Primary glaucoma surgery in Fuchs' heterochromic uveitis: a comparison of trabeculectomy versus deep sclerectomy

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Abstract

Background: Deep sclerectomy offers the potential advantage of less postoperative inflammation and better survival in Fuchs' patients. The aim of this study was to compare survival and safety profiles of Fuchs' heterochromic uveitis patients undergoing trabeculectomy or deep sclerectomy.

Methods: A retrospective study was conducted of two separate cohorts who had undergone either trabeculectomy or deep sclerectomy. Patient demographics, best-corrected visual acuity, intraocular pressure, antimetabolite used, postoperative complications and subsequent procedures were analysed.

Results: In total, 13 trabeculectomy patients and 14 deep sclerectomy patients were included. Mean preoperative intraocular pressure was similar at 30.1 mmHg in the trabeculectomy group and 35.9 mmHg in the deep sclerectomy group, with no significant difference between the two ($p = 0.22$). Kaplan–Meier survival outcomes for success at <22 mmHg and <19 mmHg showed no significant differences between the groups and this was also the case for intraocular pressure at 3 years (analysis of variance; $p = 0.47$).

Conclusion: Both procedures appear to have similar efficacy and safety profiles, suggesting that both are effective.

Keywords: deep sclerectomy, Fuchs, trabeculectomy, uveitis

Introduction

Fuchs' heterochromic uveitis (FHU) accounts for 1–11% of uveitis cases,[1] of which between 29% and 60% are susceptible to developing secondary uveitic glaucoma (UG).[2–5] The aetiology of glaucoma in FHU includes lens-induced acute glaucoma, trabecular sclerosis, phacolysis, cicatrices, anterior segment neovascularization, trabeculitis and steroid-induced glaucoma, but is largely due to chronic open angle glaucoma.[3]

Intraocular pressure (IOP) may become uncontrolled despite maximal medical therapy, requiring surgical intervention. Augmented trabeculectomy has higher failure rates in patients with UG,[6] although it has been shown to have similar success rates to glaucoma drainage implantation (GDI) in some series.[6–8] Deep sclerectomy (DS) offers an alternative intervention for UG patients, with favourable published outcomes compared with trabeculectomy.[9,10] This may be attributable to the absence of either anterior chamber penetration or surgical iridectomy.[11]

It has been suggested that FHU-related glaucoma is associated with higher trabeculectomy failure rates compared with other uveitic aetiologies.[12] The aim of this study was to compare the outcomes and safety profiles of augmented DS with 5-fluorouracil-augmented trabeculectomy (5FT) in two single-surgeon FHU patient cohorts with those of patients having UG. To the best of our knowledge, such a comparison has not previously been made.

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Methods

This was a descriptive, retrospective, nonrandomized, case note review of all patients diagnosed with FHU undergoing either 5FT or DS for secondary glaucoma in two UK tertiary centres with experience in both complex uveitis and glaucoma. The entire research has followed the tenets of the Declaration of Helsinki. Ethical approval was not sought due to the retrospective and noninterventional nature of this study.

All patients were identified from correlational ongoing glaucoma surgery and uveitis clinic databases (Microsoft Access). All DS procedures were performed by a single consultant glaucoma surgeon (N.A.) between January 2002 and July 2007 in Calderdale and Huddersfield NHS Foundation Trust. All trabeculectomy procedures were performed by a single uveitis consultant with long-standing expertise in the procedure between November 1993 and March 2011 at Manchester Royal Eye Hospital with some of the latter patients being already reported in a previous publication by these authors.[7]

Patients undergoing prior glaucoma surgery within 6 months of filtering surgery and those with incomplete medical records were excluded.

Data collected included patient demographics, Snellen best-corrected visual acuity (BCVA), pre- and postoperative IOP, use of antimetabolites, use of spacer device implantation, any postoperative complications, subsequent procedures including reoperation for glaucoma and the use of supplementary medical therapy. All pre- and postoperative management took place under the supervision of individual specialists, with subspecialty input when necessary.

A standardized technique was used for both DS and 5FT procedures, details of which have been described in separate previous publications.[7,13] For the DS cases, mitomycin C (MMC) at a dose of 0.2 or 0.4 mg/mL was applied to the subconjunctival space prior to scleral flap dissection for 2–3 min in 12 of 16 eyes (75%). The mitomycin concentration and application time were varied according to the anticipated failure risk. The surgical site was chosen after preoperative gonioscopy had identified an area free of peripheral anterior synechiae (PAS). Postoperatively, patients received strong topical steroid prednisolone acetate 1% drops 2-hourly, which was continued for a minimum of 8 weeks. All patients were seen on the first postoperative day, then at week 1 and at week 6 post-surgery or before. Subsequent postoperative visits were determined by clinical need. Where there was an elevation of IOP at any stage, Nd:YAG laser goniopuncture (LGP) was performed with a Magna View contact gonioscopy lens (Ocular Instruments, Bellevue, WA, USA). Needle revision with 5-fluorouracil (5-FU) or MMC was subsequently performed if IOP was still elevated. The need for either or both of these interventions was not classified as a failure. The detailed technique for LGP has already been described in a previous publication.[14]

All trabeculectomies were performed via a superiorly placed fornix-based conjunctival flap. After dissecting a 4 mm by 4 mm scleral flap, 5-FU (when used) was applied with soaked surgical sponges for 2–3 min and washed away with a balanced salt solution. A 'block' sclerectomy was performed, followed by a peripheral iridectomy. The scleral flap was closed with interrupted 10-0 nylon sutures. No releasable sutures were placed. Postoperatively, patients received dexamethasone 0.1% drops 2-hourly and cyclopentolate 1% three times a day, which were continued in a tapering regime for a minimum of 3 months. All patients were seen on the first postoperative day, then each subsequent week for the first month after surgery and week 6 post-surgery. Subsequent postoperative visits were determined by clinical need. Needling with 5-FU was performed if IOP was suboptimal postoperatively. Preoperatively, topical steroids were adjusted depending on the inflammation activity.

The data compared examination findings prior to surgery with those of postoperative day 1, weeks 1–2, weeks 3–6 and months 3, 7, 13, 17, 23, 29, 35, 41, 47, 53, 59, 65 and 71 thereafter. Complete (unqualified) success criteria were defined as follows: (a) IOP < 22 mmHg or a 20% decrease from baseline IOP off any glaucoma medications and (b) IOP < 19 mmHg or a 30% drop from baseline IOP off glaucoma medications. Partial (qualified) success was defined as any of the above but with at least one topical IOP-lowering medication. The IOP had to be above the predetermined level on two consecutive visits to be considered as failure. IOP < 6 mmHg on two consecutive time points 3 months after surgery was also considered as failure. If a patient had an unsuccessful LGP or needle revision, failure was considered to have occurred on the visit when the decision to undertake that procedure was taken.

Reoperation for glaucoma or for a complication was defined as additional surgery. Serious complications were defined as those associated with the loss of two or more lines of Snellen VA for more than 6 months or reoperation to manage a complication. Eyes that tested Seidel positive within the first month of follow-up were classified as wound leaks, whereas those occurring after 1 month were categorized as bleb leaks. Data from patients who underwent additional glaucoma surgery were censored from that time point.

Statistical analysis

MedCalc Software (Broekstraat 52, 9030 Mariakerke, Belgium) was used for statistical analysis. Kaplan–Meier survival outcomes were calculated for each surgical intervention and represented graphically for ease of comparison. Repeated-measures analysis of variance (ANOVA) was used to investigate any differences between groups at measured time intervals up to 3 years postoperatively. The Kruskal–Wallis test was used to look for differences in postoperative medication usage. The log-rank test was used to check for differences in success rates between eyes with or without previous intraocular surgery. Nonparametric comparisons were made with the χ^2 test with Yates correction or Fisher's test where appropriate.

Results

In total, 13 patients underwent 5FT and 14 underwent DS. The mean follow-up duration was 6 years for 5FT (73.3 ± 28.1 months) and 13 years for DS (152.91 ± 127.32 months). These and further patient demographics, including previous intraocular surgery, antimetabolite use and preoperative medications, are detailed in Table 1. Mean preoperative IOP was 30.5 ± 8.01 mmHg in the 5FT group and 33.6 ± 11.6 mmHg in the DS group; this difference was not significant ($p = 0.43$). Phacoemulsification was combined with 5FT in four eyes (30.8%) and with DS in two eyes (14.3%). In total, 12 eyes (44%) had previous intraocular surgery (Table 1).

The Kaplan–Meier survival outcomes for both the trabeculectomy and DS groups are detailed in Table 2 with no significant differences shown. Figure 1 shows Kaplan–Meier curves for both unqualified and qualified success rates at <22 mmHg and <19 mmHg. Figure 2 shows IOP changes for each group over time, including 95% confidence intervals. No difference was measured between the groups during a 3-year follow-up period (repeated-measures ANOVA; $p = 0.47$). Figure 3 shows medications prescribed before and after surgery. For the 60-month period, no significant difference in mean postoperative number of glaucoma drops was found between the groups at all time intervals ($p > 0.05$) except for the 11- to 13-month interval where $p = 0.02$ (Kruskal–Wallis test). The mean number of medications in both groups at 60 months was less than 1 (DS $= 0.52 \pm 1.02$, 5FT $= 0.62 \pm 0.96$).

Table 3 shows pre-operative and post-operative status after Trabeculectomy and Deep Sclerectomy including visual acuity, IOP and inflammatory flare ups. Table 4 shows the complications that occurred during follow-up, any postoperative adjustments and reoperations carried out. Three eyes from the 5FT group underwent further surgery for uncontrolled IOP (two requiring glaucoma drainage tubes and one repeat trabeculectomy). In comparison, only one eye from the DS group required a further drainage procedure. In the DS group, three eyes had no intraoperative flow due to thickened trabecular meshwork-Descemet's membrane (TDM), presumably from trabecular fibrosis.

Discussion

The surgical management of UG is challenging, with the main indication for surgery being uncontrolled IOP on maximal medication. The results of filtering surgery in uveitis are variable and are generally associated with higher failure rates compared with nonuveitic glaucoma.[15,16] Both trabeculectomy and DS have been evaluated in UG previously.[7,17] The aim of this study was to compare the survival and safety profile of patients with FHU syndrome, who had undergone either trabeculectomy or augmented DS. We included 26 eyes of 26 patients with Fuchs' uveitis syndrome (FUS). To our knowledge, no published results of DS in FHU are available in the literature, with scarce evaluation of trabeculectomy in this condition.[18,19] This is the first cohort comparing outcomes of trabeculectomy with DS in FHU patients.

In primary open angle glaucoma (POAG), both DS with a collagen implant and trabeculectomy procedures can result in equal control of IOP.[20] However, DS may be associated with fewer postoperative complications than trabeculectomy.[21] This has been attributed to the presence of an intact globe with the TDM acting both as a barrier to infection

Table 1. Summary of patient demographics and history (baseline characteristics).

	Trabeculectomy	Deep sclerectomy	*p* value
Eyes (*n*)	13	14	–
Age at surgery (years), mean $\pm$ SD	60.2 $\pm$ 13.2	50.7 $\pm$ 16.2	0.1
Sex – male/female	8/5	10/4	
Laterality – right eye/left eye	7/6	6/8	
Ethnicity			
Caucasian	14	13	
Indian	0	1	
Mean follow-up (months), mean $\pm$ SD	73.3 $\pm$ 28.1	152.91 $\pm$ 127.32	0.03
IOP at decision to operate	30.5 $\pm$ 8.01	33.6 $\pm$ 11.6	0.43
Number of preoperative medications (*n*)	2.7	2.5	0.6
$Previous intraocular surgeries (*n*)			
None	7	8	
Phacoemulsification	1	4	
Extracapsular cataract extraction	1	1	
Trabeculectomy	0	1	
Pars plana vitrectomy	1	1	
Cyclodiode laser	1	1	
Antimetabolite			
None	6	1	
5-Fluorouracil	6	0	
Mitomycin C	0	9	
Bevacizumab	0	2	
Concomitant phacoemulsification	4	2	

IOP, intraocular pressure; SD, standard deviation.
$Some eyes had more than one intraocular procedure.

and as a flow restrictor, thus reducing the risk of hypotony in situations of ciliary body shutdown. The presence of the TDM which potentially restricts aqueous outflow of proinflammatory cytokines and the absence of a surgical iridectomy during DS should theoretically result in less postoperative inflammation with several studies reporting this including improved surgical success with the application of MMC.[11,14,17,22] This study has shown however that the risks of postoperative inflammation and other untoward events were relatively similar (and low) in both the trabeculectomy and the DS groups. The number of patients with significant complications, including hypotony, was also low in both groups. Needling rates were equivalent, whereas postoperative laser manipulation, mainly LGP, was only performed in the DS group. It is now our standard practice to inform patients that LGP will most likely be required at some point in their surgical aftercare.

Table 2. Kaplan–Meier survival IOP outcomes.

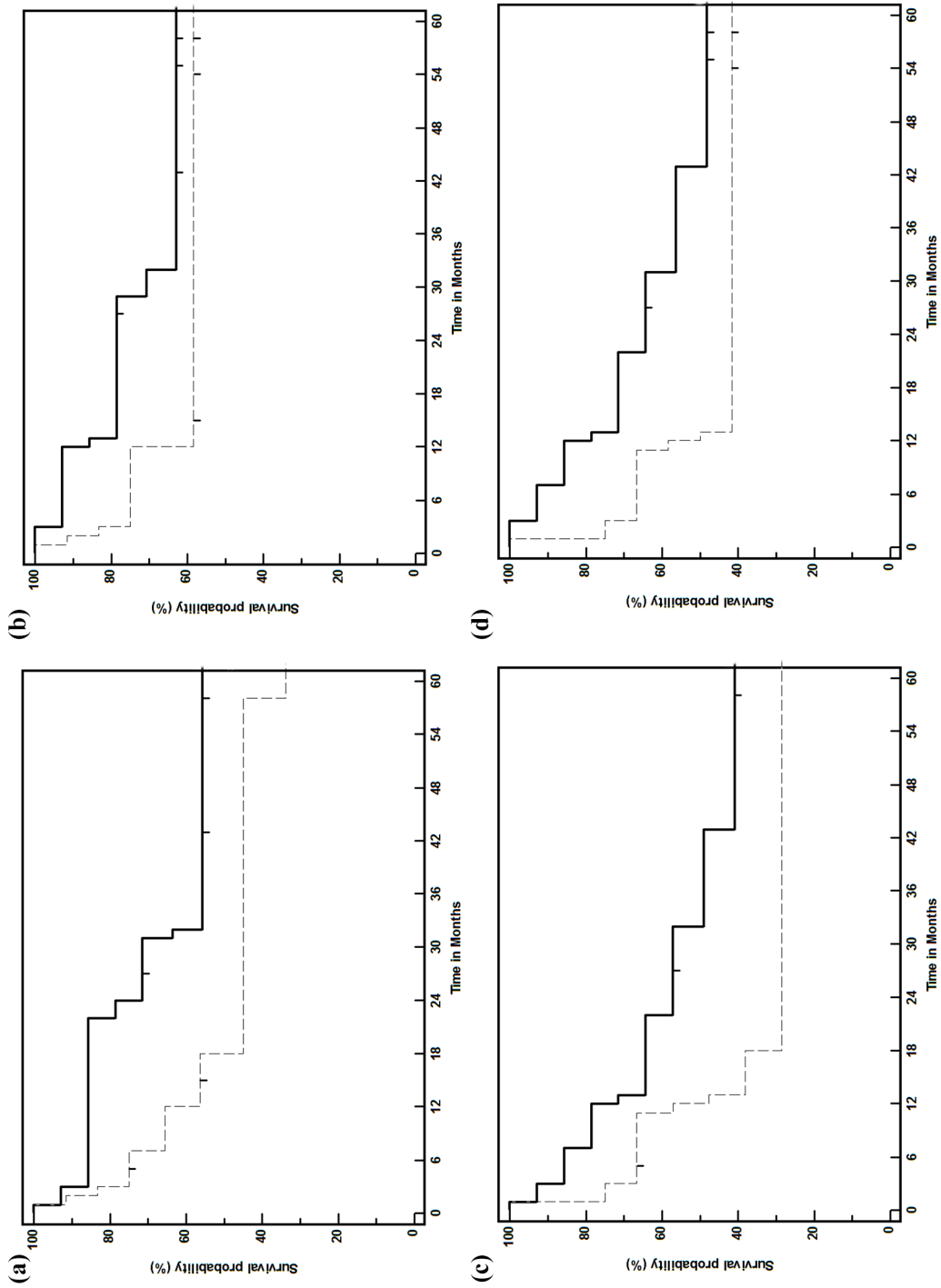|	Trabeculectomy (95% CI)	Deep sclerectomy (95% CI)	p (log-rank test)
IOP < 22, no meds			0.21
Year 1	56.2 (33.6–94.3)	85.7 (69.3–100)	
Year 2	45.0 (22.9–88.6)	71.4 (51.3–99.5)	
Year 3	45.0 (22.9–88.6)	55.6 (34.3–89.9)	
IOP < 22, meds			0.48
Year 1	58.3 (36.2–94.1)	85.7 (69.2–100)	
Year 2	58.3 (36.2–94.1)	78.6 (59.8–100)	
Year 3	58.3 (36.2–94.1)	62.9 (41.6–95.0)	
IOP < 19, no meds			0.28
Year 1	38.1 (17.9–81.1)	71.4 (51.3–99.5)	
Year 2	28.6 (11.1–73.5)	57.1 (36.3–89.9)	
Year 3	28.6 (11.1–73.5)	49.0 (28.4–84.5)	
IOP < 19, meds			0.40
Year 1	50.0 (28.4–88.0)	78.6 (59.8–100)	
Year 2	41.7 (21.3–81.4)	64.3 (43.5–95.0)	
Year 3	41.7 (21.3–81.4)	56.2 (35.2–90.0)	

CI, confidence interval; IOP, intraocular pressure.
Complete (unqualified) success criteria were defined as follows: (a) IOP < 22 mmHg or a 20% decrease from baseline IOP off any glaucoma medications and (b) IOP < 19 mmHg or a 30% drop from baseline IOP off glaucoma medications. Partial (qualified) success was defined as any of the above but with at least one topical IOP-lowering medication.

However, as DS is a nonpenetrating procedure, it may fail to address glaucoma in eyes that exhibit inflammatory changes throughout the trabecular meshwork as the corneoscleral and uveal parts of the meshwork are not removed. It is not uncommon therefore to find a heavily fibrosed TDM during DS in UG which may limit aqueous flow through the membrane and may necessitate earlier LGP postoperatively.

The mean preoperative IOP in this study was greater than 30 mmHg in both groups, representing a higher than average listing IOP compared with POAG. This may reflect a tendency to defer surgery in patients with uveitis and may contribute to the relatively high IOP-lowering success rates in this study. It also means that a target IOP of <19 mmHg, a successful outcome quoted in recent multicentre trabeculectomy study,[23] would be more likely to represent a clinically significant

percentage drop in IOP compared with other glaucoma aetiologies where lower IOPs might be targeted (e.g. normal-tension glaucoma). In this study, the IOP reduction was substantial, with the mean 1-year values being less than 19 mmHg in both groups and with similar success rates at 3 years. This was also mirrored by a reduction in the number of glaucoma medications after surgery. Importantly, the safety profiles of the two techniques were similar, with no statistical significance found between the two groups in terms of complication rates.

There are limited data available for DS and trabeculectomy in FHU, with previous studies comparing DS and trabeculectomy in POAG,[24,25] and nonspecific UG.[17] In our study, the probability of IOP < 22 mmHg and <19 mmHg without medications (unqualified success) or further glaucoma procedures was 58% and 38%, respectively, at

Figure 1. Kaplan–Meier survival for maintaining IOP.

DS, deep sclerectomy; IOP, intraocular pressure; TRAB, trabeculectomy.

Kaplan–Meier survival plots showing cumulative survival percentage of success of TRAB and DS over time after initial surgery: (a) <22 mmHg with laser goniopuncture and needle revision but no glaucoma medications or further glaucoma surgery; (b) <22 mmHg with laser goniopuncture and needle revision and one or more glaucoma medications; (c) <19 mmHg with laser goniopuncture and needle revision but no glaucoma medications or further glaucoma surgery; (d) <19 mmHg with laser goniopuncture and needle revision and one or more glaucoma medications. y-axis – cumulative survival percentage and x-axis – time in months. Solid lines represent DS and broken lines, trabeculectomy.
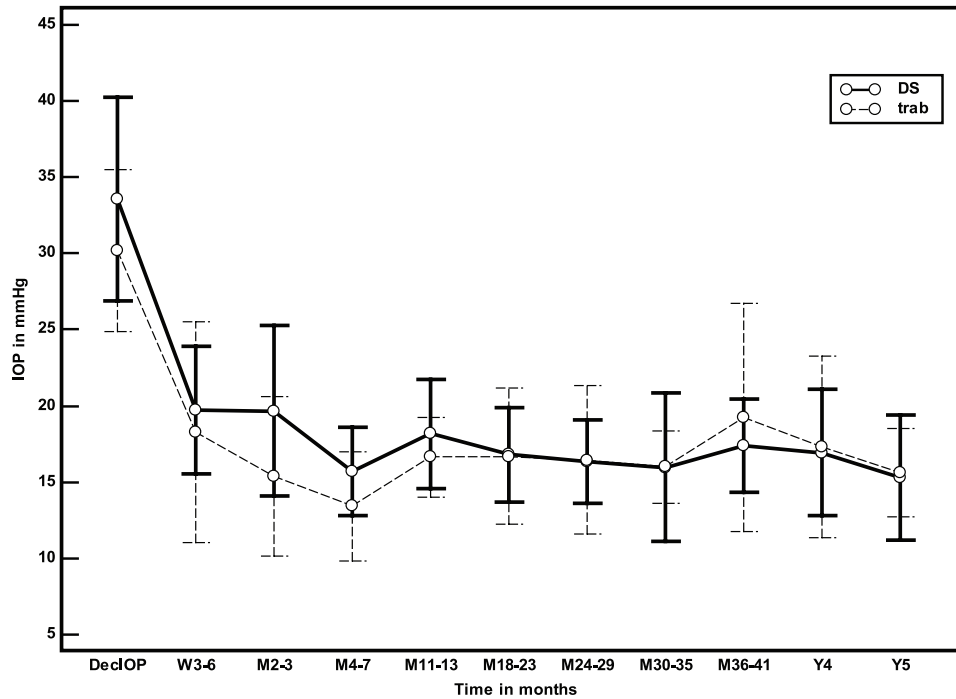
Figure 2. IOP evolution with time between groups before and after TRAB and DS.
ANOVA, analysis of variance; DecIOP, intraocular pressure at decision to perform surgery; DS, deep sclerectomy; IOP, intraocular pressure; M, month; TRAB, trabeculectomy; W, week; Y, year.
IOP changes after surgery. Error bars represent 95% confidence intervals. No difference in groups at all measured time intervals up to 3 years (repeated-measures ANOVA; $p = 0.47$).
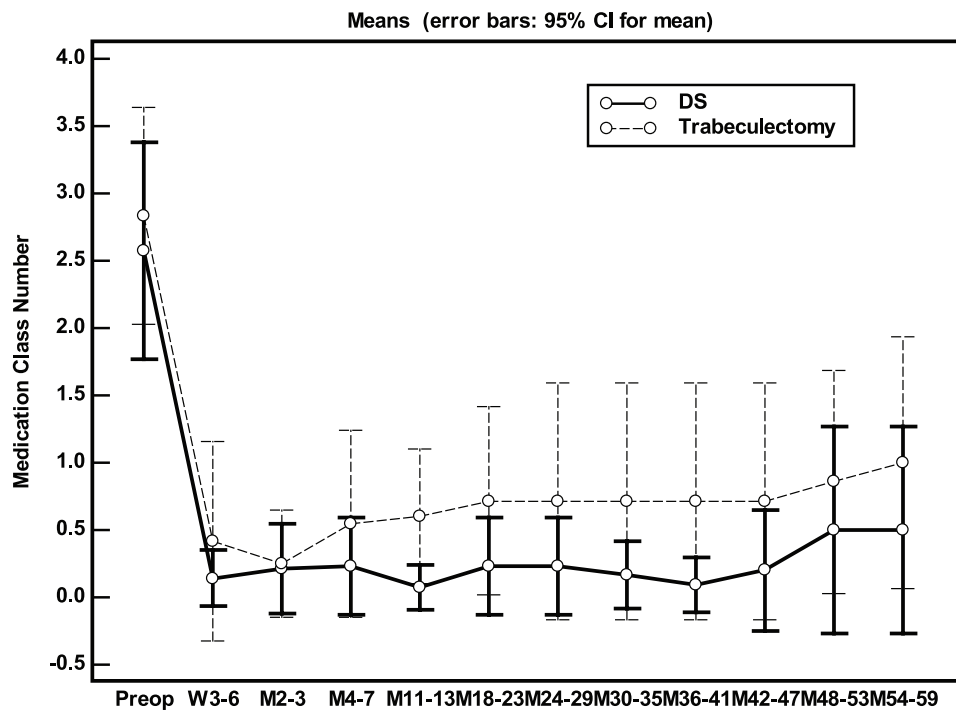
Figure 3. Glaucoma medications before and after surgical interventions.
CI, confidence interval; DS, deep sclerectomy.
No significant difference was found between the groups at all time intervals ($p > 0.05$) except at the 11- to 13-month interval where $p = 0.02$ (Kruskal–Wallis test).

Table 3. Pre- and postoperative status after trabeculectomy and deep sclerectomy.

	Trabeculectomy (n = 13)	Deep sclerectomy (n = 14)	p value
Preoperative IOP (mean ± SD)	30.5 ± 8.01	33.6 ± 11.6	0.43
Preoperative VA – number of patients with VA of 6/12 or better (n)	9	9	
Preoperative VA – number of patients with VA of 6/12 or better (n)	8	14	
Mean postoperative IOP			
Month 1	17.6 ± 11.5	19.3 ± 7.39	0.64
Month 6	13.4 ± 5.6	19.6 ± 4.87	0.37
Year 1	17.0 ± 4.15	18.1 ± 6.03	0.62
Year 2	16.4 ± 6.32	15.5 ± 3.10	0.66
Year 3	19.2 ± 9.71	16.6 ± 3.50	0.47
Year 4	17.3 ± 7.71	16.9 ± 4.93	0.90
Year 5	15.6 ± 3.50	14.7 ± 4.50	0.66
More than 2 Snellen lines lost postoperatively	2	0	
Flare-up over postoperative follow-up	6	3	

IOP, intraocular pressure; SD, standard deviation; VA, visual acuity.

1 year for the trabeculectomy group. These outcomes appear less successful when compared with those of You and colleagues, who report a complete plus qualified success of IOP < 22 mmHg in 90.9% at 1 year, 77.9% success at 2 years and 62.3% success at 3–4 years. This is derived from 11 patients that underwent augmented trabeculectomy in FHU.[18] Other authors report a 72% success rate with trabeculectomy in FHU patients (50% of cases augmented with 5-FU), after a mean follow-up of 26 months.[19] Our results showed lower success rates than those reported by previous authors, with a range of 78%–91.7%, although these studies were not specific to FHU patients.[8,16,17,22] The discrepancy in results may possibly reflect the change in practice preferences over time with respect to the use of antimetabolites in our cohort; only half of our trabeculectomy cases involved the use of antimetabolites. All the aforementioned studies used antifibrotic agents and have been associated with significantly lower failure rates.[26] Another variable in our cohort could be the inclusion of combined phacotrabeculectomy cases, which are

associated with a higher failure rate in UG.[12] Furthermore, one subject had a previous extracapsular cataract extraction and was noted to have had vitreous in the anterior chamber at the time of trabeculectomy. Due to the small number of patients in this study, we decided to include these combined cases and recognize that this is a potential limitation for strict comparison to DS in our study.

In this study, the probability of unqualified success was 85.7% and 71.4%, respectively, at 1 year for DS. This value is comparable to those reported by Al Obeidan and colleagues[10] (72.7% for <23 mmHg), Dupas and colleagues[17] (88%), Souissi and colleagues[27] (88%) and Auer and colleagues[28] (90%) in UG. It was lower than the value reported by Shaarawy and Mermoud[29] (100%) but comparable to that of Kozobolis and colleagues[22] (50%–95%), both of which report nonuveitic cases. The probability of unqualified success in our study at 3-year follow-up was 55.6% and 49%, respectively. This is lower than the value reported in a previous study assessing DS with

Table 4. Complications, postoperative adjustments and reoperations.

	Trabeculectomy ($n = 13$)	Deep sclerectomy ($n = 14$)	*p* value
Complications			
Hyphaema	5	3	
No intraoperative flow (thickened TDM)	0	3	
TDM microperforation	0	1	
Conjunctival leak with shallow AC	1	1	
Hypotonous maculopathy	0	1	
Total	7	9	0.67
Postoperative manipulations			
Needling	4	5	
Iridoplasty		1	
Goniopuncture		14	
Total	4	20	0.47
Reoperations			
Phacovitrectomy		1	
Drainage tube	2	1	
Selective laser trabeculoplasty		1	
Trabeculectomy	1		0.27

AC, anterior chamber; TDM, trabeculo-Descemet's membrane.

MMC in UG, which suggests that surgery in FHU is associated with a higher failure rate compared with other forms of uveitis.[14]

All patients in the DS group underwent LGP, a higher rate when compared with other studies. A total of 36% required needling which is comparable to previously published data. Reported intervention rates within the literature are quoted as 36% needling, 29% LGP[28] and 15% LGP[10] in UG and 35% needling and 45% LGP[25] in nonuveitic glaucoma. Factors contributing to the 100% LGP rate in our study may include the fact that one eye did not have concurrent use of antimetabolite and also that three eyes had no intraoperative aqueous flow due to a thick hyalinized trabecular descemet's window.

The most common complication was microhyphaema (five and three eyes in the trabeculectomy and DS groups, respectively) which may compromise postoperative IOP control and bleb formation, but no patients required subsequent anterior chamber washout. Surgical hyphaema (Amsler sign) is common in patients with FHU and results from reduced intraoperative IOP. It is interesting that this was not observed rather more frequently in the 5FT group, compared to DS. Serious complications included hypotony with macular folds in one eye from the DS group which is comparable to that reported in UG by Al Obeidan and colleagues[10] (7%), but lower than that reported by Mercieca and colleagues[9] (28.3%). This patient required bleb compression sutures to be performed which resulted in a final Snellen unaided visual acuity of 6/9 postoperatively. One eye in each group had a conjunctival bleb leak which was managed conservatively. Three eyes had subsequent glaucoma surgical procedures in the 5FT group (23%) and one eye in the DS group (7.1%). Two 5FT patients lost

more than two Snellen lines of vision compared with none in the DS group.

There are several limitations in this study. It is retrospective, did not follow a predefined study protocol and is a direct surgeon-to-surgeon comparison in addition to a procedure comparison. There was also a choice bias for surgical technique for patients in the individual groups, as the procedure was chosen according to individual surgeon preference. This bias however enabled us to identify two distinct and comparable groups. The prevalence of FHU results in small numbers of patient data, which reduces the ability to make robust statistical distinctions.

This study did not examine postoperative inflammation, as our objective was to determine surgical outcomes and complications. Nine eyes demonstrated postoperative uveitis (three after DS and six after 5FT). However, the significance of this is uncertain. Interestingly, Mercieca and colleagues[9] report that the recurrence of inflammation had no bearing on subsequent postoperative IOP control in eyes undergoing augmented DS.

Conclusion

In conclusion, our study suggests that augmented DS and trabeculectomy appear to have a similar efficacy in terms of IOP reduction and safety profile when used in FHU-related glaucoma. This study does not allow us to make a clear recommendation on the optimal procedure for these patients. A multicentre prospective study using larger patient numbers would be necessary to answer this question accurately. Our small cohort suggests that either of the procedures can be used safely and effectively to manage secondary glaucoma related to this condition.

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