·Clinical Research·

Combined pars plana vitrectomy and Baerveldt glaucoma implant placement for refractory glaucoma

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Abstract

• AIM: To evaluate outcomes of combined pars plana vitrectomy and Baerveldt glaucoma implant (PPV-BGI) placement for refractory glaucoma.

• METHODS: The medical records of 92 eyes (89 patients) that underwent PPV-BGI were retrospectively reviewed, including 43 eyes with neovascular glaucoma (NVG) and 49 eyes with other types of glaucoma (non-NVG).

• RESULTS: Outcome measures were visual acuity (VA), intraocular pressure (IOP), glaucoma medical therapy, complications, and success [VA >hand motions (HM), IOP ≥6 mm Hg and ≤21 mm Hg, no subsequent glaucoma surgery]. Cumulative success rates for the non-NVG group and NVG group were 79% and 40% at 1y, respectively (P=0.038). No difference in the rates of surgical success were found between pars plana and anterior chamber tube placement. Preoperative IOP (mean±SD) was 30.3±11.7 mm Hg in the Non-NVG group and 40.0±10.6 mm Hg in the NVG group, and IOP was reduced to 15±9.5 mm Hg in the non-NVG group and 15±10.5 mm Hg in the NVG at 1y. Number of glaucoma medications (mean±SD) decreased from 2.7±1.3 in the non-NVG group and 2.8±1.3 in the NVG group preoperatively to 0.76±1.18 in the non-NVG group and 0.51±1.00 in the NVG group at 1y. Improvement in VA of ≥2 Snellen lines was observed in 25 (27%) eyes, although only 33% of non-NVG eyes and 2.3% of NVG eyes maintained VA better than 20/200 at 1y. Nonclearing vitreous hemorrhage was the most common postoperative complication occurring in 16 (17%) eyes, and postoperative suprachoroidal hemorrhages developed in 5 (5.4%) eyes.

• CONCLUSION: PPV-BGI is a viable surgical option for eyes with refractory glaucoma, but visual outcomes are frequently poor because of ocular comorbidities, especially in eyes with NVG. The location of tube placement does not influence surgical outcome and should be left to the discretion of the surgeon.

• KEYWORDS: glaucoma drainage device; pars plana vitrectomy; refractory glaucoma; neovascular glaucoma
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INTRODUCTION

Glaucoma drainage devices (GDDs) have traditionally been used in eyes at high risk for trabeculectomy failure, such as those with pediatric glaucoma, uveitic glaucoma, secondary glaucoma after penetrating keratoplasty, and neovascular glaucoma (NVG)[1-8]. The GDD tube is usually inserted into the anterior chamber (AC), but it may be placed through the pars plana into the vitreous cavity if corneal endothelial decompensation or AC angle abnormalities are present[3,5,9-20]. Pars plana vitrectomy (PPV) is required to avoid vitreous occlusion of the tube ostium if placed into the vitreous cavity. A vitrectomy may also be required with tube insertion into the AC in the presence of vitreous prolapse, as is commonly seen in aphakia eyes. Glaucoma patients with coexisting posterior segment diseases may be considered for combined PPV and GDD implantation, such as patients with NVG who require both panretinal laser photocoagulation (PRP) and intraocular pressure (IOP) reduction[21-23]. Successful IOP reduction has been reported with the combination of PPV with implantation of various types of GDD's in case reports and small case series in eyes with complex diseases[2,9-18]. Studies of Baerveldt glaucoma implants (BGI) (Abbott Medical Optics,

Santa Ana, California, USA) combined with PPV and insertion into the vitreous cavity have not been widely published [11,14,20]. The purpose of this study is to report the outcomes of a large cohort of patients who underwent PPV and BGI placement (PPV-BGI), and to compare the outcomes between the NVG and non-NVG cases.

SUBJECTS AND METHODS

This study was approved by the Human Subjects Committee of the University of Miami Miller School of Medicine, and was conducted in accordance with the Declaration of Helsinki for research in human subjects. The medical records of all patients who underwent PPV-BGI at the Bascom Palmer Eye Institute between January 1, 1992 and May 31, 2007 by one vitreoretinal surgeon (Smiddy WE) were identified using Current Procedural Terminology (CPT) codes and retrospectively reviewed. Implantation of a BGI was performed by one of the other authors (Gedde SJ, Budenz DL, Parrish RK Ⅱ and Palmberg PF). Demographic information, surgical indication, lens status, number of previous intraocular surgeries, preoperative AC angle status, presence of preoperative hyphema, presence of iris or angle neovascularization, adjunctive procedures performed during surgery, complications, pre- and post-operative best-corrected visual acuity (BCVA) and IOP, number of antiglaucoma medications, and post-operative interval until last follow-up examination were extracted from the medical record.

The surgical procedure consisted of a three-port, 20-gauge PPV performed in conjunction with the placement of a BGI in the superotemporal quadrant. Temporary restriction of aqueous flow through the implant was achieved with a tube ligation with a 7-0 polyglactin suture near the tube-plate junction. Fenestrations were created in the tube with a TG-130 needle just anterior to the polyglactin ligature with a needle for early IOP control according to the glaucoma surgeon's judgment. The tube was placed through the pars plana into the vitreous cavity either through a sclerotomy created by the 20-gauge microvitreoretinal blade or through a separate 23-gauge needle tract. It was the consensus of the glaucoma specialist that the Hoffman elbow modification of the BGI was not necessary and, hence, it was not used. A donor corneal or scleral patch graft was applied over the anterior portion of the tube to prevent erosion. Patients were monitored post-operatively by both the glaucoma and vitreoretinal surgeons.

Patients were categorized by diagnosis as NVG or non-NVG for the purpose of data analysis. The main outcome measure was success defined as BCVA≥hand motions (HM), normal IOP (≥6 and ≤21 mm Hg) with or without antiglaucoma medication, and no additional ocular surgery. Eyes that did not fail but required adjunctive glaucoma medications were classified as qualified successes, while those without glaucoma medications were categorized as complete successes. Hypotony was defined as IOP ≤5 mm Hg. Data from the clinic visit nearest to 12mo post-operatively (range, 7 to 18mo) were analyzed for 1y outcomes.

Table 1 Baseline characteristics of the study population

Data analyzed	NVG	Non-NVG	*P*
No. of eyes	43	49	
No. of patients	41	48	
Age (a)			
Mean (SD)	65 (15)	62.51 (22.95)	0.55[a]
Median (range)	64 (36-92)	69 (5-90)	
Gender			
Male, *n* (%)	23 (53)	22 (45)	0.34[b]
Follow-up (mo)			
Mean (SD)	16 (15)	23 (21)	0.031[a]
Median (range)	11 (1-84)	15 (1-84)	
Lens status, *n* (%)			0.02[c]
Phakic	20 (47)	10 (20)	
Aphakia	2 (5)	5 (10)	
ACIOL	2 (5)	9 (18)	
PCIOL	19 (44)	25 (51)	
VA, logMAR			
Mean (SD)	2.23 (0.48)	1.51 (0.75)	<0.001[a]
Median (range)	2.3 (0.7-3.0)	1.3 (0.18-3.0)	
IOP (mm Hg)			
Mean (SD)	40.0 (10.6)	30.3 (11.7)	<0.001[a]
Median (range)	39 (17-60)	31 (6-55)	
Extent of angle closure by PAS, *n* (%)			0.24[c]
PAS (-) /open angle	13 (30)	15 (31)	
<180 degrees	13 (30)	8 (16)	
≥180 degrees	17 (40)	26 (53)	
Antiglaucoma medications, *n* mean (SD)	2.8 (1.3)	2.7 (1.3)	0.56[a]
Mean number previous intraocular surgeries, *n* mean (SD)	0.7 (0.5)	1.8 (1.4)	<0.001[a]

ACIOL: Anterior chamber IOL; IOP: Intraocular pressure; logMAR: Logarithm of minimal angle resolution; NVG: Neovascular glaucoma; PAS: Peripheral anterior synechia; PCIOL: Posterior chamber lens; VA: Visual acuity. [a]Two-sample *t*-test; [b]Fisher Exact test; [c]Pearson Chi-square test.

SPSS (Version 17, SPSS Inc. Chicago, Il, USA) was used for statistical analysis. Demographic data and preoperative data between the NVG group and non-NVG group were analyzed with a paired 2-sample *t*-test. IOP comparisons between two groups were analyzed with a paired 2-sample *t*-test. Rates of surgical success, surgical failure, postoperative hypotony, and visual acuity change were analyzed by Chi-square test. The incidence of complications was analyzed with the Fisher Exact test. Kaplan-Meier survival analysis was used to calculate success rates.

RESULTS

Baseline Characteristics Table 1 shows the baseline

characteristics of the study population. Ninety two eyes from 89 patients were included in the study. The NVG group consisted of 43 eyes from 41 patients, and proliferative diabetic retinopathy (14 eyes, 33%) and central retinal vein occlusion (4 eyes, 9%) were the most common underlying etiologies. The non-NVG group consisted of 49 eyes of 48 patients, and the most common surgical indications were prior penetrating keratoplasty (8 eyes, 16%) and aphakia with vitreous prolapse (6 eyes, 12%). The median age (64y *vs* 69y), male gender (53% *vs* 45%), median follow-up interval (11mo *vs* 15mo), rate of ≥50% angle closure (40% *vs* 53%), and number of preoperative glaucoma medications (2.8 *vs* 2.7) were not significantly different between the NVG group and non-NVG group, respectively. The non-NVG group had better preoperative vision (median logMAR 1.3 *vs* 2.3, P<0.001), lower median IOP (31 mm Hg *vs* 39 mm Hg, P <0.001), and more previous intraocular surgeries (mean 1.8 *vs* 0.7, P <0.001) in comparison to the NVG group.

Preoperatively there were a total of 55 pseudophakic, 7 aphakic, and 30 phakic eyes. Cataract extraction was performed during follow-up in the study in 8 (27%) phakic eyes. The NVG group was more commonly phakic (47%) than the non-NVG group (20%) at the time of BGI placement (P=0.023). Other ocular comorbidities included tractional retinal detachment (2 eyes; one due to PDR and one due to sickle cell retinopathy), retained lens material, aqueous misdirection, traumatic glaucoma, and aniridia (one each). Tube fenestrations were performed in 33 (67%) of non-NVG and in 40 (93%) of NVG eyes.

Surgical Outcomes Surgical outcomes are provided in Table 2. Surgical failure occurred in 34 (37%) of the 92 eyes with at least 1y follow-up, including 26 (60%) of the NVG group and 8 (16%) of the non-NVG group (P=0.038). Vision loss to NLP (16 eyes, 23%), IOP <6 or >21 mm Hg (6 eyes, 18%), phthisis or enucleation (14 eyes, 41%) and glaucoma reoperations (6 eyes, 18%) were the causes for treatment failure. Two eyes in the NLP category underwent enucleation due to a blind, painful eye. The reoperations included PPV due to vitreous hemorrhage (VH) or fibrovascular proliferation (2 eyes), BGI revision (1 eye), BGI replacement (2 eyes), and BGI removal (1 eye). Failure on treatment was evident within 6mo post-operatively in 20 (59%) of the 34 eyes. The cumulative probability of success at 1y using Kaplan-Meier survival analysis was worse in the NVG group than in the non-NVG group (40% *vs* 79%; P<0.001), a difference that persisted thereafter (Figure 1).

Tube Location The tube was placed into the AC in 48 (52%) eyes (including 20 pseudophakic, 4 aphakic, and 24 phakic eyes) and into the vitreous cavity in 44 (48%) eyes (including 35 pseudophakic, 3 aphakic, and 6 phakic eyes). The tube was more frequently placed into the AC in the NVG group (81%) than in the non-NVG group (27%) (P<0.001), and in phakic (80%) compared to aphakic or pseudophakic (38%) eyes.

Table 2 Surgical outcomes

Data analyzed	NVG n=43	Non-NVG n=49	P
Tube location, n (%)			<0.001[a]
AC	35 (81)	13 (27)	
PP	8 (19)	36 (73)	
Visual Outcome at final visit, n (%)			0.007[a]
Improved	10 (23)	27 (55)	
Stable	13 (30)	10 (20)	
Worse	20 (47)	12 (24)	
NLP	14 (33)	2 (4)	<0.001[b]
≥20/200	1 (2.3)	16 (33)	
Mean IOP at 1a, mm Hg (SD)	15 (10.5)	15 (9.5)	0.425
Treatment outcomes at final visit, n (%)			<0.001[a]
Complete success	8 (19)	26 (53)	
Qualified success	9 (21)	15 (31)	
Failure	26 (60)	8 (16)	
Mean number of glaucoma medications at 1a, n (SD)	0.51 (1.00)	0.76 (1.18)	0.343

AC: Anterior chamber; IOP: Intraocular pressure; NLP: No light perception; NVG: Neovascular glaucoma; PP: Pars plana. [a]Analyzed by Pearson Chi-square test; [b]Fisher Exact test.

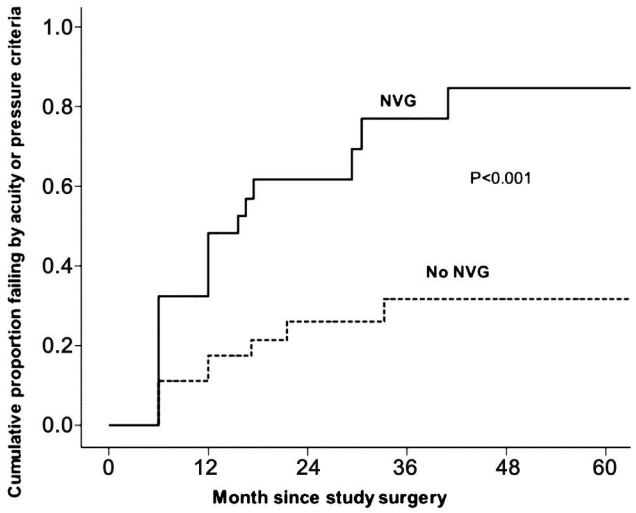

Figure 1 Kaplan-Meier plot of cumulative proportion of eyes failing visual acuity or intraocular pressure criteria for successful outcome.

Mean IOP at one-year follow-up visit was 15 mm Hg for both NVG and Non-NVG groups (P=0.425) and the mean number of antiglaucoma medications was reduced from a mean of 2.8 in the NVG group and 2.7 in the non-NVG preoperatively to 0.51 and 0.76, respectively (P=0.343). Paired t-test for postoperative compared to preoperative.

Visual Results Visual results were better in the non-NVG group (Table 2). After one-year follow-up, 16 (37%) of the NVG eyes presented visual acuity ranging between HM and

counting fingers and only one eye (2%, VA = 20/70) presented visual acuity ≥20/200, while 16 (33%) of 42 non-NVG eyes achieved Snellen visual acuity ≥ 20/200 (P=0.001). Visual acuity was stable or improved in 75% of non-NVG eyes (*vs* 53% in the NVG group).

Complications Table 3 shows complications and associated surgical procedures during the first year of follow-up. The only intraoperative complication, a suprachoroidal hemorrhage, occurred in a non-NVG patient after a penetrating keratoplasty. Postoperative complications occurred in 28 (65%) NVG and 24 (49%) non-NVG eyes. The most common complications that were present at or beyond 1wk post-operatively in NVG patients included non-clearing VH and/or hyphema in 16 eyes (37%). In contrast, none of the non-NVG eyes had a VH by the first post-operative week. The persistence of VH/hyphema likely indicated continuing hemorrhage due to progressive underlying disease. Postoperative VH was an important prognostic factor in the NVG group; 88% of NVG patients with non-clearing VH ultimately were surgical failures. Postoperative suprachoroidal hemorrhage requiring surgical drainage within 2wk post-operatively occurred in 5 (10%) non-NVG eyes, two of which developed phthisis. Suprachoroidal hemorrhage did not occur in any NVG cases. Post-operative retinal detachment (3 cases in each group, 7% of total) or retinal breaks without retinal detachment (1 eye in the non-NVG group, 1% of total) also occurred (Tables 3, 4).

Table 3 Complications and associated surgical procedures during 1y follow-up

Complications	NVG n=43	Non-NVG n=49
Choroidal detachment	3	6
Retinal breaks with RD	3	3
Retinal breaks without RD	0	1
Unclearing VH[a]	16	0
Endophthalmitis	2	0
Flat AC	1	0
Tube blockage by vitreous	0	2
IOL dislocation	0	3
Exposed tube	0	1
Corneal endothelial failure	2	4
Enucleated	2	0
Phthisis	12	2
Repeated surgery	3	3
Cataract progression (18 phakic eyes)	1	0
VA LP or NLP	8	0
IOP <6 or >21 mm Hg	3	3
Total (number of eyes)	56 (28)	28 (24)

IOL: Intraocular lens; IOP: Intraocular pressure; NLP: No light perception; NVG: Neovascular glaucoma; RD: Retinal detachment; SCH: Suprachoroidal hemorrhage; VH: Vitreous hemorrhage; VA: Visual acuity; LP: Light perception. [a]Unclearing VH: Vitreous hemorrhage not cleared till 1mo post-operatively.

Table 4 Postoperative complications on first postoperative day

Complications	NVG n=43	Non-NVG n=49
Hypotony	3	13
Hyphema	26	7
VH	25	10
SCH	0	5
Total (number of eyes)	54 (26)	35 (20)

SCH: Suprachoroidal hemorrhage; VH: Vitreous hemorrhage.

DISCUSSION

This study has demonstrated that PPV combined with GDD can offer respectable results, considering it is a treatment option for the most advanced cases, and specifically that eyes with non-NVG have a better prognosis. Potential advantages of this procedure in selected patients with uncontrolled IOP includes simultaneous management of glaucoma and posterior segment disorders and the option of pars plana placement of the drainage tube for patients with anterior segment comorbidities [12,14,16,20]. Previous studies of combined procedures have been limited to small cases of various types of GDD's[2,9-18], offered limited comparison outcomes of NVG to other indications, used broader criteria for success (*e.g.* inclusion of light perception final visual acuity as success), or lacked details of visual acuity results [14,16,17,20]. The present study included a large number of patients who underwent a single type of GDD, and outcomes are subdivided into eyes with NVG and those with other glaucoma diagnoses.

Glaucoma type was a major factor affecting surgical success in this study, with NVG eyes fairing substantially worse than non-NVG eyes. The Kaplan-Meier cumulative success one year post-operatively (40% in NVG eyes and 79% in the non-NVG eyes) in the current study was similar to previously reported success rates of 43% to 78% for BGI which lumped all glaucoma categories [24-26]. Our study design did not permit a controlled evaluation of combined PPV/BGI in regards to BGI placement only or placement by location, but a reasonable inference from these data is that the tube site may be effectively decided by the surgeon based upon constraints in an individual eye. The more frequent pars plana placement in non-NVG eyes (73%) was probably due to associated anterior segment pathology that was more chronic or reflected previous surgical attention, such as vitreous prolapse commensurate with aphakia and pseudophakia.

The poor visual outcome of NVG patients in the current series is consistent with those reported previously, and is likely attributable to their poorer baseline visual acuity and natural history. A previous study reporting 56% success and 28% qualified success among 50 NVG eyes considered eyes with LP visual acuity as successes, and did not offer a detailed visual acuity analysis [20]. Still they acknowledged "serious complications" in 10% of eyes, consistent with the findings of the current study which offers a sober prognosis among NVG eyes. A recent retrospective study evaluated the

performance of PPV-BGI in 89 NVG eyes and found a cumulative success rate of 67% in 73 eyes (82% of total) that completed follow-up (6mo post-operatively), however, the authors also considered eyes with LP visual acuity as successes cases [27]. Fifty-five eyes (62%) in the aforementioned study presented improved or stable visual acuity, a result that somewhat resembles ours, once 53% of the NVG eyes in this series presented stable or improved visual acuity and 8 (19%) had light perception at 1-year follow up visit. Also of note is that fifty-one eyes (58% of total) in this recent case series received intravitreal anti-VEGF injection perioperatively, in contrast to only 2 eyes (2%) in our study.

Progression of NVG implies increasing retinal ischemia and increased production of vascular endothelial growth factor (VEGF)[28,29]. The principal weakness of the current study is that the interval during which these cases were studied predated our more regular use of anti-VEGF therapy for eyes undergoing combined PPV-BGI. Studies using off-label intravitreal injection of bevacizumab (IVB) have reported short-term efficacy and safety in NVG treatment, in association with or not with other treatment modalities[30-35]. IVB has also been reported as an effective adjuvant for surgical treatment of NVG [36-48]. Blocking anti-VEGF activity to interrupt the vicious cycle of NVG aggravation is probably helpful in improving the surgical outcome of NVG, but a prospective randomized trial, or at least a larger, case-control study specifically aiming to define the best setting (s) for its surgical adjunctive use would likely be more definitive, but at this point probably impractical. Any retrospective study is subject to the biases of case ascertainment and individual surgeon preferences; these were at least mitigated by this being a consecutive case series, there being one vitreoretinal surgeon (but several glaucoma surgeons), and little variation in the retinal portion of the procedure.

Any surgical case series could have longer follow-up examination intervals, but the nature of the tertiary practice setting of the current study dictated these constraints; the rapid declaration of clinical course in these sorts of cases probably establishes the long term outcome early post-operatively.

The current study, although retrospective and non-randomized, shows encouraging results with the performance of PPV-BGI (especially for non-NVG eyes), offering the glaucoma specialist a viable option in selected cases of refractory glaucoma. The best suited eyes for pars plana insertion of the GDD are those with narrow or flat angles, corneal decompensation, or those with florid rubeosis iridis. The apparently disappointing results with NVG in our series suggest the need to optimize the treatment approach for those eyes, possibly through earlier PPV-BGI intervention and/or use of anti-VEGF agents.

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