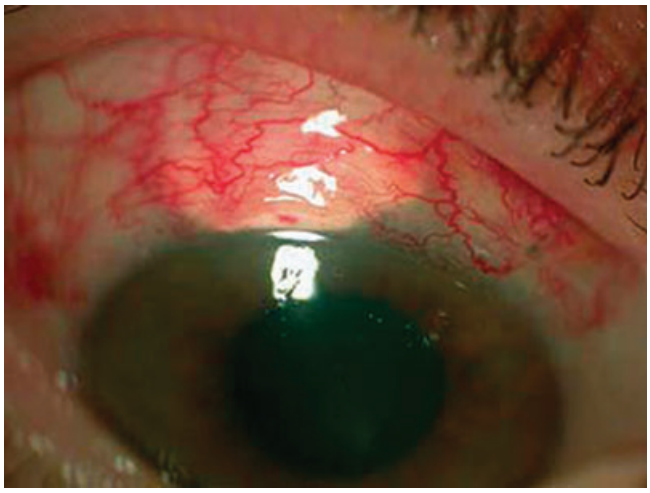

Fig. 5. Trabeculectomy with expanded polytetrafluoroethylene (ePTFE) membrane implant: postoperative appearance after 48 hr.

Table 4. Frequency (%) of postoperative complications in the study groups.

	T	TMMC	TG	TGMMC	P^*
Hyphaema	5 (33)	5 (33)	4 (27)	4 (27)	0.960
Inflammation	2 (13)	3 (20)	3 (20)	4 (27)	0.841
Hypotony	7 (47)	7 (47)	1 (6)	3 (20)	0.035
Shallow AC	5 (33)	4 (27)	2 (13)	2 (13)	0.448
Flat AC	1 (6)	1 (6)	0	1 (6)	0.788
Choroidal detachment	3 (20)	4 (27)	2 (13)	1 (6)	0.493
Cystic/avascular bleb	0	3 (20)	0	3 (20)	0.08

T, trabeculectomy; TMMC, trabeculectomy with mitomycin-C; TG, trabeculectomy with ePTFE; TGMMC, trabeculectomy with mitomycin-C and ePTFE; AC, anterior chamber.
*Chi-square test.

When the complete and qualified endpoint success rates are considered, significant intergroup difference is lacking both at ≤21 and ≤17 mmHg target IOP. In particular, the groups behave quite similarly at the ≤21 mmHg IOP target and rates are comparable with those of other medium-to-long-term studies (Kitazawa et al. 1991; Skuta et al. 1992; Smith et al. 1997; Wilkins et al. 2005; Anand et al. 2006). However, at the ≤17 mmHg target IOP the success rates – especially the complete ones – increase from the simple trabeculectomy eyes through the MMC-augmented eyes to the ePTFE with or without MMC eyes, even if the differences are still not significant. This trend is clearly shown by the survival curves and could indicate, if statistically confirmed by a larger series, a complementary or additive mechanical non-stick effect of the ePTFE patch on the antifibrotic MMC action.

The ePTFE membrane tolerance was optimal. Eyes in the TG and TGMMC groups showed no adverse reaction to the material; neither inflammation nor extrusion nor conjuctival erosion were noted. Progressive discolouration with disappearance of the membrane, as already reported in cardiosurgical practice, was present in all cases (Minale et al. 1988).

Early hypotony was the only postoperative complication significantly more frequent in non-ePTFE groups. This finding is in agreement with the instability of IOP during the first month in trabeculectomy cases where the patch was not inserted (as mentioned earlier). The degree and incidence of late MMC-related complications are not severe with the technique we performed, irrespective of the use of ePTFE. However, a limit of this study could be that the sample size, which was designed for the assessment of equivalence in IOP reduction, may be too small to properly assess all safety issues. On the other hand, we chose not to increase the number of participants because of the unknown clinical medium-term ePTFE effects on the trabeculectomy site.

In conclusion, our results suggest that ePTFE implant in trabeculectomy for POAG or PEXG is well tolerated and could act as a filtration-modulating device; therefore, it is useful in reducing early hypotony-related complications, and contributes to attaining a medium-term IOP control comparable to that achieved through the use of low-dosage MMC. The adjunct of other adjuvant procedures we do not perform in our study, such as releasable sutures, could enhance these results. Even if our study indicates that the ePTFE implant is a viable alternative to low-dosage MMC in terms of medium-term IOP control, this does not seem enough to allow a routine switching from MMC to ePTFE adjuvant. At the moment, ePTFE use can be taken into account when the antimetabolite-related risk is to be avoided. Moreover, the question of whether ePTFE plus MMC-augmented trabeculectomy implies a better medium-term IOP reduction than MMC or ePTFE alone is unanswered: larger randomized clinical trials and longer follow-up are required to investigate these issues.

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Correspondence:
Prof. Salvatore Cillino
Dipartimento di Neuroscienze Cliniche
Sezione di Oftalmologia
Università di Palermo
Via Liborio Giuffrè 13–90127
Palermo
Italy
Tel: +39 91 6553904
Fax: +39 91 6261438
Email: casuccio@unipa.it