• Clinical Research •

Deep sclerectomy-trabeculectomy with mitomycin C in treating glaucoma: postoperative long-term results

Chung Shen Chean, Li Jiang, Gayathri Kanchana Niroshani Pati Arambage, Punithawathy Ranjit

Ophthalmology Department, Royal Stoke University Hospital, Newcastle Road, Stoke-on-Trent ST4 6QG, United Kingdom
Correspondence to: Chung Shen Chean. Ophthalmology Department, Royal Stoke University Hospital, Newcastle Road, Stoke-on-Trent ST4 6QG, United Kingdom. shen920815@gmail.com
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Abstract

● **AIM:** To determine the long-term postoperative outcomes of deep sclerectomy-trabeculectomy (DST) with mitomycin C (MMC) in the treatment of glaucoma.

● **METHODS:** Patients who underwent DST with MMC between 2010 and 2017 were included in this retrospective observational study. Complete success was defined as postoperative intraocular pressure (IOP) ≤21 mm Hg or 30% reduction of IOP from baseline without any topical IOP-lowering agent, and qualified success defined as IOP≤21 mm Hg or 30% reduction of IOP from baseline with/without single topical agent. We evaluated the surgical success rates and complication rates of this procedure, as well as described the IOP profiles, best corrected visual acuity (BCVA) profiles and mean deviations (MD) of Humphrey visual field (HVF) 24-2 performance at each follow-up time point. Mixed linear regression models were constructed to determine estimated predictive values of demographic data, use of topical IOP-lowering agents, baseline and postoperative IOP and optical profiles (*e.g.*, BCVA and MD).

● **RESULTS:** Totally 98 eyes (mean postoperative follow-up 67.5mo) showed mean IOP reduction at every follow-up interval. Both median BCVA and MD of visual fields were maintained throughout the follow-up intervals when comparing to baseline. The number of IOP-lowering medications decreased from 2.8±0.8 to 0.3±0.7 (P=0.068). Totally 84 (85.7%) eyes achieved complete success at final follow-up. Transient hyphaema and transient choroidal effusion developed in 15 eyes (15.3%) and 11 eyes (11.2%) respectively. Other complications included shallow anterior chamber in 5 eyes (5.1%), bleb leak in 4 eyes (4.1%), bleb revision in 7 eyes (7.1%), bleb needling in 9 eyes (9.2%) and repeat trabeculectomy in 1 eye (1.0%). There was no endophthalmitis, blebitis or macular oedema. There was no significant correlation between postoperative IOP control and postoperative BCVA.

● **CONCLUSION:** DST with MMC demonstrates effective and sustained long-term outcomes in the treatment of glaucoma with no major complication.

● **KEYWORDS:** glaucoma; surgical outcome; deep sclerectomy; trabeculectomy; mitomycin C

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INTRODUCTION

Trabeculectomy is the current gold standard in the surgical management of glaucoma and its efficacy has been compared to many other glaucoma surgical procedures[1-2]. Intraoperative anti-metabolites such as mitomycin C (MMC) are used to improve the success rate of trabeculectomy[3]. Despite its efficacy in reducing intraocular pressure (IOP), trabeculectomy is far from ideal due to its association with significant complications such as hypotony and endophthalmitis[4]. Non-penetrating surgery such as deep sclerectomy (DS) is introduced as a potentially safer and effective method for lowering IOP with less incidence of postoperative endophthalmitis and hypotony[5]. In DS, a clinically significant intra-scleral space is created by de-roofing the Schlemm's canal to form a trabeculo-Descemet's membrane to allow the aqueous to percolate through it[6], whilst achieving additional drainage *via* the intrascleral and suprachoroidal pathways[7]. However, these non-penetrating techniques have not gained popularity to replace trabeculectomy as it can be time consuming and technically more challenging with a steep learning curve[8-9]. Recent systematic reviews and Meta-analyses showed that although DS is associated with significantly lower postoperative complication rates, it is less effective in reducing IOP than trabeculectomy for patients with open angle glaucoma[5,10].

The quest for safer surgical techniques compared to trabeculectomy whilst achieving effective IOP reduction in glaucoma patients prompted the authors' interests in deep sclerectomy-trabeculectomy (DST). DST, also known as "penetrating DS"[6] combines both modified DS and trabeculectomy[1,11]. This modified surgical technique is believed to help in achieving effective and sustained IOP reduction due to the existence of additional routes for aqueous outflow and the presence of "intra-scleral lake"[6], whilst maintaining respectable safety profile. The healing response and the resistance of sub-Tenon tissue can affect the external sub-conjunctival drainage pathway, which may compromise the success of filtration surgery[12]. Intraoperative application of MMC to the sub-Tenon space will help to inhibit the proliferation of fibroblasts, thereby increasing the survival of filtration bleb and consequently increasing the success rate of any anti-glaucoma bleb-dependent surgical procedure[6,13].

There is limited evidence of its long-term postoperative outcomes. This study intends to determine the long-term success rate and complication rate of DST with MMC for patients with glaucoma.

SUBJECTS AND METHODS

Ethical Approval Institutional Review Board (IRB) or Research Ethics Committee ruled that approval was not required for this study. The study was approved as a clinical audit (CA09021) by the review board at the University Hospitals of North Midlands (UHNM) Quality, Safety and Compliance Department and the study methodology adhered to the tenets of the Declaration of Helsinki. Written consents were obtained for all patients preoperatively after discussing the benefits and risks of the procedure as well as available alternative treatment options.

Patients In this retrospective observational cohort study, we evaluated patients with glaucoma who underwent DST with MMC at a tertiary university hospital in the United Kingdom (UK) between 2010 and 2017. All patients were enrolled consecutively in the study if they fulfilled the following eligibility criteria: 1) diagnosis of any type of glaucoma (primary or secondary, open or closed angle glaucoma) characterised by unsatisfactory IOP reduction with maximally tolerated medications, or progression of visual field defects or progression of glaucomatous optic disc cupping with or without good IOP control who had undergone DST with MMC; 2) completion of at least one year follow-up postoperatively.

Exclusion criteria were as follow: 1) previous ophthalmic surgery (including glaucoma surgery); 2) previous argon or selective laser trabeculoplasty; 3) ocular trauma; 4) patients who had other co-existing ocular pathology (*e.g.*, history of posterior segment pathology).

Preoperative Data Preoperative data consisted of patient demographics which included age, gender, diagnosis of glaucoma type determined using gonioscopy, examination of anterior and posterior segment using slit lamp biomicroscopy (including dilated fundus examination of the optic disc), number of IOP-lowering medications, logMAR distance best-corrected visual acuity (BCVA) assessed by a well-trained nursing officer or a healthcare assistant, IOP measured using Goldmann applanation tonometry (GAT) by an ophthalmologist and mean deviation (MD) of visual field examination using static automated Humphrey visual field (HVF) with 24-2 full threshold test or 10-2 threshold test at the time of listing for surgery. For patients using topical combinations, the medications were counted according to the number of active drugs. The use of systemic acetazolamide was counted as one drug.

Operative Procedures All surgeries were performed by a single experienced glaucoma surgeon (Ranjit P). The type of anaesthesia was determined preoperatively according to patient suitability, with the majority performed under general anaesthesia. If general anaesthesia was unsuitable, sub-Tenon anaesthesia was administered in 3 mL of 2% lignocaine and 300 IU of hyaluronidase.

Before anaesthesia, topical apraclonidine 1% was used to reduce intraoperative bleeding. The surgical steps of DST were illustrated in Figure 1. A traction suture 6-0 prolene (Ethicon®, USA) was applied in clear cornea superiorly to mobilise the globe for better exposure of the surgical site. Fornix-based conjunctival and Tenon's flap was created to expose sclera and blunt dissection was carried out to expose sub-Tenon space posteriorly on either side of the superior rectus (Figure 1A). A sponge soaked with 0.2 mg/mL MMC was applied to the sub-Tenon "pocket" for 3min, followed by continuous thorough irrigation with 20 mL of balanced salt solution (BSS). The episcleral vessels were cauterised as minimal as possible using wet-field bipolar diathermy, avoiding the perforators, which were connected to the collector channels. One in 10 000 of topical adrenaline were administered on the scleral bed before making the scleral flap. A thin limbus-based 4×4 mm^2 superficial flap of one-third of the scleral thickness was then created with a diamond knife (John Weiss®, United Kingdom), which was extended 1.5 mm anteriorly into clear cornea (Figure 1B). Under the superficial flap, a second 3.5×3.5 mm^2 deep scleral flap was created with the diamond knife (John Weiss®, United Kingdom) and a crescent knife (Mani® Inc. Japan), leaving a residual sclera bed of 50 to 100 μm over the uvea (Figure 1C). This second flap was extended anteriorly from the scleral spur 1.5 mm into clear cornea, de-roofing the Schlemm's canal. Then, the deeper flap was excised, creating a 3.5×1.5 mm^2 trabeculo-descemets window (Figure 1D). The juxtacanalicular

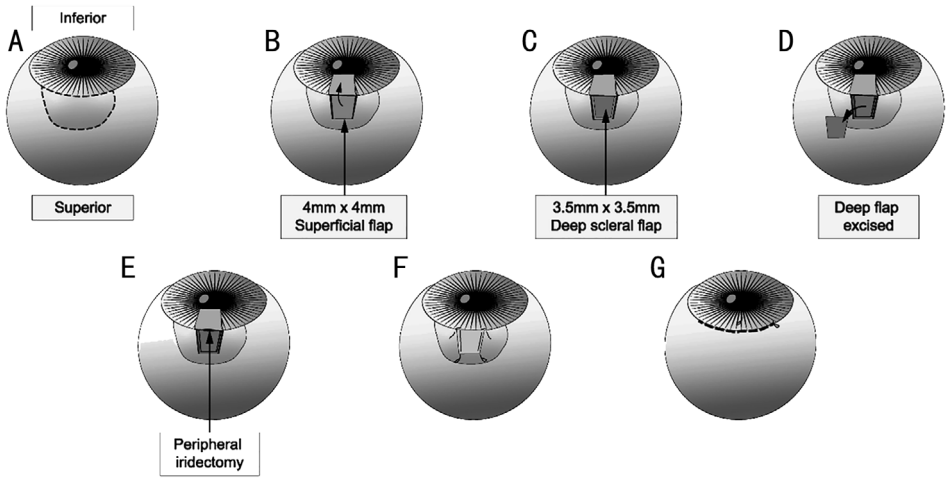

Figure 1 Surgical steps of a deep-sclerectomy trabeculectomy with mitomycin C A: A fornix-based conjunctival flap was created; B: A thin limbus-based 4×4 mm^2 superficial flap of one-third of the scleral thickness was created; C: A 3.5×3.5 mm^2 deep scleral flap was created; D: The deeper flap was excised, creating a 3.5×1.5 mm^2 trabeculo-descemets window; E: After removing the juxtacanalicular trabecular meshwork, a peripheral iridectomy was performed; F: The superficial scleral flap was repositioned using two cardinal 10-0 Nylon (Alcon®, USA) pre-placed releasable sutures. Additional two 10-0 Vicryl sutures (Ethicon®, USA) were used anteriorly to secure scleral flap to prevent anterior flow of aqueous; G: The conjunctiva and Tenon fascia were repositioned and repaired with 10-0 Vicryl (Ethicon®, USA) and 10-0 Nylon (Alcon®, USA).

trabecular meshwork was then removed with suture tier forceps. Cut ends of Schlemm's canal were dilated with viscoelastic 1.4% sodium hyaluronate (Healon GV, Alcon®, USA) on either side. A self-sealing corneal paracentesis was performed and pre-placed two 10-0 nylon (Alcon®, USA) releasable sutures were secured on either side of the superficial flap before penetrating the trabeculo-descemets window using diamond knife (John Weiss®, United Kingdom). A subsequent peripheral iridectomy was also performed with Vanass scissors (Altomed®, UK; Figure 1E). For the closure of the superficial scleral flap, the two cardinal 10-0 nylon (Alcon®, USA) releasable sutures were then tied. Additional two 10-0 vicryl sutures (Ethicon®, USA) were used anteriorly to secure scleral flap to prevent anterior flow of aqueous (Figure 1F). The conjunctiva and Tenon fascia were repositioned and repaired with 10-0 vicryl (Ethicon®, USA) and 10-0 nylon (Alcon®, USA), and the anterior chamber (AC) was reformed with BSS (Figure 1G). Finally, a subconjunctival injection of dexamethasone 2 mg/0.5 mL and cefuroxime 125 mg/mL in the lower fornix were given; a stat dose of atropine 1% topical eye drop and a sterile eye pad was applied.

All patients were treated postoperatively with topical chloramphenicol 0.5% eye drops four times per day for one week and prednisolone acetate 1% eye drops two-hourly for two to four weeks and then tapered accordingly for another two to three months. Cyclopentolate 1% eye drops twice a day was given to all phakic patients for one week.

Intraoperative and Postoperative Data Data on intraoperative anaesthesia and any intraoperative complication were noted. Postoperative data included distance BCVA, slit lamp examination and IOP measurements using GAT at within 1wk, 1, 3, 6, 12mo and then yearly thereafter to up to 7y. MDs of visual field examination with static automated perimetry (HVF 24-2 full threshold test or 10-2 threshold test) at 6, 12mo then yearly thereafter to up to 7y, and the use of IOP-lowering medications at 12mo and yearly thereafter to up to 7y were also recorded.

Postoperative complications such as hyphaema, transient choroidal effusion, shallow AC, bleb leak, macular oedema, hypotony, choroidal detachment, blebitis and endophthalmitis were recorded. Any postoperative interventions such as AC reformation with viscoelastic 1.4% sodium hyaluronate (Healon GV, Alcon®, USA), conjunctiva resuturing, bleb needling with anti-metabolite injection, bleb revision, laser suturelysis, removal of releasable sutures and repeat trabeculectomy were also noted.

Outcome Measures The outcome measures of our study were in keeping with the recommendations of the World Glaucoma Association Guidelines on Design and Reporting of Glaucoma Surgical Trials[14] and also with other studies reporting surgical success and complications of glaucoma filtering procedures[1,6,15]. Surgical success or failure was determined by several measures: 1) IOP measurement, 2) percentage of postoperative IOP reduction, 3) number of topical IOP-lowering medications postoperatively, 4) need for further glaucoma surgery. Only single IOP measurement was used at each follow-up time point due to the retrospective nature of our study. Postoperative IOP of ≤21 mm Hg or 30% reduction of IOP from baseline without any topical IOP-lowering agent was considered as complete success.

Postoperative IOP of ≤21 mm Hg or 30% reduction of IOP from baseline with/without single topical IOP-lowering agent was considered as qualified success. Failure of the procedure was concluded when more than one topical IOP-lowering medication and/or repeat glaucoma surgery was required to control IOP postoperatively.

With regards to postoperative complications, hypotony was defined based on clinical findings and was classified as transient or long-term hypotony. Transient hypotony included hypotony which were temporary and not affecting vision or causing any long-term visual complication. Long-term hypotony was defined as hypotony which persisted for more than six weeks with retinal folds, causing hypotonic maculopathy affecting visual acuity and/or requiring intervention[16]. Bleb leak was explained as a visible conjunctival leak and/or a positive Seidel's test after surgery[17]. Transient choroidal effusion was defined as an abnormal accumulation of fluid in the suprachoroidal space which resolved spontaneously during the first month postoperatively without visual complication[18]. The term choroidal detachment described persistent choroidal effusion secondary to severe or long-term hypotony[19-20].

Statistical Analysis Outcome data were presented as numbers and percentages, mean values and standard deviation (SD) as well as median and range or interquartile range (IQR). A Kaplan-Meier survival curve of the complete and qualified success rates was performed using MedCalc Statistical Software version 19.6.3 (Med Calc Software Ltd, Ostend, Belgium).

Student's paired *t*-test was used to assess differences in parametric data (IOP, BCVA, and MD) before and after surgery. Wilcoxon signed-rank test was used for non-parametric data (number of IOP-lowering medications). Multivariate logistic regression (including demographic information, use of topical IOP-lowering medication, preoperative variance) was performed for postoperative profiles that included three factors: IOP, BCVA, and MD. A *P*-value of less than 0.05 was considered statistically significant. Mixed linear regression models were constructed to determine estimated predictive values of demographic data, use of topical IOP-lowering agents, baseline and postoperative IOP and optical profiles (*e.g.*, BCVA and MD). These statistical analyses were performed using MATLAB R2013b (The Mathwork, Natick, MA, USA).

RESULTS

A total of 98 eyes of 74 Caucasian patients who underwent DST with MMC between 2010 and 2017 (mean follow-up period of 67.5mo, range 12-84mo) were included for analysis after 19 eyes were excluded due to the following reasons: wrong glaucoma surgery recorded (*n*=3, 2.6%), postoperative follow-up duration of less than one year (*n*=3, 2.6%), pre-existing ophthalmic surgery (*n*=1, 0.9%), previously had glaucoma laser procedure (*n*=2, 1.7%), had other co-existing ocular pathology affecting outcome measures (*n*=1, 0.9%), incomplete case notes documentation (*n*=9, 7.7%).

Table 1 Patients' demographics and baseline characteristics

Demographics	DST with MMC
Total number of patients, *n*	74
Gender, *n* (%)	
Male	34 (46.7)
Female	40 (53.3)
Age, mean±SD (range)	77.4±10.4 (49-97)
Total number of eyes, *n*	98
Glaucoma type, *n* (%)	
POAG	76 (77.6)
PACG	7 (7.1)
Other types	15 (15.3)
Ocular characteristics, *n* (%)	
Left eye	47 (48.0)
Right eye	51 (52.0)
Anaesthesia, *n* (%)	
Local anaesthetics	8 (8.2)
General anaesthetics	90 (91.8)
Presenting IOP, mean±SD (range), mm Hg	25.5±10.6 (10-68)
Preoperative IOP, mean±SD (range), mm Hg	23.1±7.6 (10-46)
Preoperative IOP-lowering medications, mean±SD	2.8±0.8
Presenting BCVA, median logMAR (IQR)	0 (0-0.2)
Preoperative BCVA, median logMAR (IQR)	0.12 (0-0.22)
Preoperative HVF 24-2, MD, mean±SD	-12.23±5.93
Total follow-up (mo)	
Mean±SD	67.5±18.8
Median (IQR)	72 (60-84)
Range	12-84

DST: Deep sclerectomy-trabeculectomy; MMC: Mitomycin C; SD: Standard deviation; IQR: Interquartile range; POAG: Primary open angle glaucoma; PACG: Primary angle-closure glaucoma; IOP: Intraocular pressure; BCVA: Best corrected visual acuity; HVF: Humphrey visual field; MD: Mean deviation. Preoperative IOP was defined as the IOP measured using Goldmann applanation tonometry on listing for DST with MMC.

Table 1 showed our patients' demographic and baseline characteristics in the duration of follow-up. Most patients had DST with MMC under general anaesthesia (*n*=90, 91.8%) and for primary open angle glaucoma (*n*=76, 77.6%).

Table 2 demonstrated the percentages of decrease of mean IOP, IOP profiles and the proportion of patients with complete and qualified success at each follow-up time point. A significant decrease in IOP compared to preoperative level of approximately 44%-47% at each follow-up interval was achieved. The proportion of patients with IOP≤21 mm Hg at one, three, five and seven years after surgery were 95.9%, 97.8%, 97.5% and 100.0% respectively. At similar time points

Table 2 Mean IOP decrease, IOP profiles, complete and qualified success rates at each follow-up time point

n (%), mm Hg

Time (mo)	Number of eyes at each follow-up time point, *n*	Mean IOP, mean±SD	Mean IOP decrease (preop./postop.), %	Proportion of eyes with IOP ≤21	Proportion of eyes with IOP ≤18	Proportion of eyes with IOP ≤15	Proportion of eyes with IOP ≤12	Complete success rate	Qualified success rate
0	98	23.1±7.6	N/A	47 (48.0)	30 (30.6)	11 (11.2)	4 (4.1)	N/A	N/A
12	97	12.4±4.3	46.3	93 (95.9)	86 (88.7)	71 (73.2)	58 (59.8)	91 (93.8)	91 (93.8)
24	95	12.6±3.9	45.4	93 (97.9)	89 (93.7)	69 (72.6)	56 (58.9)	83 (87.4)	87 (91.6)
36	91	12.5±4.2	46.0	89 (97.8)	82 (90.1)	68 (74.7)	53 (58.2)	76 (83.5)	80 (87.9)
48	84	12.6±4.1	45.6	83 (98.8)	78 (92.9)	63 (75.0)	45 (53.6)	73 (86.9)	76 (90.5)
60	79	12.7±4.4	45.2	77 (97.5)	73 (92.4)	59 (74.7)	43 (54.4)	66 (83.5)	69 (87.3)
72	71	12.9±4.4	44.4	69 (97.2)	64 (90.1)	50 (70.4)	37 (52.1)	58 (81.7)	64 (90.1)
84	30	12.3±4.6	47.0	30 (100.0)	28 (93.3)	22 (73.3)	16 (53.3)	25 (83.3)	27 (90.0)

IOP: Intraocular pressure; SD: Standard deviation; N/A: Not applicable. Complete success defined as postoperative IOP of ≤21 mm Hg or 30% reduction of IOP from baseline without any topical IOP-lowering agent. Qualified success defined as postoperative IOP of ≤21 mm Hg or 30% reduction of IOP from baseline with/without single topical IOP-lowering agent.

Table 3 Complete and qualified success rates at final follow-up[a]

n (%), *n*=98

Success/failure rates	Data
Complete success	
All eyes	84 (85.7)
POAG	62 (63.3)
PACG	7 (7.1)
Normotension glaucoma	10 (10.2)
Secondary glaucoma	5 (5.1)
Qualified success	
All eyes	89 (90.8)
POAG	67 (68.4)
PACG	7 (7.1)
Normotension glaucoma	10 (10.2)
Secondary glaucoma	5 (5.1)
Failure	
All eyes	9 (9.2)
POAG	9 (9.2)
PACG	0
Normotension glaucoma	0
Secondary glaucoma	0

POAG: Primary open angle glaucoma; PACG: Primary angle-closure glaucoma. Complete success defined as postoperative IOP of ≤21 mm Hg or 30% reduction of IOP from baseline without any topical IOP-lowering agent. Qualified success defined as postoperative IOP of ≤21 mm Hg or 30% reduction of IOP from baseline with/without single topical IOP-lowering agent. [a]Analysis performed demonstrating 98 eyes up to final follow-up time points with median follow-up duration of 72mo, and interquartile range (IQR) of 60-84mo.

as aforementioned, 73.2%, 74.7%, 74.7% and 73.3% had IOP ≤15 mm Hg, whereas 59.8%, 58.2%, 54.4% and 53.3% had IOP ≤12 mm Hg respectively. All patients achieved considerably low IOP measurements with a mean IOP of 12.4, 12.5 and 12.7 mm Hg at one, three, and five years after surgery respectively. High percentages of patients achieving complete success were demonstrated at each follow-up interval.

At final follow-up, the complete success rate was 85.7% (Table 3). Considering the median follow-up duration of 72mo of our patient cohort (*n*=98), the Kaplan-Meier survival curve demonstrating cumulative probability of complete and qualified success rates of DST with MMC up to 72-month follow-up was depicted in Figure 2.

Postoperative profiles were interpreted with a focus on our 6-year follow-up data to provide both long-term results and acceptable low dropout rate to maintain validity. We demonstrated sustained IOP reduction postoperatively at every follow-up interval that was statistically significant (Table 4). Preoperative BCVA [0.12 (IQR 0-0.22)] and postoperative BCVA were comparable in the long term. Postoperative MD also

Table 4 IOP profiles, BCVA profiles, HVF 24-2 performance and number of IOP-lowering medication of DST with MMC

Follow-up time point	Mean±SD	*P*
IOP, mm Hg		
Preoperative	23.1±7.6	0.0005
1mo	10.0±4.2	0.0249
3mo	11.8±5.1	0.0012
6mo	11.9±4.4	0.0003
1y	12.4±4.3	0.0012
2y	12.6±3.9	0.0012
3y	12.5±4.2	0.0022
4y	12.6±4.1	0.0014
5y	12.7±4.4	0.0026
6y	12.9±4.4	0.0032
7y	12.3±4.6	-
BCVA, median (IQR)		
Preoperative	0.12 (0-0.22)	0.0642
1mo	0.20 (0.10-0.30)	0.0933
3mo	0.20 (0.10-0.24)	0.0642
6mo	0.20 (0.05-0.24)	0.0642
1y	0.20 (0.10-0.22)	0.1701
2y	0.20 (0.10-0.26)	0.1285
3y	0.16 (0.10-0.23)	0.0022
4y	0.20 (0.06-0.26)	0.1101
5y	0.18 (0.10-0.24)	0.4076
6y	0.16 (0.04-0.32)	0.0641
7y	0.11 (0.06-0.34)	-
Mean deviation 24-2 HVF		
Preoperative	-12.23±5.93	0.0278
6mo	-11.57±6.79	0.0482
1y	-12.14±5.84	0.0223
2y	-10.91±5.56	0.0572
3y	-10.78±5.77	0.0167
4y	-10.60±5.50	0.4076
5y	-10.78±4.00	0.0704
6y	-10.58±4.58	0.0299
7y	-11.35±3.37	-
IOP-lowering medications		
Preoperative	2.8±0.8	-
Postoperative at final follow-up	0.3±0.7	0.0684

DST: Deep sclerectomy-trabeculectomy; MMC: Mitomycin C; IOP: Intraocular pressure; BCVA: Best-corrected visual acuity; HVF: Humphrey visual field; SD: Standard deviation; IQR: Interquartile range.

did not demonstrate significant progression. The mean number of IOP-lowering medications reduced from preoperative 2.8±0.8 to postoperative 0.3±0.7 (*P*=0.068).

Surgical complications and postoperative interventions were presented in Table 5. There was no intraoperative complication. Hyphaema developed in 15 eyes (15.3%) and in all cases

Table 5 Summary of main postoperative complications and interventions *n*=98

Complications/interventions	Eyes, *n* (%)
Hyphaema	15 (15.3)
Transient choroidal effusion	11 (11.2)
Shallow anterior chamber requiring reformation	5 (5.1)
Bleb leak requiring conjunctival suturing	4 (4.1)
Macular oedema/hypotonic maculopathy	0
Bleb needling with 5-fluorouracil injection	9 (9.2)
Bleb revision or transconjunctival suturing of bleb for hypotony	7 (7.1)
Laser suturelysis or removal of releasable sutures	6 (6.1)
Repeat trabeculectomy	1 (1.0)
Choroidal detachment	0
Blebitis	0
Endophthalmitis	0

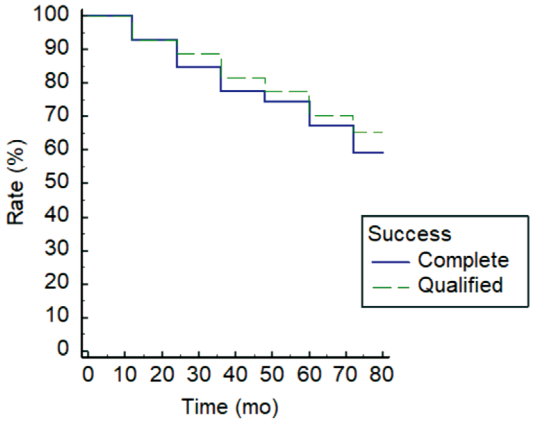

Figure 2 Kaplan-Meier survival curve showing the cumulative probability of success rate (complete and qualified) of deep sclerectomy-trabeculectomy with mitomycin C up to 72-month follow-up (*n*=98).

were transient which resolved during the first week. Totally 11 eyes (11.2%) had transient choroidal effusion, which resolved spontaneously during the first month without visual complication. No choroidal detachment or persistent choroidal effusion was observed. Other complications included shallow AC requiring reformation in 5 eyes (5.1%), bleb leak requiring conjunctival suturing in four eyes (4.1%), bleb needling with 5-fluorouracil injection in 9 eyes (9.2%), revision of bleb or transconjunctival suturing of bleb for hypotony in 7 eyes (7.1%), laser suturelysis or removal of releasable sutures in 6 eyes (6.1%), and repeat trabeculectomy in one eye (1.0%). The repeat trabeculectomy with MMC was successful and was performed as the IOP was not well controlled and there was very little drainage. There was no endophthalmitis, blebitis or macular oedema. Of all eyes included in our analysis, 65 eyes (66.3%) had no intraoperative or postoperative complication.

Mixed linear regression model constructed showed that presenting demographics (age, gender) and ocular characteristics (profiles of IOP, BCVA, and MD) were not statistically significant,

likely due to immense variability. Calculated data beyond one-year follow-up were unreliable, and thus discarded due to insufficient follow-up for time series analysis. Table 6 showed no significant correlation between postoperative IOP control and postoperative BCVA. T-statistic for each coefficient and *P*-value for the *F* statistic were calculated to test the null hypothesis that the corresponding coefficient was 0 against the alternative that it is different from 0, given the other predictors in the model.

Table 6 Linear regression estimated coefficients of IOP at one-year follow-up post DST with MMC

Parameters	Estimate	Standard error	*t*-statistics	*P*
(intercept)	3.7534	1.328	2.826	0.006
Preoperative BCVA	0.705	2.595	0.272	0.787
Preoperative IOP	0.0226	0.047	0.485	0.629
Preoperative MD	0.0869	0.047	1.855	0.068
Postoperative BCVA at 3mo	0.3833	3.157	0.121	0.904
Postoperative IOP at 3mo	0.1212	0.09	1.344	0.184
Postoperative BCVA at 6mo	3.4347	3.392	1.013	0.315
Postoperative IOP at 6mo	0.6779	0.097	6.97	0
Postoperative BCVA at 1y	-6.0439	3.11	-1.943	0.056

Number of observations: 76; Error degrees of freedom: 67; Root mean squared error: 3.54. R^2: 0.684, Adjusted R^2: 0.646, *F*-statistic *vs* constant model: 18.12. DST: Deep sclerectomy-trabeculectomy; MMC: Mitomycin C; IOP: Intraocular pressure; BCVA: Best-corrected visual acuity; MD: Mean deviation.

DISCUSSION

Our current study showed that DST with MMC is an effective surgical technique for a sustained IOP control in the management of different types of glaucoma, mainly primary open angle glaucoma (POAG). A significant IOP decrease was achieved at every follow-up interval, with a high proportion of patients (more than 80%) achieving complete surgical success. Our study also demonstrated long-term (up to 7y) stable BCVA and MD after surgery. There was no intraoperative and no major postoperative complication such as endophthalmitis, blebitis or macular oedema.

Trabeculectomy has always been considered the gold standard surgical technique in the management of POAG[1]. However, higher incidences of postoperative complications such as hypotony, shallow AC and choroidal detachment were reported as compared to non-penetrating alternatives[5]. Non-penetrating DS offered a safer profile but were considered less effective in lowering IOP than trabeculectomy[21-22]. Combining these two surgical procedures by performing a DST with MMC appears to provide a comparable result to trabeculectomy in IOP reduction but with relatively fewer complications[1,6,11]. The trabeculo-Descemets window created intraoperatively allows long-term sufficient filtration of aqueous humour giving sustained IOP reduction, as well as ensuring gentle drainage of aqueous using the alternative pathways. We believe that the "intra-scleral lake" is important to act like a reservoir, allowing aqueous humour to fill the space before gently leaving the eye, reducing the risks of complications associated with hypotony[6]. Combining non-penetrating and penetrating surgical techniques is not new and these have been performed in paediatric glaucomas[23]. Since then among adult glaucoma patients, different surgical approaches combining non-penetrating and penetrating surgical techniques have been described[1,6,24-25], with a recent study demonstrating higher success rates when combining penetrating and non-penetrating techniques[26]. Kalala *et al*[24] showed that by performing a penetrating DS, similar efficacy and safety results to traditional non-penetrating DS can be achieved. Of similar surgical technique to our current study, Sangtam *et al*[1] published the outcomes of combining modified DS and trabeculectomy, who reported complete success of approximately 50% with a median follow-up of 40mo. Kozobolis *et al*[6] also reported complete success of 58.6% and qualified success of 75.9% after a follow-up of three years. Our current study with a larger sample size reported higher complete success and qualified success rates at a longer follow-up duration (up to 7y). Whilst our current study used releasable sutures for closure of the scleral flap similar to techniques performed in standard trabeculectomy, Sangtam *et al*[1] closed the flap using interrupted 10-0 nylon sutures whereas Kozobolis *et al*[6] used sodium hyaluronate 1% to fill the created space under the scleral flap before repositioning the conjunctiva. It should be noted that inclusion criteria, surgical techniques and surgical success criteria differed amongst the aforementioned studies evaluating DST, precluding direct comparison of its surgical efficacy and safety.

Our current study reported effective and sustained IOP reduction postoperatively throughout the follow-up period, which was comparable to other studies reporting IOP outcomes after trabeculectomy[27-30]. Our study with a median follow-up duration of 72mo reported a complete success rate of 85.7% and a qualified success rate of 90.8%. The reported complete success rate in studies comparing DS to trabeculectomy varied from 40%-79% in DS versus 45%-92.6% in trabeculectomy, whereas qualified success rate varied from 76.5%-95% in DS versus 88.9%-95% in trabeculectomy[21,31-32]. The number of postoperative IOP-lowering medications in the studies mentioned earlier ranged from 0.3±0.4 to 1.0±1.0 and 0.27±0.5 to 1.2±1.1 in DS and trabeculectomy respectively[21,27,31-32]. These results were also comparable to our current study.

Transient hyphaema was observed in 15.3% of eyes included in our study as compared to other similar studies reporting 13.8% and 6.8% respectively[1,6]. Its rate was still generally low and in between that of reported for DS (2%-15%)[31] and trabeculectomy (7.7%-41%)[21]. We did not encounter

any persistent choroidal effusion or choroidal detachment, however, 11.2% of eyes developed transient choroidal effusion, which resolved spontaneously during the first month; this was still better than trabeculectomy[27]. The incidence of shallow AC requiring reformation in our study was superior to trabeculectomy, which had a rate varying from 7.7%-33.3%[27,31]. The incidence of bleb leak in our study was also comparable to studies evaluating glaucoma filtering procedures[1,31].

The rate of hypotony requiring bleb revision in our study was lower than other similar studies and those reporting complications of DS and trabeculectomy[1,33]. Bleb needling with anti-fibrotic agent when there were signs of bleb failure evidenced by increased bleb vascularity with progressive IOP elevation or bleb encapsulation in our current study were less common than that reported by Sangtam *et al*[1] and Kozobolis *et al*[6], which were 50% and 20.7% respectively. The significant difference in rates of bleb fibrosis requiring intervention could be explained by the different intraoperative surgical techniques and materials used, which might have contributed to alterations in wall tension and biomechanical factors that may influence bleb fibrosis[34]. None of the eyes in our study experienced serious sight-threatening complications such as endophthalmitis, as compared with 3% in the trabeculectomy group in the study performed by Gedde *et al*[27]. These indicated that our DST with MMC techniques demonstrated high safety profile, and it maintained the safety profile of the classic DS with no additional major complication.

Strengths and Limitations Strengths of our study included a larger sample size and a longer follow-up period (up to 7y) as compared to previous similar studies[1,6]. Limitations of our study included the retrospective study design with potential missing data and recall bias. There was high dropout rate towards the end of the follow-up time point (only 30 eyes completed follow-up of 84mo), therefore some of our results could only be confidently interpreted till the follow-up time point of 72mo. Besides, all surgeries were performed by the same surgeon. Our study used a non-comparative design, and with different success criteria and diagnostic profiles, it was difficult to make any definitive conclusion comparing our results to that of standard trabeculectomy.

DST with MMC is an effective surgical procedure as it provides long-term sustained IOP reduction with no major complication encountered. Our proposed anti-glaucoma surgical modification combining the advantages of both trabeculectomy and DS can be considered for open-angle glaucoma. Further prospective randomised controlled study comparing standard trabeculectomy with our surgical technique is required to determine its true place in terms of its efficacy and safety in the armamentarium of glaucoma surgical procedures.

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