Surgical Approach and Outcomes of Uveitic Glaucoma in a Tertiary Hospital

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Abstract

Aim and objective: This study aimed to evaluate the performance of and indication for different surgical techniques in the management of uveitic glaucoma (UG).

Materials and methods: A retrospective audit of records of all patients with UG who underwent ≥1 glaucoma surgery, between January 2007 and December 2016. The main outcomes were intraocular pressure (IOP) and the need for antihypertensive medication at each follow-up visit. The total number of surgical interventions needed to control IOP was recorded. Postoperative interventions and complications were analyzed.

Results: Forty eyes from 34 patients were assessed. Overall, baseline IOP was 30.7 ± 8.2 mm Hg, and postoperative mean IOP at the last visit was 16.4 ± 2.0 mm Hg, with a mean follow-up of 28 months. Antihypertensive medications were reduced from 2.8 ± 0.8 to 0.8 ± 1.2. During the follow-up, 61.8% of the eyes required only one glaucoma surgery. There was no correlation between the location of uveitis and the total number of glaucoma surgeries required. The greatest IOP reductions were in cases treated with non-penetrating deep sclerectomy (21%), Ahmed valve (23%), and cyclophotocoagulation (CPC) (51%); in cases where an Ahmed implant was the first surgical option, a 43% reduction was achieved.

Conclusion: Filtering procedures, glaucoma drainage devices, and CPC are all good options for IOP control in UG, but all are prone to failure over time. With respect to IOP reduction, the safety profile, and postoperative care, Ahmed implants and CPC might be the best first surgical option.

Clinical significance: The article highlights the versatility of the surgical techniques required to treat UG, which is one of the most difficult types of glaucoma to manage.

Keywords: Glaucoma filtering surgery, Implant drainage devices, Uveitic glaucoma.

Introduction

Patients with uveitis have a high risk of developing glaucoma, which varies between 10% and 54%, depending on the etiology.1,2 Aqueous production is reduced due to ciliary body inflammation and a presumed shift from the conventional route to the uveoscleral pathway has been hypothesized;3 however, intraocular pressure (IOP) elevation may occur by several mechanisms, including trabecular mesh cell dysfunction, angle abnormalities like peripheral synchia, and the role of corticosteroids, otherwise of capital importance for the control of uveitis.

It is accepted that making the diagnosis of uveitic glaucoma (UG) may solely rely on an IOP of ≥21 mm Hg, with or without a glaucomatous appearance of the optic nerve4 as other ancillary tests may be substantially altered due to the uveitis itself. Therefore, the aim in these patients should be the lowest IOP with the maximum tolerated medication. As in other types of glaucoma, antihypertensive medications are considered the first option; however, the relative contraindications of prostaglandin analogs4 and the chronic course of uveitis usually lead to suboptimal IOP control.

Reports on surgical glaucoma techniques show variable rates of success for two main reasons: first, while any intraocular surgery should be performed within a minimum timeframe of 3 months without active inflammation, IOP control may be an emergent condition. Second, inflammatory activity generates extensive and accelerated scarring of most bleb-dependent surgeries, leading to earlier surgical failure.5 In this scenario, more than one intervention may be required. This study aimed to report clinical data on the efficacy and safety of different filtering surgeries, glaucoma drainage implants, and cyclodestructive procedures in a Spanish tertiary reference hospital.

Materials and Methods

Study Design

We made a retrospective, non-comparative audit of records of patients who underwent any type of glaucoma surgery due to a diagnosis of UG. The study adhered to the tenets of the Declaration of Helsinki. The study was approved by the Hospital Clinic of Barcelona Research Ethics Committee and, due to its retrospective, non-interventional design, a waiver of informed consent was granted. Each patient gave signed written informed consent before each surgery.
All patients were operated on by the same glaucoma surgeon (EM) between January 2007 and December 2016. Data on both eyes from the same patient were included if they met the inclusion criteria. All patients with a diagnosis of UG, defined as no previous history of glaucoma or ocular hypertension before the onset of uveitis who required ≥1 glaucoma surgery were included.

Surgical Technique

All surgeries were conducted in a standard fashion, similar to non-UG cases. We briefly describe each surgical technique.

All filtering procedures were performed in the upper quadrants. A fornix-based conjunctival flap and cautery were made. Mitomycin C (MMC) 0.2 mg/mL or 5-fluorouracil (5-FU) was used as antiproliferative agents. Mitomycin C was applied for 2 minutes on sponge fragments placed under the conjunctival flap and followed by profuse irrigation, while 5-FU was applied as a 0.1 mL subconjunctival injection after conjunctival suture.

A fornix-based conjunctival flap and cautery were made. Each surgical technique is covered with a scleral patch graft, and the tenon and conjunctiva were sutured with a 7/0 vicryl ligature placed around the tube. The tube was trimmed to an anchor in the limbus. In the Baerveldt implant, a 3/0 intraluminal prolene suture was inserted and a 7/0 vicryl ligature was placed around the tube or posterior chamber through a sclerostomy 3 mm posterior to the limbus. In the Ahmed valve was placed 8 mm posterior to the limbus, and the tube was trimmed to an anchor in the limbus. In the Ex-PRESS and TBC groups, the scleral flap was closed using nylon 10/0 sutures. Finally, hermetic conjunctival suturing was made.

Both glaucoma drainage devices (GDD) employed (Ahmed FP7 Glaucoma Valve (New World Medical Inc., Rancho Cucamonga, CA, USA) and Baerveldt BG101-350 (Abbott Medical Optics Inc., Santa Ana, USA)) was placed similarly, either in the superotemporal or superonasal quadrants. After conjunctival peritomy, the tube plate in the Ahmed valve was placed 8 mm posterior to the limbus, and behind the rectus muscles in the Baerveldt implant, and then anchored with a 5/0 Dacron suture. The tube was trimmed to an appropriate length with a beveled tip and placed in the anterior or posterior chamber through a sclerostomy 3 mm posterior to the limbus. In the Baerveldt implant, a 3/0 intraluminal prolene suture was inserted and a 7/0 vicryl ligature was placed around the tube to avoid abrupt hypotony-related complications. Additionally, tube fenestrations with the vicryl suture were made. The intraluminal suture could be further extracted after spontaneous vicryl suture release if the OP values were not satisfactory. Finally, the suture was covered with a scleral patch graft, and the tenon and conjunctiva were sutured.

Transscleral diode laser cyclophotocoagulation (CPC) was applied in three eye quadrants (leaving the superior temporal quadrant untreated) at a standard regimen of 2,000 ms/2,000 mW but tailored according to the audible "pops". The procedure could be repeated after 6 months if the IOP did not reach the target. Postoperative medical therapy was initiated with topical prednisolone and prednisolone acetate 1% drops every 2 hours during the first months and tapered during the following 2 months. An additional regimen of oral prednisone (2.5 mg/12 hours) and diclofenac (25 mg/12 hours) was started in the GDD group. Colchicine (0.25 mg or 3 mg/8 hours) was added in patients with a tendency to fibrosis.6

As an overall protocol guide, NPDS was the first surgical option in eyes with a low degree of intraocular or conjunctival inflammation, followed by Ex-PRESS implant if eye inflammation (intra or superficial) was moderate, and first intention drainage implants were preferred when eyes showed a high degree of uncontrollable intraocular inflammation or severe conjunctival hyperemia or vascularization. Trabeculectomy was not used as a first intervention if possible, to avoid surgical peripheral iridotomy and increased intraocular inflammation. Cyclophotocoagulation was performed initially in eyes with a low visual prognosis and extremely high refractory ocular hypertension.

Outcome Measures and Data Analysis

Medical records were reviewed and recorded in a database: age, sex, anatomic classification according to the SUN Working Group’ uveitis etiology, previous and subsequent surgeries, IOP with a Goldmann applanation tonometer, antihypertensive drugs, and postoperative complications and maneuvers.

The main outcomes measures were IOP reduction and the number of antihypertensive medications. Success was defined as a reduction in IOP >20% at the last follow-up visit for each eye receiving surgery. Eyes included in the analysis required a minimum follow-up of 6 months.

The normality of numerical variables was verified using the Shapiro–Wilks test and graphic analysis. The Chi-square test of independence was used to determine differences between the distribution of categorical variables. The Student’s t-test and the Wilcoxon signed-rank test (WSRT) were used to comparing the IOP and number of glaucoma medications on two occasions. Statistical significance was set at a two-tailed p < 0.05. A multivariate logistic regression analysis of preoperative data was performed. The analysis was made using Stata V14.1 (StataCorp, College Station, TX, USA).

Results

The medical records of 40 eyes from 34 patients diagnosed with UG with any glaucoma surgery were included. Overall, 15 (44.1%) were male and the mean age was 51.1 ± 9.8 years. The mean follow-up of the 40 cases was 28.1 ± 21.6 months (range 1–90). Uveitis characteristics are described in Table 1.

The baseline mean IOP was 30.7 ± 8.9 mm Hg with the maximum tolerated medical therapy. At the last follow-up, IOP decreased to 16.4 ± 2.0 mm Hg, after accounting for a 33% cut-off (p < 0.001, Student’s t-test). Antihypertensive medications were significantly reduced from 2.8 ± 0.8 to 0.8 ± 1.2, a 71% reduction (p < 0.001, WSRT). At the last follow-up visit, 16 (47%) cases met the criteria for success. With respect to the preoperative variables, the logistic regression model showed that only anterior uveitis [odds ratio (OR) = 1.5], the number of glaucoma medications (OR = 1.4), and the preoperative use of oral acetazolamide (OR = 1.2) were noticeable, but none were significant (p = 0.978).

Twenty-one (61.8%) eyes required one glaucoma surgery during the follow-up and 13 (38.2%) required ≥2 surgeries. Three eyes (8.8%) required >3 surgeries: in these cases, re-interventions were cases requiring several applications of CPC. With respect to the uveitis classification according to location, the Kruskal–Wallis test
Table 1: Uveitis classification by location and etiology

| Type of uveitis                  | n (%)          |
|---------------------------------|----------------|
|Anterior                         | 14 (35.0)      |
|Panuveitis                       | 14 (35.0)      |
|Intermediate                     | 2 (5.0)        |
|Posterior                       | 10 (25.0)      |

Uveitis diagnosis n (%)

- Unknown                        | 4 (10.0)        |
- Infectious                     | 26 (65.0)       |
- HLA-B27 positive               | 2 (5.0)         |
- Sympathetic ophthalmia         | 1 (2.5)         |
- Birdshot chorioretinopathy     | 2 (5.0)         |
- Fuchs heterochromic iridocyclitis| 1 (2.5)      |
- Sarcoidosis                    | 4 (10.0)        |
- Posner–Schlossman syndrome     | 1 (2.5)         |
- Vogt–Koyanagi–Harada disease   | 1 (2.5)         |
- Uveitis-glaucoma-hyphema       | 2 (5.0)         |
- Eales disease                  | 1 (2.5)         |
- Peripheral vasculitis           | 3 (7.5)         |
- Juvenile idiopathic arthritis  | 3 (7.5)         |
- Chronic retinal detachment + coloboma | 1 (2.5) |
- Idiopathic retinal vasculitis, aneurysms, and neuroretinitis | 2 (5.0) |
- Chronic endophthalmitis         | 2 (5.0)         |
- Infectious                     | 9 (22.5)        |
- Tuberculosis                   | 1 (2.5)         |
- Toxoplasmosis                  | 1 (2.5)         |
- Hepatitis B virus              | 1 (2.5)         |
- Herpes simplex virus           | 5 (12.5)        |
- Syphilis                       | 1 (2.5)         |
- Neoplastic                     | 1 (2.5)         |

HLA, human leukocyte antigen

showed no correlation between the type of uveitis and the total number of glaucoma surgeries ($\chi^2 = 1.86, p = 0.602$).

Data on the surgeries are summarized in Table 2.

Overall, NPDS was the first surgical approach in 18 (45%) cases, although 1 patient had undergone a prior trabeculectomy (data not available). Intraocular pressure decreased from 30.4 ± 7.9 to 22.7 ± 0.8 mm Hg, a 23% reduction from baseline ($p = 0.033$, WSRT). Glaucoma medications were non-significantly reduced from 2.7 ± 1.1 to 1.4 ± 0.2 postoperatively ($p = 0.602$, WSRT). A 43% reduction was found in eyes without prior glaucoma surgeries; however, the logistic regression model showed no correlation between meeting the target and total previous interventions ($p = 0.305$). Baerveldt implants were the second and third surgical procedures in three and one patient, respectively. Three eyes were followed for >6 months; the IOP fell from 31.5 ± 11.8 to 20.3 ± 12.3 mm Hg, a 28% reduction ($p = 0.285$, WSRT). Antihypertensive medications were reduced from 2.5 ± 1.7 to 1 ± 1.7 ($p = 0.317$, WSRT).

Cyclophotocoagulation was used in 13 cases. Due to a poor visual prognosis, CPC was the first intervention in seven (54%) eyes, and in 69.2% of cases, only one treatment was required. The IOP fell from 35 ± 7.8 to 16.9 ± 8.2 mm Hg ($p = 0.002$, WSRT). Antihypertensive medications were reduced from 2.4 ± 1.3 to 1.6 ± 1.4 ($p = 0.157$, WSRT).

Postoperative management of the filtering procedures is summarized in Table 3.

In all cases, bleb needling also required subconjunctival injection of 5-FU. Post-surgical complications are shown in Table 4.

Most were transient and did not require surgery, except for a case of intrascleral implant extrusion (Esnoper®, A.JL Ophthalmics, Álava, Spain) and a tube extrusion in an Ahmed device, both requiring scleral graft covering. Corneal edema was described in two cases in the Ahmed group and one in the Baerveldt group; in one case in the Ahmed group, the patient developed bullous keratopathy and required surgical removal of the Ahmed implant and relocation in the posterior chamber.

**Discussion**

During the course of UG, medical treatment does not control IOP in a high proportion of cases. It is estimated that 30% of UG patients will require surgery while on maximal medical therapy.8 However, surgery often does not result in optimal outcomes due to the accelerated healing process, and the postoperative inflammation, both causing early fibrosis of the filtering bleb or in the GDD capsule. The choice of the initial glaucoma surgical technique relies on the surgeons’ experience, but also on the degree of intraocular inflammation and the visual prognosis. However, the different surgical techniques may not contribute in the same way to reach target IOP. This study aimed to evaluate the surgical management of UG as a whole over 10 years.

Filtering procedures have long been used, with variable rates of efficacy and safety. Non-penetrating deep sclerectomy has been shown to reduce IOP to <19 mm Hg in up to 51% of cases at 5 years.9–11 Our results showed a lower reduction than previously reported, although IOP control was achieved in 38% of cases without further glaucoma surgery. Non-penetrating deep sclerectomy outperformed trabeculectomy in terms of IOP and antihypertensive medication reduction. Few studies have compared NPDS and trabeculectomy in UG. The more controlled outflow and lack of surgical iridotomy in NPDS are hypothesized to generate less bleb scarring and postoperative complications although the persistence of the trabecular meshwork in UG could result in less efficacy. Dupas et al. found less inflammation during...
the first postoperative week with NPDS, although the IOP was more effectively reduced in patients with trabeculectomy since fewer postoperative maneuvers were required to further control IOP compared with NDPS.12 Our NPDS group showed a lower rate of goniopuncture. However, our three filtering surgery groups were not strictly comparable.

Theoretically, Ex-PRESS could overcome some of the disadvantages of trabeculectomy in UG patients, due to the lack of iridectomy that could ultimately lead to less inflammation and less risk of blockage. However, few studies have reported the results of Ex-PRESS in UG patients. Dhanireddy et al.13 retrospectively compared Ex-PRESS results in open-angle glaucoma and UG patients, with a similar rate of postoperative complications and IOP control between the two groups. In our series, in three cases, Ex-PRESS was the only surgical treatment necessary to further control IOP. Studies are required to investigate whether a shift towards Ex-PRESS implant instead of trabeculectomy could benefit UG patients.

The increased use of tube shunts in the past two decades has been remarkable. In the tube vs trabeculectomy study, better outcomes overall were found with Baerveldt implants,14,15 although the results do not seem strictly applicable while deciding whether trabeculectomy or a GDD is preferable as the first glaucoma surgery.16 The same conclusions cannot be drawn in UG, as most reported data on glaucoma drainage implants and the comparisons with trabeculectomy come from retrospective studies. We performed NPDS—trabeculectomy or Ex-PRESS in narrow angles or cases with anterior synechiae, if there was no inflammation, reserving GDD for patients with active inflammation.

We also considered the IOP reduction achieved with each technique. We obtained greater IOP reductions in GDD compared with NPDS and trabeculectomy.17–19 Patients who underwent Ahmed implantation without prior surgery had a lower IOP at the

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### Table 2: Characteristics of surgical techniques

|               | NPDS (n=18) | Ex-PRESS (n=8) | TBC (n=3) | Ahmed (n=13) | Baerveldt (n=4) | CPC (n=13) |
|---------------|-------------|----------------|-----------|--------------|----------------|------------|
| Previous glaucoma surgeries | | | | | | |
| First         | 17          | 6              | 2         | 5            | –              | 7          |
| Second        | 1           | 2              | 1         | 6            | 3              | 1          |
| Third         | –           | –              | –         | 2            | 1              | 5          |
| Antifibrotic agents n (%) | | | | | | |
| 5-FU          | 9 (50)      | 5 (63)         | 2 (66)    | –            | –              | –          |
| MMC           | 8 (44.4)    | –              | 1 (33)    | –            | –              | –          |
| N/S           | 1 (5.6)     | 3 (37)         | –         | –            | –              | –          |
| Ologen        | 3 (16.7)    | 3 (37.5)       | 1 (33)    | –            | –              | –          |
| Implants      | | | | | | |
| SKGel         | 1 (5.6)     | –              | –         | –            | –              | –          |
| T-Flux        | 9 (50)      | –              | –         | –            | –              | –          |
| Esnoper       | 7 (38.9)    | –              | –         | –            | –              | –          |
| N/S           | 1 (5.6)     | –              | –         | –            | –              | –          |
| Number of treatments | | | | | | |
| Median (IQR)  | –           | –              | –         | –            | 1 (1–2)        | –          |
| Follow-up, months | 15.6 (1–36) | 11.6 (3–24) | 27 (12–42) | 22.8 (6–36) | 18 (3–24) | 15.7 (6–42) |
| IOP, mm Hg (mean ± SD) | | | | | | |
| Baseline      | 30.4 ± 7.9  | 29 ± 10.3      | 27.3 ± 11.2| 30.0 ± 9.6  | 31.5 ± 11.8   | 35.0 ± 7.8 |
| Reduction, last follow-up visit | –8 ± 13.3 | –12 ± 10 | –2.0 ± 9.8 | –10.5 ± 14.3 | –13.0 ± 24.1 | –18.1 ± 9.0 |
| Glaucoma medications. median (IQR) | | | | | | |
| Baseline      | 3 (3–3)     | 3 (2.5–3)      | 4 (3–4)   | 3 (2–3)     | 3 (1.5–3.5)   | 3 (2–3)    |
| Reduction, last follow-up visit | –0.5 (–1 to 0) | –2 (–2 to –0) | 0 (–1 to 0) | –2 (–3 to 0) | –0 (–3 to 0.0) | –2 (–3 to 0) |
| Oral acetazolamide n (%) | | | | | | |
| Preoperative  | 11 (61.1)   | 0 (0)          | 2 (66.7)  | 6 (46.2)    | 3 (75.0)      | 9 (69.2)   |
| Postoperative | 1 (7.1)     | 0 (0)          | 1 (33.3)  | 2 (15.4)    | 1 (25.0)      | 1 (8.3)    |

**Table 3: Postoperative adjustments**

|               | NPDS (n=18) | Ex-PRESS (n=8) | TBC (n=3) |
|---------------|-------------|----------------|-----------|
| Postoperative maneuvers n (%) | | | |
| Goniopuncture | 5 (27.7)    | –              | –         |
| Needling + 5-FU injection | 7 (38.9)    | 2 (25.0)       | 1 (33.3)  |
| Suture lysis  | 2 (11.1)    | 1 (12.5)       | 1 (33.3)  |

CPC, cyclophotocoagulation; IOP, intraocular pressure; IQR, interquartile range; MMC, mitomycin-C; NPDS, non-penetrating deep sclerectomy; N/S, non-specified; SD, standard deviation; TBC, trabeculectomy; 5-FU, 5-fluorouracil

1Applies only to CPC
end of follow-up. In line with other studies, we obtained similar reductions in both the Ahmed and Baerveldt groups, although the two groups were not strictly comparable. It has been theorized that the Ahmed valve could lead to higher failure rates, although this could be biased, since the Ahmed valve may be a preferred option when the patient has a higher preoperative value and, in the Baerveldt group, tube ligature is needed to prevent early hypotony until the capsule is formed.

Cyclophotocoagulation is an alternative to invasive procedures. Due to the potentially devastating consequences, it is not in the first line of glaucoma procedures, although there is increasing interest in using it as the first procedure, both transscleral and endoscopic.20,21 In inflammatory glaucoma, our results are similar to those reported by Schlote, who found a higher re-application rate than did our study22 and reported no major complications. However, we found one case of phthisis bulbi.

The study has some limitations. First, the retrospective design could have resulted in selection bias. Patients missed appointments and, although the clinical management of uveitis and glaucoma was made in the same hospital in the majority of the cases, patients not infrequently missed glaucoma visits, maybe due to less awareness of the potential sight-threatening effects of uncontrolled IOP. Second, we did not include medically-treated UG, as our patients were those referred for surgical management in the glaucoma unit. The total number of surgical cases in 10 years is relatively small, considering the prevalence of uveitis, especially in our hospital. The multidisciplinary approach and the comorbidities of uveitis patients might have influenced glaucoma management, opting for conservative control of the IOP. However, this could be foreseen as, even with primary open-angle glaucoma, only 41.5% of referrals for incisional glaucoma surgery are “appropriate and timely”, with the majority of cases with advanced glaucomatous damage.23 Third, the surgical choice was at the surgeon’s criteria, timely”, with the majority of cases with advanced glaucomatous damage.

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### Table 4: Postoperative complications

| Type of complication | NPDS | Ex-PRESS | TBC | Ahmed | Baerveldt | CPC |
|----------------------|------|---------|-----|-------|---------|-----|
| Flattened chamber | 0 | 0 | 0 | 1 (7.7) | 1 (25) | – |
| Seidel | 0 | 0 | 0 | 1 (7.7) | 1 (25) | – |
| Hyphema | 2 (11.1) | 0 | 0 | 0 | 0 | – |
| Implant extrusion | 1 (5.6) | – | – | – | – | – |
| Tube extrusion | – | – | – | 1 (7.7) | 1 (25) | – |
| Corneal edema | 0 | 0 | 0 | 2 (15.4) | 1 (25) | 0 |
| Obstruction | 0 | 0 | – | 1 (7.7) | 0 | – |
| Phthisis bulbi | 0 | 0 | 0 | – | – | 1 (7.7) |

**CPC,** cyclophotocoagulation; **NPDS,** non-penetrating deep sclerectomy; **TBC,** trabeculectomy; **S-FU,** 5-fluorouracil

†Applies only to NPDS

**Conclusion**

Glaucoma surgeons facing the surgical management of UG should have experience in more than one technique, as a myriad of surgical procedures is often required to control UG. Although up to 62% of cases may require only one surgery, patients should be warned that more than one procedure may be necessary to achieve further control, considering the inflammatory nature of the disease and, therefore, the higher risk of early postoperative conjunctival scarring. In our series, NPDS, the Ahmed implant, and CPC were the options with the greatest IOP reductions. Ahmed valves and CPC could be a good choice as the first glaucoma surgery option in UG, probably because they are bleb-independent surgical techniques.

**Disclosure**

All the authors have read and approved the final manuscript.
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