Change in Corneal Endothelial Cell Density after Baerveldt Shunt Implantation in Glaucoma Patients

Sakaorat Petchyim, M.D., Ratchadaporn Tantimala, M.D., Pinnita Prabhasawat, M.D., Pratuangsri Chonpimai, M.D., Manachaya Prukajorn, M.D., Ngamkae Ruangvaravate, M.D.

Department of Ophthalmology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

ABSTRACT

Objective: To evaluate changes in corneal endothelial cells density (EDC) at 1 one, six, and twelve months after Baerveldt shunt implantation.

Materials and Methods: This prospective study included 24 patients who underwent Baerveldt shunt implantation for refractory glaucoma, and who had one full year of post-surgical follow-up. Best corrected visual acuity (BCVA), intraocular pressure (IOP), number of glaucoma medications, central corneal thickness (CCT), corneal endothelial cell density (EDC), and morphology in central, inferior, and superotemporal (stEDC) areas were recorded at baseline, and 1, 6, and 12 months after surgery. Distance between the tip of tube to corneal endothelium (TTC) was measured using optical coherence tomography at one month after surgery.

Results: Twenty-four eyes from 24 patients were analyzed. Sixty-two percent were primary open-angle glaucoma, and 73.1% of patients had previous trabeculectomy. Mean BCVA was not significantly changed. The mean IOP at six months (12.2±4.35 mmHg) and at one year (11.1±4.31 mmHg) was significantly lower than baseline (20.1±9.24 mmHg) (p<0.001 and p<0.001 respectively). Median (min, max) number of anti-glaucoma medications significantly decreased from 4 (1, 6) at baseline to 1 (0, 3) and 1 (0, 3) at six months and one year after surgery (p<0.001 and p<0.001, respectively). Mean baseline stEDC was 1,527±644 cells/mm^2. From linear mixed model, stEDC showed the most significantly decreasing slope (y=1365.54 – 18.6125t, p=0.014), and CCT showed a significant increase over time (y=533.65 + 1.8853t). Pearson's correlation coefficient between TTC and stEDC change at one year was not statistically significant (-0.403, p=0.172).

Conclusion: After Baerveldt shunt implantation, EDC loss over time was found in the area closest to where the tube was placed in addition to increasing CCT. Distance from tip of tube to cornea is not the only factor that can cause EDC loss after shunt implantation. Additional study to identify other possible mechanisms is warranted.

Keywords: Corneal endothelial cells; Baerveldt shunt implantation; glaucoma; Thailand (Siriraj Med J 2021; 73: 252-258)

INTRODUCTION

Drainage implant surgery is one of the most effective treatments for refractory glaucoma.[1] Compared to conventional trabeculectomy, drainage implant surgery was shown to have a higher success rate for controlling intraocular pressure (IOP) during 5 years of follow-up in patients who had previous trabeculectomy and/or cataract extraction.[1] Many types of shunts have been introduced since Molteno introduced his first glaucoma drainage devices.[2] Baerveldt shunt is one of the contemporary drainage devices that was shown to achieve satisfactory pressure reduction in many studies.[1,3,4] Many studies

Corresponding author: Ngamkae Ruangvaravate
E-mail: ngamkae1@gmail.com
Received 28 October 2020 Revised 2 December 2020 Accepted 7 January 2021
ORCID ID: http://orcid.org/0000-0002-4342-0174
http://dx.doi.org/10.33192/Smj.2021.33

have compared the efficacy and complications of widely used devices. Among those, a randomized controlled trial compared the Baerveldt shunt with the Ahmed shunt. The results of that study revealed a higher success rate in the Baerveldt group; however, the Baerveldt shunt requires a greater number of interventions than the Ahmed shunt.[4]

Although glaucoma drainage implantation has demonstrated good efficacy in refractory glaucoma cases, this intervention can result in endothelial cell density (EDC) loss with severe adverse effect in some cases.[5-12] Various mechanisms of EDC loss have been proposed. One hypothesis is that mechanical trauma caused by introduction of a silicone tube into the anterior chamber could effectuate EDC loss. The result from a two-year prospective study of 41 eyes after superotemporal Ahmed implantation found endothelial cell loss compared to control eyes, and cell loss was greatest in the superotemporal cornea where the tube was placed.[8] Another theory suggests that change in flow or composition of aqueous humor after glaucoma surgery could be a cause of EDC loss. This hypothesis arose after EDC loss was observed in eyes whose anterior chamber had not been penetrated by a silicone tube.[13,14]

The primary aim of this prospective study was to evaluate changes in EDC after Baerveldt shunt implantation by comparing post-surgical EDC parameters at one, six, and twelve months to baseline. Due to the uncertain mechanism of EDC loss, our secondary aim was to investigate whether tube and endothelial distance correlate with endothelial cell change.

MATERIALS AND METHODS

This prospective study enrolled patients under the care of one of the authors (N.R.) who was scheduled for Baerveldt shunt implantation at the Department of Ophthalmology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand during July 2010 to July 2017. The indication for surgery were secondary glaucoma and any cases with uncontrolled intraocular pressure after conventional trabeculectomy. The exclusion criteria were patients with corneal opacity or lesion that could obscure corneal endothelial cell count examination such as Haab striae in congenital glaucoma and pseudophakic bullous keratopathy. Any patient that developed serious complication or who required additional intraocular surgery was withdrawn from the study. Only patients with at least one full year of postoperative follow-up were included in the final analysis. Eventually, 24 eyes from 24 patients were enrolled, and written informed consent was obtained from all participants. The protocol for this study was approved by the Siriraj Institutional Review Board (SIRB) (Si 676/2010).

Age at surgery, gender, type of glaucoma, history of previous laser or intraocular surgery, other ocular disease, and anti-glaucoma drugs were recorded. Best corrected visual acuity (BCVA), a thorough eye examination using slit-lamp biomicroscope, and IOP using a Goldmann applanation tonometer were obtained at every visit. Postoperatively, any surgical complication and number of anti-glaucoma medications were recorded. After shunt operation, anti-glaucoma medication was initiated to maintain individual target IOP.

Corneal endothelial cell density (EDC) and central corneal thickness (CCT)

EDC and CCT were measured at baseline, and at 1, 6, and 12 months after surgery. EDC was measured in 3 different areas of the cornea, including central, superotemporal, and inferior by one experienced technician (PC) using a Nidek-CS4 confocal microscope (Nidek Co. Ltd, Japan). Only the manual center dot method was used. CCT was measured by optical coherence tomography (Visante; Carl Zeiss Meditec, Germany).

Distance from tip of the tube to corneal endothelium (TTC)

Tip of tube to corneal endothelium distance perpendicular to posterior cornea was measured using optical coherence tomography (Visante; Carl Zeiss Meditec) at one month after surgery by the same technician. Patients were asked to look at the internal fixation light and the scanning axis was placed along the tube. The technician took special care not to apply pressure to the eye.

Surgical details

All cases were implanted with the same Baerveldt shunt model (model BG101-350, which has a surface area of 350 mm^2; Abbott Medical Optics, Inc., Santa Ana, CA, USA) at the superotemporal region. Using the standard technique, all shunts was inserted by a single surgeon (NR). A 7-0 traction suture was placed at the superotemporal cornea to expose the superotemporal conjunctiva. A conjunctival flap was made by 12-14 mm length conjunctival incision that was made parallel to and 8 mm posterior to the limbus. Muscle hooks were used to identify the superior and lateral rectus muscles. The superior rectus was isolated and retracted from the globe with a muscle hook. A second muscle hook was inserted under the belly of the muscle more posteriorly to aid in elevation and retraction. Both implant wings were placed under the superior and medial rectus muscles.

The implant was then sutured to the sclera with 8-0 virgin silk suture through the suture holes. The suture knots were rotated into the suture hole eyelets. Scissors were used to cut the tube so that approximately 1-2 mm of tube length would be inside the eye with an upward-facing bevel. The tube was then ligated within a few millimeters of the implant flange with 6-0 Vicryl. The tube was checked for complete occlusion by inserting a 30-gauge cannula at the cut end, and an attempt was made to flush saline. A clear cornea paracentesis was made at 9 o'clock using a 15-degree blade. The anterior chamber at the intended area for needle track internal opening was deepened with viscoelastic. A 23-gauge needle was used to create a track aim for the tube parallel to the iris plane. The tube was then inserted through the track. Once it was in proper position, the tube was sutured to the episclera with 10-0 nylon. Early filtration was aided by piercing the tube anterior to the ligation using a 15-degree blade (Sherwood's method). The tube was then covered with scleral graft with interrupted 10-0 nylon anchoring sutures. Tenon along with conjunctiva were sutured using 8-0 virgin silk and 10-0 nylon running suture. The wound was tested for water tightness. Dexamethasone (4 mg/ml) 0.5 ml was injected subconjunctivally into the inferior quadrant.

After the operation, a 1% prednisolone acetate eye drop was given every 2 hours during the first few weeks, with a tapered decrease to discontinuation by the 3-month postoperative time point. A 0.5% levofloxacin eye drop was given 4 times daily, and a 0.3% tobramycin and 0.1% dexamethasone eye ointment was given once before bedtime for several months according to wound healing and inflammation. Anti-glaucoma drugs were managed according to the target IOP level.

Statistical analysis

All data analyses were performed using SPSS software version 18 (SPSS, Inc., Chicago, IL, USA). Descriptive statistics were used to summarize patient demographic and clinical characteristics, and those results are reported as number and percentage, mean plus/minus standard deviation, or median (minimum, maximum). Wilcoxon signed-rank test was used to compare non-normally distributed continuous data, while paired *t*-test was used to compare normally distributed continuous data. Random intercept mixed model was used to create the equation to evaluate EDC and CCT change over time. Pearson's correlation coefficient was used to determine the correlation between TTC and EDC loss. A *p*-value less than 0.05 was considered statistically significant for all tests.

RESULTS

There were 31 patients (31 eyes) who underwent uneventful Baerveldt shunt implantation at Siriraj Hospital by a single experienced surgeon (NR) during June 2010 to July 2017. Two eyes were withdrawn from the study due to conjunctival wound leak with hypotony and recurrent granulomatous anterior uveitis. Five eyes were excluded from analysis due to ≤ 2 postoperative EDC measurements. All 24 patients completed one full year of follow-up, and all patients had baseline EDC measurement and at least 3 postoperative EDC measurements. P demographic and clinical data is summarized in Table 1. The mean preoperative stEDC was 1,527±644 cell/mm^2.

Mean visual acuity was not significantly changed between before and after surgery; however, mean IOP and the median number of anti-glaucoma medications were significant lower compared to baseline (Table 2). Table 3 showed mean EDC in particular regions at baseline and post-operative time points. Table 4 showed mean CCT at baseline and post-operative time points. According to the results of mixed model analysis (Table 5), EDC decreased over time during the one-year period after Baerveldt shunt implantation, with the greatest rate of decrease in the superotemporal region, and CCT was observed to have increased. Endothelial cell loss at 1 year was 18.07%, 8.79%, and 9.18% at the superotemporal, central, and inferior cornea, respectively. The mean CCT at baseline, and at 1, 6, and 12 months is shown in Fig 1.

Pearson's correlation coefficient revealed no statistically significant correlations between TTC and EDC change for any region (Table 6).

DISCUSSION

In this study, we investigated whether there is EDC loss after Baerveldt shunt implantation, and whether TTC correlates with EDC loss.

We found EDC loss, which is supported by the result from linear mixed model (Table 3). The greatest negative multiplier with time of stEDC emphasized the greatest EDC loss rate in that region.

The percentage of EDC loss at one year was consistent with previous studies.[15,16] One retrospective study showed 10.7% of endothelial cell loss at one year, which is comparable to our findings (8.79%). We measured EDC loss at the superotemporal cornea, whereas the previous study made their measurement at the central cornea. Other studies reported EDC loss to be greatest at the cornea quadrant where the tube was placed.[11,16,17] Iwasaki and associates found 13.1% EDC loss, which is lower than our findings. This difference may have resulted from their greater

TABLE 1. Patient characteristics.

Characteristics	N
Number of patients, n	24
Age, median (min, max), years	65 (29,80)
Gender, n (%)	
Male	15 (62.5%)
Type of glaucoma, n (%)	
POAG	15 (62.5%)
PACG	3 (12.5%)
JOAG	1 (4.2%)
Secondary glaucoma	5 (20.8%)
Uveitis	3
Steroid induced glaucoma	1
Lens subluxation	1
Lens status	
Pseudophakia	23 (92%)
Aphakia	1 (8%)
Previous trabeculectomy, n (%)	19 (73.1%)
Number of previous intraocular surgery, n (min, max)	1.76 (1,3)
Baseline stEDC	1527 ± 644
Distance between tip of the tube to endothelium	1.4 ± 0.6

Abbreviations: JOAG, juvenile open angle glaucoma; PACG, primary angle closure glaucoma; POAG, primary open angle glaucoma; SD, standard deviation; VKH; stEDC, superotemporal endothelial cell density.

TABLE 2. IOP and number of anti-glaucoma medications before and after Baerveldt shunt implantation.

Parameters	N	Value	p-value
IOP, mean ± SD, mmHg			
Baseline	26	20.12 ± 9.24	
1 month	26	17.73 ± 8.12	0.288*
6 months	26	12.15 ± 4.35	<0.001*
12 months	24	11.08 ± 4.31	<0.001*
Number of anti-glaucoma medications, median (min,max)			
Baseline	26	4 (1,6)	
1 month	26	1 (0,5)	<0.001 †
6 months	26	1 (0,3)	<0.001 †
12 months	24	1 (0,3)	<0.001 †

Notes: * Paired T-test, † Wilcoxon signed-rank test
p-value < 0.05 was considered statistical significance.
Abbreviations: IOP, intraocular pressure; SD, standard deviation.

TABLE 3. Mean EDC before and after Baerveldt shunt implantation.

Region	Baseline after operation	1 month after operation	6 months after operation	12 months
stEDC (mean ± SD)	1526.6±644.29	1420.8± 558.85	1364.8± 625.9	1289.3± 594.24
cEDC (mean ± SD)	1504.9±486.21	1588.2±534.10	1545.5±534.82	1476.2±542.51
iEDC (mean ± SD)	1406.3±497.01	1387.8±474.42	1401.7±482.72	1319.6±528.67

Abbreviations: stEDC, superotemporal endothelial cell density; cEDC, central endothelial cell density; iEDC, inferior endothelial cell density

TABLE 4. The correlation between distance from tip of the tube to corneal endothelium and EDC change.

Time	CCT (micron) Mean ± SD
Baseline	529.61±29.919
1 month after operation	521.55±39.946
6 months after operation	525.20±29.169
12 months after operation	535.80±25.548

Abbreviation: CCT, Central corneal thickness

TABLE 5. Linear mixed model equations for EDC and CCT change over time.

Parameters	Equation (mixed model)	p-value t, t^2
stEDC	y=1365.54-18.6125t	0.0144
cEDC	y=1518.44-5.2495t	0.1775
iEDC	y=1373.54-6.0106t	0.2210
CCT	y=533.65 + 1.8853t	0.0137

t = month

Abbreviations: stEDC, superotemporal endothelial cell density; cEDC, central endothelial cell density; iEDC, inferior endothelial cell density

TABLE 6. The correlation between distance from tip of the tube to corneal endothelium and EDC change.

Time	Site	Pearson correlation	p-value
6 months	stEDC	-0.340	0.112
	iEDC	0.172	0.382
	cEDC	0.130	0.510
12 months	stEDC	-0.403	0.172
	iEDC	-0.049	0.869
	cEDC	0.165	0.541

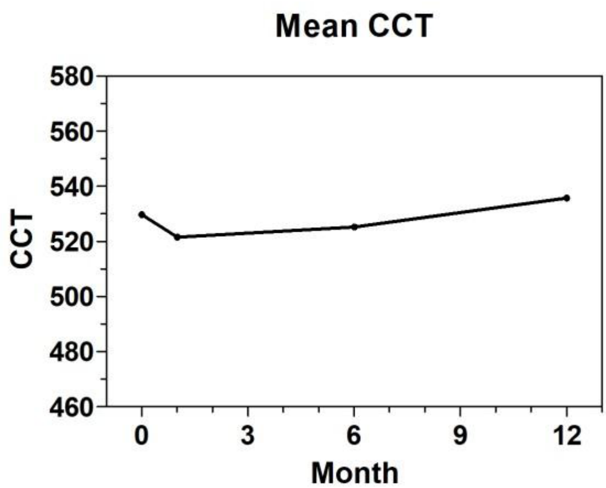

Fig 1. Mean Central corneal thickness after baerveldt shunt implantation

baseline EDC compared to our patients (2,107±625 cells/mm^2 *vs*. 1,527±644 cells/mm^2, respectively) since the lower EDC cornea is more susceptible to any cause of damage. There was one prospective study that found a rate of EDC loss of 7.43% per year, which is comparable to our study.[17]

From linear mixed model - stEDC, which was the quadrant closest to the tube in the anterior chamber, was found to be the most affected region of the 3 evaluated regions (Table 5). The local effect of EDC loss is comparable to previous reports.[11,15,17] Moreover, from the model we found increased CCT, which might represent early sign that could lead to corneal decompensation. Corneal decompensation after glaucoma drainage device implantation has been reported previously.[9,18] In the present study, we found increased CCT and decreased stEDC, which is comparable to Koo and colleagues who found an inverse correlation between CCT and superotemporal endothelial cell count in patients with EDC less than 1,000 cells/mm^2.[11]

Even though we found local EDC loss at the cornea quadrant where the tube was placed, we did not find TTC to be significantly correlated with EDC loss. In contrast, Iwasaki and colleagues reported that tube to cornea angle negatively correlated with EDC loss (Pearson's correlation -0.55, p=0.0013).[16] In the present study, we used a different tube to cornea parameter that may not be comparable. A cross-sectional study reported TTC to be the only significant predictor of EDC loss at superotemporal cornea compared to inferior cornea.[11] The lack of baseline and longitudinal data is the limitation of the study mentioned. Apart from that, the mean tube to cornea distance in the previous study was 1.1±0.8 mm compared to 1.4±0.6 mm in our study. The closer the tube is to cornea might result in greater damage to endothelium.

Many theories have been proposed to explain corneal endothelial cell loss after shunt surgery. Mechanical trauma could be caused by tube motility. Tan and associates found greater EDC loss in the 'Free' tube in the anterior chamber subgroup compared to 'Transiridial' tube, which may suggest that the tube is more stable with transiridial technique. There was no significant difference between those two subgroups relative to TTC (1.7±0.5 mm and 1.6±0.7 mm for 'Free' tube and 'Transiridial' tube, respectively). Another possible mechanism is a change in composition and/or flow of aqueous humor. Cytokines that are released due to a foreign body reaction to the plate could flow from bleb to the anterior chamber via the tube.[19] Instead of flowing symmetrically through the trabecular meshwork, aqueous humor flow to the tube could alter the environment with resulting adverse impact to endothelial cells.[19,20] In the future, study of how aqueous humor change in composition and flow could affect EDC after glaucoma shunt implantation should be conducted.

There are several limitations in this study. First, the tube parameter was TTC at 1-month post-operation, which may have been too early to determine whether or not tube migration occurred during follow-up time. There were 12 eyes from 24 eyes that had tube distance measured at 1st and 6th to 12th months. The mean difference in tube distance between 1st and 6th to 12th month was 0.08±0.189 mm closure to cornea (range: 0.53 mm closer to cornea to 0.14 mm away from cornea). This represents a small change in tube distance.

Second, tube to cornea angle, tube motility, and tube length were not measured, and one, two, or all three of these factors could influence EDC loss. Third, we included primary and secondary glaucoma, which could result in corneal endothelial cell loss. However, 79.2% of patients were primary glaucoma with no history of acute angle closure that could result in dramatic endothelial cell loss. Comparing secondary and primary glaucoma, there is no statistically significant difference in the mean EDC and stEDC at every time point. The effect of previous surgeries cannot be totally eliminated since in clinical practice, shunt surgery is reserved for refractory glaucoma cases. In this study, all cases had undergone cataract surgery. We found that after shunt surgery, endothelial cell loss (8.79%) is greater compared to a previous report of corneal endothelial cell loss in cataract surgery alone (2.06%)[21]. Therefore, the observed endothelial cell loss resulted from shunt surgery rather than cataract surgery.The only previous glaucoma surgery was trabeculectomy with mitomycin-C, which was performed in 69.2% of patients. Moreover, all of those operations were performed more than 6 months before shunt operation. In trabeculectomy, endothelial cell loss was found during the immediate postoperative period, which is less than 3 months post-operation. Our patients had trabeculectomy performed longer than 6 months; therefore, the effect from trabeculectomy should be considered minimal at best. Lastly, we did not measure the level of inflammation or cytokine release before and after shunt implantation. Further study designed to investigate or account for these factors about these possible factors will yield more information about tube-induced EDC loss.

The present study emphasizes that the tube can induce local EDC loss in the cornea quadrant nearest to the tube after Baerveldt shunt implantation. The mechanism is still unclear, but other mechanisms apart from the distance from tip of tube to cornea should be studied.

CONCLUSION

After Baerveldt shunt implantation, EDC loss over time was found in the area closest to where the tube was placed in addition to increasing CCT. Distance from tip of tube to cornea is not the only factor that can cause EDC loss after shunt implantation. Additional study to identify other possible mechanisms is warranted.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the patients that agreed to participate in this study, and Assist. Prof. Dr. Chulaluk Komoltri for her assistance in the statistical analysis.

Conflict of Interest: All authors declare no personal or professional conflicts of interest, and no financial support from the companies that produce and/or distribute the drugs, devices, or materials described in this report.

Funding disclosure: This was an unfunded study.

REFERENCES

1. Gedde SJ, Schiffman JC, Feuer WJ, Herndon LW, Brandt JD, Budenz DL, et al. Treatment outcomes in the Tube Versus Trabeculectomy (TVT) study after five years of follow-up. Am J Ophthalmol 2012;153:789-803.e2.
2. Lim KS, Allan BD, Lloyd AW, Muir A, Khaw PT. Glaucoma drainage devices; past, present, and future. British journal of ophthalmology, Br J Ophthalmol 1998;82:1083-9.
3. Seah SKL, Gazzard G, Aung T. Intermediate-term outcome of Baerveldt glaucoma implants in Asian eyes. Ophthalmology 2003;110:888-94.
4. Christakis PG, Kalenak JW, Zurakowski D, Tsai JC, Kammer JA, Harasymowycz PJ, et al. The Ahmed Versus Baerveldt study: one-year treatment outcomes. Ophthalmology 2011;118:2180-9.
5. Hau S, Barton K. Corneal complications of glaucoma surgery. Curr Opin Ophthalmol 2009;20:131-6.
6. Hollander DA, Giaconi JA, Holland GN, Yu F, Caprioli J, Aldave AJ, et al. Graft failure after penetrating keratoplasty in eyes with Ahmed valves. Am J Ophthalmol 2010;150:169-78.
7. Casini G, Loiudice P, Pellegrini M, Sframeli AT, Martinelli P, Passani A , et al. Trabeculectomy Versus EX-PRESS Shunt Versus Ahmed Valve Implant: Short-term Effects on Corneal Endothelial Cells. Am J Ophthalmol 2015;160(6):1185-90.e1.
8. Lee E-K, Yun Y-J, Lee J-E, Yim J-H, Kim C-S. Changes in corneal endothelial cells after Ahmed glaucoma valve implantation: 2-year follow-up. Am J Ophthalmol 2009;148:361-7.
9. McDermott ML, Swendris RP, Shin DH, Juzych MS, Cowden JW. Corneal endothelial cell counts after Molteno implantation. Am J Ophthalmol 1993;115:93-96.
10. Hau S, Scott A, Bunce C, Barton K. Corneal endothelial morphology in eyes implanted with anterior chamber aqueous shunts. Cornea 2011;30:50-55.
11. Koo EB, Hou J, Han Y, Keenan JD, Stamper RL, Jeng BH, et al., Effect of glaucoma tube shunt parameters on cornea endothelial cells in patients with Ahmed valve implants. Cornea 2015;34:37-41.
12. Koo EB, Hou J, Keenan JD, Stamper RL, Jeng BH, Han Y.Effects of Glaucoma Tube Surgery on Corneal Endothelial Cells: A Review. Eye Contact Lens 2016;42:221-4.
13. Rososinski A, Wechsler D, Grigg J. Retrospective review of pars plana versus anterior chamber placement of Baerveldt glaucoma drainage device. J Glaucoma 2015;24:95-99.
14. Gedde SJ, Schiffman JC, Feuer WJ, Herndon LW, Brandt JD, Budenz DL, et al. Treatment outcomes in the Tube Versus Trabeculectomy (TVT) study after five years of follow-up. Am J Ophthalmol 2012;153:789-803.e2.
15. Kim CS, Yim JH, Lee EK, Lee NH. Changes in corneal endothelial cell density and morphology after Ahmed glaucoma valve implantation during the first year of follow up. Clin Exp Ophthalmol 2008;36:142-7.
16. Iwasaki K, Arimura S, Takihara Y, Takamura Y, Inatani M. Prospective cohort study of corneal endothelial cell loss after Baerveldt glaucoma implantation. PLoS One 2018;13:e0201342.
17. Tan AN, Webers CAB, Berendschot TTJM, Brabander J, Witte PM, Nuijts RMMA, et al. Corneal endothelial cell loss after Baerveldt glaucoma drainage device implantation in the anterior chamber. Acta Ophthalmol 2017;95:91-96.
18. Kim KN, Lee SB, Lee YH, Lee JJ, Lim HB, Kim CS. Changes in corneal endothelial cell density and the cumulative risk of corneal decompensation after Ahmed glaucoma valve implantation. Br J Ophthalmol 2016;100:933-8.
19. Freedman J, Iserovich P. Pro-inflammatory cytokines in glaucomatous aqueous and encysted Molteno implant blebs and their relationship to pressure. Invest Ophthalmol Vis Sci 2013;54:4851-5.
20. Tuulonen A, Risteli J, Risteli L, Välimäki J, Airaksinen PJ. Collagen synthesis activity in the aqueous humour of eyes with glaucoma surgery: a pilot study. Br J Ophthalmol 1996;80:74-77.
21. Choi JY, Han YK. Long-term (≥10 years) results of corneal endothelial cell loss after cataract surgery. Can J Ophthalmol 2019;54:438-44.