



Review of the Ahmed versus Baerveldt study—5-year treatment outcomes

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Abstract: The results from the tube versus trabeculectomy (TVT) study provided the evidence to support the use of aqueous shunt surgery and its increasing popularity in the world. The Ahmed versus Baerveldt (AVB) study, a randomized controlled study, compared the efficacy and safety between two of the most commonly used glaucoma drainage implants. A significant proportion of the participants had failed trabeculectomy, neovascular or uveitic glaucoma. The 5-year results showed that the cumulative probability for failure is significantly lower for Baerveldt compared to Ahmed group (52.3% *vs.* 40.0%, $P=0.039$). The most common reason for failure was high intraocular pressure (IOP) but 4% of the Baerveldt group has refractory hypotony. Both surgeries were also effective in reducing dependency on intra-ocular pressure lowering medications but the Baerveldt group is superior in this aspect (median of 1 medication compared to 2 medications for Ahmed group). Both surgeries experienced 60–70% rate of complications but most were self-limiting. The most common long-term complication was corneal decompensation (10%). Overall, the results of the AVB study mirrored the results from the Ahmed Baerveldt Comparison (ABC) study. In conclusion, the 5-year report from the AVB study suggested that the Baerveldt tube is more appropriate for eyes which require much lower IOP such as eyes with advanced glaucoma or in young patients. The Ahmed tube would be more suitable for patients who are at risk of hypotony (such as uveitic and neovascular glaucoma) and those who require immediate IOP lowering after surgery.

Keywords: Glaucoma drainage implant; Ahmed glaucoma valve implant; Baerveldt implant

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Introduction

Glaucoma is an irreversible blinding disease which affects more than 70 and 100 million people in the world by year 2020 and 2040 respectively (1). The reduction of intraocular pressure (IOP) remains the mainstay of glaucoma management. Surgical intervention is indicated for patients who cannot reach their target IOP even on maximum tolerable medical therapy. Despite the emergence of minimally invasive glaucoma surgery, the more conventional aqueous drainage shunts and trabeculectomy are still the first choices for eyes with moderate to severe glaucoma.

In the tube versus trabeculectomy (TVT) study, a significant proportion of the participants had prior cataract surgery or failed trabeculectomy. The trabeculectomy group had close to 2 mmHg lower IOP than the Baerveldt implant group but this is not statistically significant ($P=0.12$). However, the cumulative failure rate (defined as IOP between 5 and 21 mmHg) was significantly lower in the tube group (29.8%) compared to the trabeculectomy group (46.9%) ($P=0.002$). The risk of trabeculectomy failure is twice as high compared to tube surgery. In addition, the rate of re-operation for high IOP was also higher in the

trabeculectomy group (29%) compared to the tube group (9%) ($P=0.025$) (2). Early complications were more frequent in the trabeculectomy group (37%) than in the tube group (21%) ($P=0.012$) but late complications were similar for both groups—one-third developed late complications ($P=0.81$) (3). The TVT study has showed us that tube surgery is both efficacious and safe when it comes to reducing IOP. One can argue that the superior safety profile of tubes makes it a more attractive “one-stop” solution for IOP control. The results of the TVT study had influenced clinical practice and an American Glaucoma Society survey showed that between 1996 and 2008, there is a 3-fold increase in the use of tubes and a corresponding nearly 50% reduction in trabeculectomy being performed (4). The authors believe that this trend will persist in future and strengthen the need for long-term data for tube shunt surgery to justify its use.

The Ahmed Versus Baerveldt (AVB) study reporting the 5-year outcomes is timely and shed light on the two most important questions about long-term outcomes of aqueous shunt surgery—efficacy and safety. In brief, the AVB was a multi-centre randomized trial comparing the Ahmed Valve (New World Medical Inc., CA, USA) and the Baerveldt implant (Abbott Medical Optics, CA, USA) in eyes with previous failed trabeculectomy or at high risk of trabeculectomy failure. The 3-year results showed that the Baerveldt tube surgery achieved a lower post-operative IOP but are at higher risk of hypotony and re-operations. Although significantly different, the IOP-lowering effect of both surgeries were clinically comparable but one can argue that the Ahmed valve implant's better safety profile potentially makes it a better option for high-risk eyes.

Population characteristics

The mean age of participants was 66 ± 16 years and equal distribution of gender (55% female). The majority was white ethnicity (71%) and half had primary open angle glaucoma. The mean pre-operative IOP was 31.4 ± 10.8 mmHg and mean number of IOP medications was 3.1 ± 1.0 . This indicated that the participants' IOP were severely sub-optimal despite on nearly maximum medical therapy. It is also interesting to note that one-third of the eyes had neovascular glaucoma or uveitis and more than one-third had previous trabeculectomy. As such, the participants included in the AVB study were prone to conjunctival scarring and inflammation which typically cause glaucoma filtration surgery to fail in the long-term.

Efficacy

At 5 years, the cumulative probability of failure (standard error) was 53.2% (4.7%) in the Ahmed group and 40.0% (5.0%) in the Baerveldt group ($P=0.039$). The rate for complete and qualified successes were very low for both groups— $<5\%$ and $<20\%$ respectively. The most common reason for failure in both groups was high IOP (IOP above 18 mmHg or less than 20% reduction from baseline IOP for two consecutive visits occurring at least 3 months after surgery). This accounted for 45% and 23% of the failures in the Ahmed and Baerveldt groups respectively. Although the rate of failure for high IOP seem to be lower for the Baerveldt group, this was counter-balanced by higher rates of hypotony in the Baerveldt group (4%) compared to none in the Ahmed group. In addition, when the upper limit of IOP was more stringent (<14 mmHg), the cumulative probability of failure was as high as 83.5% (3.5%) and 72.2% (4.5%) for the Ahmed valve and Baerveldt group respectively.

In the clinical setting, it is more useful to look at the cumulative failure rate as compared to the absolute reduction in IOP after surgery. Target IOP has to be individualized based on the severity of glaucoma, presenting IOP and age/life expectancy of each glaucoma patient. As such, although the world glaucoma association's definition of surgical failure or success has its inherent limitations, it is also the most clinically applicable standardized definition. The guidelines also encourage authors to report success rates based on three different upper limit cut-offs for IOP— <15 , 18 and 21 mmHg so that the results can be generalized to different target post-operative IOP. In the AVB study, at 5 years, the mean reduction in IOP was 47% and 57% for the Ahmed and Baerveldt groups respectively ($P=0.02$). This may sound promising but using mean reduction in IOP was a misrepresentation of the complete picture. When interpreted together with the high cumulative failure rates of both groups, this suggested that there was a huge variation in the post-operative IOP outcomes using current aqueous shunt techniques. In the long-term, the low complete success rates or high cumulative failure rates for both Ahmed valve and Baerveldt tube surgeries showed that current commercially-available aqueous shunts have considerable deficiencies in achieving long-term visual preservation.

The AVB 3-year study showed that the cumulative probability of failure was 51% for the Ahmed group and 34% for the Baerveldt group. This suggested that most of

the failure occurred within the first 3 years after the surgery which is consistent with the duration for bleb remodeling and wound healing to occur after surgery. Once the bleb has matured, the risk of failure from either high IOP or hypotony becomes much less. Despite this, the overall low success rates throughout the post-operative period leaves the authors to conclude that aqueous shunt techniques are not effective in both short-term and long-term IOP control. From the patients' perspective, they will probably require adjunctive medications or additional surgeries in the long run, not unlike trabeculectomy surgery.

The other aspect of efficacy involves the change in dependency on IOP-lowering medications and the need for additional glaucoma procedures. Both groups of eyes had a mean of about three medications before surgery and the mean number of IOP medications reduced significantly to less than two even after 5 years after surgery. However, the Baerveldt group required a median of just one medication compared to two medications in the Ahmed group ($P=0.038$). This seemed to suggest that the Baerveldt tube could be the preferred choice in patients who are highly intolerant to their eye drops, not compliant to eye drops or in eyes with IOP that are difficult to control with medications. The most common procedure performed is cyclodestructive procedure followed by additional aqueous shunt procedures. In addition, the associated complications and the interventions should also be considered (see below). This may have implications when the glaucoma patient is counseled on the long-term prognosis and treatment plan. In a sub-analysis, the authors also reported that amongst eyes with previous failed trabeculectomy, the 5-year success rate was 71% which suggested that tube surgery is effective option although the authors did not specify if this was complete or qualified success.

Safety

The safety of a procedure is based on the post-operative visual outcomes and complications. For the latter, one has to consider the frequency, severity and the subsequent re-operations required to treat the complications. In this study, both groups of eyes had a similar reduction in visual acuity. It is important to note that the baseline mean visual acuity was already very poor (Snellen equivalent of approximately 20/400) which deteriorated moderately over 5 years (Snellen equivalent of approximately 10/800). This could be attributed to natural progression of glaucoma, cataract formation or maculopathy. Progression to no light

perception occurred in 6% of the participants at 5 years.

For complications, both groups reported similar rates of between 60–70% within 5 years but most were self-limiting. Of these, half of the eyes required an intervention to treat the complication. The rate of bleb encapsulation was higher in the Ahmed group compared to Baerveldt group. This is probably due to the small base plate area of the FP7 Ahmed valve design, the use of a valve within the tube as well as the early conjunctival exposure to the pro-inflammatory mediators from the aqueous or the uneven surface texture of the Ahmed base plate (5-7). This could also explain the slightly inferior IOP-lowering effect of the Ahmed valve group. On the other hand, the Baerveldt group experienced a higher risk of refractory hypotony (5% *vs.* 1%, $P=0.057$). There is a significantly higher proportion of eyes requiring paracentesis in the Baerveldt group (14% *vs.* 4%, $P=0.007$) due to high IOP indicating that huge IOP fluctuations are more common in the Baerveldt group of eyes and the long-term implications on glaucomatous damage and visual prognosis is uncertain. It is also interesting to note that among the phakic eyes, a significant proportion of patients develop cataracts requiring phacoemulsification within 5 years (26% in the Ahmed group and 38% in the Baerveldt group, $P=0.92$). The rate of severe complications was relatively low. Explantation of tube was required for 4 (1.7%) patients for various reasons including malposition resulting in cornea decompensation, refractory hypotony and persistent motility disorder. Three patients had to undergo evisceration/enucleation due to serious complications—1 for endophthalmitis and 2 for blind painful eye (all in the Ahmed valve group). The most common long-term complication was corneal edema for both groups (10%) and this could be due to anterior chamber depth fluctuation, inflammation, cornea-tube contact or pre-existing cornea endothelial compromise (8,9).

Discussion

It is important to consider the baseline characteristics of the participants to gain a fair perspective on the outcomes reported in this study. These patients had poor baseline visual acuity, very high IOP despite on maximum tolerable medical therapy, more than one third had a failed trabeculectomy, more than 2/3 had previous cataract surgeries and one-third had secondary glaucoma due to neovascular glaucoma or uveitis. Clinically, this group of patients are at a high risk of blindness or visual impairment over a short period of time without any surgical

intervention. This would also explain the relatively poor 5-year success rates of aqueous shunt surgeries where only approximately half did not fail at 5 years. The most common cause of failure was uncontrolled high IOP. The Baerveldt group had a significantly lower failure rate compared to Ahmed. In general, compared to Ahmed valve group, the Baerveldt group provided a 3 mmHg lower post-op IOP at 5 years and also a significantly lower dependence on IOP medications. However, this is at the expense of higher risk of hypotony in eyes with a Baerveldt tube implant. The most common procedure performed for high IOP after aqueous shunt surgery was cyclodestructive procedures such as TCP which also indicates the lack of options for these eyes with severe glaucoma.

Comparison with the Ahmed Baerveldt Comparison (ABC) study

The ABC study also showed that at 5 years, the Ahmed group has a 2 mmHg higher post-op IOP compared to the Baerveldt group [14.7 ± 4.4 vs. 12.7 ± 4.5 mmHg respectively ($P=0.015$)] (10). There was no difference in number of glaucoma medications or cumulative probability of failure (44.7% for Ahmed and 39.4% for Baerveldt). Most of the failures happened in the first 2 years after surgery. However, the reason for failure was different between the two groups. The cause of failure from high IOP is higher for the Ahmed valve group (80% of failure in this group) compared to Baerveldt group (53% of failure in this group) ($P=0.003$). However, the reverse is true as well and the Baerveldt group has a higher risk of persistent hypotony (47% of failures) compared to Ahmed group (20% of failures only).

It is important to note that the settings in clinical trials are usually not reproducible in the real-world clinical settings. In the clinical trials, only experienced surgeons performed the surgeries. The patients who are part of the study tend to be more motivated to return for the follow-up regularly. The high rates of failure and low rates of complete success at the end of 5 years suggested that current tube implants are still far from ideal. This is especially important when patients undergo surgery when they are young and the studies suggested that re-operations or returning back to medical therapy is expected. However, the AVB study still provided insights on how one should select the type of implant surgery to perform. For eyes which require much lower IOP such as advanced glaucoma or in younger patients, the Baerveldt tube seems to be more appropriate. However, the Ahmed tube would be more

suitable for patients who are at risk of hypotony (such as uveitic glaucoma, neovascular glaucoma or highly-myopic eyes) and those who require immediate IOP lowering after surgery.

In conclusion, the AVB study showed that, in general, both Ahmed and Baerveldt were effective in reducing IOP if one considers 50% reduction in mean IOP reduction at 5 years after surgery. However, the cumulative surgical failure was high for both groups and the minority can be considered as complete success. The long-term rates of complications were similar but the Baerveldt group has a higher risk of refractory hypotony which was not seen in the Ahmed group.

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Footnote

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