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Original Article

Factors Affecting the Results of Ahmed Glaucoma Valve Implantation in Diabetic Neovascular Glaucoma With or Without Previous Pars Plana Vitrectomy

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Abstract

Objectives: The aim of this study was to compare the outcomes of Ahmed glaucoma valve implantation (AGVI) in neovascular glaucoma (NVG) due to proliferative diabetic retinopathy (PDR) with or without a pars plana vitrectomy (PPV) history and to analyze the factors affecting surgical failure.

Methods: Patients with NVG secondary to PDR undergoing AGVI at a single center were reviewed retrospectively. The surgical failure rates and post-operative complications were compared between eyes with (PPV-AGVI group) and without previous PPV (AGVI group). Failure was defined as loss of light perception or intraocular pressure (IOP) >17 mmHg despite maximum medication, or need of additional intervention for IOP control or for the management of complications. Survival analysis was investigated by Kaplan–Meier test. The possible factors for failure were analyzed with logistic regression analysis.

Results: The failure rates were 21.9% during the mean follow-up of 27.56±15.38 months and 14.3% during 23.63±12.38 months, in PPV-AGVI group (n=32) and in AGVI group (n=49), respectively (p=0.37). The frequency of complications and surgical intervention need for management of post-operative complications was similar between groups (p>0.05). There was no significant difference in survival analysis (p=0.13). The history of intravitreal anti-vascular endothelial growth factor (anti-VEGF) injection before AGVI was significantly associated with failure (odds ratio = 26.941, p=0.02).

Conclusion: The results of AGVI performed with long scleral tunnel technique were comparable in terms of failure rates, between NVG patients with and without previous diabetic vitrectomy. The only significant factor for failure was intravitreal anti-VEGF pre-treatment. This may be related to the necessity of anti-VEGF therapy in aggressive PDR, and also, anti-VEGF agents may increase fibrosis in the anterior chamber angle.

Keywords: Ahmed glaucoma valve, diabetic vitrectomy, intravitreal anti-vascular endothelial growth factor, neovascular glaucoma.

Introduction

Neovascular glaucoma (NVG) is a refractory glaucoma characterized by iris and anterior chamber angle neovascularization. The neovascularization occurs following ocular ischemia/hypoxia. The release of angiogenesis factors in the presence of ischemia leads to neovascular growth in the iris and fibrovascularization in the anterior chamber angle, thus obstructing the trabeculum and causing increased intraocular pressure (IOP) (1).

The management of NVG includes panretinal photo-

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coagulation (PRP), intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF), (2,3) if required vitrectomy for the treatment of the retinal neovascularization and anti-glaucomatous medication and surgery for IOP control (4). When most of the angle is closed due to synechiae, surgical treatment is necessary for lowering IOP. High failure rates of conventional trabeculectomy (5,6) have led to increased use of glaucoma drainage implants for NVG (7,8). The Ahmed glaucoma valve (AGV) provides an alternative aqueous pathway with its one-way pressure-sensitive control valve (9).

The neovascularization is most often secondary to proliferative diabetic retinopathy (PDR). The basis of surgical therapy for the blinding complications of advanced PDR is pars plana vitrectomy (PPV) (10). However, many published studies report that 0.3–23.6% of patients with PDR still develop NVG even after PPV (11-13). Vitrectomy can cause increased flow of vasoformative factors into the anterior chamber, scarring of the conjunctiva, and delayed wound healing, which may affect the results of subsequent glaucoma surgery (5,6). Sutureless 23-gauge vitrectomy has some advantages such as shorter wound healing time, and less damage to the conjunctiva, especially for further glaucoma surgery (14). There is only one self-control study that has reported the outcomes of AGV implantation (AGVI) for the treatment of NVG after 23-gauge vitrectomy for PDR (15). This retrospective study aims to compare the outcomes of AGVI in NVG due to PDR with or without a history of 23-gauge PPV and to determine the possible factors affecting surgical failure.

Methods

The clinical records of 89 patients with NVG secondary to PDR, who underwent AGVI at a single center between 2015 and 2022, were reviewed in this retrospective and comparative study. All research and measurements followed the tenets of the Declaration of Helsinki, and the protocol was approved by the Ethical Committee of the same hospital. The informed consent was waived.

The diagnostic criteria of NVG were the iris neovascularization (NVI) and/or the anterior chamber angle neovascularization (NVA), IOP ≥22 mm Hg before IOP-lowering medications, and glaucomatous optic nerve head changes. If there was an uncontrolled IOP with glaucoma progression in the retinal nerve fiber layer despite maximum medical therapy, we injected 0.1 mL intracameral bevacizumab (100 mg/4 mL Avastin, Genentech Inc, South San Francisco, CA), 3–5 days before the surgery into all enrolled eyes, and then, AGV was implanted. The cases were divided into the PPV-AGVI group and the AGVI group according to the PPV history before AGVI.

The eyes with no light perception before AGVI, the aphakic eyes, the patients with a history of laser or surgery for glaucoma treatment before AGVI, the patients undergoing AGVI more than 2 years after PPV, AGVI combined with cataract surgery and/or PPV, and the patients with a follow-up period of <6 months were excluded from the study. The eyes that did not receive PRP before glaucoma surgery were not included in the study, as it may be a possible factor for surgical failure (9). Among the eyes filled with intravitreal SO during PPV, only those with SO removal before AGVI were included in the study, as the presence of SO may affect the surgical results (16). The cases who required AGV revision or removal during the first post-operative 6 months due to malposition and tube or plate exposure were not included in the study. In the patients who had bilateral AGVI for NVG, the eye with longer follow-up was enrolled in this study.

Surgical Technique

One experienced glaucoma surgeon (SI) performed all surgical procedures. Under local or general anesthesia, a fornix-based conjunctival flap was created. The sclera was exposed by posterior dissection, with attention to the rectus muscles. Three scleral incisions, 2.5 mm long and two-thirds thick of the sclera, were made parallel to the limbus and 10–12 mm, 6–8 mm, and 1.5–2 mm away from the limbus, respectively. The scleral incisions were combined using a 60° bevel-up 2.0 mm crescent knife, and scleral tunnel was made. The plate of the AGV-FP7 model (New World Medical, Rancho Cucamonga, CA, USA) was inserted behind the rectus muscles and behind the equator with two 6/0 vicryl sutures at the superotemporal quadrant. The silicone tube of the AGV was placed into the long scleral tunnel. After partial paracentesis parallel to the iris was performed through the third scleral incision with a 23-gauge knife, the tube was placed 1–2 mm into the ciliary sulcus or into the anterior chamber. The scleral incision close to the limbus was sutured with a 10/0 nylon suture and conjunctival flap was sutured with 8/0 vicryl. After AGVI, moxifloxacin eye drops 0.5% (Vigamox) for 4 weeks and prednisolone acetate ophthalmic suspension 1% (Pred Forte) for 6–8 weeks were used.

Data Collection

Demographic characteristics of patients, lens status, the presence of angle-closure, whether intravitreal anti-VEGF injection (100 mg/4 mL Avastin, Genentech Inc, South San Francisco, CA) was performed before AGVI, pre-operative data including IOP measurement using Goldmann applanation tonometer, the number of anti-glaucomatous medications, and corrected-distance visual acuity (CDVA) converted to the logarithm of the minimum angle of resolution were recorded. In the PPV-AGVI group, the preexistence of NVI and/or NVA before vitrectomy and the interval time

between PPV and AGVI were noted. Post-operative data included IOP and medication numbers at the first post-operative day, 1st week, 1st month, 3rd, 6th, 12th, 24th, 36th months, and the last follow-up, and also CDVA at the last follow-up.

The post-operative complications such as overplate encapsulation, hyphema, hypotony, decompression retinopathy, choroidal detachment, fibrinous reaction in the anterior chamber, early IOP spikes, and tube or plate exposure were recorded. Layered blood in the anterior chamber was considered as hyphema. During the post-operative 1st week, IOP >25 mmHg was considered as an IOP spike and IOP ≤6 mmHg was noted as a hypotony. In the presence of encapsulated bleb, the treatment was needling of overplate bleb with 0.1 cc 5-Fluorouracil (5-FU) (50 mg/mL), and also, overplate fibrosis excision was performed in the eyes that had inadequate IOP control despite needling. Surgical evacuation was required when hyphema was not resolved for 2 weeks despite subconjunctival atropine and dexamethasone injection, or uncontrolled IOP was observed due to clogging of the tube tip with coagulum. Fibrinous reaction in the anterior chamber was treated with topical 1% prednisolone acetate (12 times/day) and subconjunctival dexamethasone injection. The treatment of an early IOP spike was oral acetazolamide and intravenous injection of 20% mannitol solution. Tube or plate exposure was revised using a pericardial patch graft.

Surgical failure was defined as the last IOP >17 mmHg despite maximum medication or loss of light perception. Furthermore, the eyes that required additional glaucoma surgery or laser treatment to control IOP and AGV revision surgery due to tube or plate exposure were considered as failed. Eyes that underwent additional intervention after AGVI (glaucoma surgery or laser, revision surgery, cataract extraction, and PPV) were excluded from any further IOP, and medication number analysis. Final values before additional surgery were taken as the last follow-up values in these eyes.

Statistical Analysis

The SPSS for Windows (v.20.0, IBM Corp., Armonk, NY, USA) was used for all statistical analysis. The variables were investigated using Kolmogorov–Smirnov or Shapiro–Wilk's test to determine the distribution normality. Mann–Whitney U-test was used to compare IOP and medication numbers between the two groups. The Chi-square test or Fisher's exact test was performed for the intergroup comparison of the categorical variables. The pre-operative and post-operative IOP and the number of glaucoma medications were analyzed using the Wilcoxon test. The values were given as mean±standard deviation, and categorical variables were presented as percentages (%). The possible predictive factors for surgical failure were analyzed with univariate model of Binary Logistic Regression analysis. Variables with $p<0.10$ in univariate analyses were included in multivariate analyses. The roles of variables were expressed in 95% confidence interval and odds ratio. Kaplan–Meier test was carried out for survival analysis of surgical success and the survival rates were compared between two groups with the Mantel-Cox log-rank test. $P<0.05$ was statistically significant.

Results

Two patients who required tube reposition at the first post-operative 6 months, and six patients with <6 months follow-up were not included in the study. Therefore, 81 eyes of 81 patients (32 eyes in the PPV-AGVI group, and 49 eyes in AGVI group) were enrolled in the final analysis. In the AGVI group, tractional retinal detachment was seen in two patients, 8 months and 15 months after AGVI, respectively. These two cases were not included in any further analysis.

The demographic and clinical features before AGVI are presented in Table 1. The only statistically significant difference was in the percentage of pseudophakic eyes between the two groups ($p=0.02$). In the PPV-AGVI group, the AGV was implanted into the ciliary sulcus in 16 patients (50%) and into the anterior chamber in 16 patients. In the AGVI group, the tube tip was into the sulcus in 21 patients (42.9%) and into the anterior chamber in 28 patients ($p=0.52$). The mean follow-up times were 27.56±15.38 (12–75 months) and 23.63±12.38 (7–55 months) in the PPV-AGVI group and AGVI group, respectively ($p=0.23$).

When compared with the baseline, the post-operative IOPs and the number of anti-glaucomatous medications were statistically significantly lower in both groups, at all post-operative periods ($p<0.05$). No statistically significant intergroup difference was detected in terms of IOP measurements (Table 2) and the medication numbers throughout the follow-up (Table 3).

After AGVI, the most frequent complications were overplate encapsulation (43.2%) and hyphema (25.9%). Post-operative complication rates and the need of surgical intervention for the management of complications did not differ significantly between the two groups ($p>0.05$) (Table 4). The need of overplate fibrosis excision was 12.5% (four eyes) in the vitrectomized eyes, and 6.1% (3 eyes) in the non-vitrectomized eyes ($p=0.27$). Among those who underwent fibrosis excision, IOP control was achieved in two of them in the PPV-AGVI group and in all of them in the AGVI group. In the AGVI group, anterior chamber irrigation and injection of tissue plasminogen activator were required in two patients due to obstruction of tube tip with coagulum, others reabsorbed with subconjunctival injection or spontaneously, in both groups. Decompression retinopathy, choroidal detachment, IOP spike, and fibrinous reaction were treated without any surgical intervention.

Table 1. The demographic and clinical features before AGVI

	PPV-AGVI (n=32)	AGVI (n=49)	p
Age (years)	58.90±12.41	62.93±12.76	0.16
Gender (female/male)	12/20	18/31	0.94
Lens status			
Crystalline lens (n, %)	6 (18.8)	21 (42.9)	0.02
Pseudophakia (n, %)	26 (81.3)	28 (57.1)	
Synechial angle closure (n, %)	19 (59.4)	31 (63.3)	0.72
Intravitreal anti-VEGF injection (n, %)	10 (31.3)	22 (44.9)	0.21
Intraocular pressure (mmHg)	39.93±6.81	41.10±8.55	0.35
Number of medicÇation	3.75±0.50	3.73±0.60	0.80
Previous PPV surgery			
PPV (n, %)	10 (31.3)	-	-
PPV+Phaco (n, %)	7 (21.8)		
PPV+SOI (n, %)	13 (40.6)		
PPV+Phaco+SOI (n, %)	2 (6.3)		
NVI and/or NVA before PPV (n, %)	6 (18.8)	-	-
Time interval between PPV and AGVI	13.50±8.30 (2–24 months)	-	-

AGVI: Ahmed glaucoma valve implantation; CDVA: Corrected distance visual acuity; NVA: Neovascularization of angle; NVI: Neovascularization of iris; Phaco: Phacoemulsification + intraocular lens implantation; PPV-AGVI: Pars plana vitrectomy before AGVI; SOI: Silicone oil injection; VEGF: Vascular endothelial growth factor.

Table 2. Intraocular pressure measurements after AGVI

	PPV-AGVI	AGVI	p**
Day 1	12.09±6.48 (n=32)	14.16±9.77 (n=49)	0.58
p*	<0.0001	<0.0001	
Week 1	14.12±6.83 (n=32)	14.87±9.78 (n=49)	0.95
p*	<0.0001	<0.0001	
Month 1	17.68±7.71 (n=32)	16.89±7.21 (n=49)	0.78
p*	<0.0001	<0.0001	
Month 3	17.56±6.13 (n=32)	16.32±6.53 (n=49)	0.32
p*	<0.0001	<0.0001	
Month 6	15.40±4.79 (n=32)	14.91±5.81 (n=49)	0.50
p*	<0.0001	<0.0001	
Month 12	15.62±6.43 (n=32)	14.23±4.12 (n=47)	0.59
p*	<0.0001	<0.0001	
Month 24	16.90±6.69 (n=20)	15.29±5.18 (n=27)	0.39
p*	<0.0001	<0.0001	
Month 36	14.42±3.69 (n=14)	14.94±3.61 (n=17)	0.37
p*	<0.0001	<0.0001	
Last follow-up	16.06±7.0 (n=32)	15.20±5.36 (n=49)	0.67
p*	<0.0001	<0.0001	

AGVI: Ahmed glaucoma valve implantation; PPV-AGVI: Pars plana vitrectomy before AGVI. *Comparison between pre- and post-operative intraocular pressure. **Comparison between two groups.

Table 3. Change in the number of anti-glaucomatous medications after AGVI

	PPV-AGVI	AGVI	p**
Week 1	0.0±0.00 (n=32)	0.16±0.68 (n=49)	0.15
p*	<0.00001	<0.00001	
Month 1	0.46±0.94 (n=32)	0.67±1.14 (n=49)	0.47
p*	<0.00001	<0.00001	
Month 3	1.40±1.29 (n=32)	1.48±1.20 (n=49)	0.90
p*	<0.00001	<0.00001	
Month 6	2.12±1.23 (n=32)	1.85±1.22 (n=49)	0.24
p*	<0.00001	<0.00001	
Month 12	2.31±1.20 (n=32)	2.29±1.17 (n=47)	0.88
p*	<0.00001	<0.00001	
Month 24	2.35±1.34 (n=20)	2.81±0.62 (n=27)	0.42
p*	0.001	<0.00001	
Month 36	2.35±1.15 (n=14)	2.94±0.55 (n=17)	0.18
p*	0.004	0.001	
Last follow-up	2.53±1.07 (n=32)	2.63±1.14 (n=49)	0.56
p*	<0.00001	<0.00001	

AGVI: Ahmed glaucoma valve implantation; PPV-AGVI: Pars plana vitrectomy before AGVI. *Comparison between pre- and postoperative medication numbers. **Comparison between two groups.

Table 4. Post-operative complications

	PPV-AGVI (n=32) (%)	AGVI (n=49) (%)	p
Overplate encapsulation (n, %)	14 (43.8)	21 (21.9)	0.93
Hyphema (n, %)	7 (21.9)	14 (28.6)	0.50
Hypotony (n, %)	2 (6.3)	4 (8.2)	0.55
Decompression retinopathy (n ,%)	3 (9.4)	5 (10.2)	0.60
Choroidal detachtment (n, %)	3 (9.4)	2 (4.1)	0.30
Intraocular pressure spike (n, %)	2 (6.3)	3 (6.1)	0.66
Fibrinous reaction (n, %)	1 (3.1)	4 (8.2)	0.33
Tube or plate exposure (n, %)	3 (9.3)	3 (6.1)	0.44
Need for surgical intervention (n, %)	6 (18.8)	7 (14.3)	0.59

AGVI: Ahmed glaucoma valve implantation; PPV-AGVI: Pars plana vitrectomy before AGVI.

Mean survival times for surgical success were 30.33±3.43 months and 25.13±1.88 months in the PPV-AGVI group and AGVI group, respectively (Log-rank test; p=0.13) (Fig. 1). The surgical failure rates are presented in Table 5. In the vitrectomized group, 7 patients (21.9%) were failed at the final visits. Inadequate IOP control was noted in four patients, two of them required transscleral cyclophotocoagulation (TS-CPC) and the other two patients lost light perception. One patient showed plate exposure 13 months after AGVI, and the valve was removed, and then TS-CPC was performed. One patient had tube exposure 14 months after AGVI; TS-CPC was required after the tube revision

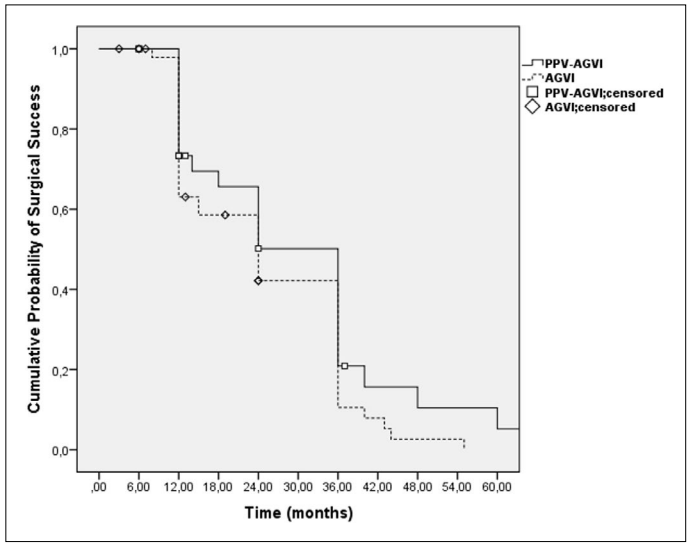

Figure 1. Cumulative probabilities of the surgical success after Ahmed glaucoma valve ımplantation (AGVI) for neovascular glaucoma with (pars plana vitrectomy-AGVI group) and without previous diabetic vitrectomy (AGVI group).

Table 5. Surgical failure rates

	n (%)	p
Month 6		
PPV-AGVI (n=32)	2 (6.3)	0.51
AGVI (n=49)	2 (4.1)	
Month 12		
PPV-AGVI (n=32)	3 (9.4)	0.45
AGVI (n=48)	3 (6.3)	
Month 24		
PPV-AGVI (n=22)	6 (27.3)	0.74
AGVI (n=30)	7 (23.3)	
Month 36		
PPV-AGVI (n=18)	6 (33.3)	0.84
AGVI (n=23)	7 (30.4)	
Last follow-up		
PPV-AGVI (n=32)	7 (21.9)	0.37
AGVI (n=49)	7 (14.3)	
Failure time (months)		
PPV-AGVI (n=32)	15.71±11.14	0.71
AGVI (n=49)	13.71±8.75	

AGVI: Ahmed glaucoma valve implantation; PPV-AGVI: Pars plana vitrectomy before AGVI.

with pericardial patch graft. The tube exposure was seen in one patient 37 months following AGVI, and the tube was revised with a pericardial graft. In the AGVI group, 7 patients (14.3%) had failure at the last follow-up. Uncontrolled IOP was noted in four patients, three of them required TS-CPC and the other one lost light perception. One patient had plate exposure 13 months after AGVI, the valve was removed. One patient showed tube exposure 7 months after AGVI, the valve was removed after revision. The tube exposure was seen in one patient 24 months following AGVI, TS-CPC was required after the revision with pericardial graft. These three patients with tube or plate exposure lost light perception eventually.

Two patients (6.3%) in the PPV-AGVI group and 4 patients (8.2%) in the AGVI group lost light perception during the follow-up. In the vitrectomized group, after AGVI, the CDVA at the final visits improved in four patients, worsened in four patients, and remained stable in 22 patients. In the non-vitrectomized group, when compared to the baseline, the CDVA at the last follow-up was better in six patients, worse in six patients, and post-operative CDVA was comparative with pre-operative values in 33 patients (Table 6). As the decrease in visual acuity was due to cataract,

Table 6. Visual acuity before and after AGVI

	PPV-AGVI (n=32) (%)	AGVI (n=49) (%)	p
Pre-operative CDVA (LogMAR)			
≤1.0 (n,%)	9 (28.1)	6 (12.2)	0.19
≥1.0-count fingers (n,%)	10 (31.3)	18 (36.7)	
Hand motion (n,%)	13 (40.6)	25 (51.0)	
Post-operative CDVA (LogMAR)			
≤1.0 (n,%)	10 (33.3)	8 (17.8)	0.29
≥1.0-count fingers (n,%)	7 (23.3)	14 (31.1)	
Hand motion (n,%)	13 (43.3)	23 (51.1)	
Loss of light perception (n,%)	2 (6.3)	4 (8.2)	0.55

AGVI: Ahmed glaucoma valve implantation; CDVA: Corrected distance visual acuity; PPV-AGVI: Pars plana vitrectomy before AGVI; LogMAR: Logarithm of the minimum angle of resolution.

three patients in the PPV-AGVI group (50.0%) and six patients in the AGVI group (28.6%) required cataract extraction (p=0.30).

Demographic and ocular characteristics, PPV, and AGVI-related factors were investigated as potential determinants for surgical failure at the final visit (Table 7). The univariate model of logistic regression analysis revealed that high pre-operative IOP (p=0.04) and the history of intravitreal anti-VEGF injection (p=0.04) were statistically significantly related with failure. In the multivariate analysis, the only statistically significant factor was intravitreal anti-VEGF injection before AGVI (p=0.02).

Discussion

Many published studies have reported the effectiveness and safety of AGVI in vitrectomized eyes with different indications for PPV (17-21). However, AGVI results may vary depending on etiology. The presence of diabetes mellitus and neovascularization in the anterior chamber has been found to be risk factors for failure in AGVI after vitrectomy (22). In the vitrectomized eyes, vasoformative factors may easily diffuse into the anterior chamber, causing to more severe inflammation and neovascularization (23). Another potential factor affecting the results of glaucoma surgery is post-operative hyphema associating with increased concentrations

Table 7. Logistic regression analysis of risk factors for surgical failure

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.039 (0.98–1.09)	0.14		
Gender	1.913 (0.59–6.11)	0.27		
Pre-operative factors				
Lens status	0.880 (0.26–2.94)	0.83		
Synechial angle closure	1.687 (0.48–5.93)	0.41		
Intravitreal anti-VEGF	3.443 (1.03–11.47)	0.04	26.941 (1.66–435.85)	0.02
Intraocular pressure	1.082 (1.00–1.16)	0.04	1.111 (0.91–1.35)	0.29
Medication numbers	1.568 (0.55–4.43)	0.39		
PPV-related factors				
NVA and/or NVI before PPV	5.50 (0.80–37.60)	0.08	10.929 (0.64–185.02)	0.09
PPV	0.595 (0.18–1.89)	0.38	8.771 (0.60–127.61)	0.11
PPV+phaco	5.333 (0.89–31.91)	0.06		
PPV+SOI	0.369 (0.06–2.27)	0.28		
Time between PPV and AGVI	0.908 (0.80–1.02)	0.11		
AGVI-related factors				
Location of the tube tip	0.871 (0.27–2.78)	0.81		
Overplate encapsulation	0.983 (0.30–3.14)	0.97		
Post-operative hyphema	2.600 (0.78–8.67)	0.12		

AGVI: Ahmed glaucoma valve implantation; CDVA: Corrected distance visual acuity; NVA: Neovascularization of angle; NVI: Neovascularization of iris; Phaco: Phacoemulsification + intraocular lens implantation; PPV-AGVI: Pars plana vitrectomy before AGVI; SOI: Silicone oil injection; VEGF: Vascular endothelial growth factor.

of some cytokines, increased conjunctival inflammation, and scarring (9,24). In the present study, the outcomes of AGVI in NVG were analyzed by comparing the eyes with or without a history of 23-gauge PPV. We included only eyes diagnosed with NVG due to PDR, to exclude the effects of underlying disease on surgical outcomes. Our retrospective study found that AGVI had similar outcomes in terms of reduction in IOP and medication numbers, and failure rates in PPV-AGVI and AGVI groups. The history of intravitreal anti-VEGF injection before AGVI was associated with surgical failure.

A limited number of studies involving heterogenous etiologies of NVG have been indicated a significant improvement in IOP and medication consumption after AGVI in the vitrectomized eyes (22,25,26). However, variations in underlying diseases make comparisons with the previous studies difficult, as the effects of NVG etiology on the outcomes of glaucoma drainage implant surgery have been previously demonstrated in some studies. Mermoud et al. (27). reported better outcomes with Molteno implant in diabetic NVG compared to central retinal vein occlusion (CRVO). In Yalvac et al.'s study, (7) the success rates were higher in CRVO patients than diabetic patients in both AGVI (52.9 and 48.1%) and Molteno implant groups (26.3 and 23.5%).

There are a few studies evaluating the outcomes of AGVI after diabetic vitrectomy in the eyes with NVG.[15,28,29] In a non-comparative study by Cheng et al., (15) it was reported that in 12 patients with NVG who previously underwent 23-gauge vitrectomy for PDR, there was a significant decrease in IOP and drug counts after AGVI, and no failure was observed during a short follow-up of 15.4±4.3 months. Park et al. (28) have compared AGVI results in 42 NVG patients with 20-gauge PPV history and 31 patients without prior PPV. The success rates were 89.9% and 83.8% after 12 months, 74.8% and 74.7% after 24 months, and 62.5% and 68.5% after 36 months in the vitrectomized group and the non-vitrectomized group, respectively. In this previous study, the success rates were comparable between groups (28). In a self-control study, Lee et al. (29) have reported the success rates of 85.7% at 1 year in 35 NVG eyes with the previous diabetic vitrectomy, but they did not specify the technique of vitrectomy.

In the present study, at all post-operative periods, the IOP and the number of anti-glaucomatous medications were significantly lower than baseline in both groups, with no intergroup difference. The success rate of the PPV-AGVI group (78.1% with 27.56±15.38 months follow-up) was similar to that of the AGVI group (85.7% with 23.63±12.38 months follow-up). Although, the target IOP for surgical success was ≤21 mmHg in the Park et al. and Lee et al.'s studies, our results were consistent with theirs (28,29). Unlike our study, Yalvac et al. (7) reported the success rates of AGVI in the non-vitrectomized eyes with NVG due to PDR as 48.1% after 5 years. The longer follow-up period in this study (7) may be the reason for these worse outcomes.

In our study, the most common post-operative complication was overplate encapsulation (43.2%), and 7–35 eyes (8.6%) with encapsulation necessitated fibrosis excision despite needling with 5- FU. To the best of our knowledge, no study reported the rates of overplate encapsulation after AGVI in the NVG eyes with prior diabetic vitrectomy. Eibschitz-Tsimhoni et al. (30) demonstrated that 13–57 patients (23%) developed an encapsulated cyst after AGVI. In Erçalık and İmamoğlu study, (19) encapsulation was seen in 69.2% of 13 vitrectomized eyes following AGVI. It has been reported that previous ocular surgery alters the surface of conjunctiva and subsequent surgery may cause fibrous cell proliferation leading to bleb encapsulation (31). Yalvac et al. (7) reported a percentage of 7.9% encapsulation following AGVI, in the non-vitrectomized NVG eyes with heterogeneous etiologies. In the eyes with NVG due to PDR, conjunctival exposure of the high concentration of proinflammatory mediators from the aqueous may be the reason for our high encapsulation rate in both groups.

In our research, there were no significant differences in the complication rates and in the surgical intervention need for the management of the complications between the two groups. Seven patients in the AGVI group (18.8%) and six patients in the PPV-AGVI group (14.3%) required additional operations. In Park et al.'s study, (28) while 12% of vitrectomized eyes required surgical intervention for post-operative complications, such complications did not occur in any of the non-vitrectomized eyes. However, encapsulation and its treatment were not mentioned, in this study (28).

The technique of AGV implantation performed by creation of a long scleral tunnel with a crescent knife has been previously described (19,32). In Erçalık and İmamoğlu study, (19) tube exposure was seen in one of 13 vitrectomized eyes (7.6%). In Kugu et al.'s study, (32) detecting an exposure rate of 2.5% after 46 months of follow-up, AGVI performed with the long scleral tunnel technique was reported to be safe for tube exposure. In our study, tube exposure was seen in 2 patients (6.3%) in the PPV-AGVI group and in 2 patients (4.1%) in the non-vitrectomized group. The fact that the inclusion of only NVG cases with and without previous diabetic vitrectomy may explain our higher exposure rates compared to this previous study (32). When we reviewed the studies conducted on vitrectomized NVG eyes due to PDR, there were similar tube and plate exposure rates with 7.1% in Park et al.'s study (28). The other two published studies (15,29) have not detected any exposure after AGVI; however, their follow-up times were approximately 1 year.

Several risk factors for failure after AGVI including age, (33) baseline IOP, (34) presence of NVI before surgery, (22) the presence of SO, (28) no PRP before AGVI, (9) and bleb encapsulation (30) have been reported in NVG eyes. In our series, the eyes filled with SO were excluded and PRP was performed before AGVI in all enrolled eyes. Bleb encapsulation was frequent, but it was not significantly related with failure, this may be due to performing bleb needling with 5-FU and if required fibrosis excision for the management of the encapsulation. Univariate analysis showed that pre-operative high IOP and the history of intravitreal anti-VEGF treatment were related with surgical failure; however, in multivariate analysis, the only factor associating with failure was anti-VEGF therapy before AGVI. The results about the effect of previous intravitreal anti-VEGF injection on the outcomes of glaucoma surgery for the treatment of NVG are controversial (9,34-37). It has been reported that pre-operative intravitreal anti-VEGF injection in NVG patients could increase the success rate of AGVI in some studies, (35,36) while others have not been demonstrated any difference between the groups between eyes with and without anti-VEGF pretreatment (9,34). Kwon and Sung (35) demonstrated that injection of anti-VEGF agents before AGVI improves the prognosis of AGVI when PAS is <½. In a meta-analysis, Zhou et al. (36) reported greater complete success rates in the eyes with anti-VEGF therapy compared with the controls; however, it did not show a significant difference for the qualified success rate. In a recent study, (37) a higher number of anti-VEGF injections before trabeculectomy were related with a higher failure risk in NVG. The need of anti-VEGF injection in PDR indicates more severe retinal ischemia and neovascularization that represent poor control of the ocular disease, thus contributing to failure. In addition, anti-VEGF agents provide rapid reduction of neovascularization but it has been shown that intravitreal anti-VEGF treatment may accelerate vitreoretinal fibrosis in PDR patients (38,39). The association between failure and intravitreal anti-VEGF injection in our analysis may be due to the increased fibrosis effect of anti-VEGF in the anterior chamber angle as well as in the retina.

Although analyzing AGVI results performed by one experienced glaucoma specialist with the same technique in a homogeneous group are strong features of this study, it has some limitations. First, our study is a retrospective study. Second, the patients had a variable follow-up. Twenty-four months of follow-up data were available for 58% of eyes, with 36 months of data being available for 38.2%. The reason for this loss of follow-up was the lack of contact with the patients and the fact that the cases who underwent additional intervention after AGVI were not included in further IOP analysis. Third, given the lack of records of gonioscopic grading, we could not reach the information of extent of PAS, and angles were documented only as open angle or synechial closed angle. Finally, there was no data about the number of intravitreal anti-VEGF injections, and the time interval between AGVI and the last injection, so we could not analyze the effect of these parameters on outcomes.

Conclusion

AGVI performed with the long scleral tunnel technique was found to have comparable results in reducing IOP and medication numbers and in terms of surgical failure rates in NVG patients with and without a previous history of 23-gauge PPV. The most common post-operative complication was overplate encapsulation, which was successfully treated with bleb needling and fibrosis excision when necessary. The only significant factor for surgical failure was intravitreal anti-VEGF injection before AGVI. This may be linked with the requirement of anti-VEGF therapy in the presence of aggressive disease, as well as the fact that anti-VEGF agents may increase fibrosis in the anterior chamber angle. Future prospective studies demonstrating the effect of the intravitreal anti-VEGF injection on the angle configuration may elucidate the possible underlying mechanism.

Disclosures

Ethics Committee Approval: The study was approved by the Ethical Committee of Haydarpasa Numune Training and Research Hospital (No: HNEAH-KAEK 2024/KK/10) in the light of the tenets of the declaration of Helsinki.

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