Clinical Characteristics of Fast and Slow Progressors of Glaucoma Secondary to Iridocorneal Endothelial Syndrome

Min Gu Huh, MD\textsuperscript{1,2}, Young Kook Kim, MD, PhD\textsuperscript{1,2}

\textsuperscript{1}Department of Ophthalmology, Seoul National University Hospital, Seoul, Korea
\textsuperscript{2}Department of Ophthalmology, Seoul National University College of Medicine, Seoul, Korea

\textbf{Purpose:} To investigate the clinical characteristics of patients diagnosed with glaucoma secondary to iridocorneal endothelial (ICE) syndrome according to the degree of glaucoma progression.

\textbf{Methods:} We retrospectively analyzed the medical records of 19 eyes of 19 patients with glaucoma due to ICE syndrome who had been observed for more than 4 years. The patients were then categorized into slow progressor and fast progressor groups based on the rate of mean deviation (MD) change (-1.0 decibel [dB]/yr), and the clinical characteristics of the two groups were compared and analyzed.

\textbf{Results:} A total of 19 eyes from 19 glaucoma patients with ICE syndrome were included in the study, with 11 eyes in the slow progressor group and 8 eyes in the fast progressor group. Baseline characteristics showed no significant differences in age, ICE type, retinal nerve fiber layer thickness or MD of visual field tests between the two groups, but the fast progressor group had a significantly lower corneal endothelial cell density (ECD) and larger cup-to-disc ratio (CDR) compared to the slow progressor group. In the slow progressor group, only 2 eyes (18.2\%) required glaucoma surgery, and intraocular pressure was managed with medication alone. In contrast, 7 eyes (87.5\%) in the fast progressor group underwent surgery. Kaplan–Meier survival analysis revealed that there were significant difference in requiring glaucoma surgery and progression to advanced glaucoma during follow up between fast and slow progressor group.

\textbf{Conclusions:} In patients with glaucoma secondary to ICE syndrome, the fast progressor group had significantly lower ECD and larger CDR in the baseline examination, and progressed to advanced glaucoma more rapidly despite undergoing surgery relatively early.

\textbf{Key words:} Glaucoma, Iridocorneal endothelial syndrome

\textbf{Received:} 2023. 4. 12. \hspace{1cm} \textbf{Revised:} 2023. 6. 12. \hspace{1cm} \textbf{Accepted:} 2023. 6. 12.

\textbf{Corresponding Author:} Young Kook Kim, MD, PhD
Department of Ophthalmology, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea
Tel: +82-2-2072-4301, Fax: +82-2-741-3187
E-mail: md092@naver.com

www.koreanglaucoma.org
the formation of peripheral anterior synechiae (PAS), resulting in an increase in IOP.\textsuperscript{5-8}

Although glaucoma occurs frequently in individuals with ICE syndrome, there have not been many studies on the long-term clinical course of this disease.\textsuperscript{9,10} Therefore, in this study, we aimed to compare the clinical characteristics of patients diagnosed with glaucoma and ICE syndrome who have had long-term follow-up at our hospital, by categorizing them as slow progressors and fast progressors based on their clinical course and degree of glaucoma progression.

Materials and Methods

This study received approval from the Institutional Review Board of Seoul National University Hospital in Seoul, Korea (IRB number: 2304-010-1418), and followed the principles outlined in the Declaration of Helsinki.

Study subjects

To begin with, we conducted a retrospective search for patients diagnosed with ICE syndrome who had visited Seoul National University Hospital from January 2010 to December 2022. Next, we identified patients who had developed glaucoma as a secondary condition to ICE syndrome. Additionally, patients who had a follow-up period of less than 4 years or an insufficient glaucoma examination were excluded. As a result, a total of 19 eyes were enrolled in this study (Fig. 1).

On the initial visit to the Clinic, all underwent a full ophthalmic examination entailing a medical history review, slit-lamp biomicroscopy, Goldmann applanation tonometry (Haag-Streit, Koniz, Switzerland), funduscopic examination (90 diopter lens), stereoscopic optic disc photography, red-free retinal nerve fiber layer (RNFL) photography (TRC-50IX; Topcon Corporation, Tokyo, Japan), circumpapillary retinal nerve fiber layer thickness measurement, and optic nerve head (ONH) parameter measurement by Cirrus spectral-domain optical coherence tomography (SD-OCT) (Carl Zeiss Meditec, Dublin, CA, USA), and central 24-2 threshold testing of the Humphrey visual field (HFA II; Humphrey Instruments Inc., Dublin, CA, USA).

Glaucomatous eyes were defined by their characteristic localized or diffuse neuroretinal rim thinning of the optic disc (on stereo disc photography) or by the presence of RNFL defect (on red-free fundus imaging). Glaucomatous visual field (VF) defect was defined as follows: (1) a 3-point cluster of lower than 5% probability in a location typical for glaucoma of a pattern deviation map, at least 1-point cluster with a lower than 1% probability; (2) glaucomatous hemifield test results outside the normal limits; or (3) a pattern standard deviation (PSD) of more than 95% of the normal limits, as confirmed on at least 2 reliable examinations (false-positives/false-negatives <15%, fixation losses <15%).

The advanced glaucoma was defined as a “Severe” category of VF loss of Hodapp-Parrish-Anderson criteria.\textsuperscript{11} This category includes the following criteria: mean deviation (MD) >-12 dB, more than 50% of the points are depressed below the 5% level or more than 20 points are depressed below the 1% level on the pattern deviation plot, At least one point in the central 5° has a sensitivity of 0 dB, Points within the central 5° with sensitivity <15 dB in both hemifields.

The diagnosis of ICE syndrome was made by the examining physician or by descriptive features in the examination recorded in the medical chart. It based on the presence of characteristic ICE cells (cell surface is dark instead of light, Figure 1. Study enrollment flow chart. dB = decibel; F/U = follow-up; ICE = iridocorneal endothelial; MD = mean deviation.
hyperreflective nucleus, and the intercellular junctions are light instead of dark) observed through specular microscopy and the typical findings for three subtypes observed during slit-lamp examination. The classification criteria for the 3 subtypes are as follows, patients with a diagnosis of ICE and iris holes or atrophy were categorized as PIA, those with iris nodules were categorized as CRS, and those without or less iris findings but corneal changes of ICE syndrome (corneal edema, epithelial bullae, hammered silver appearance of the endothelium) were categorized as CS. All three subtypes of ICE syndrome were included in the analysis (Fig. 2).

Data collection

The medical records of the patients were analyzed to extract information on their age, sex, ICE subtype (CS, PIA, CRS), and the number of glaucoma surgeries they had

---

**Table 1.** Comparison of baseline characteristics between slow progressor and fast progressor

<table>
<thead>
<tr>
<th>Variable</th>
<th>Slow progressor</th>
<th>Fast progressor</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (eye)</td>
<td>11</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>52.7 ± 19.0</td>
<td>50.1 ± 14.5</td>
<td>0.750*</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>7 (63.6)</td>
<td>6 (75.0)</td>
<td>0.894†</td>
</tr>
<tr>
<td>ICE syndrome subtype</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chandler syndrome</td>
<td>1 (9.1)</td>
<td>1 (12.5)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Progressive iris atrophy</td>
<td>7 (63.6)</td>
<td>4 (50.0)</td>
<td>0.901†</td>
</tr>
<tr>
<td>Cogan-Reese syndrome</td>
<td>3 (27.3)</td>
<td>3 (37.5)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Baseline IOP (mmHg)</td>
<td>18.4 ± 6.3</td>
<td>21.9 ± 6.5</td>
<td>0.251</td>
</tr>
<tr>
<td>Average RNFL thickness (µm)</td>
<td>95.4 ± 10.4</td>
<td>92.4 ± 4.4</td>
<td>0.356*</td>
</tr>
<tr>
<td>Value of visual field test</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean deviation (dB)</td>
<td>-3.0 ± 1.2</td>
<td>-3.3 ± 1.2</td>
<td>0.811†</td>
</tr>
<tr>
<td>Pattern standard deviation (dB)</td>
<td>2.3 ± 1.4</td>
<td>3.0 ± 2.0</td>
<td>0.531†</td>
</tr>
<tr>
<td>Visual field index (%)</td>
<td>95.7 ± 2.7</td>
<td>94.4 ± 4.0</td>
<td>0.574†</td>
</tr>
<tr>
<td>Central corneal thickness (µm)</td>
<td>582.3 ± 46.1</td>
<td>602.3 ± 65.9</td>
<td>0.446</td>
</tr>
<tr>
<td>Corneal endothelial cell density</td>
<td>1,961 ± 647</td>
<td>1,395 ± 329</td>
<td>0.045†</td>
</tr>
<tr>
<td>Cup-to-disc ratio</td>
<td>0.45 ± 0.06</td>
<td>0.69 ± 0.09</td>
<td>&lt;0.001†</td>
</tr>
</tbody>
</table>

Values are presented as number only, mean ± standard deviation, or number (%).

dB = decibel; ICE = iridocorneal endothelial; IOP = intraocular pressure; RNFL = retinal nerve fiber layer.

*Comparison was performed using Student’s t-test.

†Comparison was performed using chi-square test.
undergone during the follow-up period. Patients were evaluated through ophthalmic examinations, which included measurements of the IOP at baseline, mean, maximum, and minimum values during the follow-up period, endothelial cell density (ECD), cup-to-disc ratio (CDR), average RNFL thickness by Cirrus SD-OCT, and VF indexes (MD, PSD, visual field index [VFI]).

**Statistical analysis**

In this study, we compared the clinical characteristics between fast progressors and slow progressors. The eyes were grouped as “slow progressors” when the MD change rate was greater than or equal to -1.0 dB/yr, and as “fast progressors” when the MD change rate was less than -1.0 dB/yr.\(^2\),\(^1\) Continuous variables were compared between the two groups using Student’s t-test, while categorical variables were compared using the chi-square test. The rate of MD change for each eye was calculated using ordinary least squares regression analyses. The Kaplan–Meier survival analysis and the log-rank test were conducted to compare the timing of when glaucoma surgery was required and progression to advanced glaucoma in event-based analysis between slow progressors and fast progressors.

The data in this study are presented as the mean with standard deviation (range) for normally distributed continuous variables and as frequency (percentage) for categorical variables. The generalized estimating equation and the generalized linear mixed model were performed using R software version 4.2.3. A p-value of less than 0.05 was considered statistically significant.

**Results**

**Subject baseline demographics comparing slow progressors and fast progressors**

The baseline characteristics of age, sex, IOP, and ICE

<table>
<thead>
<tr>
<th>Variable</th>
<th>Slow progressor</th>
<th>Fast progressor</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (eye)</td>
<td>11</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Follow-up duration (yr)</td>
<td>7.4 ± 3.7</td>
<td>9.6 ± 3.0</td>
<td>0.147(^*)</td>
</tr>
<tr>
<td>IOP factor during F/U</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean IOP (mmHg)</td>
<td>15.7 ± 2.9</td>
<td>17.9 ± 3.1</td>
<td>0.143(^*)</td>
</tr>
<tr>
<td>Maximum IOP (mmHg)</td>
<td>21.3 ± 5.6</td>
<td>29.1 ± 6.8</td>
<td>0.013(^*)</td>
</tr>
<tr>
<td>Minimum IOP (mmHg)</td>
<td>12.3 ± 3.7</td>
<td>10.1 ± 2.2</td>
<td>0.158(^*)</td>
</tr>
<tr>
<td>Average RNFL thickness (µm)</td>
<td>86.2 ± 11.7</td>
<td>54.6 ± 8.4</td>
<td>0.001(^*)</td>
</tr>
<tr>
<td>RNFL change rate (µm/yr)</td>
<td>-0.73 ± 0.37</td>
<td>-2.31 ± 0.42</td>
<td>&lt;0.001(^*)</td>
</tr>
<tr>
<td>Value of VFI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MD (dB)</td>
<td>-7.7 ± 2.6</td>
<td>-17.5 ± 4.3</td>
<td>&lt;0.001(^*)</td>
</tr>
<tr>
<td>PSD (dB)</td>
<td>3.7 ± 0.6</td>
<td>7.5 ± 2.0</td>
<td>&lt;0.001(^*)</td>
</tr>
<tr>
<td>VFI (%)</td>
<td>79.5 ± 5.2</td>
<td>54.7 ± 16.0</td>
<td>&lt;0.001(^*)</td>
</tr>
<tr>
<td>MD change rate (dB/yr)</td>
<td>-0.7 ± 0.3</td>
<td>-1.9 ± 1.1</td>
<td>0.002(^*)</td>
</tr>
<tr>
<td>Progression to advanced glaucoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (9.1%)</td>
<td>7 (87.5)</td>
<td>0.003(^*)</td>
<td></td>
</tr>
<tr>
<td>Cornea endothelial cell density (µm)</td>
<td>1,747 ± 621</td>
<td>751 ± 324</td>
<td>0.001(^*)</td>
</tr>
<tr>
<td>Glaucoma surgery during F/U</td>
<td>2 (18.2)</td>
<td>7 (87.5)</td>
<td>0.015(^*)</td>
</tr>
<tr>
<td>Trabeculectomy</td>
<td>1 (50.0)</td>
<td>2 (28.6)</td>
<td>0.763(^*)</td>
</tr>
<tr>
<td>Ahmed implant</td>
<td>1 (50.0)</td>
<td>5 (71.4)</td>
<td>0.049(^*)</td>
</tr>
</tbody>
</table>

Values are presented as number only, mean ± standard deviation, or number (%).
\(dB = \) decibel; \(F/U = \) follow-up; \(IOP = \) intraocular pressure; \(MD = \) mean deviation; \(PSD = \) pattern standard deviation; \(RNFL = \) retinal nerve fiber layer; \(VFI = \) visual field index.
\(^*\)Comparison was performed using Student’s t-test.
\(^*\)Comparison was performed using chi-square test.
type did not show any significant difference between the slow progressor and fast progressor groups. The average RNFL thickness, MD, and VFI tended to be slightly lower in the fast progressor group, but there was no significant difference between the two groups. However, the ECD was significantly lower in the fast progressor group ($p = 0.045$), and the CDR was higher in the fast progressor group ($p < 0.001$) (Table 1).

Figure 3. Representative case of fast progressor of patients with glaucoma with ICE syndrome. (A1) Cogan-Reese syndrome in 56-year-old woman with glaucoma. (B1) Large cupping & rim narrowing. (C1, D1) Inferior RNFL thinning shown in RNFL thickness & deviation map. (E1) Gray scale of visual field test. (F1) Visual field test shows superior field defect in pattern deviation (VFI 90%, MD -4.04 dB, PSD 5.81 dB) correspond to the inferior RNFL thinning (C1, D1). (G1) Specular microscopy shows that fine hammered silver appearance, dark areas within the cells and 1,555 endothelial cell density. (A2) Follow-up slit lamp photo. Increased corneal edema is seen. B2. In the follow-up disc photo, there was no significant change in the cup-disc ratio. (C2, D2) Follow-up RNFL thickness & deviation map shows that widening of inferior RNFL thinning and newly developed superior RNFL thinning. (F2) Follow-up visual field test shows that progression of superior field defect and newly detected inferior field defect in pattern deviation (VFI 57%, MD -16.86 dB, PSD 10.23 dB). (G2) Follow-up specular microscopy shows reduced endothelial cell density by 454 compared to the baseline and pleomorphism size and shape of endothelial cells. $dB =$ decibel; F/U = follow-up; ICE = iridocorneal endothelial; MD = mean deviation; PSD = pattern standard deviation; RNFL = retinal nerve fiber layer; VFI = visual field index.
Follow-up characteristics comparing slow progressors and fast progressors

The study found that at the last follow-up, the group of patients with fast progression of glaucoma in ICE syndrome had significantly lower average RNFL thickness, RNFL change rate, MD, VFI, MD change rate and CEC density compared to the group of patients with slow progression (Table 2). And the clinical progress of a representative patient case in the fast progressor group is attached as a figure that shows RNFL changes, worsening of VF defects, and CEC loss (Fig. 3). Although there was no significant difference in basal and mean IOP between the two groups, the maximum IOP during follow-up was significantly higher in the fast progressors group (29.1 mmHg, \( p = 0.013 \)) than slow progressors group (21.3 mmHg). Almost half of the total patient group (9 eyes, 47.4%) underwent glaucoma surgery during follow-up, with Ahmed implant being performed in 6 eyes (31.6%) and trabeculectomy in 3 eyes (15.8%). The proportion of patients who underwent glaucoma surgery during follow-up was also significantly higher in the fast progressor group (7 eyes, 87.5%, \( p = 0.015 \)) than slow progressors group (2 eyes, 18.2%) (Table 2).

Survival analysis comparing slow progressors and fast progressors

The Kaplan–Meier survival analysis was used to compare the cumulative probabilities of patients requiring glaucoma surgery and progressing to advanced glaucoma in the fast and slow progressor group. The Kaplan–Meier survival curve shows that cases requiring glaucoma surgery in 18.2% of slow progressor group at 3.0 years of follow-up and 87.5% of fast progressor group at 5.2 years of follow-up (\( p = 0.005 \)). And 33.3% of slow progressor group progressed to advanced glaucoma at 10.5 years, and 87.5% of fast progressor group progressed to advanced glaucoma at 11.0 years of follow-up (\( p = 0.018 \)) (Fig. 4).

Discussion

Glaucoma with ICE syndrome

The prevalence of glaucoma in eyes with ICE syndrome has been reported to range from 46% to 82%.\(^5\) This is due to the angle obstruction caused by the migration of abnormal endothelial cells and the development of PAS, which can lead to increased IOP and glaucoma.\(^14\) The severity of glaucoma is known to be worse in PIA and CRS compared to CS, possibly because of the higher prevalence of ICE cell proliferation over the iridocorneal angle and secondary PAS in these ICE syndrome variants. Additionally, IOP control is more challenging in PIA and CRS than in CS.\(^8\) This study found no difference in ICE variants between slow and fast progressors. Both groups had a higher proportion of PIA among the three variants. In this study, despite the small sample size, we tried to compare the baseline and follow-up characteristics and relatively long-term clinical course of glaucoma secondary to ICE syndrome according to the progression rate of glaucoma.

Figure 4. (A) Kaplan–Meier survival curve shows that cases requiring glaucoma surgery in 18.2% of slow progressor group at 3.0 years of follow-up and 87.5% of fast progressor group at 5.2 years of follow-up. (B) Another Kaplan–Meier curve shows that 33.3% of slow progressor group progressed to advanced glaucoma at 10.5 years, and 87.5% of fast progressor group progressed to advanced glaucoma at 11.0 years of follow-up.
Treatment of glaucoma with ICE syndrome

In a retrospective study by Chandran et al., which included 223 eyes of 203 subjects with ICE syndrome, 163 eyes (73%) were found to have glaucoma, and 50% were managed medically. Glaucoma surgery was required in 54% of subjects with PIA, 47% of CRS, and 45% of CS. In the slow progressor group of the current study, the majority of patients had their IOP controlled with medical treatment, and only 2 patients (18.2%) required surgery. In the entire group of this study, 9 patients (47.4%) required surgery for IOP control during follow-up, and 6 patients (31.6%) of them required surgery relatively early within 3 years. Particularly in the fast progressor group, 7 patients (87.5%) underwent surgery. Although most of the patients in the fast progressor group underwent surgery relatively quickly and controlled their IOP, the glaucoma continued to progress further in the later stages.

Endothelial cell loss in glaucoma with ICE syndrome

The tall and conical shape of ICE cells gives rise to the characteristic specular microscopic appearance of the light-dark reversal pattern observed in ICE syndrome. This pattern is caused by the reflection of light from the tall and narrow cells. The ICE cells located in the vicinity of normal CECs are non-motile and have high metabolic activity, which may play a role in damaging nearby endothelial cells through a toxic effect. As a result, these abnormal endothelial cells migrate toward the iridocorneal angle and iris. Although this pathophysiology of ICE syndrome causes endothelial cell loss and can lead to corneal damage, elevated IOP can also cause endothelial cell loss.

Liu et al. reported that there was no correlation between ECD and IOP, but they found a correlation with angle involvement. However, Cho et al. reported a significant decrease in ECD in the primary open-angle glaucoma (POAG) patient group compared to the normal-tension glaucoma patient group. Other studies also reported a lower ECD in the POAG patient group compared to healthy eyes, supporting the association between IOP and decreased ECD. In this study, the ECD was significantly lower in the fast progressor group at baseline and the last follow-up. Particularly in the fast progressor group, the ECD was significantly lower even in the early stage of glaucoma before glaucoma progressed, suggesting that abnormal endothelial cells may have already damaged normal endothelial cells and migrated to the iridocorneal angle. Lower ECD is thought to be related to the severity of the ICE disease group, but there seems to be no study that has analyzed severity in relation to ECD. However, considering Campbell's membrane theory, it is thought that the change in iris and angle will be more pronounced in the order of CS, PIA, and CRS, and the severity of the disease is expected to be greater. However, in this study, the difference in ICE subtypes between the two groups did not manifest.

Other characteristics of fast and slow progressors

In the treatment of glaucoma patients, the current stage of glaucoma is important, but the rate of progression is also an important factor in determining the direction of treatment. Several factors have been reported to determine the rate of progression of glaucoma. In a study by Chan et al., older patients with lower CCT and baseline IOP, and those with pseudoxfoliation, disc hemorrhages, ocular medication changes, IOP-lowering surgery, cardiovascular disease, and hypotension were found to progress more rapidly. In this study, in common with the above study, glaucoma surgery was also more frequently performed in the fast progressor group during the course. However, no significant difference was observed in baseline IOP and CCT between fast and slow progressor groups. But, similar to the above study, the average baseline IOP tended to be higher in the fast progressor group (21.9 mmHg) than slow progressor group (18.4 mmHg). Unlike the above study, the average baseline CCT tended to be higher in the fast progressor group (602.3 µm) than slow progressor group (582.3 µm). The ICE cells that border normal endothelial cells are often damaged or necrotic at boundary zones, suggesting that ICE cells may have a toxic effect on normal neighboring endothelial cells. For this reason, it is thought that normal endothelial function is impaired, which can cause corneal edema and increase corneal thickness.

In this study, a significant difference was observed in
CDR, which could help predict rapid progression in patients with glaucoma and ICE syndrome. In the baseline characteristics, the fast progressor group had a higher CDR compared to the slow progressor group. The CDR is an important indicator for screening and diagnosing glaucoma and plays a crucial role in early detection of the disease. Siesky et al. reported the baseline ONH and RNFL structural characteristics were associated with a significantly shorter time to functional glaucomatous progression and VF loss in OAG patients. They reported that patients with a larger baseline CDR was associated with shorter time to functional glaucoma progression. Similarly, Gordon et al. investigated the baseline factors that predict the onset of POAG in the ocular hypertension treatment study, and they reported the larger vertical and horizontal CDR were good predictors for onset of POAG. As in the studies above, the baseline CDR in this study was significantly greater in the fast progressor group. While the CDR alone cannot be used to diagnose glaucoma, the findings of this study suggest that a higher CDR in the early stage of the disease may be associated with more rapid progression of glaucoma and should be closely monitored.

The maximum IOP during follow up was significantly higher in the fast progressor group in this study. Several studies reported peak IOP during follow-up was significantly associated with glaucoma progression. And De Moraes et al. reported that peak IOP was a better predictor of progression than mean IOP or IOP fluctuation, and a peak IOP of greater than 18 mmHg increased the risk of progression by 81%.

In a study by Asrani et al., large diurnal fluctuations in IOP were identified as a significant risk factor for glaucoma progression. In a case report of ICE syndrome by Mogil et al., it was observed that the ICE eye showed larger diurnal IOP fluctuations than the normal eye. And the large IOP fluctuation may be due to a clinically invisible membrane of transformed corneal endothelium that migrates onto and progressively obstructs the trabecular meshwork. It is unfortunate that diurnal IOP fluctuations were not measured in this study, but it is suggested that future studies on glaucoma patients caused by ICE should supplement this data.

**Study limitations**

The present study has several limitations that need to be addressed. Firstly, the study participants were recruited from only one tertiary referral hospital, and all of them were of Korean ethnicity. Therefore, the findings of this study may not be generalizable to other populations or settings. Secondly, the sample size was relatively small as the study only included patients who had undergone long-term follow-up. Therefore, future research with a larger sample size is necessary to better understand glaucoma in ICE syndrome patients. Thirdly, there may be a presence of selection bias. We selected 51 glaucoma patients from the ICE syndrome patients who visited our hospital. It is possible that patients with different clinical courses were excluded during the process of excluding patients with a short follow-up period or lack of glaucoma-related exams. In the excluded patient group, there were quite a few patients who underwent penetrating keratoplasty (PKP), and the fact that no analysis of glaucoma progression after PKP was conducted could be considered a limitation. Fourth, the study did not include sufficient records of gonioscopy and anterior OCT tests to evaluate PAS. Given the mechanism of how ICE syndrome causes glaucoma, it is essential to evaluate PAS, and future studies should include these factors in their analyses.

**Conclusion**

This study provides long-term follow-up data on patients with secondary glaucoma due to ICE syndrome. The slow progressor group exhibited relatively well-controlled IOP and slow glaucoma progression with medication alone. However, in the fast progressor group, glaucoma progressed more rapidly despite early surgery. In the early stage of glaucoma, there were differences in the number of ECDs and CDR between the fast and slow progressor groups. A lower ECD count and higher CDR were associated with more rapid progression of glaucoma, highlighting the need for careful observation in these patients. It is important to note that this study had several limitations, including a small sample size, insufficient gonioscopic finding and recruitment from a single tertiary referral hospital in Korea.
Therefore, additional studies with larger and more diverse patient populations are needed to further investigate the progression and management of glaucoma in ICE syndrome.

Conflicts of interest
The authors have no conflicts to disclose.

References

국문초록

홍채각막내피증후군으로 인한 녹내장 환자에서 녹내장 진행 정도에 따른 임상 특징

목적: 홍채각막내피증후군으로 인한 녹내장 환자에서 녹내장 진행 정도에 따른 환자군의 임상 특징을 비교해보고자 한다.

대상과 방법: 홍채각막내피증후군으로 인한 녹내장 환자 중 4년 이상 경과 관찰한 19명 19안을 대상으로 후향적으로 임상적, 성인기 준을 비교 분석하였다. 시야 검사상 mean deviation의 변화율 -1.0 dB/yr를 기준으로 녹내장 진행이 빠른 군과 느린 군으로 분류하고, 두 군 간의 임상 특징을 비교 분석하였다.

결과: 연구에 포함된 환자 19명 중 녹내장 진행이 빠른 군은 8명, 느린 군은 11명이었다. 기저 검사에서는 두 군 간에 연령, 홍채각막내피증후군의 아형, 시야 검사의 mean deviation, 망막신경섬유층 두께의 차이가 없었으며, 녹내장 진행이 빠른 군에서 느린 환자군에 비해 시신경주름의 차이가 더 크고 각막 내피세포밀도가 더 적게 관찰되었다. 녹내장 진행이 느린 군에서는 2안(18.2%)에서 녹내장 수술이 필요하였으며, 대부분이 안압을 만으로 안압이 잘 조절되었고, 녹내장 진행이 빠른 군에서는 7안(87.5%)에서 안압하강을 위한 수술을 받았다. 생존분석에서 녹내장 진행이 빠른 군과 느린 군 사이에 추적 관찰 시 녹내장 수술 필요 여부와 막기 녹내장으로의 진행에 유의한 차이가 있었다.

결론: 홍채각막내피증후군으로 인한 녹내장 환자에서 녹내장 진행이 빠른 군에서 느린 군에 비해 기저 각막 내피세포밀도가 유의하게 낮았고, 기저 시신경주름의 차이가 더 컸으며, 녹내장 진행이 빠른 군은 대부분 이른 시기에 수술적 치료를 받았음에도 불구하고 막기 녹내장으로 더 빨리 진행하였다.