ORIGINAL STUDY

Comparison of Outcomes Following Glaucoma Drainage Tube Surgery Between Primary and Secondary Glaucomas, and Between Phakic and Pseudophakic eyes

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Purpose: To report outcomes of glaucoma drainage device (GDD) surgery based on primary or secondary glaucoma diagnosis and lens status.

Design: Single-center, retrospective, consecutive cohort study.

Methods: University of Florida patients aged 18 to 93 years who underwent nonvalved GDD surgery between 1996 and 2015 with a minimum of 1-year follow-up were examined. Of the 186 eyes of 186 patients enrolled, 108 had a primary glaucoma and 78 a secondary glaucoma diagnosis. Excluding 13 aphakic patients, 57 eyes were phakic and 116 pseudophakic. Mean intraocular pressure (IOP), mean number of medications, visual acuity (VA), surgical complications, and failure (IOP $\geq$18 mm Hg, IOP <6 mm Hg, reoperation for glaucoma, or loss of light perception) were the main outcome measures.

Results: No significant difference was noted in mean IOP and mean medication use (12.8 ± 4.5 and 13.0 ± 6.6 mm Hg on 2.0 ± 1.2 and 1.5 ± 1.1 medication classes, respectively), mean VA (1.08 ± 0.98 and 0.94 ± 0.89, respectively), failure, or numbers of complications and reoperations ($P > 0.05$) between eyes with primary and secondary glaucomas at up to 5 years postoperatively. Comparison of phakic and pseudophakic eyes showed a statistically significant higher success rate for the pseudophakic patient group at the $\geq$18 mm Hg upper limit and <6 mm Hg lower limit ($P = 0.01$), and significantly fewer eyes required reoperation to lower IOP (6.9% vs 23%).

Conclusions: GDD surgery appears equally effective for secondary glaucomas as for primary glaucomas, and has a better outcome for pseudophakic eyes than phakic eyes.

Key Words: glaucoma, glaucoma drainage implant, intraocular pressure, pseudophakic, surgery

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G laucoma is the leading cause of irreversible blindness on a global scale.[1] It is estimated that worldwide, 64.3 million people in 2013 had glaucoma,[2] with an increasing incidence over time. Intraocular pressure (IOP) is the only significant modifiable factor in reducing glaucoma progression.[3] In general, glaucoma is initially managed with topical medications and/or laser therapy to lower IOP to decrease the rate of glaucomatous progression and visual disability. When these measures fail, clinicians often resort to incisional surgeries to lower IOP. Although there are numerous new minimally invasive glaucoma procedures, 2 longstanding, commonly performed glaucoma surgical procedures are trabeculectomy and glaucoma drainage device (GDD) implantation.[4]

Glaucoma can be classified as either primary or secondary. Primary glaucoma can be further categorized as open-angle (POAG) or angle-closure glaucoma (PACG), where the trabecular meshwork is obstructed by the peripheral iris.[5] When glaucoma occurs as a consequence of an acquired condition, it is classified as secondary glaucoma. These acquired conditions can be the result of a systemic pathology such as diabetes mellitus or autoimmune disease, or conditions which are intrinsic to the eye itself. Causes of secondary glaucoma include trauma, medications, inflammation, masses, and neovascularization.[5] Although pseudoexfoliation (PXF) and pigmentary glaucomas are due to potential blockage of the outflow by either pseudoexfoliative material or pigment respectively and thus, technically could be designated as a secondary glaucoma, frequently from a surgical wound healing perspective, they act more like a POAG and are frequently included in combination with this group as a primary glaucoma. Many studies looking at primary glaucoma have included PXF and pigmentary glaucoma as well as POAG. For example, in the Collaborative Initial Glaucoma Treatment Study (CIGTS),[6] the study design included randomizing primary glaucoma patients naive to prior glaucoma therapy, and the consensus for study inclusion in this group was "eligible patients must have had newly diagnosed open-angle glaucoma (primary, pseudoexfoliative, and pigmentary forms)." Another example is the Primary Trabeculectomy Versus Tube (PTVT) study, in which there were 218 POAG patients, 8 chronic angle-closure glaucoma patients, 6 pigmentary glaucoma patients, 5 PXFG patients, and 5 others enrolled. Neovascular, uveitic, iridocorneal endothelial syndromes, fibrous downgrowth, and steroid-induced glaucomas were excluded.[7] Likewise, in the Tube Versus Trabeculectomy (TVT) study there were 172 POAG, 18 PACG, 8 PXFG, 1 pigmentary glaucoma, and 13 others enrolled with the same diagnoses as above excluded.[8]

Initially, GDDs were reserved for treating secondary glaucoma where the outcome of trabeculectomy surgery was known to be poor.[9,10] The inflammation and increased risk of fibrosis, which is associated with many secondary glaucomas, is thought to limit the efficacy and outcome of trabeculectomy.[11] However, over time, GDDs have been increasingly used as an initial surgery for primary glaucoma eyes with either pseudophakia and/or a failed trabeculectomy. The randomized, prospective TVT study demonstrated equal IOP control, but a higher success rate in the Baerveldt GDD group compared to trabeculectomy with mitomycin-c (MMC).[8] Another multicenter, randomized clinical trial conducted by the PTVT study group showed at 1 and 3 years of follow-up, that phakic patients with primary glaucoma who had no prior incisional eye surgery may be better treated with trabeculectomy. Eyes randomized to trabeculectomy with MMC in this trial demonstrated superior long-term IOP control and reduced medication dependence compared to GDD surgery.[7]

Conjunctival scarring is known to reduce the probability of success in patients undergoing trabeculectomy surgery. In this procedure, pressure control depends on aqueous filtration through a surgically created scleral flap near the limbus and the formation of a subconjunctival filtration bleb. Surgeons attempt to mitigate the effects of subconjunctival fibrosis and inflammation with the use of adjunctive MMC and postoperative steroid medications. Patients with a failed previous trabeculectomy have a lower success rate with repeat trabeculectomy than those undergoing first-time trabeculectomy procedure.[12,13] In contrast, a recent paper by Dawson et al has shown that the outcome of GDD surgery is equal in patients with past failed trabeculectomy to those undergoing drainage tube surgery as a first glaucoma procedure.[14]

A 2014 prospective cohort study by Takihara et al[15] demonstrated that pseudophakic patients with open-angle glaucoma undergoing trabeculectomy had a lower probability of success at postoperative year 1 when success was defined as an IOP of less than 21 mm Hg or 18 mm Hg. Unlike trabeculectomy surgery, there is relatively little research that examines the effect of prior cataract surgery on the outcome of later GDD implantation. Likewise, there is also a paucity of data comparing the efficacy of GDD implantation in eyes with a primary versus secondary glaucoma diagnosis. Our study examines the outcome of GDD surgery by comparing eyes with primary and secondary glaucoma and comparing phakic with pseudophakic eyes to allow surgeons to make a more informed decision in choosing when to proceed with GDD implantation based on a patient's glaucoma classification and lens status.

MATERIALS AND METHODS

Before conducting research, this study protocol received the University of Florida's Institutional Review Board (IRB) approval. The IRB granted a waiver of informed consent for the compilation and use of these data. This study abides by the Declaration of Helsinki, the Health Insurance Portability Accountability Act and federal and state laws.

This retrospective, single-center, consecutive, single-surgeon study analyzed 186 eyes with various glaucoma diagnoses that received a GDD implant between the years 1996 and 2015 at the University of Florida. A search was made in the hospital database for all cases assigned current procedural terminology codes

66180 or 66185 for GDD implantation. Cases were then excluded if this was not the initial GDD surgery for that eye, or if there was less than 1 year of follow-up in the chart, or if the patient was under 18 years of age. For patients who needed GDDs in both eyes, only the initial eye was analyzed. Inclusion criteria were met by 186 eyes of 186 patients. Patients who needed additional glaucoma procedures (diode cyclophotocoagulation or an additional GDD) were censored at the time of the second procedure. Visual acuity (VA) was censored at the time of any potential vision-altering procedure, including cataract surgery, corneal graft, corneal chelation, or laser capsulotomy. As a quality control, a random 40% of the records were rechecked by a separate investigator who was masked to the prior recorded information. Almost total concordance with the original data entry was found for the diagnosis, preoperative, and postoperative IOP, VA, and glaucoma medications.

Patient demographics examined in this study include age, gender, ethnicity, lens status (phakic, pseudophakic, aphakic), study eye (left or right), glaucoma diagnosis of the study eye, and the mean baseline IOP, VA, and numbers of glaucoma medications. In accordance with the World Glaucoma Congress recommendations,[16] preoperative measurements for IOP, medication use, and VA were quantified by an average of all visits up to 42 days before the surgery. The postoperative data was obtained from the yearly visit closest to the date of surgery as recommended by these guidelines.[16]

There were 108 eyes which we designated as Group I (including POAG, PXF or pigmentary glaucoma, or PACG) and 78 eyes as Group II (including neovascular, uveitic, traumatic, aphakic, secondary angle-closure, or secondary open-angle glaucoma). The neovascular glaucomas were treated with antivascular endothelial growth factor and retinal photocoagulation by our retinal surgeons. While some were new-onset and had rubeosis and active neovascularization, others were more chronic. With the uveitis diagnoses, there was a mixture of initiating etiology including herpetic disease and sarcoidosis, etc but no one diagnosis was sufficient for individual analysis.

The study population was also divided by lens status. A hundred and sixteen eyes were pseudophakic and 57 eyes were phakic at the time of GDD surgery. Thirteen eyes were aphakic, and because of the small number, these were excluded from this second part of the study, which analyzed the effect of lens status on GDD surgical outcome.

In all eyes, either a Baerveldt (Abbott Laboratories Inc, Abbott Park, IL, US) or Molteno (Molteno Ophthalmic Ltd, Dunedin, New Zealand) nonvalved GDD implant was used. In approximately 70% to 80% of cases, local anesthesia was used primarily depending on patient preference and general health. The technique has been described in detail in our previous paper.[14] In brief, nearly all of the surgeries involved a fornix-based conjunctival flap with a high preponderance of these utilizing the superior-temporal quadrant. After securing the relevant rectus muscles with a muscle hook, the episcleral plate was sutured to the sclera with 9-0 Nylon (Ethicon, New Jersey, US) approximately 9 to 10 mm from the limbus. Either a 3-0 Supramid (Assut sutures, Switzerland) or 4-0 Prolene (Ethicon, New Jersey, US) occluding suture was inserted into the upper end of the tube at the episcleral plate and a Vicryl 8-0 polyglactin (Ethicon, New Jersey, US) suture was placed externally around the tube near its upper end and tightened to fully block flow up the tube. Basic saline solution

was injected with a 27-gauge cannula into the tube to confirm its occlusion. Westcott scissors were used to trim the drainage tube to the desired length and create an anterior bevel to the tube orifice. The anterior chamber was entered approximately 1 to 2 mm behind the limbus and parallel with the iris with a 23-gauge needle, and the tube was inserted via this path. In most cases, the tube was placed in the anterior segment. For those eyes where there was angle closure with peripheral anterior synechiae, the tube was sometimes placed in the posterior segment in front of the intraocular lens in pseudophakic eyes. The tube was anchored to the sclera and held by two 10-0 Nylon wrap-around sutures. A TG140-8 spatulated needle on the 8-0 polyglactin suture was used to create 2 to 4 venting slits in the extrascleral portion of the tube, and aqueous outflow was reviewed. A double-thickness pericardial patch graft or corneal semicircular graft covered the tube to reduce the risk of future tube erosion. The conjunctiva and Tenon capsule was repositioned and closed with 8-0 polyglactin suture, and a collagen shield soaked in tobramycin/dexamethasone combination was placed.

Postoperatively, patients received a 2-month steroid drop taper and were generally started on aqueous suppressant eye drops on the first day after surgery, unless flow through the venting slits had created already adequate or low IOPs. The GDD tube in most cases was allowed to open spontaneously at 5 to 7 weeks postoperatively when the 8-0 polyglactin suture dissolved. Once the GDD was functional, then the 4 -0 Prolene or the 3-0 Supramid occluding suture could later be removed either at the clinic slitlamp or minor operations room. In a minority of cases, where more urgent IOP control was required, or where a permanent 9-0 Nylon external tie had been used, the 4-0 Prolene or the Supramid occluding suture was removed in the minor operations room, generally with a viscoelastic being injected into the anterior chamber via the paracentesis track at the time of the removal. The stent was removed to avoid the risk of future erosion of the conjunctiva overlying the stent.

STATISTICAL ANALYSIS

Univariate analyses were conducted between both treatment groups through a 2-sample t test with a Bonferroni adjustment for continuous variables and chi-square tests for categorical outcomes implant throughout a 5-year postoperative timespan. Visual acuity was analyzed by conversion of Snellen to the logarithm of minimum angle of resolution (LogMAR) equivalents. Subanalyses were conducted for patients with baseline IOP <25 mm Hg vs ≥25 mm Hg, patients with baseline age <65 years vs age ≥65 years, for those with or without a previous failed trabeculectomy surgery, and for those receiving a Baerveldt 350 mm^2. Kaplan-Meier analyses were conducted with failure defined as being an upper limit IOP of either ≥18, or ≥15, or ≥12 mm Hg, and a lower limit of <6 mm Hg on 2 consecutive occasions or loss of light perception. Multivariate analyses were performed with a binary logistic regression with the event of interest being a failure (IOP ≥18 mm Hg or <6 mm Hg). Odds ratios were calculated for each predictor factor. An odds ratio of 1 is the baseline comparison which indicates no association between the response variable (failure event) and predictor. All statistical analyses were conducted using the statistical software R version 3.6.3 (R Core Team, Vienna, Austria) and SAS Studio version 3.8 (SAS Institute Inc, Cary, NC, US).

RESULTS

Of the 186 eyes included in this study, 108 (58%) were designated as Group I (POAG, PXFG, pigmentary glaucoma, and PACG), and 78 (42%) were designated Group II (other secondary glaucomas). In the second part of the study examining the effect of lens status, the 13 aphakic eyes were excluded due to their low number. Of the remaining 173 eyes, 57 (33%) were phakic and 116 (67%) were pseudophakic.

The groups, Group I vs Group II and between phakic and pseudophakic groups, had similar baseline data, mean number of medications, ethnicity, study eye, and type of implant used (Baerveldt or Molteno) (Table 1). There were statistically significant differences between groups in baseline mean IOP with higher baseline pressures being noted in the secondary glaucomas and the phakic eyes. A subanalysis was performed dividing patients into those with a baseline IOP of <25 mm Hg and those ≥25 mm Hg. There was no baseline statistical difference between groups for those with a starting pressure of <25 mm Hg, but group differences remained for those with initial pressures of 25 mm Hg or more (Table 1). A baseline difference in mean LogMAR VA was also noted with poorer vision in the secondary glaucoma group and a nonsignificant trend toward a poorer vision in the phakic eyes.

As expected, the patients in Group II or those in the phakic group were significantly younger at the time of surgery (57 ± 14 and 57 ± 12, respectively), compared to those in Group I or who were pseudophakic (69 ± 12 years and 69 ± 13, respectively) ($P < 0.0001$). When the patients were divided into those 65 years old or more and those less than 65, there was no statistically significant difference in average age between groups for the patients less than 65. For the comparison of Group I and Group II in those 65 years old or more, there was again no statistically significant difference in age, but there still remained a significant age difference for the groups aged 65 years or more in the phakic and pseudophakic analysis (70 ± 5 vs 76 ± 7, respectively) (Table 1).

There was an almost equal percentage of males and females for the primary and secondary glaucoma study and for the pseudophakic group, but a higher proportion of males (67%) in the phakic group. Analysis showed a lower proportion of eyes with a prior failed trabeculectomy surgery in the secondary glaucoma group, which was statistically significant ($P = 0.0003$). There was no significant baseline difference between groups for the phakic and pseudophakic analysis (Table 1).

Table 2 compares the IOP and mean medication use in eyes in Group I vs Group II and between phakic and pseudophakic eyes. As noted above, at baseline there is a significant difference in mean IOP between groups, with the higher pressures being seen in Group II and in the phakic eyes. At all postoperative time points from 1 to 5 years, there was no significant difference in either mean IOP or medication use between Group I and Group II or between the phakic and pseudophakic groups (Table 2; Figs. 1 and 2)

A posthoc power analysis was performed which showed at 3 years postoperatively there is a 93% power to detect a difference of 3 mm Hg with an alpha level of 0.05, and a 64% chance to detect a 2 mm Hg difference in IOP between the primary and secondary glaucoma groups. Similarly, at 4 and 5 years respectively, there was an 84% and 67% chance to detect a 3 mm Hg difference, and a 52% and 38% chance to detect a 2 mm Hg difference. A posthoc power analysis of the phakic and pseudophakic Kaplan-Meier curves, with an alpha level of 0.05, shows an 88% power to detect a difference of 3 mm Hg in mean IOP, and

TABLE 1. Population Demographics

	Group I	Group II	*P* value[*,†]	Phakic Eyes	Pseudophakic Eyes	*P* value[*,†]
N	108	78	–	57	116	–
Baseline IOP (mm Hg)	26.2 ± 8.8	33.3 ± 10.9	<0.0001[*]	31.7 ± 10.8	27.3 ± 9.8	0.008[*]
Baseline IOP <25 mm Hg	19.6 ± 3.0	18.6 ± 4.5	0.27[*]	19.5 ± 2.6	19.2 ± 3.7	0.75[*]
N	57	19		19	55	
Baseline IOP $\geq$25 mm Hg	34.0 ± 7.0	38.0 ± 7.5	0.005[*]	37.8 ± 7.7	34.6 ± 7.5	0.04[*]
N	51	59		38	61	
Baseline # of Glaucoma Medications Used	3.1 ± 1.0	2.9 ± 1.2	0.22[*]	3.0 ± 0.9	3.0 ± 1.2	1.00[*]
Baseline VA						
LogMAR mean $\pm$ SD	0.67 ± 0.7	1.33 ± 1.0	<0.0001[*]	1.05 ± 1.0	0.81 ± 0.8	0.09[*]
Glaucoma Diagnosis						
Primary Open-Angle	85	/		26	59	
Pseudoexfoliative	10	/		1	9	
Pigmentary	2	/		1	1	
Low Tension Glaucoma	4	/		1	3	
Primary Angle-Closure	7	/		0	7	
			–			–
Neovascular Glaucoma	/	26		14	12	
Uveitic Glaucoma	/	20		4	14	
Traumatic Glaucoma	/	14		5	4	
Secondary Open-Angle	/	9		4	4	
Secondary Angle-Closure						
Congenital Glaucoma	/	4		1	3	
Aphakic Glaucoma	/	2		0	0	
	/	3		/	/	
Age at Time of Surgery (y)	69 ± 12	57 ± 14	<0.000[*]	57 ± 12	69 ± 13	<0.000[*]
Age <65 y	54 ± 8	50 ± 10	0.06[*]	51 ± 9	54 ± 9	0.16[*]
N	31	53		39	35	
Age $\geq$65 y	76 ± 7	73 ± 6	0.06[*]	70 ± 5	76 ± 7	0.0009[*]
N	77	25		18	81	
Gender						
Female	47 (44%)	38 (49%)	0.48[†]	19 (33%)	62 (53%)	0.01[†]
Male	61 (56%)	40 (51%)		38 (67%)	54 (47%)	
Ethnicity						
Caucasian	66 (61%)	52 (67%)	0.57[†]	36 (63%)	73 (63%)	
African Descendent	38 (35%)	22 (28%)		19 (33%)	38 (33%)	0.96[†]
Other (Hispanic or Asian)	4 (3.7%)	4 (5%)		2 (4%)	5 (4.3%)	
Glaucoma Surgery						
No Prior Glaucoma Surgery	60 (56%)	63 (81%)	0.0003[†]	41 (72%)	71 (61%)	0.17[†]
Prior Failed Trabeculectomy	48 (44%)	15 (19%)		16 (28%)	45 (39%)	
Study Eye						
Left	58 (54%)	37 (47%)	0.40[†]	26 (46%)	61 (53%)	0.39[†]
Right	50 (46%)	41 (53%)		31 54%)	55 (47%)	
Lens Status						
Phakic	29 (27%)	28 (36%)		57	0	
Pseudophakic	79 (73%)	37 (47%)	–	0	116	–
Aphakic	0 (0%)	13 (17%)		–	–	
GDD Implant Model Used						
Baerveldt 350 mm^2	68 (63%)	35 (45%)		26 (46%)	69 (60%)	
Baerveldt 250 mm^2	8 (7%)	14 (19%)		9 (16%)	10 (9%)	
Molteno^3 (230 or 245 mm^2)	25 (23%)	20 (26%)		17 (30%)	27 (23%)	
Molteno^3 (175 or 185 mm^2)	1 (0.9%)	5 (6%)	0.28[†]	1 (2%)	5 (4%)	0.38[†]
Molteno Double Plate or Single Plate	6 (6%)	4 (5%)		4 (7%)	5 (4%)	

[*]Two-sample *t* test.

[†]Chi-square test.

IOP indicates intraocular pressure; GDD, glaucoma drainage device; VA, visual acuity.

a 57% power to detect a 2 mm Hg difference, at 3 years postoperative.

A Kaplan-Meier analysis was performed for IOP, with failure determined by an upper limit parameter of either $\geq$18 mm Hg, $\geq$15 mm Hg, or $\geq$12 mm Hg and a lower limit parameter of <6 mm Hg on 2 consecutive occasions, or loss of light perception. For Group I vs Group II analysis, there was no statistically significant difference for any of these 3 survival curves (Fig. 3A, C, E). However, a statistically significant higher success rate was noted for the pseudophakic eye group at the $\geq$18 mm Hg upper limit and <6 mm Hg lower limit (with a 65.3% vs 54.4% success; $P = 0.01$), and a borderline difference was noted for the $\geq$15 mm Hg upper limit and <6 mm Hg lower limit Kaplan-Meier analyses ($P = 0.05$) (Fig. 3B, D). At $\geq$12 mm Hg upper

TABLE 2. IOP and Medications in Eyes in Group I (POAG, PXFG, Pigmentary Glaucoma, and PACG) and Group II (Other Secondary Glaucomas) and Phakic vs Pseudophakic Lens Status

	Group I Mean ± SD	Group II Mean ± SD	*P* value*	Phakic Eyes Mean ± SD	Pseudophakic Eyes Mean ± SD	*P* value*
Baseline						
N	108	78		57	116	
IOP (mm Hg)	26.2 ± 8.8	33.3 ± 10.9	<0.0001	31.7 ± 10.8	27.3 ± 9.8	0.008
Medications	3.1 ± 1.0	2.9 ± 1.2	0.22	3.0 ± 0.93	3.0 ± 1.2	1.00
Post-op 1 y						
N	101	72		49	113	
IOP (mm Hg)	12.0 ± 4.6	12.0 ± 4.4	1.00	12.4 ± 4.3	11.9 ± 4.6	0.52
Medications	2.0 ± 1.1	1.7 ± 1.1	0.30	1.8 ± 1.2	1.9 ± 1.1	0.61
Post-op 2 y						
N	86	57		41	94	
IOP (mm Hg)	12.1 ± 4.4	13.1 ± 6.0	0.25	13.4 ± 7.0	12.1 ± 3.9	0.17
Medications	1.8 ± 1.1	1.9 ± 1.1	0.60	2.0 ± 1.2	1.8 ± 1.1	0.34
Post-op 3 y						
N	68	41		33	73	
IOP (mm Hg)	12.6 ± 4.8	11.9 ± 4.8	0.46	12.7 ± 4.2	12.0 ± 4.8	0.47
Medications	1.9 ± 1.2	1.8 ± 1.1	0.66	2.0 ± 1.2	1.9 ± 1.1	0.60
Post-op 4 y						
N	49	35		28	53	
IOP (mm Hg)	13.0 ± 5.2	13.2 ± 7.7	0.89	13.3 ± 5.6	12.9 ± 6.7	0.79
Medications	2.1 ± 1.1	1.9 ± 1.0	0.40	2.0 ± 1.2	2.0 ± 1.0	1.00
Post-op 5 y						
N	38	24		18	41	
IOP (mm Hg)	12.8 ± 4.5	13.0 ± 6.6	0.89	11.7 ± 5.8	13.3 ± 5.3	0.31
Medications	2.0 ± 1.2	1.5 ± 1.1	0.10	1.6 ± 1.3	1.9 ± 1.1	0.37

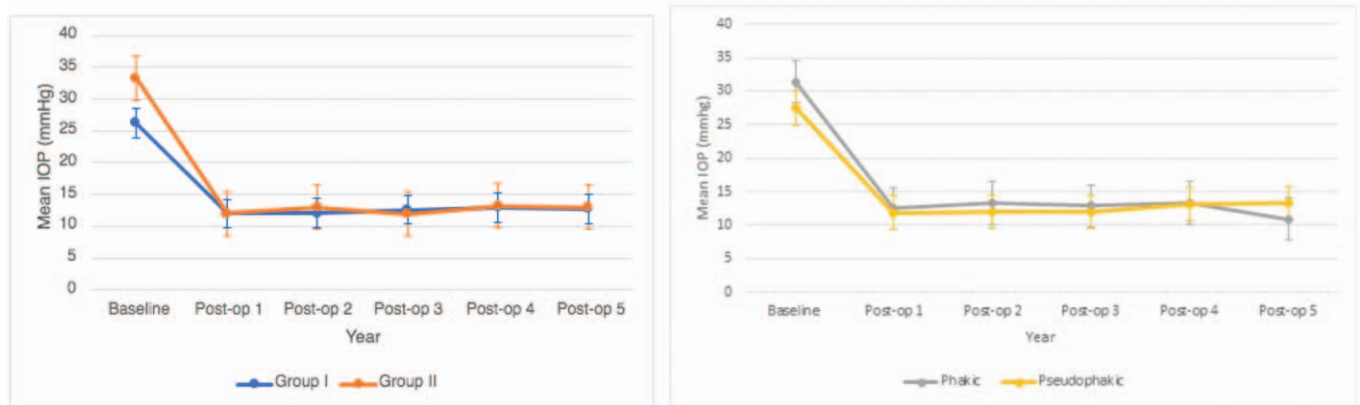*Two-sample *t* test using the Bonferroni correction for multiple comparisons.

IOP indicates intraocular pressure; PACG, primary angle-closure glaucoma; POAG, primary open-angle glaucoma; PXFG, pseudoexfoliation glaucoma.

limit Kaplan-Meier analysis, there was no longer a statistically significant difference between the success rates for the phakic and pseudophakic eye groups (Fig. 3F).

A multivariate binary logistic regression with odds ratios calculated for failure, defined as IOP ≥18 mm Hg or <6 mm Hg with 95% Wald confidence limits was performed (Table 3; Fig. 4). Observations with "other" ethnicity (n = 7 for Hispanic and Asian) were removed only for the logistic regression analysis to provide a clearer comparison of odds ratios between white and black ethnicity. Lens status (phakic or pseudophakic) was the only parameter that was significantly different between groups, and this showed an odds ratio for failure of 2.58 times higher among

phakic eyes compared to pseudophakic eyes (*P* = 0.04). No other variables, including type of implant, prior failed trabeculectomy, gender, ethnicity, primary or secondary glaucoma diagnosis, age, and starting IOP, were statistically significant in the logistic regression model.

For the comparison of the primary and secondary glaucoma eyes, there was a statistically significant difference at baseline in mean LogMAR VA with better vision being noted in the primary glaucoma eyes (*P* < 0.0001) (Table 4). These statistical differences in mean LogMAR VA continued to be noted at postoperative years 1 and 2 but were no longer seen at postoperative years 3 through 5. Over time there was a mild improvement in mean

FIGURE 1. Mean IOP in GDD recipients in Group I (POAG, PXFG, pigmentary glaucoma, and PACG) and Group II (other secondary glaucomas) (left) and phakic or pseudophakic lens status (right). The difference in IOP for Group I vs Group II patients is statistically significant (*) at baseline (*P* < 0.05 in a 2-sample *t* test). The difference in IOP for phakic vs pseudophakic lens patients is statistically significant (*) at baseline (*P* < 0.05 in a 2-sample *t* test). Error bars represent standard error of the mean. GDD indicates glaucoma drainage device; IOP, intraocular pressure; PACG, primary angle-closure glaucoma; POAG, primary open-angle glaucoma; PXFG, pseudoexfoliation glaucoma.
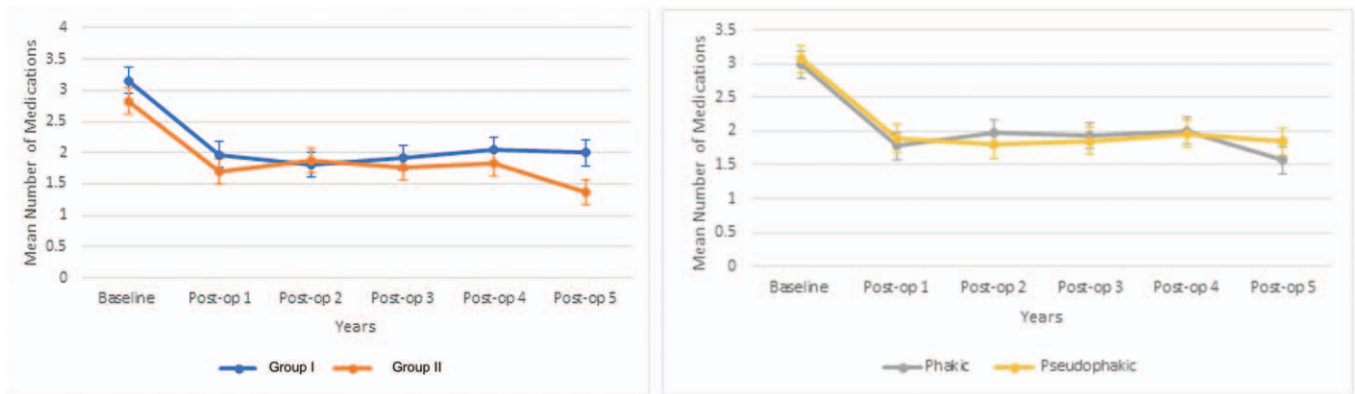
FIGURE 2. Mean number of medications in GDD recipients in Group I (POAG, PXFG, pigmentary glaucoma, and PACG) and Group II (other secondary glaucomas) (left) and phakic or pseudophakic lens status (right). There is no statistical difference in mean number of medications between Group I and Group II or the phakic and pseudophakic groups. Error bars represent the standard error of the mean. GDD indicates glaucoma drainage device; PACG, primary angle-closure glaucoma; POAG, primary open-angle glaucoma; PXFG, pseudoexfoliation glaucoma.

LogMAR VA in the secondary glaucoma group when comparing each individual with his/her baseline, but a slight decrease in the Group I eyes. Although patient numbers were small for year 5 postoperatively, there was a significant difference in mean change baseline VA in favor of the Group II eyes.

For the phakic and pseudophakic studies, there were no statistical differences in mean LogMAR VA either at baseline or at any time point in the follow-up. The mean change from baseline LogMAR VA for each individual was also similar between groups except at year 1 postoperative, where the phakic group showed a slight improvement from baseline with little change noted for the pseudophakic group (Table 4).

Postsurgical complications were classified as either early (before 30 days postoperative) or late (after the first postoperative month). There were no statistical differences noted between either Group I and Group II or the phakic and pseudophakic eye groups in the mean number of early or late complications. The number of reoperations for inadequate IOP control were not statistically different between the Group I and Group II eyes (15% vs 10%, respectively), but there were significantly more eyes in the phakic group that required a glaucoma reoperation (23% vs 6.9%, $P = 0.002$). These reoperations were most frequently laser cyclophotocoagulation for inadequate IOP control, with a small number receiving a second glaucoma drainage tube implant.

Given the baseline differences between groups, subanalyses were performed on eyes with a baseline IOP ≥ 25 mm Hg and <25 mm Hg (Supplementary Digital Content, Fig. 1A–D, http://links.lww.com/APJO/A117) and on patients aged 65 and above and below 65 years (Supplementary Digital Content, Fig. 2A–D, http://links.lww.com/APJO/A117) for mean IOP and medication use over 3 years postoperatively. No significant differences were seen between these subgroups for IOP analysis. Medication use was significantly less in the <65 age group in Group II for postoperative years 1, 2, and 3, but not in the ≥ 65 age group (Supplementary Digital Content, Fig. 2C, http://links.lww.com/APJO/A117). There were no differences in mean medication use between age groups in the phakic and pseudophakic analysis (Supplementary Digital Content, Fig. 2D, http://links.lww.com/APJO/A117).

Previous randomized studies often examined the outcome of the Baerveldt 350 mm^2 tube implant.[7,8,17] A subanalysis was performed for mean IOP and medication including only the eyes that had this specific implant. Similar to the overall group analysis, there was a difference in baseline IOP, but no differences were detected at any point postoperatively in mean IOP or medication use (Supplementary Digital Content, Table 1, http://links.lww.com/APJO/A117).

There was a significant difference at baseline in the number of eyes in the Group I vs Group II study with a prior failed trabeculectomy. An additional subanalysis was performed to compare these eyes to those undergoing a GDD surgery as an initial glaucoma procedure and again, no significant differences were noted at any time point postoperatively in mean IOP or number of medications (Supplementary Digital Content, Fig. 3A, B, http://links.lww.com/APJO/A117).

DISCUSSION

The drainage implant surgery was initially developed to help treat those patients who had already failed one or more trabeculectomy surgeries or as a first-time surgery in those patients who were in a diagnostic group where trabeculectomy surgery was unlikely to work. This latter group was generally secondary glaucomas, such as neovascular, uveitic, aphakic, post-traumatic, etc.[18–22] Over time, glaucoma drainage implants were also used as an initial glaucoma procedure in primary glaucoma eyes with pseudophakia[8,23,24] and even phakic, POAG eyes.[7,24] The TVT study showed over 3 and 5 years that GDD surgery had a higher success rate and lower reoperation rate than trabeculectomy with MMC in pseudophakic primary glaucoma eyes and/or those eyes with a prior failed trabeculectomy. Conversely, the PTVT study at 3 years showed that trabeculectomy with MMC had a higher success rate and lower mean IOPs than the GDD group in phakic, primary glaucoma eyes. Trabeculectomy surgery is known to have a higher success rate in phakic eyes rather than pseudophakics with a primary glaucoma[15] and is known to have a higher success rate in primary glaucomas, rather than secondary glaucomas.[25,26]

There has been limited direct comparison of the outcome of primary and secondary glaucomas following GDD surgery. Rachmiel et al[27] in a retrospective study of Ahmed implants compared 15 patients with a uveitic glaucoma vs 53 patients with an open-angle glaucoma, and found no significant differences in IOP outcome or success rate, although tube removal was more common in the uveitic group. Ramdas et al[28] in a retrospective study,
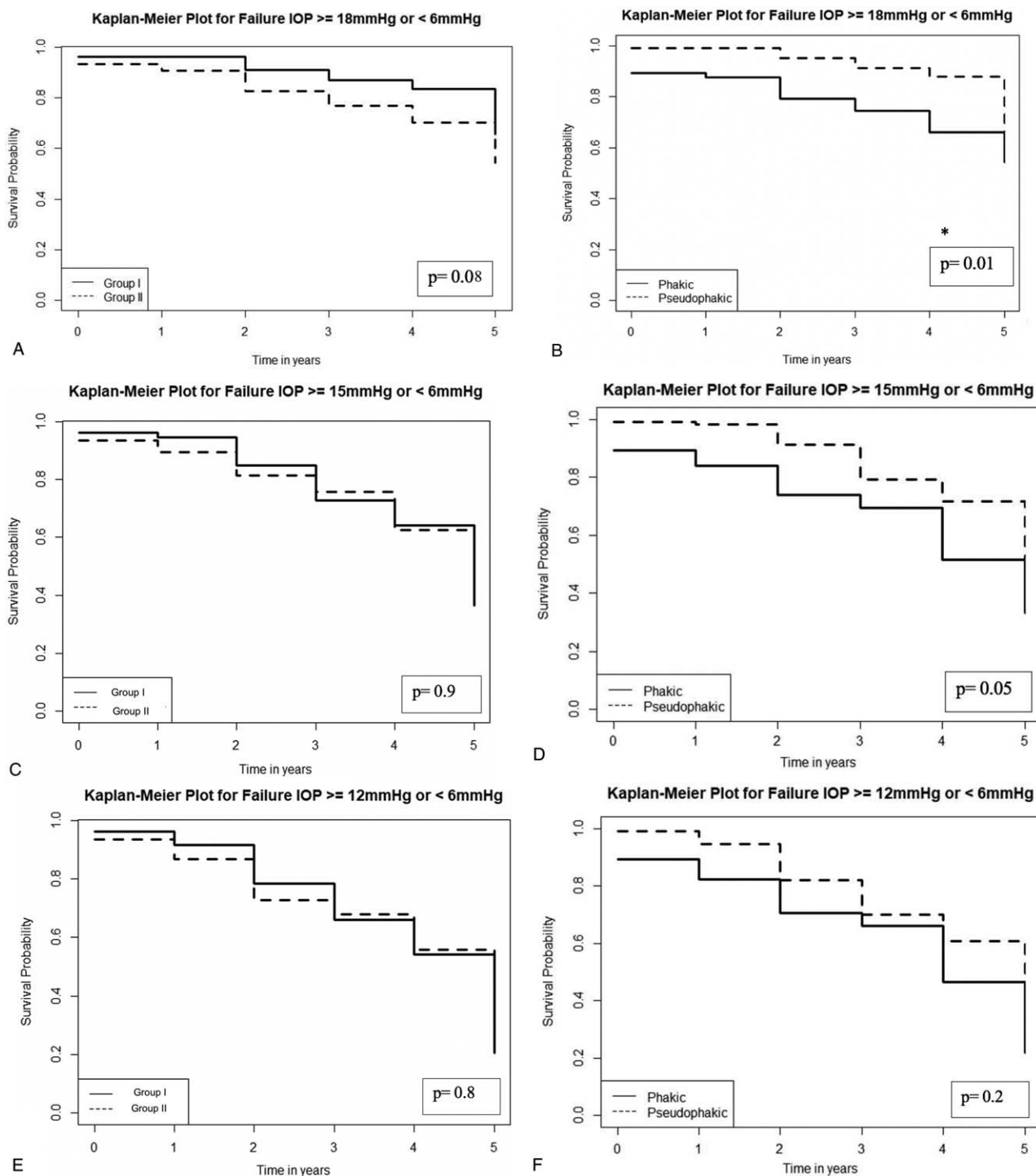
FIGURE 3. Kaplan-Meier Analysis. A, Comparison of Group I (POAG, PXFG, pigmentary glaucoma, and PACG) vs Group II (other secondary glaucomas) where failure is defined as IOP $\geq$18 mm Hg or <6 mm Hg. B, Comparison of phakic versus pseudophakic eyes where failure is defined as IOP $\geq$18 mm Hg or <6 mm Hg. C, Comparison of Group I vs Group II where failure is defined as IOP $\geq$15 mm Hg or <6 mm Hg. D, Comparison of phakic vs pseudophakic eyes where failure is defined as IOP $\geq$15 mm Hg or <6 mm Hg. E, Comparison of Group I vs Group II where failure is defined as IOP $\geq$12 mm Hg or <6 mm Hg. F, Comparison of phakic vs pseudophakic eyes where failure is defined as IOP $\geq$12 mm Hg or <6 mm Hg. *Denotes significant P value. IOP indicates intraocular pressure; PACG, primary angle-closure glaucoma; POAG, primary open-angle glaucoma; PXFG, pseudoexfoliation glaucoma.

compared 38 eyes with uveitic glaucoma to 61 eyes without uveitis with a mean follow-up of 13 months and also found no significant difference in final IOP or reduction in IOP in a mixed group of Baerveldt and Ahmed implant surgeries.

In our study, we have demonstrated no significant difference in mean IOP, medication use, VA outcome, failure rate by Kaplan-Meier analysis, and complication rate between eyes with POAG, PXFG, pigmentary glaucoma, and PACG (Group I) and other secondary glaucoma (Group II) diagnoses. The commonest cause of failure in both trabeculectomy surgery and GDD surgery is excessive fibrosis. Whereas the secondary glaucomas, which have a higher risk of scarring, have a poorer outcome than primary glaucomas with trabeculectomy surgery, the GDD procedure appears to be unaffected by this increase fibrosis potential.
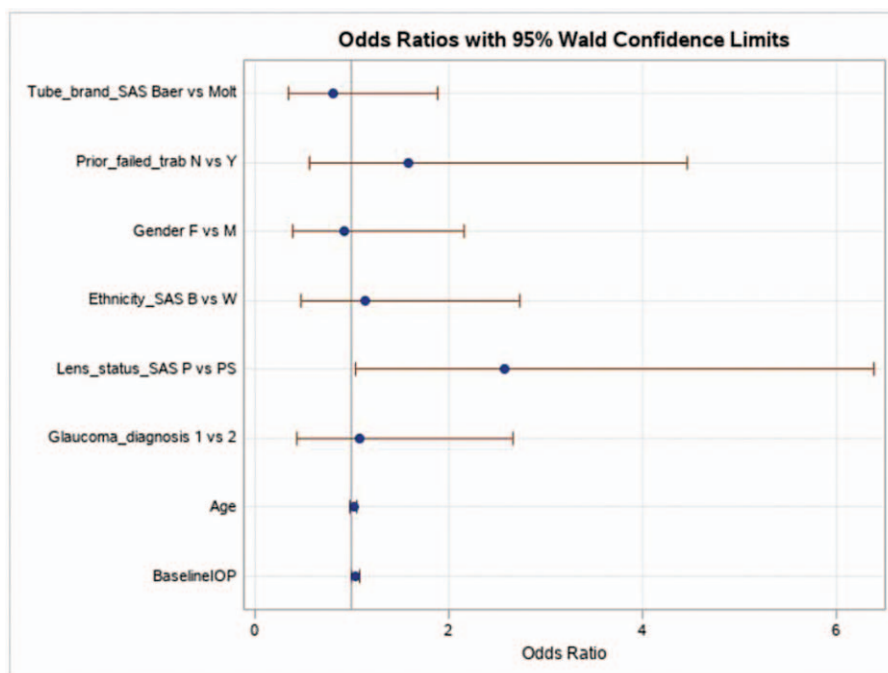
TABLE 3. Multivariate Binary Logistic Regression Results

Odds Ratio Estimates for IOP Failure ≥18 mm Hg and <6 mm Hg

Effect	Point Estimate	95% Wald Confidence Limits	*P* value
Tube Type: Baerveldt vs Molteno	0.809	0.348–1.881	0.62
Prior Failed Trabeculectomy	1.581	0.561–4.456	0.39
Gender: Male vs Female	0.917	0.390–2.154	0.85
Ethnicity: Caucasian vs African American	1.142	0.476–2.740	0.77
Lens Status: Phakic vs Pseudophakic	2.579	1.042–6.385	0.04
Glaucoma Type: Primary vs Secondary	1.080	0.438–2.667	0.87
Age	1.018	0.984–1.053	0.30
Baseline IOP	1.040	0.996–1.086	0.08

There is little in the literature regarding relative outcomes of GDD surgery in phakic and pseudophakic eyes. El Wardani et al[29] found in a randomized prospective study of 76 eyes that patients undergoing a combined phacoemulsification plus Baerveldt drainage implant, had a significantly higher failure rate (37% vs 15%) and a higher mean IOP (14 vs 12 mm Hg) at 3 years than patients undergoing Baerveldt tube surgery alone. Their conclusion was that combining phacoemulsification with aqueous shunt surgery has a negative effect on shunt bleb survival. However, given the results of our study, it might also possible that the control group, which had pseudophakic eyes and underwent Baerveldt implant alone, may have done better due to their lens status at the time of surgery, compared to the eyes that were phakic and underwent the combined surgery.

Our study has shown that GDD surgery does better in pseudophakic eyes than phakic eyes, which is the reverse of the trabeculectomy outcomes.[15,30] Indeed, on multivariate analysis, phakic/pseudophakic status appeared to be the only significant risk factor with a 95% confidence limit of 1.04 to 6.39 (risk ratio 2.59). To our knowledge, this has not been reported previously in the literature. However, these new data are in fact, somewhat supported by reviewing the 3-year results for the GDD groups in the randomized prospective TVT and PTVT studies.[7,24] Specifically, the TVT study (in which 78% of the study patients were pseudophakic) had, at 2 and 3 years postoperatively, a mean IOP of 13.4 ± 4.8 and 13.0 ± 3.9 mm Hg respectively on a mean of 1.3 glaucoma medications, while the PTVT study (in which all the patients were phakic) had a higher mean IOP of 13.7 ± 4.0 mm Hg on 2.2 medications and 14.0 ± 4.2 on 2.1 medications at 2 and 3years respectively. Thus, although the studies had some different contributing centers, the IOPs were higher at both of these time points in the PTVT study with phakic eyes, and they were on more medication than in the TVT study. Additionally, Kaplan-Meier analysis using the main study criterion for failure (<5 mm Hg to >21 mm Hg or <20% below baseline IOP on 2 consecutive occasions) showed a higher failure rate for the GDD group in the PTVT study than the TVT study (>30% vs 18%). Thus, it is possible that the overall difference in outcome between the 2 studies regarding which procedure did better might be related to improved GDD results in the pseudophakic eyes in the TVT study,

FIGURE 4. Multivariate binary logistic regression results. Using the main Kaplan-Meier failure endpoint of intraocular pressure ≥18 mm Hg or < 6 mm Hg the odds ratio was estimated for 8 potential risk factors. The only significant risk factor (*P* < 0.05) was phakic versus pseudophakic lens status. The blue dots represent the point estimates, and the orange horizontal bars represent the 95% Wald Confidence Limits. Age and intraocular pressure were analyzed as continuous variables.

TABLE 4. Visual Acuity in Eyes in Group I (POAG, PXFG, Pigmentary Glaucoma, and PACG) and Group II (Other Secondary glaucomas) and Phakic vs Pseudophakic Lens Status

	Group I[*] Mean ± SD	Group II[*] Mean ± SD	P value[†]	Phakic Eyes[*] Mean ± SD	Pseudophakic Eyes[*] Mean ± SD	P value[†]
Baseline						
N	108	78		57	116	
VA (LogMAR)	0.67 ± 0.72	1.33 ± 0.98	<0.0001	1.05 ± 1.00	0.81 ± 0.79	0.09
Post-op 1 y						
N	98	59		40	108	
VA (LogMAR)	0.71 ± 0.72	1.04 ± 0.80	0.01	0.77 ± 0.82	0.81 ± 0.73	0.83
Mean change from Baseline VA (LogMAR)	0.06 ± 0.45	−0.22 ± 0.70	0.003	−0.20 ± 0.59	0.04 ± 0.53	0.02
Post-op 2 y						
N	81	43		33	85	
VA (LogMAR)	0.72 ± 0.75	1.04 ± 0.87	0.03	0.87 ± 0.94	0.80 ± 0.71	0.66
Mean change from Baseline VA (LogMAR)	0.10 ± 0.63	−0.26 ± 0.63	0.003	−0.18 ± 0.85	0.05 ± 0.56	0.09
Post-op 3 y						
N	58	30		21	64	
VA (LogMAR)	0.78 ± 0.72	1.03 ± 0.93	0.17	0.98 ± 1.1	0.80 ± 0.70	0.35
Mean change from Baseline VA (LogMAR)	0.18 ± 0.68	−0.05 ± 0.77	0.15	0.12 ± 0.83	0.11 ± 0.67	0.96
Post-op 4 y						
N	35	21		16	38	
VA (LogMAR)	0.88 ± 0.87	0.90 ± 0.95	0.94	0.83 ± 1.05	0.88 ± 0.84	0.97
Mean change from Baseline VA (LogMAR)	0.25 ± 0.60	−0.15 ± 0.94	0.06	0.16 ± 0.97	0.07 ± 0.68	0.70
Post-op 5 y						
N	25	14		8	29	
VA (LogMAR)	1.08 ± 0.98	0.94 ± 0.89	0.66	0.99 ± 1.1	1.01 ± 0.94	0.90
Mean change from Baseline VA (LogMAR)	0.40 ± 0.57	−0.32 ± 0.82	0.003	0.06 ± 1.0	0.20 ± 0.68	0.64

[*]The visual acuity data were censored following any procedure which could improve visual acuity, including penetrating keratoplasty (PKP), Descemet stripping endothelial keratoplasty (DSEK), YAG capsulotomy, cataract extraction, or corneal chelation procedures.

[†]Two-sample *t* test.

PACG indicates primary angle-closure glaucoma; POAG, primary open-angle glaucoma; PXFG, pseudoexfoliation glaucoma; VA, visual acuity.

in addition to the comparatively improved trabeculectomy group results in the phakic eyes of the PTVT study.

A certain proportion of GDD surgeries will fail and this is most frequently due to inadequate IOP control.[7,8,17] In a previous paper on eyes receiving a nonvalved GDD at our institution, we noted that 17% of our study group required an additional procedure.[31] The randomized, prospective combined Ahmed Baerveldt Comparison (ABC)/Ahmed Versus Baerveldt (AVB) study results showed a higher incidence of GDD failure due to elevated IOP in the Ahmed group of 42% vs 23% in the Baerveldt implant group (*P* < 0.001).[17] In our current study, our overall rate of reoperation for elevated IOP was 13%, which is comparable to prior literature. In addition to the lower failure rate on Kaplan-Meier analysis in the pseudophakic eyes compared to the phakic eyes, we also found a lower incidence of reoperation for inadequate IOP control in the pseudophakic group (Table 5).

It is difficult to explain why pseudophakic eyes should exhibit better IOP and a lower reoperation rate than phakic eyes. For many years, our understanding from the outcome of trabeculectomy surgery is that pseudophakic eyes have a greater healing response than phakic eyes.[15,30] It is known, however, that the healing response in GDD surgery can be different from trabeculectomy surgery. It is clearly established that MMC is very effective in reducing fibrosis and providing lower IOPs after trabeculectomy[32–38] but, although there is some discussion, most papers have found that MMC is ineffective in GDD surgery.[39,40] Indeed, a meta-analysis study by Minckler et al[41,42] found level 1 evidence that it was not advantageous. Molteno et al[43,44] have shown that the capsule overlying the episcleral plate of the GDD implant is a dynamic structure with apoptosis

and resorption of capsule on the inner surface of the capsule facing the implant plate and the laying down of new capsule tissue by recruited fibroblasts derived from the bone marrow on the outer external surface of the capsule. Additionally, it has been shown clinically that whereas repeat trabeculectomy gives poorer results due to fibrosis than in eyes undergoing a primary trabeculectomy procedure,[12] in contrast, Bouhenni et al and Dawson et al have found equally good results for IOP control with GDD surgery in eyes with a prior failed trabeculectomy.[14,45] Furthermore, in our current paper, we have noted that eyes with in Group II (other secondary glaucomas) do equally well as eyes in Group I (POAG, PXF, pigmentary glaucoma, and PACG), which again is very different from the results following trabeculectomy.[11]

Limitations of our study include the retrospective nature of the research design, with the natural, more variable patient follow-up schedules, and some loss to follow-up. Although at 5 years only 33% of patients were available to provide data, the retention at 3 years was 58% and at 2 years 77%. For comparison, the prospective TVT study had 68% of patients available at 5 years due to death and drop-out[24] and the PTVT study had a retention rate of 70% at 3 years.[7] Another limitation is that our results may not be generalizable to all patient populations due to the single-site and single-surgeon nature of the study. All the drainage implants used in our study patients were nonvalved, but they were of mixed size and variety, including Molteno and Baerveldt implants. We performed a subanalysis of Baerveldt 350 mm² GDD implants only and found no difference in our results (Supplementary Digital Content, Table 1, http://links.lww.com/APJO/A117), but these were only 55% of the eyes enrolled in this study.

TABLE 5. Complications and Reoperations for Group I (POAG, PXFG, Pigmentary Glaucoma, and PACG) and Group II (Other Secondary Glaucomas) and Phakic vs Pseudophakic Lens Status

Complication	Group I (N = 32/108)	Group II (N = 19/78)	P value*	Phakic (N = 25/57)	Pseudophakic (N = 22/116)	P value*
Early onset: on or before the first postoperative month (30 days)						
Choroidal effusion – requiring viscoelastic to anterior chamber	1 (0.9%)	0 (0%)		0 (0%)	0 (0%)	
Aqueous removal via paracentesis tract	0 (0%)	1 (1.3%)		1 (1.8%)	0 (0%)	
Aqueous misdirection	1 (0.9%)	0 (0%)		0 (0%)	1 (1.6%)	
Total number (%§) of early postoperative complications	2/108 (1.9%)	1/78 (1.3%)	0.75	1/57 (1.8%)	1/116 (0.9%)	0.61
Late onset: after the first postoperative month (30 days)						
Choroidal effusion – requiring viscoelastic to anterior chamber	1 (0.9%)	0 (0%)		0 (0%)	1 (0.9%)	
Aqueous misdirection	3 (2.8%)	0 (0%)		1 (1.7%)	1 (0.9%)	
Tube revision or exposed tube†	2 (1.9%)	4 (5.1%)		2 (3.4%)	2 (1.7%)	
Pars plana vitrectomy†	2 (1.9%)	2 (2.6%)		2 (3.4%)	0 (0%)	
Cataract extraction and IOL implantation‡	6/29‖ (20.7%)	7/28‖ (25%)		-	-	
YAG capsulotomy‡	1/79¶ (1.3%)	2/37¶ (5.4%)		-	-	
Chelation‡	2 (1.9%)	1 (1.3%)		1 (1.7%)	2 (1.7%)	
PKP or DSEK‡	5 (4.6%)	2 (2.6%)		1 (1.77%)	5 (4.3%)	
Endophthalmitis	0 (0%)	1 (1.3%)		1 (1.7%)	0 (0%)	
Total number (%§) of late postoperative complications	22/108 (20%)	19/78 (24%)	0.51	8/57 (14%)	11/116 (9.5%)	0.38
Reoperation						
Additional glaucoma surgery with CPC† YAG or diode	12 (11%)	6 (7.7%)		11 (19%)	5 (4.3%)	
Additional glaucoma surgery with GDD implantation†	4 (3.7%)	2 (2.6%)		2 (3.5%)	3 (2.6%)	
Total number (%§) of reoperations	16/108 (15%)	8/78 (10%)	0.32	13/57 (23%)	8/116 (6.9%)	0.002

*The P value is from the "N-1" chi-square test to compare the total proportions/percentages of early and late onset complications between the 2 groups as independent events. The same test was used to compare the total percentages of additional glaucoma surgeries between the 2 groups.

†Patient IOP, medication, and visual acuity data was censored from visits following a CPC procedure or an additional GDD implantation.

‡Patient visual acuity data was censored from visits following a cataract extraction, YAG capsulotomy, or corneal transplant.

§The percentage of complications was determined by the number of individual complications divided by the total number of patients in either Group I (N = 108) and Group II (N = 78), and phakic lens (N = 57) and pseudophakic lens (N = 116). There were 4 of the 32 Group I patients that had more than 1 complication/reoperation and 7 of the 19 Group II patients with more than 1 complication/reoperation. There were 8 of the 25 phakic lens patients that had more than 1 complication/reoperation and 0 of the 22 pseudophakic lens patients with more than 1 complication/reoperation.

‖This fraction denominator represents the N value for phakic patients in Group I or Group II.

¶This fraction denominator represents the N value for pseudophakic patients in Group I or Group II.

CPC indicates cyclophotocoagulation; DSEK, descemet stripping endothelial keratoplasty; GDD, glaucoma drainage device; IOL, indicates intraocular lens; PACG, primary angle-closure glaucoma; PKP, penetrating keratoplasty; POAG, primary open-angle glaucoma; PXFG, pseudoexfoliation glaucoma; YAG, yttrium-aluminum-garnet.

In conclusion, GDDs, unlike trabeculectomy surgery, seem to perform equally well for patients in both Group I (POAG, PXF, pigmentary glaucoma, and PACG) and Group II (other secondary glaucomas). This is consistent with our previous paper,[14] which showed that prior failed trabeculectomy surgery also did not appear to influence the outcome following subsequent GDD surgery. Our study did, however, determine that GDD surgery outcomes were better regarding IOP control and reoperation rate for inadequate pressure control in pseudophakic eyes rather than phakic eyes.

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