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The Effect of Tube Location on Corneal Endothelial Cells in Patients with Ahmed Glaucoma Valve

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Purpose: To compare the effects of the Ahmed glaucoma valve (AGV; New World Medical, Rancho Cucamonga, CA) with sulcus versus anterior chamber (AC) tube placement on the corneal endothelial density and morphology over time.

Design: Nonrandomized, interventional study.

Participants: This study included 106 eyes from 101 pseudophakic patients who had the AGV tube placed in the AC (acAGV) and 105 eyes from 94 pseudophakic patients who had the AGV tube placed in the ciliary sulcus (sAGV).

Methods: All patients underwent preoperative specular microscopy, which was repeated postoperatively in 2019. The patients' demographic information, glaucoma diagnoses, and basic ocular information were obtained on chart review. Anterior segment OCT was conducted for patients who underwent sAGV to evaluate the sulcus tube position. Gonioscopy was performed to document peripheral anterior synechiae (PAS). Linear mixed-effects models were used to compare the different ocular and endothelial measurements between the 2 groups and to identify risk factors for endothelial cell density (ECD) loss over time.

Main Outcome Measures: Monthly change in corneal endothelial measurements, including ECD and coefficient of variation (CV), calculated as the difference between preoperative and postoperative measurements divided by the number of months from the time of surgery to postoperative specular microscopy.

Results: The acAGV and sAGV groups were comparable in all baseline characteristics except that the acAGV group had longer follow-up (37.6 vs. 20.1 months, respectively, $P < 0.001$). Mean monthly loss in central ECD was significantly more in the acAGV group (mean $\pm$ standard deviation: 29.3$\pm$29.7 cells/mm^2) than in the sAGV group (15.3$\pm$20.7 cells/mm^2, $P < 0.0001$). Mean monthly change in CV was similar between the 2 groups ($P = 0.28$). Multivariate analyses revealed that younger age and tube location in the AC were associated with faster central ECD loss ($P = 0.02$, $P < 0.0001$, respectively). For patients with sAGV, while PAS was associated with faster central ECD loss ($P = 0.002$), a more forward tube position tenting the iris was not ($P > 0.05$).

Conclusions: Compared with anterior segment placement, ciliary sulcus tube implantation may be a preferred surgery approach to reduce endothelial cell loss in pseudophakic patients. *Ophthalmology 2020;■:1–9 Published by Elsevier on behalf of the American Academy of Ophthalmology*

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Glaucoma drainage device (GDD) surgery is being performed with increasing frequency as an alternative to trabeculectomy.[1-3] However, one of the major long-term complications of the GDD is progressive corneal endothelial cell loss leading to corneal decompensation.[4-7] The mechanism of endothelial damage is not clear, but has been proposed to involve mechanical damage from the tube's proximity to the corneal endothelium, high fluid flow through the tube producing damage to the endothelium proximal to tube entry, and postoperative inflammation leading to corneal endothelial damage.[7,8]

Surgical techniques have been modified to avoid corneal endothelial damage by positioning the tube in the anterior chamber (AC) parallel to the iris plane and away from the cornea or by avoiding AC tube placement altogether. Pars plana tube placement has been advocated for patients with preexisting corneal disease and when the traditional AC tube insertion is not possible. This approach has been shown to be an effective way to protect against significant corneal endothelial cell loss and improve corneal graft survival.[9-14] However, pars plana tube insertion requires a concurrent or antecedent vitrectomy procedure and is associated with potential posterior segment complications such as retinal tear or detachment or tube obstruction by the vitreous. As a result, this is not a commonly performed technique.

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The ciliary sulcus is the space between the posterior iris face and a posterior chamber intraocular lens. After cataract extraction with posterior chamber intraocular lens implantation, sulcus placement of a tube offers the advantage of increased distance between the cornea and the tube with the iris acting as a barrier between them, thereby potentially minimizing mechanical damage and excessive fluid conductance force. Ciliary sulcus tube placement does not require vitrectomy, thereby avoiding additional surgery and its associated complications. Although previous studies have shown that sulcus tube placement is as effective as AC placement in lowering intraocular pressure (IOP),[15-19] this technique's effect on the corneal endothelium has not been well described in the literature. We hypothesized that GDD with sulcus tube placement is associated with a slower rate of corneal endothelial cell loss compared with the traditional AC tube location insertion. The aim of this study is to evaluate the effect of tube location on corneal endothelial cell density (ECD) after implantation of the Ahmed glaucoma valve (AGV; New World Medical, Rancho Cucamonga, CA).

Methods

This is a nonrandomized interventional study, conducted with approval from the University of California San Francisco Institutional Review Board and in accordance with the tenets of the Declaration of Helsinki. All participants provided informed consent.

Study Population

The study included consecutive patients who underwent AGV implantation in the superotemporal (ST) quadrant in the AC or the ciliary sulcus within the University of California San Francisco Glaucoma Service from 2013 to 2018, as long as none of the exclusion criteria was present. Exclusion criteria included preexisting corneal disease, previous corneal transplant, more than 1 tube shunt in the same eye, phakic status except if the patient were to undergo a combined phacoemulsification with AGV implantation, and inability to complete tests relevant for this investigation.

Patient demographics and ocular characteristics were extracted from the medical record, including the patients' age, sex, glaucoma diagnosis, IOP, and best-corrected visual acuity (BCVA) preoperatively, 1 year postoperatively, and at the time of the study.

Surgical Techniques

All surgeries were performed by a single surgeon (Y.H.). The primary surgeon's standard practice from 2013 to 2015 was to place the tube in the AC, and this practice was gradually changed to sulcus placement in 2016. Surgical techniques for AGV implantation have been described previously.[20] A fornix-based conjunctival flap was created in the ST quadrant. After being primed, the AGV plate was anchored to the sclera between the superior rectus and lateral rectus muscles. For sulcus tube implantation, a bent 20-gauge microvitreoretinal blade was used to enter into the ciliary sulcus 3.5 mm from the limbus, followed by Provisc (Alcon, Fort Worth, TX) injection along the same path. After being trimmed to the appropriate length, the Ahmed tube was inserted along the created path, with the bevel facing away from the iris. For tube implantation in the AC, a bent 20-gauge microvitreoretinal blade was used to tunnel forward and enter into the AC 3 mm from the limbus, followed by Provisc injection. After trimming to the appropriate length, the drainage tube was inserted into the AC parallel to the iris plane, with the bevel facing away from the iris. The tube was covered by an autologous scleral flap. The conjunctiva and Tenon's capsule were then secured at the limbus.

Evaluation of the Anterior Segment

All eligible patients were identified by reviewing their medical records. As a part of the preoperative evaluation before AGV implantation in the surgeon's practice, all patients had previously undergone ultrasound pachymetry (DGH Pachette 4; DGH Technology Inc, Exton, PA) to measure central corneal thickness (CCT) and noncontact specular microscopy (CellChek Konan Specular Microscope X; Konan Medical Inc, Hyogo, Japan) for corneal endothelial evaluation within 1 month before AGV surgery. During the patients' follow-up visits in 2019, these corneal measurements were repeated. The ECD and coefficient of variation (CV) were obtained on 3 prespecified corneal locations, including the central cornea, ST, and inferonasal (IN) quadrants. During the follow-up in 2019, anterior segment OCT (Visante OCT Anterior Segment Imaging, Carl Zeiss Medical Inc, Dublin, CA) was also performed to evaluate the location, position, and length of the tube. The presence or absence of peripheral anterior synechiae (PAS) was evaluated by standard gonioscopic examination using a 4-minor Zeiss gonioprism (Volk Optical Inc, Mentor, OH).

Statistical Analysis

Scatterplot was performed to evaluate the relationship between ECD change (calculated by subtracting preoperative ECD from postoperative ECD) and time lapse since surgery (calculated as the number of months from AGV surgery to postoperative repeat ECD measurements) for patients who received the AGV tube placed in the AC (acAGV) and the AGV tube placed in the ciliary sulcus (sAGV) separately. To compensate for the difference in follow-up time between the 2 AGV groups, we calculated the mean monthly change, that is, the difference between preoperative and postoperative endothelial measurements divided by the number of months since surgery, and compared these monthly changes between the 2 groups. Because some subjects had both eyes eligible for the study, linear mixed-effects models were used to compare the different ocular and endothelial measurements between the 2 AGV groups while accounting for inter-eye correlation between 2 eyes of the same subject. Randomized block design analysis of variance was used to compare endothelial measurements in central, ST, and IN locations of the same eye.

Univariate and multivariate linear mixed-effects models were used to assess risk factors for more monthly ECD loss. Factors with $P < 0.2$ from univariate analyses were included in the multivariate regression analysis. A backward stepwise selection algorithm was used until covariates had a $P < 0.05$. All statistical analyses were performed using SAS 9.4 software (SAS Institute Inc, Cary, NC). Because multiple comparisons were used to compare different specular microscopic parameters (ECD monthly change, percentage of ECD change, and CV) and different corneal locations (ST, central, and IN) between the 2 groups, Bonferroni correction was performed to adjust for multiple comparisons. Adjusted P values are indicated in associated tables.

Results

Patient Demographics and Ocular Characteristics

A total of 256 patients underwent AGV implantation with the tube implanted superotemporally in the AC or sulcus by a single surgeon (Y.H.) from 2013 to 2018. The inclusion/exclusion criteria were met by 195 patients, including 106 eyes from 101 patients who underwent acAGV and 105 eyes from 94 patients who underwent sAGV. Among these patients, 8 underwent combined phacoemulsification with acAGV, and 27 patients underwent combined phacoemulsification with sAGV.

With regard to preoperative characteristics, those who underwent acAGV and sAGV had comparable age, gender distribution, diagnoses, preoperative BCVA, IOP, and baseline corneal characteristics including CCT, ECD, and CV ($P > 0.05$ for all, Table 1). Because the surgeon shifted the surgical technique from default tube placement in the AC to placement in the sulcus in 2016, the mean months of follow-up from AGV surgery to the time when postoperative specular microscopy was conducted (mean ± standard deviation [SD]) was 37.6±20.1 months for the acAGV group, significantly longer than for the sAGV group (20.1±17.2 months, $P < 0.001$, Table 1).

With regard to the ocular characteristics postoperatively, 1 year after AGV implantation, the acAGV group had a mean IOP (mean ± SD) of 12.5±3.7 mmHg, similar to the sAGV group (11.6±3.3, $P = 0.12$). At the time when postoperative specular microscopy was performed in 2019, the acAGV and sAGV groups also had similar postoperative mean IOP (12.3±3.7 and 11.6±3.4 mmHg, respectively, $P = 0.16$). The acAGV group had significantly worse postoperative logarithm of the minimum angle of resolution (logMAR) BCVA compared with the sAGV group 1 year after surgery (logMAR 0.41±0.57 vs. 0.23±0.37, $P = 0.01$) and at the time of specular microscopy (logMAR 0.39±0.55 vs. 0.23±0.36, $P = 0.01$). In addition, the mean postoperative CCT at the time of specular microscopy in the acAGV group was thicker than in the sAGV (546±56 vs. 536±35 μm), but these differences did not reach statistical significance ($P = 0.13$). Tube length was measured on the AS-OCT images for AC tubes only, and mean AC tube length was 2.85±0.74 mm. Five eyes in the acAGV group and 4 eyes in the sAGV group developed tube-related postoperative complications, including tube occlusion, persistent inflammation longer than 3 months postoperatively, and tube-related exposure/infection ($P = 0.74$).

Comparison of Postoperative Corneal Endothelial Characteristics between the acAGV and sAGV Groups

To adjust for the effect of different time lapse since surgery on corneal endothelial cells, we calculated and compared mean monthly changes. The assumption of a linear relationship between ECD changes and time lapse since surgery was based on the observation of a linear pattern of ECD loss over time in both groups within the study period (Fig 1).

Corneal endothelial measurements were compared between the 2 AGV groups for ECD and CV in the central, ST, and IN corneal locations. The mean monthly reduction in central ECD (mean ± SD) was 29.3±29.7 cells/mm^2 in the acAGV group, which was significantly more loss than that of the sAGV group (15.3±20.7 cells/mm^2, $P < 0.0001$, Table 2). The percentage of central ECD loss (mean ± SD), which was obtained by monthly central ECD change divided by preoperative ECD, was 1.37%±1.43% per month in the acAGV group, and it was significantly higher than monthly loss seen in the sAGV group (0.72%±0.91% ECD loss per month, $P < 0.0001$, Table 2). The mean monthly change on central CV was not significantly different between the 2 groups in the central cornea ($P = 0.28$). Similar trends of corneal endothelial changes including ECD and CV described were also observed in the ST and IN locations of the cornea (Table S1, available at www.aaojournal.org).

We then examined risk factors associated with worse corneal endothelial damage for all AGV patients. In univariate analyses, younger age ($P = 0.01$) and tube location in the AC compared with sulcus location ($P < 0.0001$) were significantly associated with more monthly ECD decline in the central cornea (Table 3). In multivariate analyses, younger age ($P = 0.02$) and tube location in the AC ($P < 0.0001$) remained significant risk factors for more monthly ECD loss in the central cornea (Table 3). Tube location in the AC was also significantly associated with more monthly ECD loss in the ST and IN corneal locations, but age was not associated with ECD loss in these 2 noncentral corneal locations (Table S2, available at www.aaojournal.org). In

Table 1. Baseline Patient Characteristics

	acAGV (N = 106 Eyes, 101 Patients)	sAGV (N = 105 Eyes, 94 Patients)	P Value
Age in years, mean (SD)	64.5 (15.4)	66.4 (15.4)	0.37
Male, N (%)	46 (45.5%)	42 (44.7%)	0.62
Months since surgery (SD)*	37.6 (20.1)	20.1 (17.2)	<0.001
Glaucoma diagnoses			0.21
POAG, N (%)	77 (72.6%)	66 (62.9%)	
Uveitic glaucoma, N (%)	17 (16.0%)	17 (16.2%)	
PACG, N (%)	3 (2.8%)	9 (8.6%)	
Other, N (%)†	9 (8.5%)	13 (12.4%)	
Preoperative ocular characteristics			
Preoperative IOP, mmHg (SD)	23.4 (7.49)	23.3 (7.98)	0.96
Preoperative BCVA in logMAR (SD)	0.37 (0.49)	0.31 (0.38)	0.36
Preoperative CCT, μm (SD)	540.7 (46.6)	539.1 (36.8)	0.10
Preoperative ECD, cells/mm^2 (SD)	2190 (508)	2251 (570)	0.59
Preoperative CV (SD)	28.5 (7.13)	27.0 (5.88)	0.05

acAGV = Ahmed glaucoma valve (New World Medical, Rancho Cucamonga, CA) implant with tube placed in the anterior chamber; BCVA = best-corrected visual acuity; CCT = central corneal thickness; CV = coefficient of variation; ECD = endothelial cell density; IOP = intraocular pressure; logMAR = logarithm of the minimum angle of resolution; PACG = primary angle-closure glaucoma; POAG = primary open-angle glaucoma; sAGV = Ahmed glaucoma valve implant with tube placed in the sulcus; SD = standard deviation.

*Months since surgery indicate the number of months from the time of AGV surgery to repeat postoperative specular microscopy.

†Other glaucoma diagnoses included steroid-induced glaucoma, neovascular glaucoma, mixed-mechanism glaucoma, pigmentary glaucoma, aphakic glaucoma, pseudoexfoliative glaucoma, and normal-tension glaucoma.

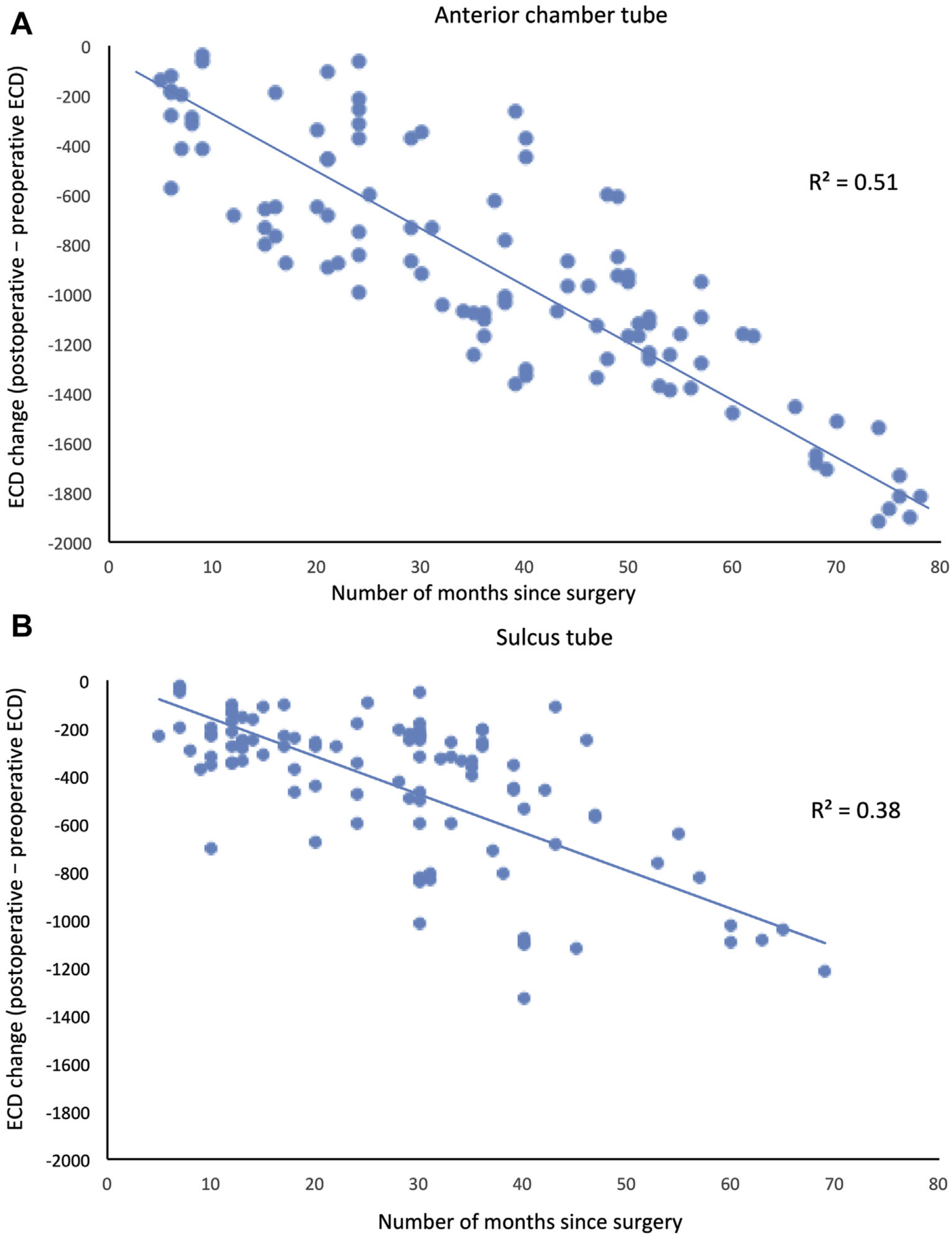

Figure 1. Scatterplot of endothelial cell density (ECD) loss over time after Ahmed glaucoma valve (AGV; New World Medical, Rancho Cucamonga, CA) with tube placement in the anterior chamber (AC) **(A)** versus sulcus **(B)**. The horizontal axis shows the time elapsed from AGV surgery to postoperative repeat ECD measurement (months). The vertical axis shows ECD change calculated by subtracting preoperative from postoperative ECD, that is, postoperative ECD − preoperative ECD (cells/mm^2). The line of best fit describes a linear relationship between ECD loss and time interval in both AGV groups, with r^2 describing how well it fits the data.

addition, we examined whether age was a risk factor for worse *percentage* monthly ECD loss and found that younger age was not associated with worse percentage ECD loss in central (P = 0.34), ST (P = 0.48), or IN cornea (P = 0.67).

We also evaluated whether the length of the AC tube was a significant risk factor for worse endothelial damage in the acAGV group. The AC tube length was not significantly associated with more monthly ECD loss in central (P = 0.73, Table 3), ST (P = 0.12), and IN cornea (P = 0.38, Table S2, available at www.aaojournal.org).

Postoperative Corneal Endothelial Characteristics in Patients with Sulcus Tube

We studied the effects of sulcus tube position on postoperative corneal endothelium in patients with sAGV. We first compared corneal endothelial parameters in 3 corneal locations in the sAGV group. The mean monthly decrease in central ECD (mean ± SD) was 15.3±20.7 cells/ mm^2, significantly lower than the decrease in the ST location (20.1±24.6, P = 0.005) but not significantly different from the ECD decrease in the IN location (17.9±20.2,

Table 2. Comparison of Monthly Change in Each of the Central Corneal Endothelial Measurements between Treatment Groups

Measurements	Mean Monthly Change (SD) acAGV (N = 106 eyes)	Mean Monthly Change (SD) sAGV (N = 105 eyes)	P Value†
ECD, cells/mm^2	−29.3 (29.7)	−15.3 (20.7)	<0.0001
%ECD change*	−1.37 (1.43)	−0.72 (0.91)	<0.0001
CV	0.08 (0.58)	0.36 (1.63)	0.28

acAGV = Ahmed glaucoma valve implant (New World Medical, Rancho Cucamonga, CA) with tube placed in the anterior chamber; CV = coefficient of variation; ECD = endothelial cell density; sAGV = Ahmed glaucoma valve implant with tube placed in the sulcus; SD = standard deviation.
*%ECD change was calculated by monthly ECD change (postoperative − preoperative ECD) divided by preoperative ECD.
†Bonferroni correction was applied to adjust for multiple comparisons. $P < 0.017$ is considered statistically significant.

$P = 0.12$, Table 4). The mean monthly changes of CV showed no significant difference whether it was measured in the central, ST, or IN cornea (overall $P > 0.05$ for all, Table 4).

Every sAGV patient underwent AS-OCT in addition to routine slit-lamp examination to evaluate the position of the sulcus tube. An example of a sulcus tube in the ideal location is shown in Figure 2A. In the sAGV group, 38 patients were found to have local shallowing of the AC on AS-OCT caused by the sulcus tube pushing the iris toward the corneal endothelium (an example is shown in Fig 2B). However, when comparing the corneas of patients with sAGV patients without tenting of the iris, these endothelial measurements were not significantly different, including corneal ECD, CV in central, ST, and IN cornea (Table 5).

Finally, we explored whether PAS affected sulcus tube position and the corneal endothelium in patients with sAGV. There were 10 eyes that were found to have PAS in more than 3 clock hours on gonioscopic examination. Among them, 6 eyes had uveitic glaucoma, 2 eyes from the same patient had primary angle-closure glaucoma, 1 eye had neovascular glaucoma, and 1 eye had traumatic glaucoma (an example of PAS on AS-OCT is shown in Fig 2C). When comparing these patients with sAGV patients who did not have PAS, the presence of PAS was significantly associated with more monthly ECD reduction in the central ($P = 0.002$) and IN cornea ($P = 0.0002$), but did not reach statistical significance in the ST cornea ($P = 0.04$). The presence or absence of PAS did not seem to have any effect on the mean monthly change of CV (Table 6).

Discussion

This study aims to directly compare postoperative corneal endothelial changes between the sulcus and AC tube locations after AGV, and to examine risk factors for corneal endothelial cell loss after the tube shunt surgery.

We found that patients in the sAGV group experienced a significantly slower rate of ECD loss in the central, ST, and IN cornea compared with the patients in the acAGV group. This supports the hypothesis that sulcus tube placement is protective against corneal endothelial cell loss over time. There are limited data describing the pattern of ECD loss after sAGV to compare with the results of the current study. However, a previous study that investigated ECD loss after phacoemulsification in patients with primary open-angle glaucoma reported a monthly ECD loss of approximately 10 cells/mm^2 (extrapolated from published data),[21] which is more comparable with the monthly ECD loss observed in the sAGV group (15.3 cells/mm^2) as opposed to that in the acAGV group (29.3 cells/mm^2). Future investigations are needed to directly compare the pattern of ECD loss after sAGV with cataract surgery. However, the results in the current investigation suggest that with regard to cornea endothelium preservation, sulcus placement might be the preferred approach for AGV implantation compared with AC placement in patients with moderate to severe glaucoma.

In the acAGV group, we found that mean central ECD decreased by 35.5%±23.4% over the course of an average of 37.6 months. Kim et al[8] reported a 10.5% decrease in central ECD 12 months after acAGV implantation; Lee et al[22] reported corneal ECD loss rates after acAGV surgery of 15.3% and 18.6% at 12 and 24 months, respectively. The yearly ECD loss is largely consistent with the reports by Kim et al[8] and Lee et al.[22] The observational period in our study was substantially longer compared with the other 2 studies, and this may explain the different results. An AGV tube in the AC presents a constant source of endothelial

Table 3. Univariate Analysis and Multivariate Analysis of Risk Factors for More Monthly Central Endothelial Cell Density Change* after Ahmed Glaucoma Valve (N = 211 Eyes, 195 Patients)

	Univariate Analysis			Multivariate Analysis		
	Estimate	Standard Error	P Value	Estimate	Standard Error	P Value
Age (per year increase)	0.30	0.12	0.01	0.27	0.12	0.02
Female	0.80	3.60	0.82			
Preoperative central ECD	−0.006	0.003	0.08			
Postoperative IOP	0.61	0.52	0.24			
Presence of PI	−2.59	3.63	0.48			
AC tube length†	1.48	4.25	0.73			
Sulcus tube location (vs. AC)	14.9	3.28	<0.0001	14.3	3.27	<0.0001

AC = anterior chamber; ECD = endothelial cell density; IOP = intraocular pressure; PI = peripheral iridotomy.
*Monthly ECD change = (postoperative − preoperative ECD)/months since surgery.
†Univariate analysis conducted for only acAGV group.

Table 4. Comparison of Corneal Endothelial Measurements at Different Corneal Locations in the Sulcus Group (N = 105)

	Mean Monthly Change (SD)			*P* Values			
Measurements	*Central*	*ST*	*IN*	*Overall*	*Central vs. ST**	*Central vs. IN**	*ST vs. IN**
ECD, cells/mm^2	−15.3 (20.7)	−20.1 (24.6)	−17.9 (20.2)	0.02	0.005	0.12	0.20
CV	0.36 (1.63)	0.10 (1.79)	0.41 (1.50)	0.35	0.25	0.85	0.18

CV = coefficient of variation; ECD = endothelial cell density; IN = inferonasal; SD = standard deviation; ST = superotemporal.
*Pairwise comparisons obtained with Bonferroni correction. $P < 0.025$ is considered statistically significant.

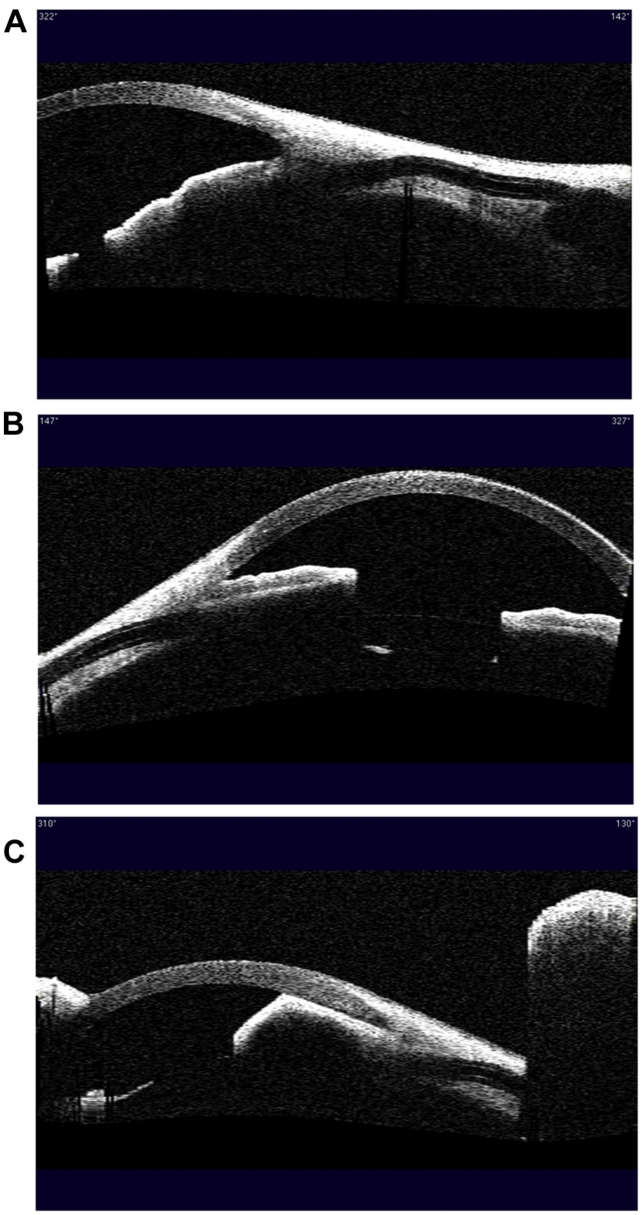

Figure 2. Evaluation of tube position and peripheral anterior synechiae (PAS) using anterior segment OCT. **A,** Example of a well-positioned sulcus tube. **B,** Example of sulcus tube pushing the iris forward toward the cornea. **C,** Example of significant PAS in a patient with traumatic glaucoma.

trauma; the longer time the tube is present in the AC, the more endothelial change it might cause.

Previously, a biexponential decay of ECD loss over time was observed after cataract surgery and penetrating keratoplasty.[23] However, ECD loss pattern after tube shunt surgery is not well understood. In our study, within the follow-up periods in each group, we observed a grossly linear relationship of ECD loss over time in acAGV and sAGV patients (Fig 1). Unlike cataract surgery and penetrating keratoplasty, damage to the endothelium during AGV surgery is limited because there is usually minimal surgical manipulation in the AC; therefore, we observed that there was no dramatic ECD loss immediately after surgery as shown in the biexponential decay model. Although there are fewer immediate postoperative corneal changes, after GDD implantation, the aqueous humor protein concentration has been observed to increase 10-fold,[24] including some proteins that are known to play a role in oxidative stress, apoptosis, and inflammation.[25] These more chronic and persistent changes are likely responsible for ongoing corneal endothelial damage in the long term. Thus, we observed a steady decline in ECD over time after surgery in both groups, and to compensate for the different follow-up durations between the 2 groups, we used monthly ECD loss to assess the rate of ECD change over time and to directly compare the 2 AGV groups.

Younger age and tube location in the AC were both significant risk factors for more monthly central ECD loss on the multivariate mixed linear regression analyses. Age has not been previously reported to be a significant risk factor for ECD loss after GDD implantation. It is reported that ECD declines by approximately 0.6% per year in normal adult subjects, whereas the annual percentage ECD decline in pediatric patients aged less than 18 years was higher.[26] Indeed, when we examined whether age was a risk factor for *percentage* monthly ECD loss, we found that age was not associated with more or less percentage monthly ECD loss. This supports our hypothesis that the effect of age on monthly ECD loss in our patient population was a reflection of natural age-related differential in ECD loss rate over time. Younger patients had more cells to lose but were not more likely to lose a higher proportion compared with older patients.

In the sAGV group, the monthly ECD loss was significantly higher in the ST corneal location, compared with the

Table 5. Comparison of Mean Monthly Change in Corneal Endothelial Measurements in sAGV Based on Sulcus Tube and Iris Relationship

	Mean Monthly Change (SD)		
Measurements	*Sulcus Tube Flat or Away from Iris (n = 67)*	*Sulcus Tube Pushing Iris Toward Cornea (n = 38)*	**P value***
Central cornea			
ECD, cells/mm^2	−17.7 (23.8)	−10.9 (12.9)	0.33
CV	0.46 (1.98)	0.19 (0.68)	0.74
ST cornea			
ECD, cells/mm^2	−21.4 (26.3)	−17.7 (21.2)	0.88
CV	0.07 (2.02)	0.16 (1.32)	0.96
IN cornea			
ECD, cells/mm^2	−21.0 (22.2)	−12.4 (14.9)	0.17
CV	0.45 (1.70)	0.33 (1.05)	0.37

CV = coefficient of variation; ECD = endothelial cell density; IN = inferonasal; sAGV = Ahmed glaucoma valve with sulcus tube; SD = standard deviation; ST = superotemporal.
*Bonferroni correction was applied to adjust for multiple comparisons. $P < 0.0083$ is considered statistically significant.

Table 6. Comparison of Mean Monthly Change in Corneal Endothelial Measurements between Eyes with versus without Peripheral Anterior Synechiae in sAVG

	Mean Monthly Change (SD)		
Measurements	*No PAS (N = 95)*	*PAS (N = 10)*	**P Value***
Central cornea			
ECD, cells/mm^2	−13.3 (18.9)	−33.8 (28.5)	0.002
CV	0.39 (1.71)	0.09 (0.47)	0.82
ST cornea			
ECD, cells/mm^2	−18.3 (22.7)	−36.7 (35.1)	0.04
CV	0.07 (1.87)	0.38 (0.82)	0.47
IN cornea			
ECD, cells/mm^2	−15.7 (17.6)	−38.5 (31.0)	0.0002
CV	0.43 (1.55)	0.20 (0.83)	0.82

CV = coefficient of variation; ECD = endothelial cell density; IN = inferonasal; PAS = peripheral anterior synechiae; sAGV = Ahmed glaucoma valve with sulcus tube; SD = standard deviation; ST = superotemporal.
*Bonferroni correction was applied to adjust for multiple comparisons. $P < 0.0083$ is considered statistically significant.

central and IN cornea. This regional difference correlates with the superotemproal location of the inserted sulcus tube in this study, and thus the area of insult and stress to the endothelial cells. This is consistent with the pattern of ECD loss in previous reports of AGV with AC tube placement.[8,22] This suggests that even though a sulcus tube may be associated with less trauma to the central corneal endothelial cells, it still induces corneal endothelial loss and corneal changes in the region closest to the tube. However, the clinical significance of preferential ECD loss at the ST location on corneal clarity and vision outcome remains to be elucidated.

When the tube is placed in the sulcus, it is not uncommon for the tube to tent the iris depending on the trajectory of the inserted tube. Our study found that the tube position, whether being flat and away from the iris, or pushing the iris toward the cornea, did not seem to significantly affect the rate of ECD loss: ECD change in all 3 corneal areas and their respective endothelial morphology did not differ significantly. It appears that as long as the tube is located in the ciliary sulcus, the iris acts as an effective barrier to reduce ECD loss from tube-cornea proximity.

The presence of PAS in sAGV patients was associated with significantly more ECD loss in central and IN corneal regions in our study. A similar finding was previously reported in a cross-sectional study that found PAS to be a significant risk factor for lower corneal ECD in patients with an AC tube.[5] Peripheral anterior synechiae may directly harm the corneal endothelium by long-term mechanical iridocorneal contact, but its effects on the central endothelium suggest a more global impact on the corneal endothelium, likely related to chronic intraocular inflammation that may have contributed to PAS formation in the first place.[27]

Study Limitations

Our study has several limitations. First, the follow-up time was significantly longer for the acAGV group compared with the sAGV group. Patients who received acAGV underwent postoperative specular microscopy on average over 17 months later than patients who received sAGV. We have reported the rate of ECD loss (i.e., mean cell loss per month) to address the differences in follow-up time, based on the linear pattern of ECD loss over time observed in both groups within the follow-up period. However, beyond the current follow-up timeframe, the ECD loss pattern is not known. Future studies with long-term longitudinal follow-up and repeated postoperative specular microscopy at prespecified time points should be conducted to more accurately examine the rate and pattern of ECD decline after AGV. Second, the study groups were not concurrent but consecutive, raising the possibility that reduced endothelial trauma in the more recently performed sulcus cases were due to greater surgeon experience and skill. However, there was substantial time overlap in the 2 groups, and the primary surgeon (Y.H.) was highly experienced with 10 years of practice at the beginning of the study. Moreover, a change in practice to sulcus placement might generate a new learning curve, thereby adversely affecting the outcomes. Yet sulcus placement demonstrated a more favorable outcome. Third, some patients underwent combined phacoemulsification and AGV implantation that could lead to worse ECD loss at the time of combined procedures and result in an overestimate of the degree of ECD loss compared with AGV surgery alone. Specifically, there were more combined cases in the sAGV group than the acAGV group. Even with a possible bias favoring the acAGV group, our results still demonstrated that sAGV as a group had significantly slower ECD loss. Furthermore, all patients in the study underwent AGV implantation, and the results may not be directly applicable to other implant types. However, similar rates of corneal endothelial cell loss have been reported with the AGV and Molteno (Dunedin, New Zealand) implants after 24 months of follow-up,[28] and all modern implants have a tube made of medical grade silicone with the same external and internal diameters. Last, all AGV procedures were performed by a single surgeon at 1 academic medical center, and this may affect the generalizability of results.

In conclusion, Ahmed glaucoma valve implantation with sulcus tube placement was associated with a slower rate of ECD loss compared with tube placement in the AC. Younger age, in addition to tube location in the AC, was a significant risk factor for faster central ECD loss. For patients with sulcus tubes, the presence of PAS was also a significant risk factor for faster endothelial cell loss, but a more forward tube position tenting the iris was not. Ciliary sulcus tube implantation may be a preferred surgery approach in pseudophakic eyes to prevent corneal endothelial cell loss while maintaining adequate IOP control. In the future, a randomized clinical trial comparing GDD with tube placement in different locations is warranted to more definitively determine the preferred surgical approach.

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Footnotes and Financial Disclosures

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Abbreviations and Acronyms:
AC = anterior chamber; **AGV** = Ahmed glaucoma valve; **acAGV** = AGV tube placed in the AC; **BCVA** = best-corrected visual acuity; **CCT** = central corneal thickness; **CV** = coefficient of variation; **ECD** = endothelial cell density; **GDD** = glaucoma drainage device; **IN** = inferonasal; **IOP** = intraocular pressure; **logMAR** = logarithm of the minimum angle of resolution; **PAS** = peripheral anterior synechiae; **sAGV** = AGV tube placed in the ciliary sulcus; **SD** = standard deviation.

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