Outcomes of Ahmed glaucoma valve and transscleral cyclophotocoagulation in neovascular glaucoma

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Purpose: To determine the outcomes of Ahmed glaucoma valve (AGV) and transscleral diode cyclophotocoagulation (CPC) in neovascular glaucoma (NVG). Methods: This was a single-center retrospective comparative case series involving chart review of consecutive patients who underwent AGV or CPC for treatment of NVG and had ≥6 months of follow-up. Surgical failure at 6 months, defined as an IOP of >21 or <6 mm Hg with hypotony maculopathy after 1 month, progression to no light perception (NLP) vision, glaucoma reoperation, or removal of AGV were the main outcome measures. Results: In total, 121 eyes of 121 patients were included (70 AGV and 51 CPC). Baseline demographics, visual acuity (VA), and intraocular pressure (IOP) were comparable between groups. At 6 months, failure was significantly higher in the CPC group than in the AGV group (43.1% vs. 17.1%, P = 0.020). Both groups had similar IOP and medication number at 6 months, but VA was significantly lower in the CPC group compared to the AGV group (2.4 ± 0.8 vs. 1.9 ± 1.0, P = 0.017). More CPC eyes required reoperation for glaucoma than AGV eyes (11.8% vs. 1.4%, P = 0.041). Multivariate regression analysis identified higher preoperative IOP (P = 0.001) and CPC surgery (P = 0.004) as independent predictors of surgical failure at 6 months. Age, sex, race, NVG etiology, bilaterality of the underlying retinal pathology, perioperative retina treatment, and prior or combined vitrectomy were not significant. Conclusion: AGV and CPC had comparable IOP and medication reduction in NVG eyes at 6 months. CPC was more frequently associated with failure, reoperation for glaucoma, and worse visual outcomes. High preoperative IOP and CPC surgery independently predicted surgical failure.

Key words: Ahmed glaucoma valve, glaucoma surgery, neovascular glaucoma, transscleral cyclophotocoagulation, tube shunts

Neovascular glaucoma (NVG) is associated with poor visual prognosis despite treatment. The most common causes of NVG are proliferative diabetic retinopathy, ischemic central retinal vein occlusion, and ocular ischemic syndrome. Retinal hypoxia stimulates the release of inflammatory cytokines, promoting fibrosis and neovascularization of the iris and anterior segment, which is associated with fibrovascular membrane formation, leading to secondary angle closure and intraocular pressure (IOP) elevation.

Management of NVG is difficult as trabeculectomy is associated with a high proportion of failure. Tube shunts, including Ahmed glaucoma valve (AGV) or Baerveldt glaucoma implant, are the standard of care for IOP-lowering in NVG. Transscleral cyclophotocoagulation (CPC) has also been investigated as a possible management strategy with variable success and possibly worse outcomes compared to tube shunt surgery. CPC has potential advantages as it may allow patients to avoid incisional surgery, can be performed in a lower-resource setting, and is a relatively short procedure.

Limited studies have reported CPC outcomes in NVG compared to tube shunt surgery. The present study aims to compare the outcomes of AGV surgery and CPC in the setting of NVG in the early postoperative period.

Methods

Study design

This was a single-center, retrospective comparative case series. The study was approved by the institute’s review board and was in accordance with Health Insurance Portability and Accountability Act regulations. As this was a retrospective study with de-identified data, informed consent was not required. The medical records of consecutive patients diagnosed with NVG who were treated with the AGV (New World Medical

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Inc., Rancho Cucamonga, CA, USA) or CPC between 2007 and 2019 at a tertiary eye care hospital were reviewed. Surgeries were performed by seven glaucoma surgeons (J. S. M., M. R. M., R. R., D. L., N. N. K., L. J. K., and A. G. S.). All surgeons were fellowship-trained glaucoma specialists, and a resident or fellow assisted in all cases. The diagnosis of NVG was based on the presence of neovascularization of the iris and/or anterior chamber angle and IOP > 21 mm Hg.

Inclusion and exclusion criteria

Patients aged ≥18 years with refractory NVG and preoperative IOP > 21 mm Hg were included. Exclusion criteria included no light perception (NLP) vision at baseline and a follow-up duration of <6 months. In patients who underwent multiple glaucoma operations, only the first tube shunt or the first CPC were included. Both continuous wave (CW) and micropulse (MP) CPC were included.

Patient visits

Visits at baseline, postoperative day 1, week 1, and months 1, 3, and 6 were reviewed from the electronic medical record. Demographic data such as age, sex, and race as well as medical and surgical history were collected. Preoperative clinical data included visual acuity (VA), IOP, topical glaucoma medications, synechial angle closure, and presence of hyphema. Details of neovascular disease, including laterality, NVG etiology, bilaterality of the underlying retinal pathology, retinal treatment in the form of panretinal photocoagulation (PRP) or intravitreal injection of anti-vascular endothelial growth factor (VEGF) within 2 weeks of surgery, and prior or concomitant vitrectomy were identified. Postoperative data included VA, IOP, glaucoma medications, postoperative complications, and need for additional glaucoma surgery.

Outcome measures

The primary outcome measure was surgical failure at 6 months, defined as IOP > 21 mm Hg with medications or <5 mm Hg at two consecutive visits after 1 month, progression to NLP vision, glaucoma reoperation (CPC or tube shunt), or removal of AGV. Eyes that failed due to IOP < 5 mm Hg had to exhibit clinically significant signs of hypotony after 1 month postoperatively. Changes in VA, IOP, and glaucoma medications at 6 months were secondary outcome measures. Eyes that met the failure criteria due to reoperation for glaucoma or removal of the implant at any time point were censored from the analysis of subsequent visits. Predictive factors for surgical failure and rate of surgical complications were also identified.

Statistical analysis

Statistical analyses were performed using SPSS software version 27.0 (IBM Analytics, Chicago, IL, USA). Snellen VA measurements were converted to logarithm of the minimum angle of resolution (logMAR) VA equivalents for the purpose of data analysis. Continuous variables were presented as mean ± standard deviation. Proportions (%) were used to describe categorical variables. Two-sided Student t-tests and Chi-square tests were used to compare treatment groups for continuous and categorical variables, respectively. Analysis of covariance was performed for between-group comparisons at 6 months after adjusting for baseline characteristics. Paired sample t tests and McNemar test were used to compare continuous and categorical variables within the same group, respectively. P < 0.05 was considered significant. Kaplan–Meier survival analysis with log-rank tests was used to report the cumulative rate of surgical failure in the AGV versus CPC eyes. Cox regression analysis was performed to identify factors predictive of surgical failure. Variables in the univariate analysis with P < 0.05 were entered into the multivariate model by using the forward stepwise Wald method. We estimated sample size (80% power and an alpha of 0.05) by considering prior outcomes from a prospective randomized study that did not detect a significant difference in surgical failure between 33 AGV eyes and 33 CPC eyes with NVG.

Results

Baseline characteristics

Of the 121 eyes of 121 patients included, 70 eyes underwent AGV and 51 eyes underwent CPC. Baseline patient characteristics are displayed in Table 1. Mean age, sex, race, underlying NVG etiology, and baseline VA, IOP, medication number, synechial angle closure, and presence of hyphema were comparable in both groups. Proliferative diabetic retinopathy (48.8%) and retinal vein occlusion (31.4%) were the most prevalent etiologies of NVG in both groups. Type of perioperative retinal treatment differed between groups. While more AGV eyes received PRP or intravitreal anti-VEGF injection (74.3% and 77.1%, respectively) within 2 weeks of surgery as compared to 11.8% and 31.4% in the CPC group (P < 0.001 for both), pars plana vitrectomy was more commonly combined in the CPC group (27.5%) as compared to the AGV group (4.3%) (P < 0.001). For the AGV group (N = 70), implants were placed in the superotemporal quadrant and the tubes were inserted into the anterior chamber in 67 (95.7%) eyes. Pars plana vitrectomy was performed concomitantly with pars plana AGV placement in the superonasal quadrant in three (4.3%) eyes. For the CPC group (N = 51), CW-CPC was performed in 25 (49%) eyes with a mean power of 1983 mW at an average duration of 2.6 s with application of 12–30 spots, and MP-CPC was performed in 26 (51%) eyes with a mean power of 2025 mW at an average duration of 220 s.

Month 6 outcomes

Clinical outcomes at 6 months are displayed in Table 2.

Surgical failure

At 6 months, a total of 34 eyes (28.1%) met failure criteria, with a significantly higher failure rate in the CPC group (22 eyes or 43.1%) compared to the AGV group (12 eyes or 17.1%) (P = 0.020). When excluding CPC eyes that failed due to CPC repeat only, the difference remained significant, with a total of 31 eyes (25.6%) meeting failure criteria, with a significantly higher failure rate in the CPC group (19 eyes or 37.3%) compared to the AGV group (12 eyes or 17.1%) (P = 0.020). Kaplan–Meier survival analysis showed that the cumulative proportion of surgical failure over 6 months was significantly higher in the CPC group as compared to the AGV group (P = 0.002) [Fig. 1]. A difference in surgical failure between the CW-CPC and MP-CPC (P = 0.57) groups was not detected. Cox regression analysis was performed to identify the predictive factors of surgical failure at 6 months. Based on the findings from the univariate analysis, a multivariate model (P < 0.001) was created and identified higher preoperative IOP (P = 0.001) and surgery type as CPC (P = 0.004) as the strongest predictors of surgical failure [Table 3]. Age, sex, race, NVG etiology, bilaterality of the underlying retinal pathology, perioperative PRP or intravitreal anti-VEGF, and prior or combined vitrectomy were not significant predictors of surgical failure.
Reasons for failure were comparable in both groups (\(P = 0.341\)). Elevated IOP > 21 mm Hg (14 eyes or 41.2%) followed by progression to NLP vision (10 eyes or 29.4%) were the most common reasons for surgical failure. Failure due to more than one reason (NLP, IOP > 21 mm Hg, or glaucoma reoperation) occurred in six (17.6%) eyes. Time to failure was also similar in both groups (3.8 ± 1.8 vs. 3.8 ± 2.3 months, \(P = 0.941\)).

Visual acuity
The mean logMAR VA remained stable from baseline to postoperative month 6 in the AGV group (2.1 ± 0.8 vs. 2.0 ± 1.0, respectively; \(P = 0.114\)) and slightly deteriorated in the CPC group (2.2 ± 0.9 vs. 2.4 ± 0.7, respectively; \(P = 0.076\)), although this did not reach significance. Additionally, although between-group differences in baseline VA were not statistically significant (\(P = 0.279\)), the CPC eyes had significantly lower VA at 6 months compared to AGV eyes (2.4 ± 0.7 vs. 2.0 ± 1.0, respectively; \(P = 0.005\)), and this difference remained significant even after adjusting for baseline VA using analysis of covariance testing (\(P = 0.009\)). Progression to NLP vision at 6 months was higher in the CPC group (nine eyes or 17.6%) compared with the AGV group (four eyes or 5.7%), but this difference was not statistically significant (\(P = 0.071\)). Progression to NLP vision was similar in CW-CPC and MP-CPC groups (\(P = 0.526\)).

Intraocular pressure
Both groups experienced significant IOP reduction through postoperative month 6. AGV eyes experienced a mean IOP reduction from 39.8 ± 9.9 mm Hg at baseline to 16.3 ± 6.1 mm Hg at month 6 (23.5 ± 10.1 mm Hg IOP reduction, \(P < 0.0001\)). CPC eyes experienced a mean IOP reduction from 37.3 ± 11.9 mm Hg at baseline to 16.2 ± 10.2 mm Hg at month 6 (21.1 ± 13.0 mm Hg IOP reduction, \(P < 0.0001\)). The IOP difference between AGV and CPC eyes at month 6 was not statistically significant (\(P = 0.940\)) and there was no significant difference between the CW-CPC and MP-CPC groups (\(P = 0.526\)). However, the AGV eyes had significantly lower IOP at the early postoperative period (day 1 and week 1) compared with the CPC group (\(P < 0.001\) for both) [Fig. 2a].

### Table 1: Baseline patient characteristics of the Ahmed Glaucoma Valve and cyclophotocoagulation groups

|                       | AGV  | CPC  | Total | \(P\) |
|-----------------------|------|------|-------|-------|
| Number of Eyes        | 70   | 51   | 121   |       |
| Number of Patients    | 70   | 51   | 121   |       |
| Age: Years            | 66.0±15.0 | 68.4±15.3 | 67.0±15.1 | 0.390 |
| Sex, Females n (%)    | 26 (37.1) | 25 (49) | 51 (42.1) | 0.199 |
| Race n (%)            |      |      |       |       |
| White                 | 27 (38.6) | 22 (43.1) | 49 (40.5) | 0.469 |
| Black                 | 26 (37.1) | 12 (23.5) | 38 (31.4) |       |
| Asian                 | 3 (4.3) | 2 (3.9) | 5 (4.1) |       |
| Hispanic              | 5 (7.1) | 4 (7.8) | 9 (7.4) |       |
| Indian                | 1 (1.4) | 0 (0.0) | 1 (0.8) |       |
| Unknown               | 8 (11.4) | 11 (21.6) | 19 (15.7) |       |
| Surgical Eye, Right n (%) | 36 (51.4) | 25 (49.0) | 61 (50.4) | 0.855 |
| NVG Etiology n (%)    |      |      |       |       |
| PDR                   | 38 (54.3) | 21 (41.2) | 59 (48.8) | 0.051 |
| CRVO                  | 23 (32.9) | 15 (29.4) | 38 (31.4) |       |
| CRAO                  | 4 (5.7) | 2 (3.9) | 6 (5.0) |       |
| OIS                   | 1 (1.4) | 4 (7.8) | 5 (4.1) |       |
| Combined              | 3 (4.3) | 2 (3.9) | 5 (4.1) |       |
| Others                | 1 (1.4) | 7 (13.7) | 8 (6.6) |       |
| Bilateral Retinal Pathology n (%) | 38 (54.3) | 19 (37.3) | 57 (47.1) | 0.069 |
| Intravitreal Injection n (%) | 54 (77.1) | 16 (31.4) | 70 (57.9) | <0.001 |
| Panretinal Photocoagulation n (%) | 52 (74.3) | 6 (11.8) | 58 (47.9) | <0.001 |
| Vitrectomy n (%)      |      |      |       |       |
| None                  | 63 (90) | 36 (70.6) | 99 (81.8) | 0.001 |
| Prior Vitrectomy      | 4 (5.7) | 1 (2.0) | 5 (4.1) |       |
| Combined Vitrectomy   | 3 (4.3) | 14 (27.5) | 17 (14.0) |       |
| Visual Acuity: LogMAR | 2.1±0.9 | 2.3±0.8 | 2.2±0.8 | 0.279 |
| Intraocular Pressure: mm Hg | 39.6±9.8 | 37.6±11.4 | 38.7±10.5 | 0.330 |
| Medication Number     | 3.3±0.8 | 3.5±1.1 | 3.4±0.9 | 0.240 |
| Synechial Angle Closure n (%) | 48 (68.6) | 28 (54.9) | 76 (62.8) | 0.133 |
| Hyphema n (%)         | 13 (18.6) | 5 (9.8) | 18 (14.9) | 0.140 |

AGV: Ahmed glaucoma valve. CPC: Cyclophotocoagulation. NVG: Neovascular glaucoma. PDR: Proliferative diabetic retinopathy. CRVO: Central retinal vein occlusion. CRAO: Central retinal artery occlusion. OIS: Ocular ischemic syndrome. Bolded values denote statistical significance.
Medical therapy

The need for medical therapy in both treatment groups was significantly reduced through postoperative month 6. The mean number of glaucoma medications in the AGV group decreased from 3.3 ± 0.8 at baseline to 2.3 ± 1.2 at 6 months (1.0 ± 1.4 medication reduction, P < 0.0001). The mean number of
glaucoma medications in the CPC group decreased from 3.5 ± 1.1 at baseline to 2.4 ± 1.5 at 6 months (1.1 ± 1.7 medication reduction, $P < 0.0001$). There was no significant difference between the medication number in the two groups at month 6 ($P = 0.836$), and there was no significant difference between the CW-CPC and MP-CPC groups ($P = 0.323$). However, the AGV eyes needed a significantly lower number of medications at all the visits prior to month 6 ($P < 0.05$ for all) [Fig. 2b].

**Postoperative complications**

Serious postoperative complications were infrequent in both groups. Suprachoroidal hemorrhage occurred in three (4.3%) AGV eyes and no CPC eyes ($P = 0.262$). Hypotony and phthisis bulbi occurred in one (2.0%) CPC eye and no AGV eyes ($P = 0.421$). In the AGV group, tube erosions requiring revisions occurred in three (4.3%) eyes, but no eyes experienced endophthalmitis at postoperative month 6. The total rate of complication was higher in the AGV group (six eyes, 8.6%) compared to the CPC group (one eye, 2.0%), but this difference was not statistically significant ($P = 0.236$).

**Reoperation for glaucoma**

In total, seven (5.8%) eyes required reoperation for glaucoma in the first 6 postoperative months, and the rate of reoperation...
was significantly higher in the CPC group (six eyes or 11.8%) compared with the AGV group (one eye or 1.4%) \( (P = 0.041) \). Among CPC eyes that required reoperation, two eyes were in the CW-CPC group and four eyes were in the MP-CPC group \( (P = 0.668) \). For all reoperated eyes, CPC was the additional glaucoma intervention.

### Discussion

Our retrospective study found that both AGV and CPC had similar outcomes in terms of IOP and medication reduction in NVG. Both procedures achieved more than 50% IOP reduction and significantly less dependence on medications at month 6. However, CPC was more frequently associated with surgical failure, reoperation for glaucoma, and worse visual outcomes as compared to AGV. High preoperative IOP and CPC surgery were independent predictors of surgical failures. While other studies have compared CPC and tube shunt surgery for NVG treatment,\cite{1,12} our study is the largest to do so. Although the literature lacks a clear recommendation regarding the optimal glaucoma surgery for the treatment of NVG, our study suggests that AGV surgery may be associated with better outcomes as compared to CPC.\cite{14}

Limited studies have compared CPC and AGV implantation for NVG.\cite{11,13} In a prospective randomized pilot study, Yildirim et al.\cite{11} did not detect a difference in success between CPC and AGV in the setting of NVG at 1 year (29% vs. 38.7%, respectively; \( P > 0.05 \)). Although our study used the same failure criteria, we detected greater surgical success with AGV compared to CPC at postoperative month 6 \( (P = 0.02) \), possibly because our study was better powered than that of Yildirim et al. (121 vs. 58). Furthermore, treatment failures or complications within the CPC group may be missed in the Yildirim study as a greater proportion of CPC patients were lost to follow-up as compared to AGV patients. Similar to ours, Yildirim et al. found that both procedures achieved significant IOP and medication reduction as compared to baseline, and there was no significant difference in the mean IOP between groups at month 6 \( (P = 0.36) \). However, at month 1 in the Yildirim study, the IOP was significantly lower in the AGV group \( (P = 0.02) \), which is in agreement with our results.

Another pilot study of a substantially smaller group \( (N = 22) \) compared AGV and CPC in NVG in a Chinese sample over an average follow-up duration of 30 months.\cite{15} This prospective randomized study reported that both AGV and CPC had a similar success rate (86% for each group) by the final visit. Of note, failure criteria in this study were based solely on IOP, without considering progression to NLP or reoperation for glaucoma as the study allowed CPC to be repeated up to five times for IOP control. These differences and a potentially inadequate sample size limit comparison with our study.

Eid et al.\cite{15} compared the outcomes of tube shunts and noncontact neodymium: YAG (Nd: YAG) CPC in NVG over a mean follow-up of 15 months. Similar to our findings, this retrospective case-matched study showed that the tube group achieved significantly lower IOP in the early postoperative period (week 1 and month 1). However, the mean IOP became nearly equal in the two groups with time. Also, the failure rate at the final visit was significantly higher in the CPC group as compared to the tube group \( (P < 0.001) \). Interestingly, the failure rate in this case series was much higher in both groups as compared to our study (33.4% vs. 17.1% for the tube group, and 79.2% vs. 43.1% for the CPC group). Although progression to NLP was not counted as failure, this higher failure rate may be attributed to longer follow-up duration (more than 1 year), inclusion of valve and non-valved tube shunts (AGV, Baerveldt implant, and Molteno implant), different CPC types (noncontact Nd: YAG), and smaller sample size (24 patients for each group).

In our multivariate model, high baseline IOP \( (P = 0.001) \) and CPC surgery \( (P = 0.004) \) were independent predictors of surgical failure, while age, sex, race, NVG etiology, bilaterality of the underlying retinal pathology, perioperative PRP or intravitreal anti-VEGF, and prior or combined vitrectomy were not found to be significant predictive factors. This was partially in agreement with a prior study that did not identify an association between PRP and anti-VEGF therapy and long-term IOP control.\cite{16} However, this study reported that synechial angle closure had the greatest impact on final IOP, which was insignificant in our study \( (P = 0.722) \). This discrepancy may be attributed to the different design and surgical treatment in both studies as they initially offered PRP with or without anti-VEGF, and trabeculectomy was only done if IOP was not controlled.\cite{16} Our study included patients who were treated with AGV or CPC indicating advanced stages of NVG, and the majority of them had synechial angle closure (62.8%). Similar to our study, a meta-analysis comparing the different NVG surgical treatments reported that CPC was associated with a higher failure rate as compared to tube shunts \( (P = 0.05) \), although both procedures had similar IOP outcomes at month 6 \( (P = 0.16) \).\cite{17}

NVG’s association with potential blindness is well-known.\cite{5,18} Our study demonstrated that while both CPC and AGV groups had similarly poor baseline VA \( (P = 0.279) \), CPC eyes demonstrated significantly worse VA at month 6 \( (P = 0.017) \). Interestingly, both groups experienced similar IOP reduction at that time point \( (P = 0.854) \). These findings agree with early studies on CPC, which demonstrated vision loss and postoperative vision-threatening complications.\cite{19,20} Of note, our study showed a comparable rate of serious postoperative complications in the CPC and AGV groups \( (P = 0.236) \). Additionally, higher IOP was seen in the CPC group as compared to the AGV group in the early postoperative period in our studies and others.\cite{11,12,13} This delayed effect on IOP may be due to the mechanism of action of CPC, which is theorized as coagulative necrosis of the secretory ciliary apparatus following the absorption of laser energy.\cite{21} Because IOP control is essential to preserve the visual field in eyes with glaucoma,\cite{22} this initially higher IOP in CPC eyes might be responsible for VA worsening.

Our study has limitations. Being a retrospective study, patient selection bias may have played a role. Although baseline VA and IOP were similar between groups, CPC has traditionally been used in eyes with poor visual prognosis,\cite{21} while AGV may have been chosen for healthier eyes with
reversible causes of vision loss (e.g., corneal edema) rather than irreversible optic neuropathy or ischemic retina. Moreover, perioperative retina treatment including PRP and intravitreal injection of anti-VEGF was significantly lower in the CPC group (P < 0.001 for both), which could have been a reason for worsening vision in the CPC group due to retinal ischemia rather than glaucoma. The modest follow-up duration of our study (6 months) is another limitation. Furthermore, differences in sample size in the AGV and CPC groups may have led to inadequately powered analyses.

**Conclusion**

Our results demonstrated that both AGV and CPC had comparable IOP and medication reduction in NVG eyes at postoperative month 6. CPC was associated with more frequent surgical failure, reoperation for glaucoma, and worse visual outcomes. High preoperative IOP and surgery type as CPC were independent predictors of surgical failure. Future randomized clinical trials on ideal surgical management in NVG may be indicated.

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**Conflicts of interest**

There are no conflicts of interest.

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