

EXTENDED REPORT

Combined cataract and glaucoma surgery with mitomycin C: phacoemulsification-trabeculectomy compared to phacoemulsification-deep sclerectomy

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Aims: To compare outcomes of phacoemulsification combined with trabeculectomy (PT) or deep sclerectomy (PDS) with intraoperative mitomycin C (MMC) application.

Methods: Non-randomised, consecutive, retrospective comparative study. 97 eyes of 97 patients (59 PDS, 38 PT) undergoing combined surgery with intraoperative MMC (0.1–0.4 mg/ml for 1–3 minutes) were identified for inclusion in the study.

Results: The probability of maintaining intraocular pressure (IOP) below 19 mm Hg and 15 mm Hg, with a 30% drop from preoperative IOP and without additional medication, 1 year after surgery were 77.6% (95% CI: 67 to 90) and 71.5% (60 to 85) for the PDS group and 89.5% (80 to 99) and 89.5 (80 to 99) for the PT group, respectively, and these differences were not statistically significant ($p > 0.05$, log rank test). After excluding ocular co-morbidity no differences were observed in the improvement of visual acuity between the two groups. There were no major differences in the complication rates except that delayed bleb leaks were seen in seven eyes (18.4%) of the PT group ($p = 0.004$).

Conclusion: In this study, no statistically significant difference was found in the IOP and visual outcomes between PDS and PT. A significantly higher frequency of late bleb leaks after PT was observed.

The decision to do sequential or combined cataract and glaucoma surgery depends on several individual patient factors including the degree of visual impairment, target intraocular pressure (IOP), stage of glaucoma, compliance, age, and life expectancy.^{1–3}

Combined phacoemulsification and trabeculectomy (PT) is the most widely reported procedure for combined surgery.⁴ Augmentation of the procedure with mitomycin C (MMC) has been shown to be beneficial when risk factors for failure are present.²

Newer surgical techniques, loosely termed as non-penetrating glaucoma surgery (NPGS), have been reported to successfully lower IOP in the long term.^{5–6} Compared to trabeculectomy, the IOP lowering efficacy of NPGS is the same or less depending on the publication but all randomised trials agree that the complication rates are less with NPGS.^{7–11} The success rates of deep sclerectomy can be improved and IOPs in the low teens achieved using by intraoperative MMC application and postoperative Nd:YAG laser goniopuncture in selected cases.¹²

Reports suggest that phaco-deep sclerectomy (PDS) and phaco-viscocanalostomy (PVCT) are effective in lowering IOP.^{13–16} MMC augmentation of PDS has not previously been reported. The aim of this study was to compare the outcomes of PT with MMC and PDS with MMC and selective Nd:YAG laser goniopuncture.

METHODS

Consecutive patients undergoing combined glaucoma and phacoemulsification surgery with intraoperative MMC between September 2001 and November 2003, were identified from an ongoing correlational database (Microsoft Access) of all glaucoma surgery performed by the glaucoma unit. The surgeries were done or closely supervised by one surgeon (NA). The decision to do PDS or PT was based on several factors including available operating theatre time and training requirements for specialist registrars. In all cases a

fornix based conjunctival flap was made. The MMC application technique was similar for both procedures and was done before dissection of the scleral flap. Two to four collagen sponges (Visitec, UK), soaked in MMC 0.1–0.4 mg/ml (0.2 mg/ml in most cases), were applied into the sub-Tenon's space for 1–4 minutes. PT was done by a same incision technique described elsewhere.¹⁷

PDS technique was standardised during this study. Firstly, a superior DS was done by a technique detailed in previous publications.^{12–18} This was followed by a temporal clear corneal phacoemulsification. In case of small, microscopic perforations, the procedure was completed as a DS. A peripheral iridectomy was performed in those with larger or posterior perforations and those with iris prolapse.

Postoperatively all patients received a topical steroid and antibiotic combination for 6 weeks or more depending on bleb appearance. If signs of bleb failure developed, subconjunctival betamethasone (0.1 ml, 0.4 mg) and 5-fluorouracil (5-FU) (0.2 ml, 5 mg) were administered. In PT eyes, selective argon laser suture-lysis or removal of scleral sutures was performed. In PDS eyes, not achieving target IOP levels, Nd:YAG laser goniopuncture was done. This involved using the YAG laser in the free running Q-switched mode, energy ranging from 2–4 mJ and a Lasag 15 gonioscopy contact lens (CGAL, Haag-Streit). Three to 20 shots were applied.¹⁹

Analysis was done on intention to treat basis and eyes complicated by perforation during DS were included in the PDS group. Statistica 6 (Statsoft Inc, USA) was used for statistical analyses. IOPs below 19 and 15 mm Hg, with a 30% reduction from preoperative IOP and without additional

Abbreviations: 5-FU, 5-fluorouracil; IOP, intraocular pressure; MMC, mitomycin C; NPGS, non-penetrating glaucoma surgery; PT, phacoemulsification combined with trabeculectomy; PDS, phacoemulsification combined with deep sclerectomy; PVCT, phacoemulsification combined with viscocanalostomy; TDM, trabeculo-Descemet's membrane

Table 1 Patient demographics and preoperative characteristics

	Phaco-deep sclerectomy	Phaco-trabeculectomy	p Value
Number of eyes	59	38	
Age (years) (SD)	78 (8.5)	78 (8)	0.55
Male/female	34/25	19/19	0.59
Race			
White	54 (91.5%)	36 (94.7%)	
Afro-Caribbean	3 (5.1%)	2 (5.3%)	
Indian	2 (3.4%)		
Diagnosis			0.46
POAG	47 (79.7%)	27 (71.1%)	
NTG	5 (8.5%)	7 (18.4%)	
PXF	6 (10.1%)	1 (2.6%)	
Steroid induced ACG	1 (1.7%)	3 (7.9%)	
Co-existing ocular pathology			
ARMD	4	3	
Retinitis pigmentosa	1	0	
Epiretinal membrane	1	1	
High myopia	3	0	
Diabetic retinopathy	1	1	
Chronic anterior uveitis	1	0	
Ocular surface disorder	3	1	
Previous laser			0.29
Peripheral iridotomy	1 (1.7%)	3 (7.9%)	
Laser trabeculoplasty	1 (1.7%)	1 (2.6%)	
Previous surgery			0.89
Trabeculectomy	3 (5.1%)	3 (7.8%)	
RD surgery	1 (1.7%)	1 (2.6%)	
Glaucoma medications			0.84
Median	2	2	
Range	1-4	0-4	
IOP control before surgery			0.86
Uncontrolled IOP (mm Hg)	31 (81.6%)	46 (78%)	
Controlled IOP (mm Hg)	7 (18.4%)	13 (22%)	
Mean follow up (months) (SD)	16.0 (9.0)	19.4 (7.6)	0.054
Target IOP (mm Hg) (SD)	14.8 (1.8)	13.6 (1.2)	0.001

ACG, angle closure glaucoma; ARMD, age related macular degeneration; NTG, normal tension glaucoma; POAG, primary open angle glaucoma; PXF, pseudoexfoliation.

medication, were the two criteria of success used in the Kaplan-Meier survival analysis. Comparisons between the two groups were done by log rank test. Needle revision and laser goniopuncture were not considered to be failures. However, a subsequent operative procedure to lower IOP was considered as failure. Dichotomous variables were analysed using χ^2 tests with Yates's correction and the Fisher's exact tests. Analyses of variance (ANOVA) were used for continuous variables. Non-parametric data were analysed by the

Mann-Whitney U tests. All tests were two tailed and p values less than 0.05 were taken to be significant.

RESULTS

A total of 97 eyes of 97 patients were eligible for the study. One patient was excluded, as she died 2 months after surgery. Six (6.1%) patients died during the course and data were censored at the point of their demise. There were no significant differences in the preoperative characteristics of the two groups, except in the PT group the target IOPs, were significantly lower and follow up was longer (table 1).

IOP changes after surgery are shown in figure 1. IOP data was included till end of follow up even if patients were placed on glaucoma medications or had another procedure to lower IOP. Figures 2 and 3 show Kaplan-Meier survival curves for IOP below 19 mm Hg and 15 mm Hg. The log rank test showed no differences in the survival analyses with both success criteria ($p > 0.05$).

At last follow up, five eyes (13.2%) of the PT group were on an average of 1.6 glaucoma medications and six eyes (10.1%) of the PDS group were on an average of 1.16 medications to control IOP. This difference between groups was not significant ($p = 0.76$). After excluding ocular co-morbidity, no differences were observed in the improvement of visual acuity between the two groups ($p = 0.48$). Causes of a decrease of two Snellen chart lines from preoperative VA included age related macular degeneration (ARMD) (one eye, PT group), epiretinal membrane (one eye, PT group), ischaemic central retinal vein occlusion (one eye, PDS group).

Surgical complications are shown in table 2 and subsequent procedures in table 3. Eight out of 59 eyes in the PDS group (13.5%) were complicated by intraoperative perforation of the trabeculo-Descemet's membrane (TDM) and the

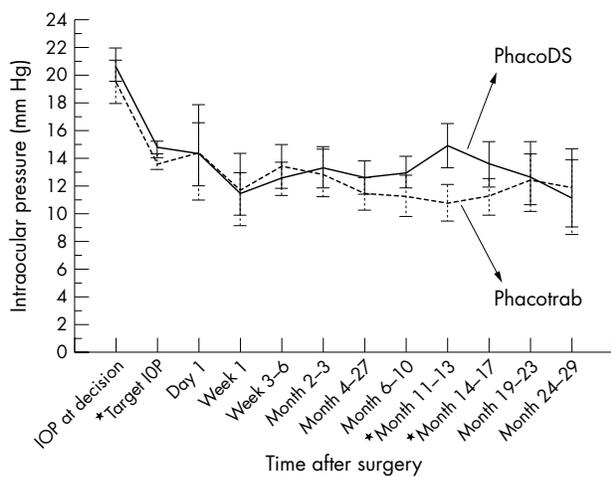


Figure 1 IOP changes after combined phacoemulsification combined with deep sclerectomy (PhacoDS) and phacoemulsification combined with trabeculectomy (PhacoTrab). Error bars represent 95% confidence intervals of means.

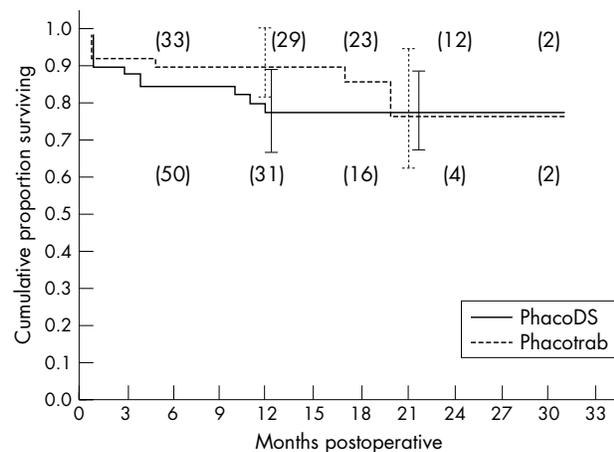


Figure 2 Comparing phacoemulsification combined with deep sclerectomy (PhacoDS) and phacoemulsification combined with trabeculectomy (Phacotrab) outcomes. Kaplan-Meier survival curves for maintaining IOP less than 19 mm Hg without medication. Error bars represent 95% confidence intervals. Numbers in parentheses represent number of eyes at risk at the specified time period. Log rank test, $p=0.5$.

complications of this subgroup are presented separately. There were no cases of bleb infection or endophthalmitis. The difference in frequency of late bleb leaks between the groups was highly significant ($p=0.004$).

DISCUSSION

Phaco-deep sclerectomy and phaco-trabeculectomy with MMC were found to have similar high success rates by the Kaplan-Meier survival analysis. Cox's proportional hazard model also showed no significant effect of the type of procedure (PT or PDS) on the success rates (table 4). However, in the 11–13 month and 14–17 month interval after surgery, IOPs were significantly lower in the PT group ($p<0.05$, ANOVA). The mean time for laser goniopuncture after PDS was 10.2 months. This explains the higher mean IOPs in the PDS group 1 year after surgery and the subsequent decline. More than half the eyes in the PDS group required laser goniopuncture for adequate IOP control. Outcomes compared well to the published literature despite more stringent definitions of success than generally reported. The National Trabeculectomy Survey reported outcomes of 64% of IOPs less than 16 mm Hg at 1 year without medication.²⁰ Gianoli *et al* found success rates of 59% for PDS and 52% for PT at 1 year¹⁶ and Wishart *et al* 77% for DS and 94% for PDS at 3 years.¹⁵ Both, however, defined success as IOP of 21 mm Hg or less without medication. This level of IOP

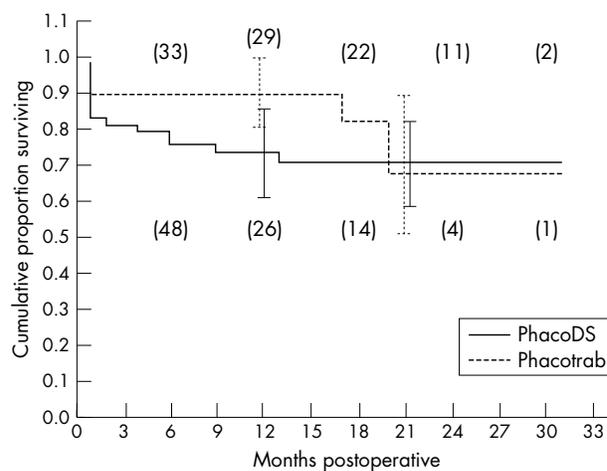


Figure 3 Comparing phacoemulsification combined with deep sclerectomy (PhacoDS) and phacoemulsification combined with trabeculectomy (Phacotrab) outcomes. Kaplan-Meier survival curves for maintaining IOP less than 15 mm Hg without medication. Error bars represent 95% confidence intervals. Numbers in parentheses represent number of eyes at risk at the specified time period. Log rank test, $p=0.3$.

control may not be sufficient to control progression in eyes with advanced glaucoma.²¹

The above reports did not use MMC, which is reported to increase success rates for PT. Shin *et al* found MMC was beneficial in PT with a high risk of failure (African-American origin, IOP >20 mm Hg on maximum tolerated medication or at least two topical medications preoperatively).²² According to this definition the majority of the patients in this study would fall into this high risk category. Kozobolis *et al* randomised patients undergoing DS without an implant, to have or not have intraoperative MMC. IOP reduction was significantly greater in the DS-MMC group; however, rates of IOP of 21 mm Hg or less at 3 years were only 42.5% of DS and 50% of DS-MMC.²³ Laser goniopuncture was not performed in these patients and this may explain these indifferent results. Goniopuncture has been reported to significantly lower IOP months to years after surgery.¹⁹

MMC augmentation is associated with thin walled blebs and a high incidence of delayed bleb leaks and hypotony.²⁴ In this study the rates of MMC related complications were low. There were no cases of bleb infections or endophthalmitis. Hypotony occurred in only two patients who underwent laser goniopuncture after PDS. The frequency of late bleb leaks was significantly higher (18.4%) in eyes in the PT group than in the PDS group (0%). One of the advantages reported by a previous study of PDS over PT was a lower incidence of

Table 2 Complications after combined surgery

Complications	Phaco-trabeculectomy	Phaco-deep sclerectomy	PDS-intraoperative perforation	p Value between PDS all and PT
No of eyes	38	51	8	
Post-capsular rupture	1 (2.6%)	3 (5.9%)	0	1.0
Transient shallow anterior chamber	3 (7.9%)	0	2 (25%)	0.4
Hyphaema	2 (5.3%)	3 (5.9%)	2 (25%)	0.7
Fibrin	3 (7.9%)	0	1 (12.5%)	0.3
Transient conjunctival edge leak	3 (7.9%)	3 (7.7%)	2 (25%)	1.0
Delayed bleb leaks	7 (18.4%)	0	0	0.004
Iris incarceration in sclerostomy/laser puncture site/perforation of TDM	1 (2.6%)	4 (7.8%)	2 (25%)	0.2
Delayed suprachoroidal haemorrhage	0	2* (3.9%)	2 (25%)	0.1
Hypotony (<5 mm Hg)	0	2* (3.9%)	0	0.5

TDM, trabeculo-Desemet's membrane.

*After Nd:YAG laser goniopuncture in one eye.

Table 3 Procedures after combined surgery (more than one procedure was done on some eyes)

Procedure	Phaco-trabeculectomy	Phaco-deep sclerectomy
Laser suture-lyses/removal of releasable scleral sutures	18 (47.4%)	2 (3.3%)*
Nd:YAG laser goniopuncture	–	30 (51.7%)†
Argon laser iridoplasty	–	7 (14.2%)
Needle revision		
Total	10 (26.3%)	12 (20.3%)
With subconjunctival 5-FU	9 (23.7%)	8 (13.5%)
With subconjunctival MMC	1 (2.6%)	4 (6.8%)
Nd:YAG laser capsulotomy	2 (5.3%)	3 (5.2%)
Conjunctival re-suturing	1 (2.6%)	0
Drainage of suprachoroidal haemorrhage	0	2 (3.3%)
Revision of trabeculectomy with intraoperative MMC	1 (2.6%)	0
Conjunctival advancement and bleb reduction for dysthaesia	2 (5.3%)	0
Bleb repair and conjunctival autograft for delayed leak	2 (5.3%)	0
Deep sclerectomy with MMC	1 (2.6%)	1 (1.7%)
IOL exchange	1 (2.6%)	1 (1.7%)
Ptosis repair	1 (2.6%)	0

*PDS eyes with intraoperative perforation.

†Includes three eyes with intraoperative perforations.

Table 4 Results of Cox's regression models for the two success criteria

	IOP <19 mm Hg		IOP <15 mm Hg	
	Hazard ratio (95% CI)	p Value	Hazard ratio (95% CI)	p Value
Age at surgery (years)	1.05 (0.99 to 1.08)	0.06	1.03 (0.67 to 1.58)	0.17
Sex	8.42 (2.18 to 32.47)	0.0019	1.66 (0.70 to 3.93)	0.24
Surgery (PT or PDS)	1.26 (0.41 to 3.90)	0.68	0.84 (0.34 to 2.64)	0.69
IOP <10 at weeks 1–2	0.60 (0.19 to 1.86)	0.36	0.91 (0.38 to 2.16)	0.82
IOP <14 at weeks 3–6	0.60 (0.01 to 0.24)	0.00009	0.25 (0.10 to 0.62)	0.002
Transconjunctival oozing	0.21 (0.04 to 1.04)	0.055	0.18 (0.05 to 0.75)	0.02

postoperative inflammation and other immediate complications like hyphaema and shallow anterior chamber.¹⁶ In this study, however, there was a low incidence of immediate side effects in both groups and the possible benefits of PDS were offset by a high incidence of intraoperative perforations (15.7%).

IOP outcomes of PDS and PT with MMC augmentation were found to be similar in this study. This similarity in outcomes has previously been found between PDS and PT, but has not been reported using MMC.¹⁶ This study shows that both PDS and PT with MMC can be safe and effective procedures for achieving low IOPs in patients with glaucoma and cataract. The significance of these results are limited by study design—a non-randomised, retrospective comparative trial. There was also a possible bias against eyes undergoing PT as they had longer follow ups and probably more advanced glaucoma, as evidenced by the lower target IOPs. Finally, the surgeon's learning curve and technique must be taken into account. It is evident that most failures of the PDS group occurred within the first three postoperative months (figs 2 and 3). This may be related to problems with surgical technique. Shaarawy *et al* have shown in a prospective trial of DS that patients with an IOP <6 mmHg on the first postoperative day had significantly fewer Nd:YAG goniopunctures and a longer median time to failure.²⁵ The low first day IOP probably signifies adequate inner scleral flap dissection and juxtacanalicular trabecular meshwork removal. A prospective randomised controlled trial with procedures performed by experienced surgeons with long term follow up is required to assess whether PT or PDS with MMC is more successful.

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