Long-Term Outcomes of Initial Trabeculectomy in Glaucoma Associated with Granulomatous and Non-Granulomatous Uveitis

Faisal A. Almobarak (✉ falmobarak@ksu.edu.sa)

King Saud University <https://orcid.org/0000-0003-3504-2828>

Ali H. Alharbi

King Abdullah Medical City

Ibrahim Aljadaan

King Khaled Eye Specialist Hospital

Hassan Aldhibi

King Khaled Eye Specialist Hospital

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Abstract

Purpose

To evaluate the outcomes of initial trabeculectomy in granulomatous and non-granulomatous uveitis.

Methods

Retrospective comparative study of 68 eyes that underwent an initial trabeculectomy.

Results

The mean follow-up was 74.18 and 74.86 months in both groups ($p = 0.95$). The intraocular pressure decreased from 40.03 mmHg (± 7.2) and 36.48 mmHg (± 11.3) to 14.00 mmHg (± 6.2) and 13.48 mmHg (± 5.7), the number of medications decreased from 3.73 (± 0.7) and 3.58 (± 0.9) to 1.00 (± 1.4) and 1.13 (± 1.4) on the last follow-up ($p < 0.01$) in the granulomatous and non-granulomatous groups, respectively. More eyes in the granulomatous uveitis group developed delayed postoperative complications like cataract, transient hypotony and glaucoma progression. Success rates were 64.9 and 71.0%, while failure rates were 35.1 and 29.0% in both groups ($p = 0.84$).

Conclusions

Trabeculectomy seems to have comparable IOP control and survival in granulomatous and non-granulomatous uveitis. Nevertheless, more eyes in the granulomatous uveitis group developed late onset complications.

Introduction

Uveitic glaucoma is a common and potentially vision threatening complication of uveitis.¹ The incidence of uveitic glaucoma among uveitis patients has been reported to be 13 to 41%.^{2, 3} Such variation is mostly related to the anatomic location and the wide range of uveitis entities which comprise infectious, non-infectious, idiopathic and systemic-related intraocular inflammatory conditions.^{2, 4, 5} Several mechanisms are involved in the pathogenesis of uveitic glaucoma, like the deposition of granuloma containing Langerhans giant cells and other inflammatory debris in the angle which can worsen the pressure control despite medical treatment.^{6, 7} Granulomatous uveitis carries a greater risk of developing uveitic glaucoma⁸, and there is need for glaucoma surgery compared with non-granulomatous uveitis.⁹ Several studies reported a favorable outcome of Mitomycin C (MMC) enhanced trabeculectomy in uveitic glaucoma, but few have looked at the outcome in glaucoma associated with major uveitis entities such as granulomatous and non-granulomatous uveitis.^{10–15} Therefore, the aim of our study was to evaluate

the outcomes of MMC enhanced trabeculectomy as a first procedure in patients with glaucoma associated with granulomatous and non-granulomatous uveitis.

Materials And Methods

Patients

We retrospectively reviewed the medical records of uveitic glaucoma patients who underwent MMC enhanced trabeculectomy at King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia between 2002 and 2017. Inclusion criteria were: (i) medically uncontrolled intraocular pressure (IOP) of ≥ 21 mmHg despite maximum tolerated antiglaucoma medications; (ii) the presence of glaucomatous optic nerve head damage; (iii) no previous history of pressure lowering procedure (except for YAG peripheral iridotomy) or any intraocular surgeries; and (iv) a minimum follow-up of 12 months. Eyes were divided into two groups based on uveitis entity: granulomatous and non-granulomatous uveitis. Granulomatous uveitis was diagnosed if larger keratic precipitates, including large (mutton-fat) keratic precipitates, Koeppe/Busacca iris nodules, optic disc or choroidal granulomas were seen while non-granulomatous uveitis was diagnosed if fine endothelial keratic precipitates were seen in the absence of iris nodules and choroidal granulomas. All patients were evaluated by uveitis specialist and the inflammation was quietened (≤ 5 cells per high power field in the anterior chamber) except for those who needed an urgent intervention because of uncontrolled IOP. Grading of the anterior chamber (AC) cells was done following the standardization of uveitis nomenclature scheme.¹⁶ Topical prednisolone drops were given preoperatively ranging from hourly to every 3 hours, while systemic steroids were initiated (or dose maximized for those already on the treatment) for cases of panuveitis and selected cases with intermediate uveitis based on the old history of relapses and the possible activation of the disease and then tapered and stopped (or went back to the preoperative maintenance dose) after the surgery. Systemic immunosuppressive agents were administered, maximized or maintained based on the patient presentation to achieve the optimal control of the inflammation. The dosage of all uveitis medications was gradually adjusted and tapered postoperatively to the preoperative maintenance dosage by the uveitis specialist. The study adhered to the tenets of declaration of Helsinki and was approved by the Ethics Review Board of King Khaled Eye Specialist Hospital, part of a retrospective study on trabeculectomy in uveitic glaucoma.

Surgical Technique

Fornix-based conjunctival peritomy was performed and hemostasis of the scleral bed was achieved. Scleral flap was dissected followed by the application of sponge soaked with either 0.2 or 0.4 mg/ml MMC, depending on the routine practice of the surgeon, under the flap and overlying Tenon tissue/conjunctiva for 2 to 5 min. Irrigation of the surgical field using balanced salt solution was carried out, then a block of tissue anterior to the scleral spur was removed followed by peripheral iridectomy. The scleral flap was closed using 10 – 0 nylon sutures and adjusted to allow adequate filtration while having a formed anterior chamber. The conjunctiva was closed using 9 – 0 vicryl suture and the wound was

checked for the presence of leakage. Finally, subconjunctival injections of antibiotics and steroids were given.

The postoperative visits considered for this study were those made at the first postoperative day, at 2 to 4 weeks and the third month, and then at 12 months intervals. Postoperative monitoring was carried out by both the glaucoma and uveitis specialists. Laser suturelysis (LSL) was performed whenever needed to enhance filtration.

Data Analysis

The following pre- and postoperative data were collected: age at time of surgery, sex, etiologic diagnosis, IOP, number of antiglaucoma medications, best corrected visual acuity (BCVA) converted into logarithm of minimal angle of resolution (logMAR) format, the need for manipulation after surgery (e.g., LSL), time to failure, postoperative complications, and the need for subsequent pressure lowering procedures to control IOP.

Variables were evaluated using the Student's t-test, Wilcoxon rank test, Mann-Whitney U test, Chi-Square test and Fisher's exact test. Cumulative probabilities of success, presented as percentage $\pm$ standard error (SE), were determined by Kaplan-Meier life table analysis for both groups and were compared using the Mantel-Cox log rank test. Trabeculectomy success was classified as: (i) absolute success (IOP between 6 and 21 mmHg without antiglaucoma medications, no loss of vision due to glaucoma progression, no postoperative vision threatening complications such as suprachoroidal hemorrhage and endophthalmitis attributed to the bleb, and no need for further glaucoma procedure to control the IOP); (ii) qualified success (same as absolute success but with antiglaucoma medications); (iii) failure (if any of the following develops: IOP > 21 mmHg despite maximum tolerated antiglaucoma medications on two visits, persistent hypotony [IOP ≤ 5 mmHg] on two visits causing hypotony maculopathy, loss of vision due to glaucoma progression, postoperative vision threatening complications, or the need for further glaucoma procedure to control the IOP). Variables were presented as mean and standard deviation (SD) and p value less than 0.05 was considered statistically significant. Statistical analyses were performed using PAWS version 23 for Windows.

Results

Thirty-seven eyes of 25 patients in the granulomatous uveitis group and 31 eyes of 21 patients in the non-granulomatous uveitis group were included in this study. Most eyes had panuveitis in the granulomatous uveitis group while anterior uveitis was the most common anatomic location in the non-granulomatous uveitis group. The most common etiologic diagnosis was Vogt-Koyanagi-Harada disease (VKH) and idiopathic uveitis, followed by Fuch's iridocyclitis and Behcet disease. There were no significant differences in the mean age, baseline: preoperative IOP, number of antiglaucoma medications nor log MAR between both groups. All eyes were phakic and there were no previous intraocular surgeries. There was no difference in the follow-up period between both groups ($p = 0.95$, Mann-Whitney U test).

Most eyes had adequate inflammatory control preoperatively (≤ 5 cells per high power field in the anterior chamber) in both groups (Table 1).

Table 1
Characteristics and ocular history*

Variable	Granulomatous Uveitis (n = 37)	Non-Granulomatous Uveitis (n = 31)	P value
Age at time of surgery, yrs**	27.60 ($\pm$ 7.9)	33.52 ($\pm$ 13.1)	0.07
Gender**	7 (30.4%)	18 (78.3%)	0.005
Male (23)	16 (69.6%)	5 (21.7%)	
Female (23)			
Uveitis location	13 (35.1%)	13 (41.9%)	0.003
Anterior	Zero	7 (22.6%)	
Intermediate	Zero	Zero	
Posterior	24 (64.9%)	11 (35.5%)	
Panuveitis			
Uveitis etiology	26 (70.3%)	—	—
VKH	7 (18.9%)	—	
Fuchs iridocyclitis	2 (5.4%)	—	
Posner Schlossman Syndrome	2 (5.4%)	—	
Herpetic	—	19 (61.3%)	
Idiopathic	—	9 (29.0%)	
Behcet	—	2 (6.5%)	
Ankylosing spondylitis	—	1 (3.2%)	
JRA			
Angle status***	28 (75.7%)	17 (54.8%)	0.07
Open	9 (24.3%)	14 (45.2%)	
Closed			

*Data are presented as mean ($\pm$ SD) and frequencies (%). Numbers are per eyes.

**Numbers are per patients.

*** Fisher's exact test.

Variable	Granulomatous Uveitis (n = 37)	Non-Granulomatous Uveitis (n = 31)	P value
MMC concentration	25 (67.6%)	19 (61.3%)	0.59
0.2 mg/ml MMC	12 (32.4%)	12 (38.7%)	
0.4 mg/ml MMC			
Duration of exposure to MMC (minutes)	3.08 (± 1.0)	2.68 (± 0.8)	0.16
0.2 mg/ml MMC	3.08 (± 0.7)	2.92 (± 0.5)	0.50
0.4 mg/ml MMC			
Anterior chamber cells	0.55 (± 0.7)	0.58 (± 1.2)	0.91
Activity of inflammation***	9 (24.3%)	3 (9.7%)	0.23
Active	28 (75.7%)	28 (90.3%)	
Inactive			
Follow-up, months	74.18 (± 41.8)	74.86 (± 42.1)	0.95
*Data are presented as mean (± SD) and frequencies (%). Numbers are per eyes.			
**Numbers are per patients.			
*** Fisher's exact test.			

There was no significant difference between both groups in the IOP, number of antiglaucoma medications, nor logMAR throughout the whole follow-up period. The intragroup analysis revealed a statistically significant difference ($p < 0.001$, Wilcoxon test) in the mean IOP and number of antiglaucoma medications compared with baseline values in both groups, but none in logMAR. Up to third of all eyes in each group required LSL within the first 4 months postoperatively to achieve adequate IOP control, but half of LSL procedures failed (Table 2).

Table 2
Follow-up data*

Characteristic	Granulomatous Uveitis (n = 37)	Non-granulomatous Uveitis (n = 31)	P Value**
Preoperative baseline	40.03 (± 7.2)	36.50 (± 11.3)	0.12
IOP, mmHg	3.73 (± 0.7)	3.58 (± 0.9)	0.43
No. of medications	0.60 (± 0.7)	0.61 (± 0.7)	0.94
LogMAR visual acuity	9 (24.3%)	3 (9.7%)	—
Activity of inflammation	28 (75.7%)	28 (90.3%)	0.23
Active	37	31	
Inactive			
No. of eyes			
1 Day postoperative	9.92 (± 10.2)	15.08 (± 14.8)	0.10
IOP, mmHg	Zero	Zero	—
No. of medications	0.78 (± 0.6)	0.90 (± 1.0)	0.64
LogMAR visual acuity	25 (67.6%)	12 (38.7%)	—
Activity of inflammation	12 (32.4%)	19 (61.3%)	0.11
Active	37	31	
Inactive			
No. of eyes			

*Data are presented as mean (± SD).

** P value calculated using unpaired student t-test, Mann-Whitney U test, Fisher's exact test and Chi-Square test.

Characteristic	Granulomatous Uveitis (n = 37)	Non-granulomatous Uveitis (n = 31)	P Value**
1 Month postoperative	10.08 (± 6.3)	12.15 (± 8.0)	0.24
IOP, mmHg	0.05 (± 0.3)	0.06 (± 0.4)	0.90
No. of medications	0.60 (± 0.6)	0.46 (± 0.5)	0.30
LogMAR visual acuity	10 (27.0%)	Zero	—
Activity of inflammation	27 (73.0%)	31	< 0.01
Active	37	31	
Inactive			
No. of eyes			
3 Months postoperative	12.11 (± 7.1)	12.86 (± 6.0)	0.65
IOP, mmHg	0.05 (± 0.2)	0.14 (± 0.5)	0.38
No. of medications	0.65 (± 0.7)	0.60 (± 0.6)	0.78
LogMAR visual acuity	8 (21.6%)	6 (19.4%)	—
Activity of inflammation	29 (78.4%)	25 (80.6%)	0.46
Active	37	31	
Inactive			
No. of eyes			
12 Months postoperative	13.76 (± 6.2)	13.97 (± 4.6)	0.88
IOP, mmHg	0.46 (± 0.8)	0.42 (± 0.9)	0.85
No. of medications	0.71 (± 0.7)	0.50 (± 0.6)	0.19
LogMAR visual acuity	7 (18.9%)	3 (9.7%)	—
Activity of inflammation	30 (81.1%)	28 (90.3%)	0.41
Active	37	31	
Inactive			
No. of eyes			

*Data are presented as mean (± SD).

** P value calculated using unpaired student t-test, Mann-Whitney U test, Fisher's exact test and Chi-Square test.

Characteristic	Granulomatous Uveitis (n = 37)	Non-granulomatous Uveitis (n = 31)	P Value**
24 Months postoperative	12.55 (± 3.7)	11.52 (± 4.2)	0.39
IOP, mmHg	0.59 (± 1.1)	0.59 (± 0.9)	1.00
No. of medications	22	22	—
No. of eyes			
36 Months postoperative	14.97 (± 8.2)	14.45 (± 4.4)	0.81
IOP, mmHg	0.71 (± 1.0)	0.75 (± 1.2)	0.91
No. of medications	17	20	—
No. of eyes			
48 Months postoperative	17.89 (± 9.1)	16.55 (± 6.8)	0.61
IOP, mmHg	0.78 (± 1.1)	1.11 (± 1.4)	0.42
No. of medications	18	20	—
No. of eyes			
60 Months postoperative	16.08 (± 3.6)	16.40 (± 6.6)	0.88
IOP, mmHg	0.75 (± 1.2)	1.33 (± 1.6)	0.30
No. of medications	12	15	—
No. of eyes			
Last visit	14.00 (± 6.2)	13.48 (± 5.7)	0.73
IOP, mmHg	1.00 (± 1.4)	1.13 (± 1.4)	0.69
No. of medications	0.70 (± 0.9)	0.56 (± 0.8)	0.49
LogMAR visual acuity	2 (5.4%)	Zero	—
Activity of inflammation	35 (94.6%)	31	0.38
Active	37	31	
Inactive			
No. of eyes			

*Data are presented as mean (± SD).

** P value calculated using unpaired student t-test, Mann-Whitney U test, Fisher's exact test and Chi-Square test.

Characteristic	Granulomatous Uveitis (n = 37)	Non-granulomatous Uveitis (n = 31)	P Value**
LSL	9 (24.3%)	9 (29.0%)	0.66
No. of eyes	4 (44.4%)	4 (44.4%)	
Success	5 (55.6%)	5 (55.6%)	
Fail			
Success status at last follow-up	24/37 (64.9%)	22/31 (71.0%)	0.84
Overall success	15/37 (40.6%)	13/31 (42.0%)	
Absolute success	9/37 (24.3%)	9/31 (29.0%)	
Qualified success	13/37 (35.1%)	9/31 (29.0%)	
Failure			
*Data are presented as mean (± SD).			
** P value calculated using unpaired student t-test, Mann-Whitney U test, Fisher’s exact test and Chi-Square test.			

The most common early complications during the first 2 postoperative weeks were hypotony (IOP $\leq$ 5 mm Hg) which did not require surgical intervention, followed by IOP spike $\geq$ 30 mm Hg requiring bleb massage and/or LSL in both groups. The most common delayed complication ($>$ 2 weeks postoperatively) in both groups was cataract development and progression ($p = 0.11$, Chi-Square test). Among the 19 eyes in the granulomatous uveitis group, 7 eyes had early hypotony in the first postoperative week, while 2 eyes had hypotony 2–8 weeks postoperatively. In the non-granulomatous uveitis group, 2 eyes out of 10 had early hypotony in the first postoperative week, while one eye had hypotony 2–8 weeks postoperatively. The mean time to cataract surgery was 26.33 ($\pm$ 29.2) months (range: 6-118) and 40.90 ($\pm$ 40.0) months (range: 6-119) in the granulomatous and non-granulomatous uveitis groups, respectively ($p = 0.28$, Mann-Whitney U test) (Table 3).

Table 3
Postoperative complications*.

Complication	Granulomatous Uveitis (n = 37)	Non-granulomatous Uveitis (n = 31)
Early (first 2 weeks)		
Transient hypotony	10 (27.0%)	8 (25.8%)
IOP spike > 30 mmHg	2 (5.4%)	5 (16.1%)
Hyphema	3 (8.1%)	Zero
Leaking bleb	1 (2.7%)	1 (3.2%)
Decompressive Retinopathy	1 (2.7%)	Zero
Hypotony maculopathy	1 (2.7%)	1 (3.2%)
Choroidal effusion	2 (5.4%)	1 (3.2%)
Delayed (more than 2 weeks)		
Cataract requiring surgery	19 (51.4%)	10 (32.3%)
Loss of ≥ 3 lines on Snellen chart	5 (13.5%)	2 (6.5%)
because of Glaucoma progression	3 (8.1%)	1 (3.2%)
Delayed transient hypotony	1 (2.7%)	2 (6.5%)
Glaucomatous complete vision loss	1 (2.7%)	1 (3.2%)
IOP spike > 30 mmHg		
Leaking bleb	Zero	2 (6.5%)
Endophthalmitis	Zero	1 (3.2%)
*Percentages are out of each group		

Complete vision loss occurred in 3 eyes at the end of the study because of progressive glaucomatous optic nerve head damage in both groups, while loss of ≥ 3 lines on the Snellen chart was documented in 13 eyes (35.1%) in the granulomatous uveitis groups, compared with 10 eyes (32.3%) in the non-granulomatous uveitis group. Factors causing this drop in vision were uveitis-related retinal pathologies such as choroidal neovascular membrane and cystoid macular edema, clinically documented glaucoma progression, cataract progression and uveitis-related corneal complications such as band keratopathy (Table 4).

Table 4
Causes of visual loss*.

Visual loss category	Granulomatous Uveitis (n = 37)	Non-granulomatous Uveitis (n = 31)
Glaucomatous complete vision loss	1 (2.7%)	2 (6.5%)
Loss of ≥ 3 lines on Snellen chart	5 (13.5%)	2 (6.5%)
Glaucoma progression	4 (10.8%)	4 (12.9%)
Uveitis-related retinal pathologies	3 (8.1%)	3 (9.7%)
Cataract progression	1 (2.7%)	1 (3.2%)
Uveitis-related corneal complication		
*Percentages are out of each group		

The cumulative probabilities of success of trabeculectomy for the granulomatous uveitis group were 75.5% ($\pm 7.1\%$), 62.2% ($\pm 8.0\%$), 54.1% ($\pm 8.2\%$), 40.5% ($\pm 8.1\%$) and 27.0% ($\pm 7.3\%$) compared with 87.1% ($\pm 6.0\%$), 77.4% ($\pm 7.5\%$), 61.3% ($\pm 8.7\%$), 41.9% ($\pm 8.9\%$) and 35.5% ($\pm 8.6\%$) in the non-granulomatous uveitis group at 12, 24, 36, 48 and 60 months, respectively ($p = 0.80$, Log Rank) (Fig. 1). In the granulomatous uveitis group, the failure rate was 35.1% (13/37): 10 eyes due to uncontrolled IOP requiring further glaucoma surgery, and 3 eyes due to visual loss secondary to glaucomatous disc progression, compared with a failure rate of 29.0% (9/31) in the non-granulomatous uveitis group: 6 eyes because of uncontrolled IOP requiring further glaucoma surgery, 2 eyes because of visual loss secondary to glaucomatous disc progression and one eye because of bleb related endophthalmitis which responded to pars plana vitrectomy and then required further glaucoma surgery ($p = 0.84$) (Table 2). Most failures occurred within 3 years after trabeculectomy: 61.5% of all failed cases ≤ 24 months and 69.2% ≤ 36 months of follow-up in the granulomatous uveitis group, compared with 44.4% of all failed cases ≤ 24 months and 55.6% ≤ 36 months of follow-up in the non-granulomatous uveitis group. Seventeen eyes (25.0%) required a second glaucoma procedure to control the IOP, 8 of which (11.8% of 68 eyes) needed a third procedure, and 3 eyes (4.4% of 52 eyes) of these required a fourth glaucoma procedure (Table 5).

Table 5
Eyes that required repeat glaucoma surgery*.

Glaucoma Surgery	Granulomatous Uveitis (n = 37)	Non-granulomatous Uveitis (n = 31)
First repeat surgery	11 (29.7%)	6 (19.4%)
Time to surgery (from previous), months	47.50 ($\pm$ 50.6)	49.50 ($\pm$ 36.3)
Trabeculectomy $\pm$ cataract extraction	7	5
Tube surgery	2	Zero
Cyclophotocoagulation	2	1
Second repeat surgery	6 (16.2%)	2 (6.5%)
Proportion out of previous repeat	6/11 (54.5%)	2/6 (33.3%)
Time to surgery (from previous), months	15.33 ($\pm$ 5.0)	3.00 ($\pm$ 1.4)
Trabeculectomy $\pm$ cataract extraction	Zero	Zero
Tube surgery	5	1
Cyclophotocoagulation	1	1
Third repeat surgery	2 (5.4%)	1 (3.2%)
Proportion out of previous repeat	2/6 (33.3%)	1/2 (50.0%)
Time to surgery (from previous), months	51.50 ($\pm$ 55.9)	11.00
Trabeculectomy $\pm$ cataract extraction	Zero	Zero
Tube surgery	Zero	Zero
Cyclophotocoagulation	2	1
*Data are presented as mean ($\pm$ SD) and frequencies (%). Numbers are per eyes.		

Discussion

Uveitis comprises a wide range of intraocular inflammatory disorders of various aetiologies. The type, clinical associations and causes of uveitis are strongly influenced by genetic, ethnic, geographic, nutritional and environmental factors.¹⁷ MMC enhanced trabeculectomy has considerably increased the success rate of glaucomas with high risk for surgical failure including uveitic glaucoma. Reports on the success rate range from 50 to 90% depending on the number of patients, the length of follow-up and uveitis entities.^{14, 18–23} Few studies evaluated the outcome of trabeculectomy in major uveitis entities such as Behcet disease and VKH while others looked at prognostic factors for surgical failure including granulomatous and non-granulomatous uveitis.^{10–15} To the best of our knowledge, this is the first study

to evaluate the outcome of MMC enhanced trabeculectomy as a first glaucoma procedure in granulomatous and non-granulomatous uveitis.

In the current study, the most common causes were panuveitis and anterior uveitis in both groups, followed by intermediate uveitis in the non-granulomatous uveitis group, but no isolated posterior uveitis. This is in line with previous report on the anatomic distribution of uveitis in Saudi Arabia.^{9, 24, 25} Nevertheless, some studies reported no difference in incidence of uveitic glaucoma in relation to anatomic classification and etiology while others found anterior uveitis as the main cause of uveitic glaucoma.^{2, 8, 26–29} The presence of anterior segment inflammation contributes to the development of glaucoma in anterior uveitis and panuveitis by directly affecting the trabecular meshwork, while aqueous outflow pathway is less influenced by posterior segment inflammation. Alrubaie *et al*⁹ reported that glaucoma surgery was most frequent in anterior uveitis and panuveitis in 1220 eyes with uveitis in Saudi Arabia. In the current study, the most common etiologic diagnosis was VKH and idiopathic uveitis, while most patients were females and males in the granulomatous and non-granulomatous uveitis groups, respectively. This is not surprising given that VKH was among the commonest uveitis entities in females in Saudi Arabia while idiopathic was the commonest among males.²⁴ Most eyes had open angle in both groups while few had closed angles. The accumulation of fibrotic tissue, granuloma containing Langerhans giant cells and other inflammatory debris in the trabecular meshwork and Schlemm's canal can obstruct the angle and result in either open or closed angle, and might block the trabeculectomy filtration site.^{7, 14}

Most patients in our study had a controlled inflammation before trabeculectomy and during the first 12 months after surgery, apart from the surgically induced inflammation, except for an increase in the first month in the granulomatous uveitis group in comparison with the non-granulomatous uveitis group. Inflammatory mediators present in aqueous during active inflammation and filtering to the subconjunctival space result in macrophages and fibroblasts activation, aggregation, collagen synthesis and eventual scarring. Interestingly, there was no difference in the immediate postoperative complications between both groups. Hypotony and IOP spikes were the most common early postoperative complications in both groups, while more eyes in the granulomatous uveitis groups developed more delayed complications compared with the non-granulomatous uveitis group mainly: cataract progression requiring surgery (51.4 and 32.3%), visual loss because of glaucoma progression (13.5 and 6.6%) and transient hypotony (8.1 and 3.2%). Yalvac *et al*¹⁰ reported cataract (23.1%) and bleb leak (15.3%) as the most common complication after trabeculectomy in Behcet disease (a major non-granulomatous uveitis entity), while choroidal effusion and hypotony were 11.5 and 7.6%, respectively in a study that included 26 eyes. Elgin *et al*¹² reported cataract development in 30.4% of 23 eye after trabeculectomy in Behcet disease and hypotony 26.1%. Iwao *et al*¹⁴ reported similar rates of cataract requiring surgery in 30 eyes (29.7%) out of 101 eyes with uveitic glaucoma which included 81 eyes (80.2%) with non-granulomatous uveitis, but lower rates of hypotony. Such results are almost comparable to our non-granulomatous uveitis group results. Complications in the granulomatous uveitis group are also comparable to our previous report on VKH (a major granulomatous uveitis entity), while Shimizu *et*

*al*¹³ reported lower rates of hypotony and choroidal detachment, bleb leak, and cataract requiring surgery in 47 eyes, 32 (68.1%) of whom had granulomatous uveitis, compared with the granulomatous uveitis group in our current study.^{11, 13} One eye developed endophthalmitis in the non-granulomatous uveitis group but with no signs of leakage on presentation. Bleb leak can be asymptomatic and could spontaneously seal due to the presence of infection and concurrent inflammation.^{30, 31} The high percentage of cataract development and progression in uveitic glaucoma is not only due to the cataractogenic effect of trabeculectomy, but also the presence of chronic inflammation and use of topical corticosteroids therapy.³²⁻³⁵ Other additional factors include old age and hypotony. The current study included patients of relatively younger age group (27.85 and 31.78 years in both groups). However, 28.57% and 33.33% of eyes which developed early hypotony had cataract development and progression in the granulomatous and non-granulomatous groups, respectively.

There were no differences between both groups in the IOP, number of antiglaucoma medications, trabeculectomy survival nor the success rates and failures. Both groups had similar follow-ups, therefore, it is unlikely that the natural course of trabeculectomy could have influenced either group outcome over the other.^{19, 36, 37} Elgin *et al*¹² reported 82.6% success rate in 23 eyes with Behcet disease at one year follow up while Yalvac *et al*¹⁰ reported 83.3% and 66.4% success rates in 26 eyes with Behcet disease at one and 4 years, respectively. Shimizu *et al*¹³ reported a success rate of about 60% in 15 eyes with non-granulomatous uveitis in 2 to 10 years follow-up period (thirty-four eyes out of 47 underwent trabeculectomy, while the remaining eyes underwent trabeculotomy and trabectome surgery). However, Iwao *et al*¹⁴ reported 94.4% success rate of 57 eyes at one year and 85.6% and around 80.0% in 39 and 19 eyes at 2 and 3 years, respectively. Our short term success rates are comparable to previous studies but the intermediate and long term rates are lower.^{10, 12-14} Shimizu *et al*¹³ reported a success rate of 90% in 32 eyes with granulomatous uveitis on the first year and 87.5% in 2 to 10 years follow-up, while Iwao *et al*¹⁴ reported 72.4% success rate in 15 eyes at one year, and 54.3% at 2 years in 8 eyes. In our previous report on VKH, the success rates were 77.8%, 74.1% and 63.0% on the first, second and third years, respectively. Similarly, our success rates in the current study are lower than previous reports (Fig. 2).

Most repeat glaucoma surgeries were done less than 3 years after the initial trabeculectomy, half of the first repeats need a second repeat glaucoma surgery. Our results are in line with Carreño *et al*³⁸ who reported a higher risk of failure of repeat glaucoma surgery in comparison to the first procedure.³⁸ In the study of Elgin *et al*¹², 4 eyes with Behcet disease (17.4%) required a repeat glaucoma surgery which is comparable to our non-granulomatous uveitis group. In our previous study on VKH, 8 eyes (29.6%) required a repeat glaucoma surgery which is comparable to our granulomatous uveitis group.^{11, 12}

This study has some limitations which include retrospective design, relatively small sample sizes and the non-standardized surgical technique and follow-up treatment. Collected data were limited to what were available in medical records. However, this is the first study to evaluate the outcome of trabeculectomy in eyes with uveitic glaucoma in two major uveitis entities with a long follow-up. In conclusion, MMC-enhanced trabeculectomy seems to have comparable outcomes in glaucoma associated with

granulomatous and non-granulomatous uveitis. More eyes in granulomatous uveitis groups developed late onset complications, while most failure and repeat glaucoma surgeries in both groups occurred in the first 3 years. Therefore, continuous monitoring after trabeculectomy is crucial in both granulomatous and non-granulomatous uveitis.

Declarations

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Figures

Figure 1

Kaplan-Meier survival curves showing the cumulative probability of success.

Figure 2

Bar chart comparing the success rates in different studies with the current study. Dark bars represent studies on trabeculectomy while light dotted bars represent the current study. Gr. Uv. : Granulomatous Uveitis. Non-Gr. Uv. : Non-Granulomatous Uveitis. BD: Behcet disease. VKH: Vogt-Koyanagi-Harada disease.