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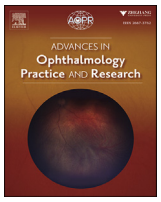

Full Length Article

Outcomes of vitrectomy, complete pan-retinal photocoagulation, and endoscopic cyclophotocoagulation surgery after anti-VEGF treatment in neovascular glaucoma

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ABSTRACT

Purpose: To establish a comprehensive treatment strategy and evaluate the efficacy of combination of anti-vascular endothelial growth factor (VEGF) injection, pars plana vitrectomy (PPV), endoscopic pan-retinal photocoagulation (PRP), and endoscopic cyclophotocoagulation (ECP) surgery for neovascular glaucoma (NVG) patients.

Methods: This retrospective study included 30 patients (30 eyes) who were suffering from NVG and treated with PPV & PRP & ECP (ECP group, 16 eyes), or Ahmed glaucoma valve implantation (Ahmed group, 14 eyes). The intraocular pressure (IOP), number of postoperative anti-glaucoma medications, best-corrected visual acuity (BCVA), successful rate of surgery, and postoperative complications were recorded and statistically analyzed at the time points of preoperative, 1-day, 1-month, 3-months, 6-months, and 12-months after operation.

Results: An obvious reduction in IOP and number of postoperative anti-glaucoma medications were observed in both the ECP group and Ahmed group after operation ($P < 0.05$), and the ECP group showed a significantly lower IOP compared to the Ahmed group at the 6-months ($P = 0.014$) and 12-months ($P = 0.047$) postoperative time points, while there was no significant difference of medication number between the two groups except for 1-day after surgery. The BCVA showed no marked difference between the two groups preoperatively and post-operatively ($P > 0.05$), while it was significantly improved in ECP group at 3-months ($P = 0.001$), 6-months ($P = 0.004$), and 12-months ($P = 0.010$) time points comparing with preoperative BCVA. The surgical success rates in ECP group were also slightly higher than Ahmed group. And the complications after operation showed no marked differences.

Conclusions: The comprehensive treatment of PPV, endoscopic PRP, and ECP surgery for NVG patients after anti-VEGF injection can control IOP effectively and be friendly to patients' BCVA without obvious serious complications throughout a 12-months follow-up period.

1. Background

Neovascular glaucoma (NVG) is an aggressive type of refractory glaucoma that is a difficult situation to manage by medical and surgical means and often results in poor visual outcomes.[1–3] The most common causes of NVG include proliferative diabetic retinopathy (PDR), ischemic retinal vein occlusion, and ocular ischemic syndrome, which are associated with neovascularization and fibrovascular membrane formation of the iris and anterior segment, leading to secondary angle closure and intraocular pressure (IOP) elevation.[4,5] Surgical interventions indicated to treat NVG are divided into two major categories, one is anti-glaucoma surgery, such as glaucoma valve implantation, filtration surgery, ciliary body freezing or photocoagulation, and the other is vitreous surgery, which is the targeted treatment of primary diseases, such as vitrectomy, pan-retinal photocoagulation (PRP), anti-vascular endothelial growth factor (VEGF) injection, etc.[6,7] However, because of the complexity and specificity of the primary diseases, none of these procedures have been found to be superior, and most of them do not offer long-term effect.[8]

Some previous literature indicated that the combination of anti-VEGF agents, complete PRP, medical reduction of IOP, and anti-glaucoma surgery (such as filtration surgery and Ahmed glaucoma valve [AGV] implantation) were the most recommended treatments for NVG.[9,10] Unfortunately, AGV implantation, whose success rate was comparable to other glaucoma drainage devices and become the common therapy for

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NVG, also showed limited IOP reduction and even postoperative complications in eyes with profoundly ischemic situation, such as choroidal detachment, shallow anterior chamber, hyphema, and hypotony, which are outstanding problems that would seriously affect the surgical effect and prognosis.[11,12]

With the improvement of endoscopic and photocoagulation techniques in ophthalmology, endoscopic cyclophotocoagulation (ECP) has shown advantages of long-term safety and efficacy for the treatment of NVG,[13,14] particularly in the lower rates of postoperative complications compared with other NVG treatment.[15] ECP allows the surgeon to endoscopically destruct the ciliary body with the least collateral tissue damage and provides the other advantage of conserving the normal structure of the conjunctiva, leaving them intact for future possible second glaucoma surgeries. Furthermore, the endolaser PRP with endoscopic facilitation through the pars plana approach would reach a wider range of photocoagulation and achieve a superior effect than the common endolaser PRP.[16,17] In addition, whenever a clear view of fundus is compromised due to corneal opacity, hyphema, dense cataract, or vitreous hemorrhage, pars plana vitrectomy (PPV) may be necessary for PRP completion.

Thus, we conducted this retrospective study to establish a comprehensive treatment strategy of combination of PPV, endoscopic PRP, and ECP surgery to control IOP and further improve the visual acuity of NVG patients. The efficacy and complications of this surgery were evaluated and compared with AGV implantation. And anti-VEGF injection, which has been verified to help block the pathogenesis of NVG and cause the neovascularization to subside,[18,19] was performed before all the surgeries.

2. Methods

2.1. Study population

This retrospective comparative study included 30 eyes of 30 patients with NVG who were assigned to receive either ECP (ECP group, n = 16) or AGV implantation (Ahmed group, n = 14) and had a regular follow-up in Chinese PLA General Hospital from January 1, 2017 to October 1, 2022 (n = 30). The surgeries were processed by the same surgeon (Dr. Baoke Hou) and followed by operation consents that had been signed by all participants. Two experienced ophthalmologists collected and recorded the data to guarantee its quality and the disagreements were resolved by their discussion. This study was conducted under the principles of the Declaration of Helsinki, and the study protocol was approved by the Ethics Committee of Chinese PLA General Hospital.

2.2. Inclusion and exclusion criteria

Patients were included if they were diagnosed with NVG, during the atrial angle closing period, with ineffective IOP lowering by maximally tolerated medical treatment and willingness for surgery owing to pain and progressive loss of vision with uncontrolled IOP. Exclusion criteria included that; (1) eyes had previous cyclodestructive procedure or the glaucoma drainage device implantation; (2) eyes that lost light perception; (3) eyes that had the retinal or choroidal detachment.

2.3. Preoperative evaluation

The information about patients' age, sex, surgical eye, NVG etiology, and ocular lens status before the operation was collected. As well as the preoperative information of ophthalmological examinations, including best-corrected visual acuity (BVCA, which was converted into a logarithm of the minimal angle of resolution [logMAR]), IOP measurement, slit-lamp microscope examination, ocular fundus examination, and B-scan ultrasound of eyes. Preoperative antiglaucoma drugs were also recorded.

2.4. Follow-up and outcome criteria

The information after the operation including IOP, BCVA, use of antiglaucoma medications, success rate, and postoperative complications were recorded on 1 day, as well as 3, 6, and 12 months postoperatively. During the follow-up period, phacoemulsification & IOL implantation or secondary operation needed for IOP control will undergo on the second stage when it is necessary.

The complete success of the surgery was defined by the following criteria[20]: (1) IOP within the range of 6–21 mmHg, and IOP reduced by more than 20% from preoperative IOP at least for two consecutive visits; (2) no loss of light perception; (3) no need of additional glaucoma procedure and (4) no need of application of anti-glaucoma drugs after surgery. And qualified success was defined that the IOP could be kept within the range of 6–21 mmHg while with the use of anti-glaucoma medications. In addition, failure of the treatment was manifested as uncontrolled IOP even with anti-glaucoma medications, the need for another anti-glaucoma surgery, IOP <6 mmHg for more than two months, no light perception, serious complications (retinal detachment, severe choroidal detachment, endophthalmitis, malignant glaucoma, etc.), or atrophy of the eyeball.

2.5. Statistical analysis

Using IBM SPSS 23.0 and GraphPad Prism 9 to analyze the data. The categorical variables were described in percentages and frequencies and Fischer's exact test was used for their analysis. The continuous variables were presented by mean ± standard deviation and adopted independent sample *t*-test for intergroup comparisons, and intragroup comparisons such as before and after operation adopted the paired sample *t*-test. A Kaplan-Meier survival curve was used to display success rates. Significant differences were defined as $P < 0.05$.

3. Surgical techniques

3.1. Intravitreal administration of anti-VEGF

Ranibizumab Injection (10 mg/ml, NOVARTIS) was used as the anti-VEGF medication. After the preoperative preparation, the patient was instructed to look down and the needle was inserted along the direction of the center of the eyeball at the position of 3–4 mm far from corneal limbus edge. After the injection, it usually took 3–5 days for the medication to exert its effects.

3.2. ECP procedure

Prior to the ECP surgery, the PPV and PRP were performed by the surgeon via a standard 3-port approach. Then the ECP was completed by the E4 Endoscopy System (BEAVER-VISITEC INT., INC./ENDO OPIKS. INC.), which could convert a visual image of the endoscope into a video image and provide a light source for the endoscope. The power of the 19-gauge endolaser delivering 810 nm diode laser was set as 0.2–0.4 W until the ciliary processes change as whitening and shrinkage. The range of treatment varied from 180 to 360° depending on the baseline IOP. After the procedure, the patients were instructed to follow the postoperative regimen, including tobramycin dexamethasone eye drops and ointment.

3.3. AGV implantation procedure

AGV implantation was performed by the standard procedure. After topical anesthesia with 2 mL lidocaine (2%), the fornix-based conjunctival flap was created and 5-FU (25 g/L) was placed under it for 5 min. Before placement of the tube implant body to the sclera, saline solution injection was performed to irrigate the drainage tube. The implant's body was secured on sclera with 6.0 polyester sutures. A 4 mm scleral tunnel posterior to corneoscleral limbus was created by a 23-gauge needle,

Table 1
Demographic characteristics.

	ECP	Ahmed	*P*
Number of cases (eyes)	16	14	
Age, years (mean ± SD)	48.88 ± 15.08	53.71 ± 13.70	0.368[a]
Male, n (%)	10 (62.50%)	7 (50.00%)	0.713[#]
Surgical eye, n (%)			0.299[#]
OD	7	9	
OS	9	5	
NVG Etiology, n			0.672[#]
Proliferative Diabetic Retinopathy	8	5	
Coats' Disease	2	1	
Recurrent Retinal Detachment	2	2	
CRAO	0	1	
CRVO	4	3	
None	0	2	
Lens, n			0.217[#]
Phakic	8	3	
Pseudophakic	6	10	
Aphakic	2	1	
Preoperative IOP, mmHg (mean ± SD)	36.03 ± 6.34	38.84 ± 8.92	0.324[a]
Mean glaucoma medication (mean ± SD)	3.31 ± 0.45	3.15 ± 0.56	0.608[a]
Preoperative BCVA (logMAR) (mean ± SD)	2.26 ± 1.85	2.52 ± 1.43	0.591[a]

BCVA, best-corrected visual acuity; CRVO, central retinal vein occlusion; CRAO, central retinal artery occlusion; ECP, endoscopic cyclophotocoagulation; IOP, intraocular pressure; SD, standard deviation.
[a] Independent sample *t*-test; [#]Fisher's exact test.

through which the tube was inserted into anterior chamber. The tube was anterior and parallel to the iris and its bevel faced the corneal. 7–0 absorbable sutures were used to fix the position of the tube and 10–0 nylon sutures were used to close the conjunctiva. All the eyes received tobramycin dexamethasone ointment for the control of inflammation.

4. Results

4.1. Patients' demographic characteristics

In this retrospective study, there are 30 patients with 30 eyes fulfilling the inclusion criteria enrolled in this study. In total, 16 eyes underwent ECP and 14 underwent AGV implantation. There is no significant difference in age ($P = 0.368$), sex ($P = 0.713$), surgical eye ($P = 0.299$), NVG etiology ($P = 0.672$), lens status ($P = 0.217$), preoperative IOP ($P = 0.324$), the number of preoperative glaucoma medications ($P = 0.608$), and preoperative BCVA ($P = 0.591$) between the two groups. Patients' mean age was 48.88 ± 15.08 for ECP group and 53.71 ± 13.70 for AGV group. The NVG etiologies in the study included proliferative diabetic retinopathy, coats' disease, recurrent retinal detachment, central retinal artery occlusion (CRAO), and central retinal vein occlusion (CRVO), except for two eyes without the identified cause. The most prevalent etiologies of NVG in both groups were diabetic retinopathy (43.3%) and CRVO (23.3%). The Patients' demographic and preoperative ocular characteristics in detail are demonstrated in Table 1.

4.2. Comparisons of IOP in the two groups

The preoperative IOP was 36.03 ± 6.34 mmHg for the ECP group, and 38.84 ± 8.92 mmHg for the Ahmed group. There was no significant difference in the preoperative IOP between the two groups ($P = 0.324$). In the ECP group, the postoperative IOP was reduced to 16.53 ± 5.42 mmHg at 1-day, 12.57 ± 3.14 mmHg at 3-months, 11.88 ± 2.31 mmHg at 6-months, and 11.81 ± 4.14 mmHg at 12-months. In the Ahmed group, the postoperative IOP was reduced to 12.19 ± 4.14 mmHg at 1-day, 14.56 ± 3.89 mmHg at 3-months, 14.40 ± 2.92 mmHg at 6-months, and 15.73 ± 6.11 mmHg at 12-months. And there was a significantly lower IOP at the 1-day postoperative time point in the Ahmed group compared to the ECP group ($P = 0.021$). At the 6-months and 12-months postoperative time points, the ECP group showed a significantly lower IOP compared to the Ahmed group ($P = 0.014$; $P = 0.047$). In addition, the mean percentage reduction of IOP in both groups at each follow-up time point was more than 50% ($P < 0.0001$). Meanwhile, the two groups showed no significant difference in IOP reduction and percentage change in follow-up periods except for postoperative day 1. The IOP, IOP reduction, and comparison between the two groups at all follow-up visits are shown in Table 2 and Table 3.

Table 2
Preoperative and postoperative intraocular pressure values during the follow-up (mmHg, mean ± SD).

Time Point	ECP	Ahmed	*P* value[a]
Preoperative	36.03 ± 6.34	38.84 ± 8.92	0.324
Postoperative			
1 day	16.53 ± 5.42	12.19 ± 4.14	0.021
3 Months	12.57 ± 3.14	14.56 ± 3.89	0.131
6 Months	11.88 ± 2.31	14.40 ± 2.92	0.014
12 Months	11.81 ± 4.14	15.73 ± 6.11	0.047

[a] Independent sample *t*-test. ECP, endoscopic cyclophotocoagulation; SD, standard deviation.

Table 3
IOP reduction between preoperative and postoperative values (mmHg, mean ± SD) and reduction percentage from preoperative values in the two groups (%, mean ± SD).

Postoperative Time Point	ECP	Ahmed	*P* value[a]
1 day			
IOP, difference	19.49 ± 9.74	26.65 ± 9.06	0.048
Reduction (%)	51.77 ± 19.84	67.57 ± 11.98	0.015
3 Months			
IOP, difference	23.46 ± 6.69	24.27 ± 10.04	0.794
Reduction (%)	64.26 ± 10.65	60.68 ± 13.30	0.420
6 Months			
IOP, difference	24.14 ± 6.70	24.44 ± 9.39	0.921
Reduction (%)	65.91 ± 9.29	61.16 ± 11.23	0.215
12 Months			
IOP, difference	24.21 ± 6.45	23.10 ± 8.61	0.690
Reduction (%)	66.82 ± 10.89	59.01 ± 14.31	0.101

ECP, endoscopic cyclophotocoagulation; IOP, intraocular pressure; SD, standard deviation.
[a] Independent sample *t*-test between ECP group and Ahmed group.

Table 4
Preoperative and postoperative number of anti-glaucoma medications during the follow-up (mean ± SD).

Time Point	ECP	Ahmed	*P* value[a]
Preoperative	3.44 ± 0.63	3.71 ± 0.73	0.273
Postoperative			
1 day	0.75 ± 0.68	0.00 ± 0.00	<0.001
3 Months	0.19 ± 0.40	0.50 ± 0.76	0.163
6 Months	0.25 ± 0.45	0.64 ± 1.08	0.194
12 Months	0.38 ± 0.72	0.79 ± 1.42	0.318

ECP, endoscopic cyclophotocoagulation; SD, standard deviation.
[a] Independent sample *t*-test.

4.3. Application of anti-glaucoma medications

The mean number of preoperative ophthalmic medications was 3.44 ± 0.63 for the ECP group, and 3.71 ± 0.73 for the Ahmed group. There was no significant difference in the number of anti-glaucoma medications before operation between the two groups ($P > 0.05$). And except for the 1-day postoperative time point, lower drug needs in the Ahmed group ($P < 0.001$), the medication number showed no marked difference between the ECP group and Ahmed group at other follow-up visits. Furthermore,

Table 5
Preoperative and postoperative BCVA (logMAR) during the follow-up (mean ± SD).

Time Point	ECP	Ahmed	*P* value[a]
Preoperative	1.98 ± 0.64	1.75 ± 0.59	0.306
Postoperative			
1 day	1.77 ± 0.55	1.84 ± 0.27	0.654
3 Months	1.25 ± 0.52[#]	1.41 ± 0.43	0.378
6 Months	1.29 ± 0.61[#]	1.61 ± 0.63	0.170
12 Months	1.39 ± 0.60[#]	1.73 ± 0.70	0.157

BCVA, best-corrected visual acuity; ECP, endoscopic cyclophotocoagulation; SD, standard deviation.
[a] Represents independent sample *t*-test between ECP group and Ahmed group.
[#]Represents paired sample *t*-test between preoperative and postoperative BCVA, and $P < 0.05$.

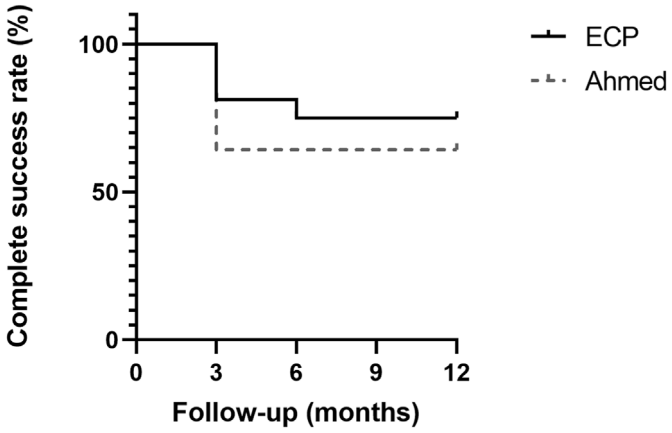

Fig. 1. Kaplan-Meier survival curve showed that there was no marked difference in complete success rate between the ECP group and Ahmed group at 12 months after surgery ($P = 0.450$).

compared with the number of preoperative anti-glaucoma medications, a significant statistical reduction of the medication number needed for control IOP was observed in both two groups at each postoperative time point ($P < 0.0001$) (Table 4).

4.4. Comparative analysis of BCVA

In the ECP group, the preoperative BCVA (logMAR) was 1.98 ± 0.64, which was changed to 1.77 ± 0.55 at 1-day after operation, 1.25 ± 0.52 at 3-months after operation, 1.29 ± 0.61 at 6-months after operation, and 1.39 ± 0.60 at 12-months after operation. In the Ahmed group, preoperative BCVA (logMAR) was 1.75 ± 0.59 and postoperative BCVA was 1.84 ± 0.27 at 1-day, 1.41 ± 0.43 at 3-months, 1.61 ± 0.63 at 6-months, and 1.73 ± 0.70 at 12-months time point (Table 5). The BCVA showed no marked difference between the ECP group and Ahmed group either preoperatively or at any time postoperatively ($P > 0.05$), while it was significantly improved in ECP group at 3-months ($\#P = 0.001$), 6-months ($\#P = 0.004$), and 12-months ($\#P = 0.010$) comparing with preoperative baseline BCVA. Each patient's BCVA in ECP group was stable or improved three months after the surgery except for one patient with cataract development which was relieved by subsequent cataract surgery, and three patients in Ahmed group presented worsening BCVA.

4.5. Surgical success

The complete success rates between the two groups during the 12-months follow-up period were manifested by Kaplan–Meier survival curves (Fig. 1). In the ECP group, the complete success rate was 81.25% at 3-months, 75.00% at 6-months, and 75.00% at 12-months time point, and the qualified success rate was 100.00% in each follow-up visit. In the Ahmed group, the complete success rate was 64.30% from 3-months to 12-months time point, and the qualified success rate was 100.00% at 3-months, 85.71% at 6-months, and 78.57% at 12-months time point, respectively. The complete success rates and qualified success rate in Kaplan–Meier survival curves between the ECP group and Ahmed group showed no significant difference throughout the 12-months follow-up period ($P = 0.450$; $P = 0.055$). And there are three cases in Ahmed group (21.43%) belonging to surgical failure because of the uncontrolled IOP and the need for another anti-glaucoma surgery.

Table 6
Complications during study and secondary operation.

Complications	ECP (n = 16)	Ahmed (n = 14)	*P* value[a]
Anterior segment inflammation	2 (12.50%)	–	0.485
Hyphema	1 (6.25%)	1 (7.14%)	> 0.999
Hypotony maculopathy	1 (6.25%)	–	> 0.999
Shallow anterior chamber	–	2 (14.29%)	0.209
Encapsulated cyst formation	–	2 (14.29%)	0.209
Corneal touch	–	1 (7.14%)	0.467
Tube occlusion	–	1 (7.14%)	0.467
Undergo Secondary Operation			
Treatment of cataract	1 (6.25%)	–	> 0.999
TCP	–	2 (14.29%)	0.209
AGV replacement	–	1 (7.14%)	0.467

AGV, Ahmed glaucoma valve; ECP, endoscopic cyclophotocoagulation; TCP, transscleral cyclophotocoagulation.
[a] [a]Fisher's Exact Test.

4.6. Complications during study and secondary operation

Complications during the postoperative follow-up period and secondary operation were listed in Table 6, including anterior segment inflammation, hyphema, hypotony maculopathy, shallow anterior chamber, encapsulated cyst formation, corneal touch, and tube occlusion. There was no severe complication that occurred postoperatively among all patients. All the complications were relieved with corresponding therapy, except for the uncontrolled IOP of three eyes in the Ahmed group due to tube occlusion or scarring of the filtration bubble, which were assigned to TPC or AGV replacement for further treatment. The rate of complications and secondary operations differed insignificantly between the ECP and Ahmed groups (Table 6).

5. Discussion

NVG, one of the most common types of refractory glaucoma, is mainly caused by extensive retinal ischemia and hypoxia situation that leads to angle neovascularization, rubeosis, and formation of fibrovascular tissue on the trabecular meshwork which would obstruct aqueous outflow through the trabecular meshwork and rapidly rising IOP.[1,21,22] Currently, the consensus about NVG treatment highlights the importance of the treatment of protopathy, improvement in retinal ischemia and hypoxia, and effective IOP control.[10,23] While the treatment of NVG remains challenging even though many surgical strategies have been proposed. This study establishes a comprehensive strategy and evaluates the efficacy of combination of anti-VEGF injection, PPV, endoscopic PRP, and ECP surgery to treat NVG patients. This study found that the ECP group presented better IOP control when compared with the Ahmed group in the long follow-up period, while the status of BCVA, number of anti-glaucoma medications, surgical success rate, and postoperative complications exist with no significant difference between the two groups.

During the follow-up period, the IOP was lower in the Ahmed group compared with the ECP group at the 1-day time point ($P = 0.021$) (Table 2). Then it rose in Ahmed eyes to become equivalent to ECP group at 3-months, and gradually higher than ECP group at 6-months ($P = 0.014$) as well as 12-months time point ($P = 0.047$). And the variation

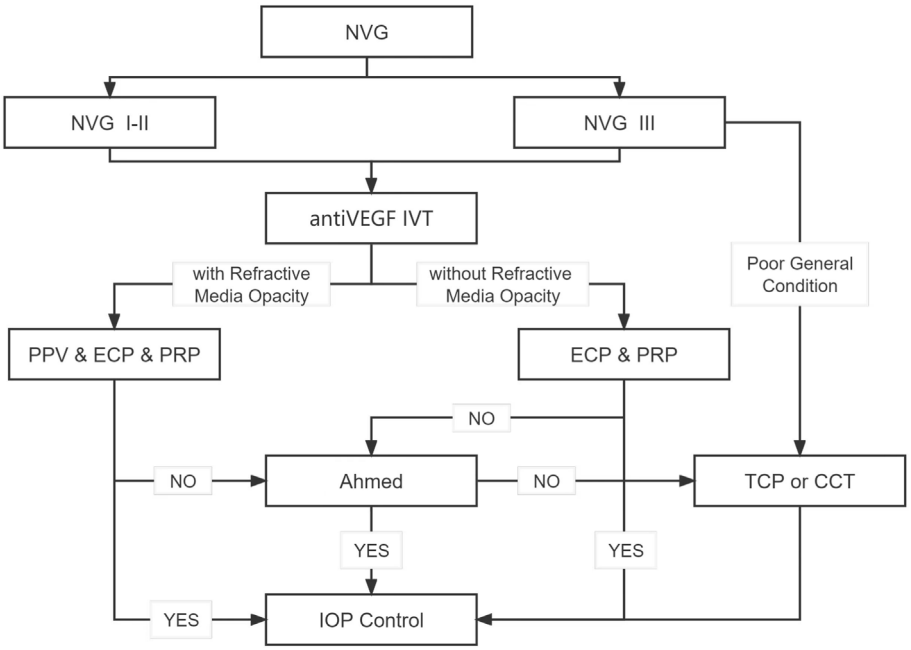

Fig. 2. A chart of the NVG (neovascular glaucoma) treatment procedure. CCT, cyclocryotherapy; ECP, endoscopic cyclophotocoagulation; IOP, intraocular pressure; PPV, pars plana vitrectomy; PRP, pan-retinal photocoagulation; TCP, transscleral cyclophotocoagulation; VEGF, vascular endothelial growth factor.

tendency of anti-glaucoma medication number needed after surgery was similar to IOP fluctuation, while it showed no evident differences between the two groups in the follow-up visits except for 1 day after surgery (Table 4). Besides, we found that the postoperative IOP in ECP eyes was more stable and lower than Ahmed group especially after 3 months. This may be explained by the increased inflammatory process in the early postoperative period after ECP. And the IOP gradually decreased and remained stable with the control of the inflammation. In addition, ECP is a precisely managed destructive procedure that avoids unnecessary collateral tissue damage and other potential overtreatments by visualizing the targeted ciliary body tissue directly and delivering laser power absorbed by the epithelium of the ciliary body specifically, thus, less tissue damage and better control of IOP are achieved.

NVG patients usually present with poor visual status. As shown in Table 5, the preoperative visual acuity was worse than 1 (logMAR) in most cases. Although the BCVA showed no marked differences between the two groups at different follow-up time points and before surgery, it was significantly improved in ECP group at 3-months ($P = 0.001$), 6-months ($P = 0.004$), as well as 12-months time point ($P = 0.010$), compared with preoperative BCVA. This may be due to the removal of cloudy vitreous by PPV surgery and effective IOP control in ECP group. IOP control is essential to maintain the visual field of NVG eyes, and uncontrolled IOP (>21 mmHg) was an important reason for worsening BCVA with three patients in Ahmed group. Besides, surgery may accelerate the progression of cataract causing vision loss, which could be relieved by subsequent cataract surgery.

This study showed that the complete success rate at 12 months was 75.00% and 64.30% for ECP and Ahmed group respectively, and the qualified success rate at 12-months time point was 100.00% and 78.57% for ECP and Ahmed groups respectively. There were no significant differences in the complete and qualified success rates between the two groups throughout the whole follow-up period ($P > 0.05$). These results were similar to previous studies where ECP or Ahmed tubes were used to treat refractory glaucoma,[14,20,24] or presented slight differences due to the differences in patient inclusion or criteria for success rate. It has also been presented that AGV implantation can rapidly reduce the IOP of NVG patients, but the long-term effect after surgery is not as good as ECP group, which may be due to its subsequent higher rate of surgery failure than ECP group (21.43% *vs.* 0.00%).

The rate of complications and secondary operations differed insignificantly between the two groups ($P > 0.05$). While they were markedly different in the distribution between the two groups. The main complication in ECP group was anterior segment inflammation, hyphema, and hypotony maculopathy which was similar to previous literature.[25,26] We observed clinically that the complications could be relieved after corresponding treatment such as the paravertebral injection of dexamethasone and the supplement of tobramycin dexamethasone ointment. The main complication in Ahmed group was the shallow anterior chamber, encapsulated cyst formation, corneal touch, and tube occlusion, consistent with the literature reports.[27,28] The occurrence of these complications demanded closer and more follow-up visits in Ahmed group with a higher number of therapy procedures after surgery, such as anterior chamber injection of viscoelastic or needling of the cystic bleb, and three eyes in the Ahmed group with uncontrollable IOP due to tube occlusion or scarring of the filtration bubble need to treat with TPC or AGV replacement. Therefore, the risk of surgical failure was higher in the Ahmed group. In addition, all patients included in this study were supplied with anti-VEGF injections preoperatively, and the protopathy of NVG was managed appropriately, above procedures may help reduce the complications of surgery further.[29,30]

After a long-term follow-up of these patients, we conclude that the comprehensive treatment for NVG combining anti-VEGF injection, PPV, endoscopic PRP, and ECP surgery can not only control IOP, they can also protect visual function by improving BCVA and manage primary disease with complete PRP treatment. Based on our clinical practice and literature materials,[6,8] we summarize a systematic and cogitative process of treatment for NVG patients (Fig. 2). Firstly, it is necessary for the second and third stages of NVG to get the anti-VEGF treatment. But if the patient has a poor body condition or poor vision potential, the procedure of PPV&PRP&ECP may be aggressive, and direct transscleral cyclophotocoagulation (TCP) or cyclocryotherapy is suggested. With the assistance of anti-VEGF, the operation of PRP and PPV can own more clear and stable operation field. If the patient has ocular vitreous opacity, PPV will be done to improve the completion of PPR and manage the primary disease as well. PPV combined PRP and ECP are important treatments to control IOP and improve the retinal situation, whose efficacy and prognosis have been identified in this study. However, if the above treatment cannot control IOP, Ahmed valve implantation can be

the further treatment option despite its frequently occurring complications that are difficult to manage.

6. Conclusions

Conclusively, the comprehensive treatment of PPV, endoscopic PRP, and ECP surgery for NVG patients after anti-VEGF injection can control IOP effectively and be friendly to patients' BCVA without obvious serious complications throughout a 12-months follow-up period. Among the surgery process, anti-VEGF treatment is the basic, while PPV&PRP is the guarantee and ECP is the key to controlling IOP and preserving visual function in NVG patients.

Study approval

This study was conducted in accordance with the principles of the Declaration of Helsinki, and the study protocol was approved by the Ethics Committee of Chinese PLA General Hospital. And patient consent for inclusion was waived because all data were anonymized and the study was retrospective in nature.

Author contributions

The authors confirm contribution to the paper as follows: Conception and design of study: HB; Data collection: ZS; Analysis and interpretation of results: LJ; Drafting the manuscript: LJ; All authors reviewed the results and approved the final version of the manuscript.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

VEGF	Vscular endothelial growth factor
PPV	Pars plana vitrectomy
PRP	Endoscopic pan-retinal photocoagulation
ECP	Endoscopic cyclophotocoagulation
NVG	Neovascular glaucoma
IOP	Intraocular pressure
BCVA	Best-corrected visual acuity
PDR	Proliferative diabetic retinopathy

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aopr.2023.05.001.

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