Changes in Corneal Endothelial Cells after Ahmed Glaucoma Valve Implantation: 2-Year Follow-up

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• PURPOSE: **To evaluate changes in corneal endothelial cells after Ahmed glaucoma valve (AGV) implantation for the treatment of refractory glaucoma.**

• DESIGN: **Observational case series.**

• METHODS: **We prospectively evaluated the change in density and shape of the corneal endothelium in 41 patients (41 eyes) who had undergone AGV implantation for the treatment of refractory glaucoma. Corneal specular microscopy was performed on the superior, supratemporal, supranasal, and central areas with a noncontact specular microscope before surgery and 1, 6, 12, 18, and 24 months after surgery. The changes at each time point were compared with those at baseline and with those of the control group, which consisted of 20 contralateral glaucomatous eyes receiving antiglaucoma medications.**

• RESULTS: **The mean follow-up was 19.1 months. The average percentage decrease in corneal endothelial cell count was 5.8% at 1 month, 11.5% at 6 months, 15.3% at 12 months, 16.6% at 18 months, and 18.6% at 24 months after surgery. The changes were statistically significant compared with those at baseline and those of the control eye at all time points during the study period ($P < .05$). The supratemporal area, the closest site to the tube, showed the greatest decrease in endothelial cell density, by 22.6%, whereas the central cornea showed the smallest decrease, by 15.4%, at 24 months after surgery.**

• CONCLUSIONS: **There was statistically significant corneal endothelial cell loss in the operated eye after AGV implant surgery. The corneal endothelial cell loss increased with time: 15.3% at 12 months and 18.6% at 24 months after surgery, on average, in all measured areas. (Am J Ophthalmol 2009;148:361–367. © 2009 by Elsevier Inc. All rights reserved.)**

IT IS WELL KNOWN THAT REFRACTORY GLAUCOMAS such as neovascular glaucoma, secondary glaucoma from uveitis or trauma, and glaucomas with wide conjunctival scars from previous surgeries do not respond well after conventional trabeculectomy.[1,2] Although the application of antifibrotic agents such as 5-fluorouracil and mitomycin C to the filtration surgery has become popular recently, the success rate of trabeculectomy in such cases remains unsatisfactory. As an alternative approach, glaucoma implant surgery has been proposed, and better outcomes have been reported.[3–5] The Ahmed glaucoma valve (AGV) (AGV-S2; New World Medical, Rancho Cucamonga, California, USA) implant has shown good surgical results with fewer postoperative complications compared with conventional trabeculectomy in treating refractory glaucoma.[6,7] Nevertheless, many complications such as hypotony, shallow anterior chamber (AC), hyphema, tube–corneal touch, choroidal effusion, cataract formation, and endophthalmitis, as well as chronic corneal endothelial loss and eventual corneal decompensation still may result from the surgery.[7]

We found few longitudinal studies of changes in corneal endothelial cells after glaucoma implant surgery by a PubMed search. In a 1-year follow-up study after AGV surgery in 30 patients, we reported a 10.5% decrease in corneal endothelial cell density (ECD) at 12 months after surgery.[8] In the present study, we evaluated changes in the corneal endothelium after AGV surgery in a greater number of subjects and for a longer follow-up period than in our previous study.

METHODS

THIS PROSPECTIVE STUDY TO EVALUATE CHANGES IN CORneal ECD and corneal shape after AGV implantation surgery received approval from the Institutional Review Board of Chungnam National University Hospital, Daejon, Korea. All surgeries were performed by a single surgeon (C.-S.K.) between August 1, 2003 and December 31, 2005, after obtaining informed consent from the patients. All patients with refractory glaucoma such as neovascular glaucoma, secondary glaucoma from uveitis or severe trauma, and glaucomas with a wide conjunctival scar from a previous surgery, including failed previous filtration surgery or retinal surgery, were included. Congenital glaucoma and cases lost to follow-up without any ocular problem within 6 months after surgery were excluded. Follow-up was stopped when any serious complication requiring surgical treatment developed or any additional surgery was needed to lower intraocular pressure

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(IOP), but the data collected before the second surgery were included. The other eye of the subject was used as a control only when that eye had glaucoma and the patient was taking antiglaucoma medication for IOP control.

Clinical information, including age, gender, type of glaucoma, number of antiglaucoma medications (a fixed combination drug was counted as 2 drugs), number of previous intraocular surgeries, and systemic illness, was recorded. Before surgery, the following evaluations were preformed: visual acuity (VA), IOP (by Goldmann applanation tonometry; average of 3 measurements at each examination), slit-lamp examination, refraction, funduscopy, and specular microscopic examination. After surgery, VA and IOP were assessed, slit-lamp and fundus examinations were performed, and the number of antiglaucoma medications and complications, if any, were recorded.

All surgeries were performed under retrobulbar anesthesia and using a standard technique, as mentioned in the previous report.[8] In brief, a clear corneal traction suture was anchored at the superior peripheral cornea (approximately 5 mm long and 75% deep) using 8-0 nylon to expose a surgical field. A conjunctiva and Tenon capsule incision of approximately 10 mm were made circumferentially at 5 mm posterior from the limbus in the supratemporal quadrant, and the sub-Tenon space was undermined. The body of the AGV was inserted into the sub-Tenon space, between the superior and lateral rectus muscles. Anchoring sutures were secured through the holes of the body onto the sclera at 8 to 9 mm posterior from the limbus with a 10-0 nylon suture. Paracentesis into the AC was made with a 23-gauge needle at the limbus. A silicone tube was cut, and a length of approximately 2 mm was inserted into the AC, in a bevel-up position. The silicone tube was anchored to the sclera by 2 anchoring sutures. A full-thickness donor scleral patch graft, 4 × 3 mm in size, was attached over the tube near the limbus and secured. The Tenon capsule and the conjunctiva were sutured with a continuous 10-0 nylon suture. In 6 cases in which shallowing of the AC during the surgical procedure was evident, a temporary occlusion suture of the silicone tube was made using an 8-0 vicryl suture (TG140-8; Johnson & Johnson, Somerville, New Jersey, USA), tied with 5-0 nylon thread (P-1; Johnson & Johnson) along with the silicone tube. A portion of the 5-0 nylon was exposed through the conjunctiva and was removed within 4 weeks after surgery. Atropine sulfate 1% solution (Ocutropine; Samil, Seoul, Korea) was used for 3 days after surgery, and 0.3% ofloxacin (Ocuflox; Samil) and 0.12% prednisolone acetate (Ocu-Pred; Samil) were prescribed 4 times daily and tapered over 3 months. If the IOP was elevated after surgery, oral acetazolamide was used for the first week, and then nonselective β-blockers, α-2 agonists, and prostaglandins were prescribed, in that order.

Specular microscopy using a noncontact-type specular microscope (Noncon Robo SP-8000; Konan Medical Inc, Tokyo, Japan) was performed by 1 experienced examiner before surgery and at 1, 6, 12, 18, and 24 months after surgery. All examinations were carried out at the central, superior, supranasal, and supratemporal areas of the cornea, while the patient maintained fixation on the target in the equipment. Cell density, hexagonality, and the coefficient of variation in cell area were calculated.

TABLE 1. Characteristics of Subject Group (underwent Ahmed Glaucoma Valve Implantation) and the Control Group (the Other Eyes of the Subject Who Had Glaucoma and Were Receiving Antiglaucoma Medications without Glaucoma Surgery)

Characteristic	Subject Group	Control Group	*P* value
No. of patients (no. of eyes)	41 (41)	20 (20)	
Mean age ± SD (years)	54.9 ± 13.6	53.8 ± 12.8	.782[a]
Gender (male/female)	26/15	12/8	.825[b]
Eye (right/left)	18/23	7/13	.964[b]
Lens status, no. eyes (%)			.831[b]
Phakia	24 (58.5)	13 (65.0)	
Aphakia or pseudophakia	17 (41.5)	7 (35.0)	
No. of past intraocular surgeries (mean ± SD)	0.6 ± 0.9	0.5 ± 0.7	.732[a]
Diagnosis, no. eyes (%)			.953[b]
Neovascular glaucoma	23 (56.1)	12 (60.0)	
Secondary glaucoma	14 (34.1)	4 (20.0)	
POAG	4 (9.8)[c]	3 (15.0)	
ACG	—	1 (5.0)	
Mean follow-up ± SD (mos)	19.1 ± 5.4	20.1 ± 5.8	.873[a]
Range	9 to 24	9 to 24	

ACG = angle-closure glaucoma; mos = months; POAG = primary open-angle glaucoma; SD = standard deviation.

[a]Two-tailed *t* test.

[b]Fisher exact test.

[c]All patients experienced a failed trabeculectomy.

All data were analyzed using SPSS software version 12.0K (SPSS Inc, Chicago, Illinois, USA). The Fisher exact test and a two-tailed *t* test were used to compare the demographic data between subjects and controls, and the Wilcoxon signed-rank test was used to compare IOP, VA, number of medications, and corneal ECD before and after surgery. A Mann–Whitney *U* test was used to compare IOP, number of medications, and percentage decrease of corneal ECD between groups. Values of $P < .05$ were deemed to be statistically significant. Kaplan-Meier survival analysis and a log-rank test were performed for cases with more than 20% loss of corneal endothelial cells after surgery.

RESULTS

WE STUDIED 41 EYES IN 41 PATIENTS (15 WOMEN, 26 MEN) with a mean age of 54.9 ± 13.6 years. The average follow-up period was 19.1 months (range, 9 to 24 months), and 31 eyes were followed up for 24 months. The control

TABLE 2. Change in Intraocular Pressure, Visual Acuity, and Number of Antiglaucoma Medications before and after Ahmed Glaucoma Valve Implantation

	Subject Eye				Control Eye			
Time of Examination	No.	IOP (mm Hg)	Eye drops	VA	No.	IOP (mm Hg)	Eye drops	VA
Baseline	41	36.7 ± 13.3	3.3 ± 0.8	0.9 ± 0.6	20	19.4 ± 3.5[b]	2.5 ± 0.6[c]	0.3 ± 0.5
1 mo	41	23.9 ± 6.1[a]	0.4 ± 0.5[a]	0.9 ± 0.7	20	19.4 ± 3.7	2.5 ± 0.6[c]	0.3 ± 0.7
6 mos	41	22.9 ± 6.2[a]	0.7 ± 0.7[a]	0.9 ± 0.7	20	19.6 ± 2.5	2.6 ± 0.7[c]	0.3 ± 0.6
12 mos	38	21.4 ± 8.5[a]	1.4 ± 0.9[a]	0.9 ± 0.6	19	19.7 ± 3.6	2.6 ± 0.6[c]	0.4 ± 0.6
18 mos	32	20.7 ± 7.5[a]	1.7 ± 0.6[a]	1.0 ± 0.8	18	19.8 ± 3.8	2.7 ± 0.6[c]	0.4 ± 0.6
24 mos	31	20.5 ± 8.9[a]	2.1 ± 0.7[a]	1.0 ± 0.8	14	20.5 ± 4.1	2.9 ± 0.7[c]	0.4 ± 0.7

IOP = intraocular pressure; mos = month(s); VA = visual acuity (in logarithm of the minimum angle of resolution units).

Data are presented as mean ± standard deviation.

[a]Postoperative IOP and number of antiglaucoma medications in the operated eye decreased significantly compared with baseline ($P < .05$, Wilcoxon signed-rank test).

[b]$P < .05$ compared with subject eye (Mann–Whitney *U* test).

[c]$P < .05$ compared with subject eye (Mann–Whitney *U* test).

group was composed of 20 eyes in 20 patients (8 women and 12 men) with a mean age of 53.8 ± 12.8 years. The average follow-up was 20.1 months (range, 9 to 24 months), and 14 eyes were followed up for 24 months. In the study group, 17 eyes (41.5%) were pseudophakic or aphakic; 7 eyes (35.0%) were so in the control group. The average number of previous intraocular surgeries was 0.6 in the subject group and 0.5 in the controls. Neovascular glaucoma was the most common type in both the subject group (23 eyes; 56.1%) and the control group (12 eyes; 60.0%). There was no statistical difference in demographics between the subject and control groups (Table 1). In the subject group, follow-up was stopped during the study period in 7 patients because of serious complications requiring surgical intervention (4 cataract, 2 retinal, and 1 glaucoma surgeries), and 3 eyes were lost to follow-up from 6 to 12 months after surgery, without any known problem or complication. In the control group, 4 eyes were followed up for fewer than 24 months because of 3 cataract surgeries and 1 glaucoma surgery, and 2 eyes were lost to follow-up from 6 to 12 months after surgery. Data before any second surgery or loss to follow-up were included in the analysis.

In the subject group, the IOP before surgery was 36.7 ± 13.3 mm Hg, and it decreased to 20.5 ± 8.9 mm Hg by 24 months after surgery; the decrease in IOP was significant at all time points ($P < .05$). The number of antiglaucoma medications was 3.3 ± 0.8 before surgery and 2.1 ± 0.7 at 24 months after surgery; the number of medications was significantly lower at all time points. VA (in logarithm of the minimum angle of resolution units) did not change significantly after surgery (0.9 ± 0.6 before surgery; 1.0 ± 0.8 at 24 months). Changes in IOP, the number of medications, and VA before and after surgery were not significant in the control group (Table 2).

In the subject group, the corneal ECD (average of 4 areas) was 2250 ± 657 (cells/mm^2) before surgery and decreased significantly after surgery to 2134 ± 698 at 1 month after surgery (5.8% decrease; $P = .021$), 2021 ± 742 at 6 months after surgery (11.5% decrease; $P = .014$), 1910 ± 794 at 12 months after surgery (15.3% decrease; $P = .024$), 1857 ± 758 at 18 months after surgery (16.6% decrease; $P = .012$), and 1785 ± 781 at 24 months after surgery (18.6% decrease; $P = .001$). Furthermore, these decreases were significantly greater than those in the control group at all time points ($P < .05$, Mann–Whitney *U* test). The change in corneal ECD differed according to the specific area measured and the time after surgery. At 1 month after surgery in the subject group, the percentage decrease in cell density was more prominent in the superior cornea (8.7% from baseline; $P = .024$) than in the other areas: supratemporal, 4.4% ($P = .001$); supranasal, 5.7% ($P = .021$); and central cornea, 4.6% ($P = .125$). At 6 months, the decreases had increased to 11.1%, 13.9%, 11.7%, and 8.6% in the superior, supratemporal, supranasal, and central areas, respectively. For all time points beginning 6 months after surgery, the densities in the subject group were significantly decreased in all areas, and the changes were significantly greater than those in the control group (Table 3). The greatest decrease was in the superior cornea at 1 month and in the supratemporal area at all subsequent time points. The smallest decrease was in the central area at all time points. The average of the changes in all areas showed a significant decrease beginning 1 month after surgery and continuing during the 24-month follow-up (Figure 1). Kaplan-Meier survival analysis for the percentage decrease in central corneal ECD of less than 20% gave survival rates of 69.3% at 12 months and 63.4% at 24 months after surgery in the subject group, whereas there was no case with a decrease of more than 20% in the control group (Figure 2).

The morphologic evaluation of the cornea after surgery revealed no significant changes in either polymegathism

TABLE 3. Change in Endothelial Cell Count in Each Measured Area and Overall Average after Ahmed Glaucoma Valve Implantation

Time of Examination	Superior		Supratemporal		Supranasal		Center		Average	
	Subject	Control	Subject	Control	Subject	Control	Subject	Control	Subject	Control
Baseline	2243 ± 705	2426 ± 566	2382 ± 655	2152 ± 658	2223 ± 764	2501 ± 628	2152 ± 658	2386 ± 620	2250 ± 657	2466 ± 589
1 mo	2089 ± 824[b]	2372 ± 550	2280 ± 708[b]	2554 ± 585	2117 ± 771	2469 ± 492	2047 ± 700	2362 ± 505	2134 ± 698[b]	2439 ± 626
%[a]	−8.7 ± 7.8[c]	−2.8 ± 6.1	−4.4 ± 6.3[c]	1.4 ± 5.8	−5.7 ± 7.2[c]	−0.8 ± 4.1	−4.6 ± 7.3	−1.2 ± 4.2	−5.8 ± 7.1[c]	−0.8 ± 6.4
6 mos	1999 ± 823[b]	2381 ± 626	2087 ± 735[b]	2478 ± 601	2040 ± 816[b]	2483 ± 668	1958 ± 717[b]	2351 ± 599	2021 ± 742	2423 ± 607
%[a]	−11.7 ± 10.2[c]	−3.2 ± 6.3	−13.9 ± 12.3[c]	−2.2 ± 6.2	−12.5 ± 10.0	−1.0 ± 6.0	−8.6 ± 10.7	−2.2 ± 5.7	−11.5 ± 9.0[c]	−2.1 ± 5.7
12 mos	1880 ± 811[b]	2385 ± 623	1939 ± 765[b]	2466 ± 610	1943 ± 843[b]	2432 ± 658	1881 ± 729[b]	2295 ± 626	1910 ± 794[b]	2395 ± 600
%[a]	−16.2 ± 14.9[c]	−3.3 ± 5.5	−18.0 ± 15.9[c]	−2.5 ± 7.2	−14.6 ± 12.7[c]	−2.9 ± 6.1	−12.6 ± 11.3[c]	−2.8 ± 6.1	−15.3 ± 13.8[c]	−2.8 ± 6.1
18 mos	1798 ± 821[b]	2345 ± 624	1911 ± 736[b]	2457 ± 628	1877 ± 832[b]	2424 ± 697	1839 ± 729[b]	2330 ± 642	1857 ± 758[b]	2389 ± 632
%[a]	−18.0 ± 16.6[c]	−4.6 ± 6.5	−18.5 ± 16.0[c]	−4.0 ± 6.9	−17.2 ± 16.5[c]	−3.7 ± 5.6	−14.1 ± 10.4[c]	−2.5 ± 6.7	−16.6 ± 13.4[c]	−3.7 ± 6.7
24 mos	1771 ± 845[b]	2266 ± 624	1795 ± 817[b]	2435 ± 590	1771 ± 817[b]	2370 ± 699	1801 ± 744[b]	2297 ± 638	1785 ± 781[b]	2342 ± 649
%[a]	−20.6 ± 18.2[c]	−4.8 ± 5.2	−22.6 ± 17.7[c]	−4.2 ± 6.9	−18.1 ± 15.9[c]	−3.8 ± 6.9	−15.4 ± 10.8[c]	−3.7 ± 5.2	−18.6 ± 16.8[c]	−4.2 ± 7.2

Mos = month(s).
[a]Percentage decrease in cell number from baseline.
[b]$P < .05$ compared with baseline (Wilcoxon signed-rank test).
[c]$P < .05$ compared with control eye (Mann–Whitney U test).

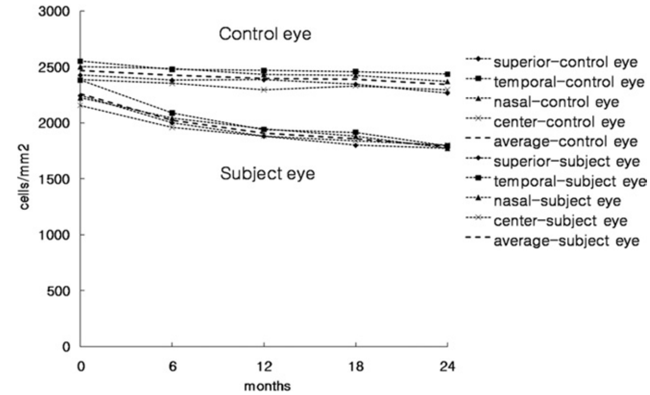

FIGURE 1. Graph showing the change in endothelial cell count after Ahmed glaucoma valve (AGV) implantation. There was a statistically significant decrease in mean percentage decrease in corneal endothelial cell count in operated eyes in all measurement areas compared with control eyes during the follow-up ($P < .05$, Mann–Whitney U test).

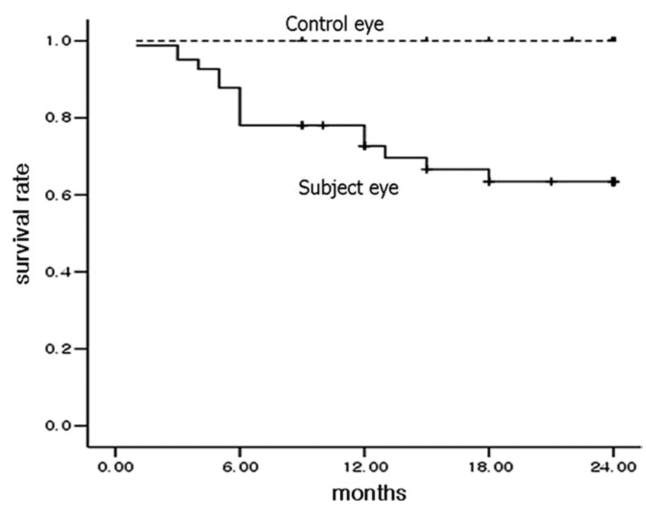

FIGURE 2. Kaplan-Meier survival curve showing survival for the percentage decrease in central corneal endothelial cell count less than 20% from baseline count after AGV implantation. The survival rates were 69.3% operated eyes and 100% in control eyes at 12 months, and 63.4% in operated eyes and 100% in control eyes at 24 months ($P < .001$, log-rank test).

(coefficient of variation in cell area) or pleomorphism (hexagonality of the cells). Furthermore, both of these parameters were the same between the subject and control groups (Tables 4 and 5).

DISCUSSION

ROLLET AND MOREAU FIRST USED A FOREIGN MATERIAL, horse hair, for refractory glaucoma surgery in 1907.[9] Since that time, many kinds of implant materials and designs have been developed and studied. The AGV, a modern type of long-tube shunt glaucoma implant, was introduced

TABLE 4. Mean Change in Coefficient of Variation after Ahmed Glaucoma Valve Implantation

	Superior		Supratemporal		Supranasal		Center	
Time of Examination	Subject	Control	Subject	Control	Subject	Control	Subject	Control
Baseline	0.366	0.342	0.332	0.351	0.331	0.349	0.343	0.351
1 mo	0.341	0.340	0.337	0.352	0.325	0.321	0.349	0.335
6 mos	0.372	0.362	0.352	0.336	0.337	0.340	0.358	0.331
12 mos	0.363	0.363	0.365	0.359	0.327	0.340	0.361	0.327
18 mos	0.365	0.374	0.358	0.338	0.332	0.357	0.346	0.341
24 mos	0.344	0.379	0.353	0.331	0.314	0.362	0.336	0.351

Mos = month(s).
$P > .05$ from baseline (Wilcoxon signed-rank test) at all follow-up visits in all areas compared with the control eye (Mann–Whitney *U* test).

TABLE 5. Mean Change in Hexagonality after Ahmed Glaucoma Valve Implantation

	Superior		Supratemporal		Supranasal		Center	
Time of Examination	Subject	Control	Subject	Control	Subject	Control	Subject	Control
Baseline	55.4	60.1	55.1	57.7	56.8	56.1	54.5	55.5
1 mo	55.8	63.1	54.6	55.7	52.0	58.5	52.5	56.8
6 mos	53.6	59.1	54.2	57.9	52.8	56.9	53.6	55.1
12 mos	51.4	57.7	54.5	56.0	53.5	54.2	55.2	59.5
18 mos	53.4	55.9	56.5	57.2	53.7	56.5	57.3	60.1
24 mos	54.7	56.8	55.5	52.4	55.2	56.3	56.8	56.2

Mos = month(s).
$P > .05$, from baseline (Wilcoxon signed-rank test) at all follow-up visits in all areas compared with the control eye (Mann–Whitney *U* test).

by Coleman and associates in 1995 and is used widely today.[10]

In long-tube shunt surgery, the tube must be connected to the AC to assist aqueous outflow. However, the existence of the tube in the AC is known to disturb the normal environment of the corneal endothelium and may induce corneal edema and decompensation.[6] The frequency of corneal complications after AGV implant surgery has been reported to be 9% to 27% after long-term follow-up.[11–13] In a 30.5-month follow-up study, Topouzis and associates reported the development of corneal decompensation in 27% of 60 eyes after AGV surgery, making decompensation one of the most frequent complications after AGV implantation.[13] However, we could find no report about changes in the corneal endothelium after implant surgery, except for a report by McDermott and associates and a 1-year follow-up study after AGV surgery reported previously by our group.[8,14] McDermott and associates studied changes in the density of the corneal endothelium after surgery using a Molteno implant, an open-type implant without a valve function; they found no clinically significant change at 10 months after surgery in 19 patients. However, because they did not determine the corneal ECD before surgery, they could not evaluate the change in density over time after surgery compared with the density before surgery.

The exact mechanism causing damage to the corneal endothelium remains unclear, and many theories have been proposed. McDermott and associates proposed the jet flow around the tube end caused by the heart beat, inflammation in the chamber, intermittent tube–corneal touch, tube–uveal touch, and a foreign body reaction to the silicone tube as possible mechanisms of corneal endothelial damage.[14] Setälä suggested that high IOP and long duration of elevated IOP before surgery may affect the endothelium directly or may cause hypoxic damage indirectly.[15] Fiore and associates proposed that the mechanism of corneal endothelial damage may involve the toxicity of the preservatives in eye drops, the duration of surgery, shallowing of the AC during or after surgery, or changes in the composition of the aqueous humor attributable to the direct connection with the sub-Tenon space.[16]

Damage to the corneal endothelium can be induced differentially according to the type of intraocular surgery. Smith and associates reported a wide range of decreases in ECD, 1.6% to 54.8%, at 3 months after filtration surgery.[17] Arnavielle and associates reported density decreases of 7.0% at 3 months and 10.6% at 12 months after trabeculectomy.[18] Shin and associates found a decrease of 7.7% at 3 months after trabeculectomy with mitomycin C soaking, but a 2.5% decrease in density when the intracameral injection of viscoelastics was used with the same surgery.[19]

Damage to the corneal endothelium also has been reported widely in cataract surgery. Wirbelauer and associates reported that the average loss of corneal endothelium was 11.4%, and Walkow and associates reported an 8.5% loss at 12 months after cataract surgery.[20,21] Lesiewska-Junk and associates also described a change in corneal endothelium within 1 month after phacoemulsification cataract surgery.[22] Damage to the corneal endothelium in cataract surgery is thought to be a one-time event associated with the surgery. In contrast, AGV surgery for glaucoma is associated with a continuing risk for damage to the corneal endothelium because of the existence of the tube within the chamber and the direct connections between the AC and the extraocular space, sub-Tenon space, and the corneal endothelium.

In this study, we excluded cases in which tube–corneal touch developed. In cases requiring additional surgery, the data after the additional surgery were excluded because of its possible effects on the corneal endothelium. In our previous study, the subjects were restricted to those who could be followed up for more than 1 year, and the decrease in corneal ECD was 10.5% at 12 months after surgery. However, in the clinical setting, some of the patients who underwent AGV surgery for refractory glaucoma were dropped from follow-up in our previous study because of secondary surgery to treat increased IOP or complications after surgery. We suggest that the cases dropped during the first year after surgery might have shown changes in the corneal endothelium that were different from those in the cases with good postoperative courses. Thus, in the present study, we did not exclude those who could not be followed up for 2 years because of additional surgeries or significant complications, and the data before a second surgery were included in our analysis. As a result, there was a greater decrease in the corneal ECD compared with that in the previous study. In the present study, the average percentage decreases for all fields of the corneal endothelium were 5.8%, 11.5%, 15.3%, 16.6%, and 18.6% at 1, 6, 12, 18, and 24 months after surgery, respectively.

As mentioned in our previous study, we believe that the density at the superior area of the cornea showed the greatest decrease because of the corneal traction suture made to expose the surgical field.[8] After 1 month, the site of the greatest decrease was the supratemporal area; the site of smallest change was the central area at all time points in the study. The decrease in ECD progressively increased during the study period, and at the end of the study, the site of the greatest decrease was the supratemporal area, where the tube end was located. Given that the corneal endothelium has no ability to reproduce, our findings suggest that the central ECD will continue to decrease with time.

It was difficult to establish a control group in this study, because we could not just wait to evaluate patients who showed significantly elevated IOP in the clinical setting. As a second choice, we used the other eye of the subject as a control, but only if that eye was diagnosed with glaucoma and the IOP was under control with one or more antiglaucoma medications. Although this group might not have been the best control given that the differences in IOP and in the number of antiglaucoma medications might have affected the changes in the corneal endothelium, other factors were matched similarly (Table 1). Additionally, it is possible that despite our best efforts, we might not have examined the exact same area of the cornea at every visit, using the same fixation target at each examination. There might have been inborn errors in the calculation of the cell density, although the same experienced examiner conducted all of the evaluations to minimize such errors.

In conclusion, we found that the corneal ECD decreased progressively up to 24 months after AGV surgery and that the change was significant compared with the baseline and control densities. Thus, attention should be paid to the corneal ECD in deciding on AGV surgery for the treatment of refractory glaucoma, especially in a patient who has any risk factor for corneal damage. Alternative treatments should be considered for patients with significantly low corneal ECD before surgery; however, if no other viable option can be identified, great care must be taken to avoid inadvertent damage to the cornea during and after AGV surgery.

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