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Five-Year Treatment Outcomes in the Ahmed Baerveldt Comparison Study

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Purpose: To compare the 5-year outcomes of the Ahmed FP7 Glaucoma Valve (AGV) (New World Medical, Cucamonga, CA) and the Baerveldt 101-350 Glaucoma Implant (BGI) (Abbott Medical Optics, Abbott Park, IL) for the treatment of refractory glaucoma.

Design: Multicenter, randomized, controlled clinical trial.

Participants: A total of 276 patients, including 143 in the AGV group and 133 in the BGI group.

Methods: Patients aged 18 to 85 years with previous intraocular surgery or refractory glaucoma and intraocular pressure (IOP) of $\geq$18 mmHg in whom glaucoma drainage implant (GDI) surgery was planned were randomized to implantation of an AGV or a BGI.

Main Outcome Measures: Surgical failure, IOP, visual acuity (VA), use of glaucoma medications, and complications.

Results: At 5 years, IOP (mean $\pm$ standard deviation [SD]) was 14.7$\pm$4.4 mmHg in the AGV group and 12.7$\pm$4.5 mmHg in the BGI group ($P = 0.015$). The number of glaucoma medications in use at 5 years (mean $\pm$ SD) was 2.2$\pm$1.4 in the AGV group and 1.8$\pm$1.5 in the BGI group ($P = 0.28$). The cumulative probability of failure during 5 years of follow-up was 44.7% in the AGV group and 39.4% in the BGI group ($P = 0.65$). The number of subjects failing because of inadequately controlled IOP or reoperation for glaucoma was 46 in the AGV group (80% of AGV failures) and 25 in the BGI group (53% of BGI failures; $P = 0.003$). Eleven eyes in the AGV group (20% of AGV failures) experienced persistent hypotony, explantation of implant, or loss of light perception compared with 22 eyes (47% of failures) in the BGI group. Change in logarithm of the minimum angle of resolution VA (mean $\pm$ SD) at 5 years was 0.42$\pm$0.99 in the AGV group and 0.43$\pm$0.84 in the BGI group ($P = 0.97$).

Conclusions: Similar rates of surgical success were observed with both implants at 5 years. The BGI produced greater IOP reduction and a lower rate of glaucoma reoperation than the AGV, but the BGI was associated with twice as many failures because of safety issues. *Ophthalmology 2014;■:1–9 © 2014 by the American Academy of Ophthalmology.*

*Supplementary material is available at www.aaojournal.org.

Glaucoma drainage implants (GDIs) have been used with increasing frequency in the management of glaucoma refractory to trabeculectomy, even in the era of antifibrotic agent use. Medicare data reveal a marked increase in the use of GDIs, from approximately 2000 in 1994 to approximately 12 000 in 2012 (Rich W III, personal communication, 2014). In addition, surveys of the membership of the American Glaucoma Society performed in 1996, 2002, and 2008 show a significant increase in the use of GDIs in patients who had undergone prior surgery or who had neovascular or uveitic glaucoma compared with trabeculectomy with mitomycin-C.[1–3] This shift in practice pattern has been validated by the results of the Tube Versus Trabeculectomy (TVT) Study,[4] which found that patients with prior trabeculectomy or cataract surgery had a higher success rate with GDI surgery compared with trabeculectomy with mitomycin-C.

Glaucoma drainage implants share a common design consisting of a tube that is inserted into the eye through a scleral fistula, which shunts aqueous humor to an end plate placed in the equatorial region. They differ with respect to the size and material composition of the end plate, as well as the presence or absence of a valve that restricts aqueous flow if the intraocular pressure (IOP) becomes too low. A limited number of studies comparing different implant designs exist, and most of these are retrospective case series.[5] A recent Ophthalmic Technology Assessment of GDIs performed by the American Academy of Ophthalmology's Technology Assessment Committee concluded that "Too few high-quality direct comparisons of various available shunts have been published to assess the relative efficacy or complication rates of specific devices…."[6] The Ahmed Baerveldt Comparison (ABC) and Ahmed Versus Baerveldt (AVB) studies were initiated to compare the safety and efficacy of the Ahmed FP7 glaucoma valve (AGV) (New World

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Medical, Cucamonga, CA) and the Baerveldt 101-350 glaucoma implant (BGI) (Abbott Medical Optics, Abbott Park, IL), the 2 most commonly used GDIs in the United States. These randomized prospective clinical trials have shown similar results through 3 years of follow-up.[7,8] Specifically, both studies showed a small difference in IOP (1.2−1.3 mmHg lower in the BGI group) on slightly fewer medications (0.5−0.7 in the BGI group), with more subjects failing because of elevated fewer IOP in the AGV group. The purpose of this study is to report the 5-year treatment outcomes in the ABC Study.

Methods

The institutional review board at each of 16 clinical centers approved the study protocol before recruitment was started, and each patient gave informed consent. The study was registered at www.clinicaltrials.gov (NCT00376363; accessed February 16, 2014). The design and methods of the ABC Study are described in detail in a baseline methodology article[9] and are summarized in the following sections.

Randomization and Treatment

Patients aged 18 to 85 years with refractory glaucoma and IOPs ≥18 mmHg in whom GDI surgery was planned were enrolled in the study. Patients with primary glaucomas with a previous failed trabeculectomy or other intraocular surgery were included. Also, patients without previous intraocular surgery were eligible if they had secondary glaucomas known to have a higher risk of trabeculectomy failure, such as neovascular glaucoma (NVG), uveitic glaucoma, or glaucoma associated with iridocorneal endothelial syndrome. Exclusion criteria included no light perception (NLP) at baseline, uveitic glaucoma secondary to juvenile rheumatoid arthritis, prior GDI or cyclodestructive procedure, need for concurrent or anticipated (within 6 months) nonglaucoma surgery (cataract, corneal, vitreoretinal), superotemporal scleral buckle, or retinal sponge precluding superotemporal placement of an implant), or inability to provide informed consent.

Eligibility was independently confirmed at the Statistical Coordinating Center at the Bascom Palmer Eye Institute. Individuals enrolled in the study were randomized to placement of an AGV or BGI according to a permuted variable block randomization scheme, stratified by surgeon within Clinical Center and type of glaucoma. Patients were allocated to 1 of 4 strata according to their type of glaucoma, as follows: (1) primary glaucomas with previous intraocular surgery; (2) high-risk secondary glaucomas (excluding uveitic glaucoma and NVG); (3) NVG; and (4) uveitic glaucoma. Neither the subject nor the investigator was masked to the randomization assignment. Only 1 eye of each patient was eligible for enrollment. Details of the inclusion and exclusion criteria, recruitment method, and surgical procedures for implantation of the AGV and BGI used in this study are described in the baseline article.[9]

Patient Visits

Follow-up visits were scheduled 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, 18 months, 2 years, 3 years, 4 years, and 5 years postoperatively. Information about data obtained at baseline and follow-up visits is contained in the baseline article.[9]

Primary and Secondary Outcome Measures

The primary outcome measure was failure, based on consensus definitions contained in the World Glaucoma Association Guidelines on Design and Reporting of Surgical Trials.[10] These criteria for failure were defined prospectively as IOP >21 mmHg or less than a 20% reduction below baseline on 2 consecutive study visits after 3 months, IOP ≤5 mmHg on 2 consecutive study visits after 3 months, reoperation for glaucoma, loss of light perception, or removal of the implant for any reason. Reoperation for glaucoma was defined as additional glaucoma surgery requiring a return to the operating room. Cyclodestruction was counted as a reoperation for glaucoma, irrespective of whether the procedure was performed in the operating room. Interventions performed at the slit lamp, such as needling procedures, removal of occluding stents, or laser suture lysis, were not considered glaucoma reoperations. The IOP, use of glaucoma medications, visual acuity (VA), visual fields, and rates of surgical complications were secondary outcome measures in the ABC Study. Eyes that had not failed by the these criteria and were not receiving glaucoma medical therapy were considered complete successes, and those requiring adjunctive medical therapy were defined as qualified successes.

Statistical Analysis

Snellen VA measurements were converted to logarithm of the minimum angle of resolution (logMAR) VA equivalents for the purpose of data analysis, as reported previously.[11] The time to failure was defined as the time from GDI placement to reoperation for glaucoma, loss of acuity to NLP in the study eye, or the first of 2 consecutive follow-up visits after 3 months in which the patient had persistent hypotony (IOP ≤5 mmHg) or inadequately controlled IOP (IOP >21 mmHg or not reduced by 20%). Data on IOP and numbers of glaucoma medications were censored once a patient underwent a reoperation for glaucoma, explantation of the implant, or loss of light perception, but not after failure due to high IOP, hypotony, or reoperation for a complication. There was no censoring of VA results. Univariate comparisons between treatment groups were performed with the 2-sided Student t test for continuous variables and the chi-square test or Fisher exact test for categoric variables. Risk factors for treatment failure were assessed for statistical significance with the Kaplan−Meier survival analysis log-rank test. Multivariate analysis was performed with Cox proportional hazard regression analysis with forward stepwise elimination. Patients' data were analyzed in the group to which they were assigned during randomization (intent-to-treat analysis). A P value of 0.05 or less was considered statistically significant in our analyses.

Results

Recruitment and Retention

A total of 276 patients were enrolled between October 2006 and April 2008, including 143 patients (52%) who were randomized to placement of an AGV and 133 patients (48%) who were randomized to placement of a BGI. Protocol violations are described in the baseline article.[9]

The retention of patients in the study through 5 years of follow-up is shown in Figure 1. In the overall study group, 174 patients (63%) completed their 5-year visit. This included 87 patients (61%) in the AGV group and 87 patients (65%) in the BGI group. We compared the numbers of patients who did not complete a 5-year visit (n = 81) by treatment group, excluding from analysis those who had died before the end of the 5-year visit window (n = 21). No significant difference was observed in the proportion of patients

who did not complete 5-year visits in the AGV group (n = 44 [34%]) and the BGI group (n = 37 [30%]) ($P = 0.59$, Fisher exact test). There was no difference between randomized treatment groups in mean IOP or mean numbers of IOP-lowering medicines between those followed until the next annual visit and those lost to follow-up (all $P > 0.2$, 2-way analysis of variance with test of interaction between treatment group and loss to follow-up during the next year).

Baseline Characteristics

There were no differences in baseline demographic or clinical characteristics between the 2 groups, as detailed in the baseline article.[9]

Intraocular Pressure Reduction

The baseline and follow-up IOPs for the 2 groups are reported in Table 1 and Figure 2. Patients who underwent additional glaucoma surgery, removal of the implant, or loss of light perception were censored from analysis after these events. Both study groups experienced a significant postoperative reduction in IOP. Among patients with 5-year follow-up in the AGV group, IOP (mean ± standard deviation [SD]) was reduced from 29.6±10.1 mmHg at baseline to 14.7±4.4 mmHg at the 5-year follow-up visit ($P < 0.001$, paired t test). In the BGI group, IOP (mean ± SD) was reduced from 28.3±9.3 mmHg at baseline to 12.7±4.5 mmHg at the 5-year follow-up visit ($P < 0.001$, paired t test). The IOP difference between the 2 treatment arms at 5 years was statistically significant ($P = 0.015$) using analysis of covariance, which takes into account baseline IOP differences. The AGV group had a significantly lower mean IOP than the BGI group at the 1-day and 1-week follow-up visits. However, the mean IOP in the BGI group was approximately 1 to 2 mmHg lower than in the AGV group thereafter, except at the 2-year visit. The 1.3-mmHg difference in baseline IOP between patients in the AGV and BGI groups who returned for 5-year follow-up was not statistically significant ($P = 0.37$). Furthermore, accounting for preoperative IOP with analysis of covariance did not alter the statistical significance of any of the comparisons of postoperative IOPs between the AGV and BGI groups. Mean IOP in the AGV and BGI groups did not vary significantly among the 4 study strata at any of the annual follow-up visits (all $P > 0.2$, 2-way analysis of variance with test of interaction).

Medical Therapy

Table 1 also shows the number of glaucoma medications in both groups at baseline and follow-up. Patients who underwent glaucoma reoperation, removal of the implant, or loss of light perception were censored from analysis. There was a significant reduction in the need for medical therapy in both treatment groups (Fig 3). The number of glaucoma medications (mean ± SD) in the AGV group decreased from 3.5±1.0 at baseline to 2.2±1.4 at the

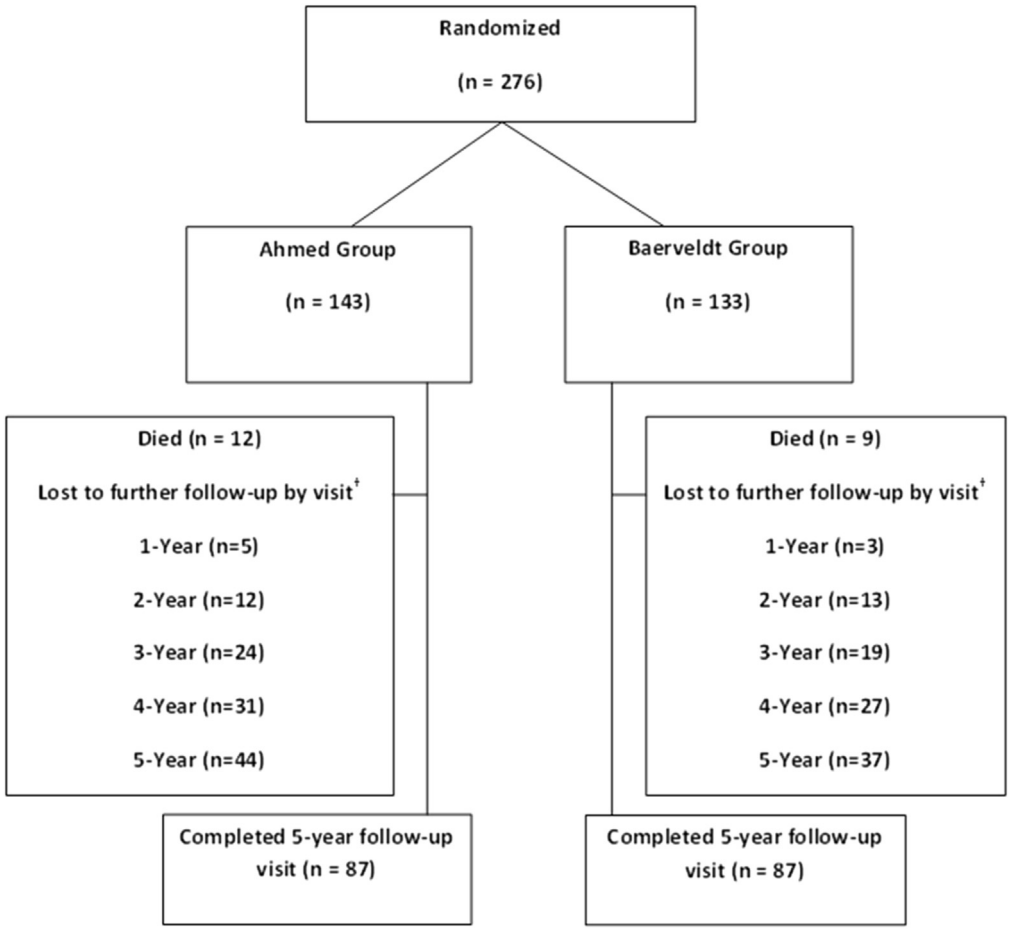

Figure 1. Recruitment and retention in the Ahmed Baerveldt Comparison Study at 5 years.

5-year follow-up visit ($P < 0.001$, paired t test). The number of glaucoma medications (mean ± SD) in the BGI group was reduced from 3.5±1.1 at baseline to 1.8±1.5 at the 5-year follow-up visit ($P < 0.001$, paired t test). Patients in the AGV group were using significantly more medications at years 2 to 4 compared with the BGI group. There was no statistical difference between treatment groups with regard to the number of medications in use at 5 years or the reduction in medications from baseline to 5 years. Mean number of medications in the AGV and BGI groups did not vary significantly among the 4 study strata at any of the annual follow-up visits (all $P > 0.2$, 2-way analysis of variance with test of interaction).

Treatment Outcomes

Table 2 compares the outcomes and reasons for failure of randomized patients, unadjusted for follow-up time. All patients who were seen at the 5-year follow-up visit or failed during the first 5 years of the study were included in this analysis. Although the total numbers of failures were similar in the 2 groups, the reasons for treatment failure were different between the AGV and BGI groups ($P = 0.012$, exact chi-square test). The number failing because of inadequately controlled IOP or reoperation for glaucoma was 46 in the AGV group (representing 80% of AGV failures) compared with 25 in the BGI group (53% of BGI failures), a statistically significant difference ($P = 0.003$). Only 11 AGV eyes (20% of AGV failures) experienced persistent hypotony, complications for which explantation was performed, or loss of light perception in the study eye compared with 22 (47% of failures) in the BGI group.

Table 1. Intraocular Pressure and Medical Therapy at Baseline and Follow-up in the Ahmed Baerveldt Comparison Study

	Ahmed Group	Baerveldt Group	P Value*
Baseline			
IOP (mmHg)	31.2±11.2	31.8±12.5	0.71
Glaucoma medications	3.4±1.1	3.5±1.1	0.34
No.	143	133	
1 yr			
IOP (mmHg)	15.4±5.5	13.4±6.9	0.018
Glaucoma medications	1.8±1.3	1.5±1.4	0.078
No. followed (% of baseline)	133 (93)	117 (88)	
2 yrs			
IOP (mmHg)	14.5±5.5	14.2±6.0	0.76
Glaucoma medications	1.9±1.3	1.4±1.5	0.020
No. followed (% of baseline)	122 (85)	110 (83)	
3 yrs			
IOP (mmHg)	14.4±4.7	13.1±4.5	0.078
Glaucoma medications	2.0±1.4	1.5±1.4	0.018
No. followed (% of baseline)	106 (74)	100 (75)	
4 yrs			
IOP (mmHg)	15.5±6.2	13.4±4.4	0.017
Glaucoma medications	2.2±1.7	1.7±1.4	0.025
N followed (% of baseline)	102 (74)	99 (74)	
5 yrs			
IOP (mmHg)	14.7±4.4	12.7±4.5	0.015
Glaucoma medications	2.2±1.4	1.8±1.5	0.28
No. followed (% of baseline)	87 (61)	87 (65)	

IOP = intraocular pressure.
Data are presented as mean ± SD unless otherwise indicated. The IOP and number of medications are censored after treatment failure by no light perception, reoperation for glaucoma, or explantation for complication.
*Student t test.

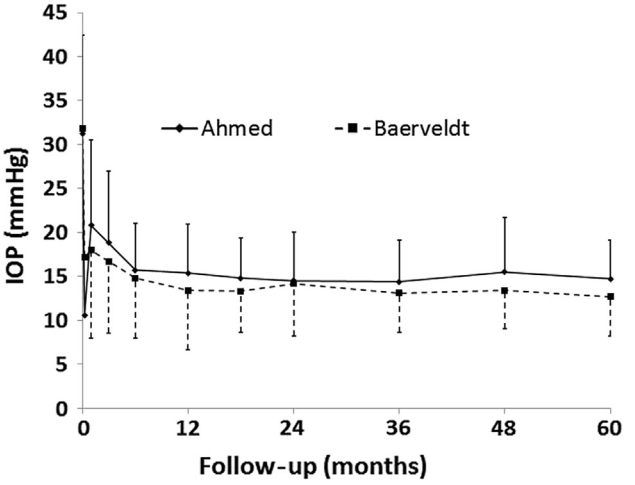

Figure 2. Graph of intraocular pressure (IOP) (mmHg) in the Ahmed Baerveldt Comparison Study by study group from preoperative level to 5-year follow-up visit (mean ± standard deviation).

Kaplan–Meier survival analysis was used to compare failure rates between the 2 treatment groups (Fig 4). The cumulative probability of failure (standard error [SE]) was 44.7% (4.6%) in the AGV group and 39.4% (4.6%) in the BGI group at 5 years ($P = 0.65$, log-rank test). The relative risk of treatment failure in the AGV group was 1.1 times that in the BGI group (95% confidence interval, 0.8–1.7; $P = 0.52$ Cox proportional hazards regression). There was no suggestion of different treatment effects in the 4 randomized strata ($P = 0.52$, 3 degrees of freedom test of treatment group by stratum interaction). To investigate the timing of failures over follow-up, we calculated annual hazard rates during each of the 5 study years. The hazard rate (SE) of failure was highest in the first 2 years of follow-up, 1.5% (0.02%) and 1.3% (0.2%), respectively, and decreased in years 3 and 4 to 0.5% (0.2%) and 0.4% (0.8%), respectively, with a modest increase in the last year

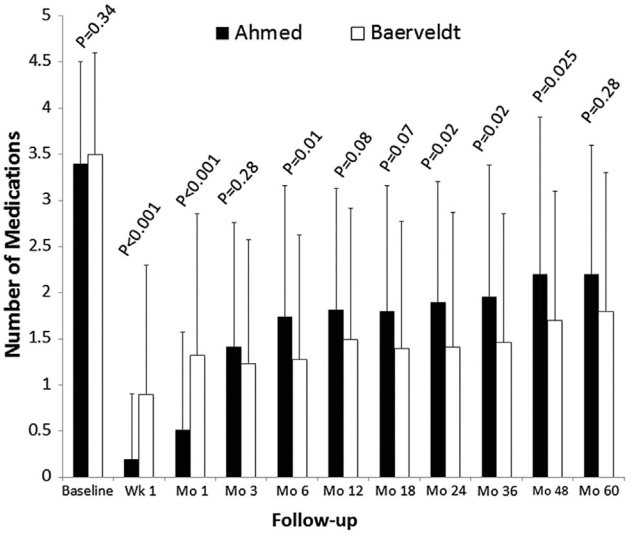

Figure 3. Histogram of the number of classes of ocular hypotensive medication used from before surgery to 5-year follow-up visit (mean ± standard devitation). mo = months.

Table 2. Reasons for Treatment Failure in the Ahmed Baerveldt Comparison Study

	Ahmed Group	Baerveldt Group
Inadequate IOP control without additional glaucoma surgery*	23 (40%)	17 (36%)
Reoperation to decrease IOP	23 (40%)	8 (17%)
Explantation for complication	3 (5%)	4 (8%)
Persistent hypotony†	1 (2%)	6 (13%)
Loss of light perception	7 (12%)	12 (26%)
Total	57	47

IOP = intraocular pressure.
Data are presented as number (percentage of the total number) of failures in each respective treatment group). There was a statistically significant difference in the distribution of types of failures between the Ahmed FP7 glaucoma valve and Baerveldt 101-350 glaucoma implant ($P = 0.012$, exact chi-square test).
*IOP >21 mmHg at 2 consecutive visits after 3 months.
†IOP ≤5 mmHg at 2 consecutive visits after 3 months.

of the study (0.8% [0.2%]). There was no difference in the pattern of hazard rates over time between the study strata.

The cumulative proportion of patients undergoing reoperation for glaucoma during 5 years of follow-up was 20.8% in the AGV group compared with 8.6% in the BGI group ($P = 0.010$, log-rank test; Fig 5). The relative risk of reoperation for glaucoma in the AGV group was 2.6 times that of the BGI group (95% confidence interval, 1.2–5.3; $P = 0.012$, Cox proportional hazards regression). Table 3 presents the specific reoperations for glaucoma performed in the 2 treatment groups.

The failure rates for the AGV and BGI treatment groups were examined using alternative outcome criteria. Patients with persistent hypotony, reoperation for glaucoma, or loss of light perception were still classified as treatment failures; however, the upper IOP limit defining success and failure was changed. When inadequate IOP control (with or without medications) was defined as IOP greater than 17 mmHg or not reduced by 20% on 2 consecutive follow-up visits after 3 months, the cumulative probability of failure at 5 years (SE) was 60.4% (4.5%) in the AGV group and 46.1% (4.7%) in the BGI group ($P = 0.048$, stratified log-rank test). When inadequate IOP control was defined as IOP greater than 14 mmHg or not reduced by 20% on 2 consecutive follow-up visits after 3 months, the cumulative probability of failure was 77.6% (3.9%) in the AGV group and 64.4% (4.5%) in the BGI group at 5 years ($P = 0.003$, stratified log-rank test).

Patients with a 5-year follow up visit who were still successful through that visit were divided into complete and qualified success on the basis of the requirement for IOP-lowering medical therapy at 5 years. The number of complete successes at 5 years was 9 (8%) in the AGV group compared with 14 (14%) in the BGI group ($P = 0.27$; Table 4). Table 4 also reviews in detail the percentage of treatment failures and complete and qualified success in the 2 arms of the study by stratum. The study was not adequately powered to reach conclusions about the differences between treatment arms in

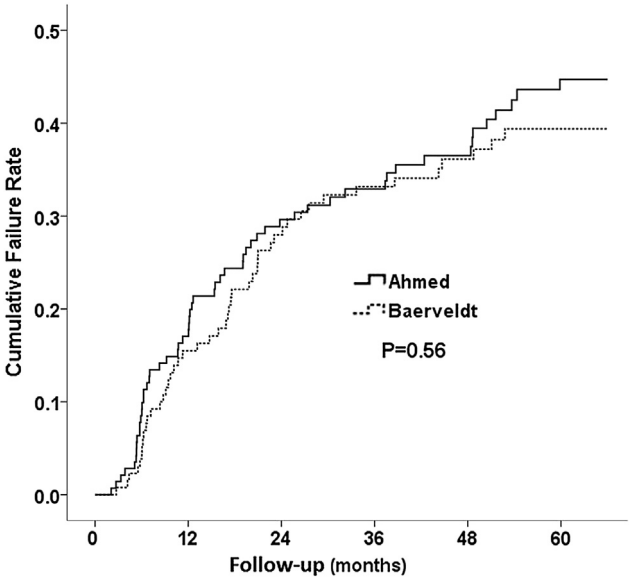

Figure 4. Kaplan–Meier survival curve of cumulative surgical failures through 5 years of follow-up by treatment group.

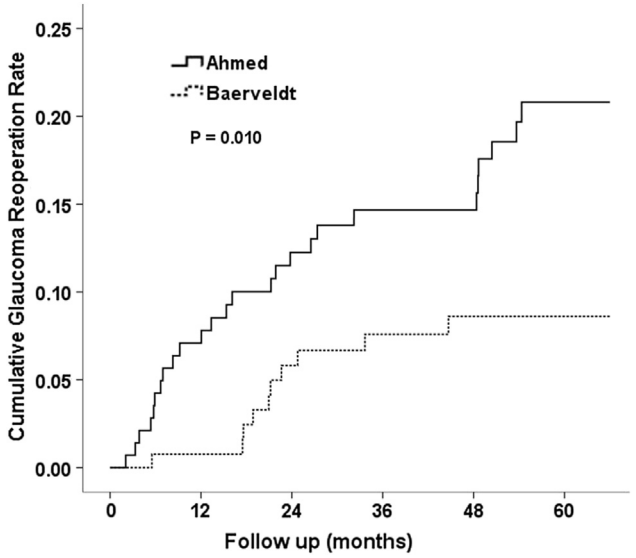

Figure 5. Kaplan–Meier survival curve of cumulative reoperation rates through 5 years of follow-up by treatment group.

Table 3. Reoperations for Glaucoma in the Ahmed Versus Baerveldt Study

	Ahmed Group (n = 143)	Baerveldt Group (n = 133)
Additional tube shunt	13	8
Cyclodestructive procedure	12	2
Tube revision followed by cyclodestructive procedure	1	0
Total no. of patients (5-yr cumulative Kaplan–Meier percentage ± SE) with reoperation for glaucoma*	26 (20.8±3.7%)	10 (8.6±2.6%)

SE = standard error.
Data are presented as number of patients unless otherwise indicated.
*$P = 0.010$ for the difference in 5-year cumulative reoperation rates for glaucoma between treatment groups from Kaplan–Meier analysis (log-rank test adjusted for stratum).

Table 4. Treatment Outcomes After 5 Years of Follow-up in the Ahmed Versus Baerveldt Comparison Study

	Ahmed Group	Baerveldt Group
Stratum 1—primary glaucomas with previous intraocular surgery		
Failure	26 (47)	18 (35)
Qualified success	25 (46)	23 (44)
Complete success	4 (7)	11 (21)
Stratum 2—secondary glaucomas (excluding neovascular and uveitic glaucomas)		
Failure	7 (50)	7 (58)
Qualified success	5 (36)	4 (33)
Complete success	2 (14)	1 (8)
Stratum 3—NVG		
Failure	19 (66)	20 (71)
Qualified success	9 (31)	6 (21)
Complete success	1 (3)	2 (7)
Stratum 4—uveitic glaucoma		
Failure	5 (56)	2 (33)
Qualified success	2 (22)	4 (67)
Complete success	2 (22)	0 (0)
Overall group		
Failure	57 (53)	47 (48)
Qualified success	41 (38)	37 (38)
Complete success*	9 (8)	14 (14)

NVG = neovascular glaucoma.
Data presented as number of patients (percentage).
*$P = 0.27$ for the difference in complete success rates between treatment groups (binomial logistic regression model including both randomized treatment group and stratum as independent variables).

these subgroups. That being said, there does not seem to be much difference in outcomes within the diagnostic strata.

Because the surgeon was not masked to the treatment assignment, a potential bias in the decision to reoperate for IOP control existed. To evaluate for reoperation bias, the IOP levels were compared between treatment groups among patients who failed because of inadequate IOP control. For cases failing by high IOP at 2 consecutive study visits without reoperation, the average of the failing IOPs was calculated and compared between the 2 treatment groups. The failing IOP (mean ± SD) in the AGV group was 20.0±4.4 mmHg compared with 23.0±6.4 mmHg in the BGI group ($P = 0.089$, 2-sample t test). The IOP immediately before glaucoma reoperation was also compared between treatment groups. Among AGV cases reoperated for glaucoma, the preoperative IOP (mean ± SD) immediately before reoperation was 28.9±9.0 mmHg compared with 29.4±6.3 mmHg in the BGI group ($P = 0.90$).

Visual Acuity

Visual acuity results are shown in Table 5. There was a significant decrease in Snellen VA in both treatment groups during the 5 years of follow-up. In the AGV group, logMAR Snellen VA (mean ± SD) decreased from 1.07±1.01 at baseline to 1.42±1.15 at the 5-year follow-up visit ($P < 0.001$, paired t test). In the BGI group, logMAR Snellen VA (mean ± SD) decreased from 1.04±1.00 at baseline to 1.43±1.40 at the 5-year follow-up visit ($P < 0.001$, paired t test). There was no significant difference in logMAR Snellen VA between the 2 groups at 5 years ($P = 0.97$, Student t test).

Table 5. Visual Acuity Results in the Ahmed Baerveldt Comparison Study

	Ahmed Group (n = 86)	Baerveldt Group (n = 87)	P Value†
Snellen VA, logMAR mean ± SD			
Baseline (n = 276)	1.07±1.01	1.04±1.00	0.80
5 yrs (n = 174)	1.42±1.15	1.43±1.40	0.94
Change at 5 yrs (n = 174)	0.42±0.99	0.43±0.84	0.97
Loss of ≥2 Snellen lines at 5 yrs, n (%)*	36 (42)	38 (44)	0.88‡
Glaucoma	14 (39)	17 (45)	
Retinal disease	10 (28)	5 (13)	
Corneal opacity, edema, graft failure	3 (8)	10 (26)	
Cataract	3 (8)	3 (8)	
Other§	1 (3)	5 (13)	
Unknown	5 (14)	2 (5)	

logMAR = logarithm of the minimum angle of resolution; SD = standard deviation; VA = visual acuity.
*Patients may have >1 reason for decreased vision.
†Two-sided Student t test.
‡Fisher exact test.
§Other reasons for vision loss included phthisis bulbi (n = 3), posterior capsule opacification (n = 2), and inability to perform acuity test (Alzheimer's disease, n = 1).

Snellen VA was decreased by 2 or more lines from baseline in 36 patients (42%) in the AGV group and 38 patients (44%) in the BGI group at 5 years, and this difference was not significantly different ($P = 0.88$, Fisher exact test) (Table 5). The most frequent causes of vision loss during 5 years of follow-up were glaucoma, retinal disease, and anterior segment pathology. The reason for decreased vision was unknown in 5 patients (14%) in the AGV group and 2 patients (5%) in the BGI group. The other miscellaneous cause for reduced vision in the AGV group was Alzheimer's disease in 1 patient who did not perform the acuity test well. Other causes of vision loss in 5 patients in the BGI group included phthisis bulbi and posterior capsular opacification. There were no significant differences in the reasons for VA loss between the 2 treatment groups. Of 161 patients with visual acuities measured at both the 3- and 5-year visits, 32 (20%) lost 2 or more Snellen lines of acuity between their 3- and 5-year visits. Reasons for acuity loss were glaucoma alone or in combination with another cause in 14 patients (44%), retinal disease in the absence of glaucoma in 7 patients (22%), corneal disease in 5 patients (16%), and cataract alone in 1 patient (3%); in 4 patients (13%) the reason was not recorded.

Twenty-five patients (9%) progressed to NLP vision, 6 of whom had previously failed by one of the other criteria, and all but 1 of these (96%) were in the NVG stratum. We compared the incidence of NLP between randomized treatment groups among the 80 patients with NVG. At 5 years, the cumulative proportion of patients with NVG who progressed to NLP in the AGV group was 28.3% (SE, 8.9%) compared with 51.1% (SE, 9.2%) in the BGI group, a difference that was statistically significant ($P = 0.030$, log-rank test). In the judgment of the surgeons, neovascular eyes that lost light perception in the AGV group did so for the following reasons: glaucoma (n = 4), progressive diabetic retinopathy (n = 3), and no reason provided (n = 1). In the BGI group, the reasons included macular disease (n = 2), phthisis bulbi (n = 3, n = 1 after retinal detachment), vitreous hemorrhage/hyphema (n = 1), glaucoma (n = 2), enucleation of painful eye (n = 1),

undetermined because of anterior segment pathology (n = 1), progressive diabetic retinopathy (n = 1), ischemia (n = 1), and no reason provided (n = 4).

Discussion

The ABC Study is a multicenter prospective clinical trial comparing the 2 most popular GDIs. Patients with previous intraocular surgery or refractory glaucoma were enrolled in the study and randomly assigned to surgical treatment with the AGV or BGI. The BGI was more effective in providing long-term IOP control than the AGV implantation. The BGI produced greater IOP reduction with fewer adjunctive medications and required fewer glaucoma reoperations compared with the AGV during 5 years of follow-up.

We recognize that the goal of glaucoma therapy is the prevention of further glaucomatous optic nerve damage and visual field loss with preservation of visual function. The degree of IOP reduction is a surrogate for successful glaucoma therapy, primarily because IOP is easily measurable and the only known treatable risk factor for glaucoma progression. As such, it serves as an important measure of surgical success. Both the AGV and BGI produced profound reductions in IOP, from baseline averages of 31 to 32 mmHg to final average IOPs of 14.7 mmHg in the AGV group and 12.7 mmHg in the BGI group. The total IOP reduction was greater than 50% in both treatment groups, which is comparable to previous studies of GDIs.[5] The BGI group had a mean IOP approximately 2 mmHg lower than the AGV group at most of the annual study visits, including at 5 years, and this represents a statistically significant difference. The lower IOPs in the BGI group were achieved with fewer glaucoma medications compared with the AGV group at most time intervals.

There are 2 reasons that may be offered to explain the superior IOP control observed with the BGI relative to the AGV. First, studies have shown that glaucoma drainage devices with larger end plates result in lower IOPs.[5] Heuer et al[12] found higher success rates and lower long-term IOPs using the double-plate compared with the single-plate Molteno implant (IOP Ophthalmics, Costa Mesa, CA). However, there may be an upper limit of benefit of end plate size; Britt et al[13] subsequently noted similar outcomes when comparing the Baerveldt 500 mm^2 implant with the 350 mm^2 implant in a prospective clinical trial. A recent retrospective study by Seah et al[14] comparing the Baerveldt 250 mm^2 with the 350 mm^2 implant found no difference in final IOP between the 2 implant sizes. A prospective randomized trial comparing these 2 end plate sizes is underway (clinicaltrials.gov, NCT01159314, registered July 8, 2010). The second possible explanation for lower long-term IOPs with the BGI relates to exposure of the filtering bleb to postoperative inflammatory material. In the valved AGV, there is immediate flow of aqueous to the bleb, exposing it to inflammatory cells, cytokines, and proteins resulting from the surgery, which may produce more vigorous scarring of the fibrous capsule surrounding the end plate.[5,15] In the nonvalved BGI, complete occlusion of the tube for the first 4 to 6 weeks is critical to prevent early hypotony and hypotony-related complications, such as flat anterior chambers, choroidal effusions, and suprachoroidal hemorrhages.[16] By occluding the BGI for a period of several weeks, the bleb is exposed to less inflammatory material. Whatever the explanation, the larger, nonvalved BGI tends to produce better long-term IOP control, which may make it the preferred implant in patients in whom one is trying to achieve the lowest possible IOP postoperatively.

The primary outcome in the ABC Study was cumulative failure rate at 5 years. Approximately 40% of subjects in both groups failed by criteria defined a priori, based on failure criteria recommended by a consensus group of the World Glaucoma Association.[10] It is interesting to note that the 2 treatment groups failed at approximately the same rate, but they did so for different reasons. The AGV group failed because of high IOP end points, whereas the BGI group failed because of safety end points. Higher IOPs in the AGV group resulting in failure or reoperation for glaucoma may be related to the smaller end plate or immediate release of inflammatory factors to the sub-Tenon's space, as discussed above. The higher rate of hypotony in the BGI group is likely related to the larger size of the end plate and the lack of a flow restrictor, the same design features that resulted in fewer failures because of lack of IOP control. A higher rate of surgical success was seen with the BGI compared with the AGV in post hoc analyses when IOP failure was stringently defined as IOP greater than 14 mmHg.

Only 8% of subjects who received the AGV and 14% of those who received the BGI had controlled IOP without medications at 5 years (complete success). In the TVT Study, the tube (BGI) group had a complete success rate of 25%, but the subjects in the TVT Study were at lower risk of surgical failure than in the current study because the TVT Study excluded patients with secondary glaucomas, such as iridocorneal endothelial syndrome, uveitis, and NVG. Table 4 shows the complete success rate by stratum in the ABC Study at 5 years. In stratum 1, which is identical to the subjects addressed by the TVT Study, the complete success rate in the BGI group is 21%, similar to the 25% complete success rate in the TVT BGI group.

The rate of reoperation for glaucoma was higher in the AGV group relative to the BGI group. Patients who required additional glaucoma surgery underwent placement of a second GDI or cyclodestruction in both treatment groups. Because investigators were not masked to the treatment assignment and the decision to reoperate was left to the surgeon's discretion, a potential for bias existed in the decision to reoperate for glaucoma. No significant difference in mean IOP at the time of failure was seen between treatment groups in patients who had a reoperation for glaucoma or in patients who failed because of inadequate IOP reduction but did not have additional glaucoma surgery. These observations suggest that no selection bias was present for glaucoma reoperation.

Visual acuity decreased in both treatment groups during the 5 years of follow-up. Approximately 43% of subjects lost 2 or more lines of Snellen VA. Snellen acuity was the same in the treatment groups at year 5, and no significant differences in the rates and reasons for vision loss were present in the AGV and BGI groups. Many of the causes of

vision loss, such as progression of diabetic retinopathy or age-related macular degeneration, were not directly attributable to the surgical procedures being studied. Compared with the 3-year study results,[7] there were no additional subjects in the AGV group who lost 2 or more lines of vision, but there were 8 additional subjects in the BGI group who lost 2 or more lines of vision. The proportion of subjects who lost 2 or more lines of vision in the current study and the magnitude of vision lost between the preoperative and 5-year visit were similar to those seen in the 5-year results of the TVT Study.[4]

Several retrospective case series have compared the AGV and BGI.[17–21] Unfortunately, the surgeon's GDI selection in these studies may have been influenced by the patient's presumed risk of failure and could bias the results. Randomized clinical trials are designed to produce comparison groups that differ only by the treatment provided, and they offer the highest level of evidence-based medicine. The AVB Study is another multicenter, randomized, prospective clinical trial comparing the safety and efficacy of the AGV and BGI. Both the ABC and AVB Studies observed significantly greater long-term IOP reduction and less need for glaucoma medical therapy with the BGI compared with the AGV, with similar success rates after 3 years of follow-up. The similarity in results between these clinical trials has allowed each study to validate the other.

There are several limitations to the ABC Study. Neither the patient nor the surgeon was masked to the implant used. The study evaluated only the AGV and BGI, and the results cannot be extrapolated to other GDIs or different models of the AVG or BGI. Patients were excluded if other ocular procedures were required in conjunction with glaucoma surgery, so the study does not provide information about the preferred implant when concurrent ocular surgery is needed. Although aspects of both surgical procedures were standardized, some variation in surgical technique occurred between surgeons. We thought that it was important to provide latitude for the surgeon to perform the procedures being studied in a manner in which he/she was proficient. Also, the results apply only to the diagnostic groups included in the study. Specifically, these results cannot be generalized to patients without prior incisional surgery who are lowrisk for failure of standard surgery (e.g., trabeculectomy).

The ABC Study does not demonstrate clear superiority of one implant over the other. In addition to efficacy and safety data, there are other important considerations. The individual patient characteristics and surgeon's comfort and experience with each implant are critical in device selection. The benefits of each implant in reducing IOP must be interpreted in light of its surgical complications (manuscript forthcoming). The valve mechanism of the AGV allows the implant to function immediately postoperatively, and this may be particularly advantageous in patients with markedly elevated IOP preoperatively. For instance, patients with NVG with completely closed anterior chamber angles typically have markedly elevated IOP that is unresponsive to medical therapy and need immediate IOP lowering; one would prefer a valved implant in this instance because one would not want to wait the typical 5 to 7 weeks for a suture ligature to dissolve in an nonvalved implant such as the BGI. In addition, patients with NVG typically do not have significant glaucomatous cupping at presentation because their IOP has been elevated for a relatively short period of time. For these reasons, perhaps one would prefer the smaller-plated valved AGV implant and be willing to sacrifice the modestly lower average IOP achievable with the larger, nonvalved BGI. The AGV also may be preferred in patients at greater risk for postoperative hypotony, such as those with uveitic glaucoma or prior cyclodestruction. In these patients, decreased aqueous humor production may induce hypotony if there is excess outflow in a large nonvalved implant such as the BGI. In either group of patients, NVG or inflammatory glaucomas, if the IOP is too high in the longterm, a larger, nonvalved implant usually can be placed in a second quadrant. However, these clinical suggestions should be backed up with future properly powered randomized clinical trials because the current study did not have enough subjects in these subgroups to come to definitive conclusions on which implant is best used in which subgroup.

It is interesting to compare the results of the ABC Study at 3 and 5 years. From zero to 3 years, the failure rates in the 2 groups were approximately 10% per year, with a cumulative failure rate of 30% in both groups at year 3. From 3 to 5 years, the failure rate seems to flatten such that an additional 10% of subjects failed in the last 2 years of follow-up, for a rate of 5% failure per year. It seems that once patients make it through the first 3 years, there is a lower rate of failure going forward, although longer follow-up would be helpful to confirm this. Also, it is interesting to note that the IOP and number of medications remained stable between years 3 and 5, as they had been in years 1 to 3. Similar to the 5-year results of the BGI in the TVT Study,[4] IOP was, on average, between 13 and 15 mmHg on an average of 2 medications.

In conclusion, the use of BGIs produced greater IOP reduction and a lower incidence of glaucoma reoperation than AGV implantation after 5 years of follow-up. The AGV decreased IOP to a greater degree in the early postoperative period compared with the BGI. Similar rates of surgical success were observed with both implants during 5 years of follow-up, but the reasons for treatment failure were different. Failure after AGV was usually due to high IOP end points, whereas failure with the BGI was most commonly related to safety end points (hypotony, implant explantation, and loss of light perception). The additional approximately 2-mmHg-lower IOP obtained with the BGI must be weighed against the larger number of safety end points in the BGI group compared with the AGV group. A detailed account of the complications after 5 years of follow-up from this study is forthcoming.

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Footnotes and Financial Disclosures

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Abbreviations and Acronyms:
ABC = Ahmed Baerveldt Comparison; **AGV** = Ahmed FP7 Glaucoma Valve; **AVB** = Ahmed Versus Baerveldt; **BGI** = Baerveldt 101-350 Glaucoma Implant; **GDI** = glaucoma drainage implant; **IOP** = intraocular pressure; **logMAR** = logarithm of the minimum angle of resolution; **NLP** = no light perception; **NVG** = neovascular glaucoma; **SD** = standard deviation; **SE** = standard error; **TVT** = Tube Versus Trabeculectomy; **VA** = visual acuity.

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