Long-term follow-up of endothelial cell loss after implantation of collamer posterior chamber intraocular lenses

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PURPOSE: To assess long-term endothelial cell density (ECD) changes in eyes undergoing Implantable Collamer Lens (ICL, STAAR surgical, Nidau, Switzerland) surgery for the correction of moderate to high levels of anisometropia.

SETTING: Fernández-Vega Ophthalmological Institute, Oviedo, Spain.

METHODS: This study involved 36 eyes of 36 patients who received unilateral V4 ICL implantation to correct anisometropia. Mean age of the patients at the time of surgery was 33.78 ± 6.99 years (range: 24 to 49 years) and mean manifest spherical equivalent (SE) was −13.65 ± 5.40 diopters (D; range: −25.25 to −0.75 D). Mean follow-up after ICL implantation was 7.4 years (range: 4 to 10 years). The Specular Microscope SP-3000P (Topcon, Europe) was used to measure ECD in operated and non-operated eyes after the follow-up period.

RESULTS: Mean ECD decreased significantly from 2803 ± 423 cells/mm² preoperatively to 2,580 ± 357 cells/mm² after surgery. Endothelial cell loss between the preoperative evaluation and at 7.4 years was 10.8 ± 18.6% in operated eyes. Mean ECD was also seen to decrease from 2,690 ± 440 cells/mm² at baseline to 2,628 ± 400 cells/mm² after 7.4 years in the non-operated eyes, although these changes were not statistically significant. Thus, endothelial cell loss due to ICL surgery was 7.7% after 7.4 years of follow-up.

CONCLUSIONS: Despite significant endothelial cell loss throughout the follow-up period, ICL implantation is a safe procedure for correcting low to high anisometropia. The outcomes also showed endothelial cell loss in the non-operated eyes over the follow-up period, but this finding could be attributed to natural physiological changes and aging.

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The Visian Implantable Collamer Lens (ICL, STAAR surgical, Nidau, Switzerland) is a posterior phakic intraocular lens implantation (pIOL) approved by the US Food and Drug Administration (FDA) for myopia correction. The effectiveness, safety, predictability and stability of the ICLs in the correction of high and low levels of myopia, hyperopia and astigmatism have been demonstrated. The main advantages of this technique are its simplicity and reversibility, good visual outcomes and the precision of the achieved refraction correction. Nevertheless, some postoperative complications have been reported, such as increased intraocular pressure (IOP), pupillary block, pigment dispersion, glaucoma, anterior subcapsular cataract and endothelial cell loss. The integrity of the corneal endothelium is essential for long-term maintenance
of corneal clarity after intraocular surgery. Corneal endothelium is affected by age, disease and intraocular surgery. Intraocular surgery causes cell loss in the superior cornea which requires transformation and migration of endothelial cells from the central and inferior cornea. In most corneas, endothelial mosaic is reestablished, although some retain a bizarre endothelial appearance which is correlated with continued cell loss. Furthermore, in addition to chronic cell loss, intraocular surgery causes acute cell loss greater than the normal attrition due to aging.

The aim of the present study was to evaluate corneal endothelial cell density (ECD) after unilateral pIOL implantation in highly anisometropic eyes with long-term follow-up.

PATIENTS AND METHODS

Thirty-six eyes, 5 from men (14%) and 31 from women (86%), of 36 patients undergoing unilateral ICL implantation for the correction of high anisometropia were included in this retrospective, observational study at the Fernandez-Vega Ophthalmological Institute, Oviedo, Spain. The inclusion criteria for pIOL implantation were age over 18 years, anterior chamber depth (ACD) less than 2.8 mm, ECD more than 2,000 cells/mm², cataract, history of glaucoma or retinal detachment, macular degeneration or retinopathy, neuro-ophthalmic disease, and history of ocular inflammation. Before pIOL implantation, patients had a full ophthalmologic examination. The examination included manifest and cycloplegic refractions, keratometry, corneal topography and pachymetry (Orbscan II, Bausch & Lomb), ECD measurement (SP 3000P, Topcon Europe BV), slit lamp evaluation, Goldmann applanation tonometry, and binocular indirect ophthalmoscopy through a dilated pupil. This study was approved by the Institutional Review Board of the University of Valencia Research Group of Optometry and followed the tenets of the Declaration of Helsinki. After being fully informed of the details and possible risks of the surgical procedure, all patients provided written informed consent.

**Phakic intraocular lens size and power calculation**

A Visian Implantable Collamer lens ICMV4 pIOL model was used in all patients. The pIOL diameter was individually determined based on the horizontal white to white (WTW) distance and ACD, measured from the endothelium with the Orbscan II device, following the pIOL manufacturer’s recommendations. For eyes with an ACD measurement of 3.5 mm or less, the pIOL size was calculated by adding 0.5 mm to the horizontal WTW measurement. For eyes with an ACD measurement greater than 3.5 mm, up to 1.0 mm was added to the WTW measurement. Calculated IOL sizes between the available IOL diameters (in 0.5 mm steps) were usually rounded down if the ACD was 3.5 mm or less, and rounded up if the ACD was greater than 3.5 mm. The pIOL power was calculated using the pIOL power table software provided by the manufacturer and a modified vertex formula.

**Surgical Technique**

All surgeries were performed by the same experienced surgeon (JFA) through a 3.2 mm clear corneal tunnel incision in the horizontal meridian using peribulbar anesthesia. Intraoperative iridectomy was performed 1 week before surgery. Thirty minutes before surgery, tropicamide and phenylephrine eye drops were instilled. Five minutes before surgery, povidone–iodine 5% (Betadine®) was applied. The anterior chamber was filled with sodium hyaluronate 1% (Provisc®), which was completely removed at the end of surgery. Tobramycin and dexamethasone 0.1% eye drops were used 4 times a day for 10 days, after which diclofenac sodium eye drops were started 4 times a day for 2 weeks.

**Outcomes**

The Specular Microscope SP-3000P (Topcon, Europe) was used to analyze the corneal endothelium throughout the mean follow-up in both eyes. Mean follow-up after pIOL implantation was 7.4 years (range: 4 to 10 years). Data analysis was performed using SPSS statistical software (version 22.0, SPSS, Inc.). Comparison of means was performed using the nonparametric Wilcoxon signed-rank test. Differences were considered statistically significant when the P value was less than 0.05.

**RESULTS**

Preoperative patient demographics data are summarized in Table 1. The mean age of patients at the time of surgery was 33.78 ± 6.99 years (range: 24 to 49 years). The preoperative manifest spherical equivalent (SE) was −13.65 ± 5.40 diopters (D; range: −25.25 to −0.75).

Mean follow-up after pIOL implantation was 7.4 years (range: 4 to 10 years). In 1 case (2.8%) the follow-up was 8 years; in 2 eyes (5.6%), 5 years; in 12 eyes (33.3%), 6 years; in 4 eyes (11.1%), 7 years; in 6 eyes (16.7%), 8 years; in 6 eyes (16.7%), 9 years; in 4 eyes (11.1%), 10 years; and in 1 eye (2.8%) 11 years (Figure 1). Figure 2 shows mean preoperative cumulative ECD and 7.4 years post-surgery for the eye undergoing pIOL implantation and for the non-operated eye. We found a statistically significant decrease in ECD at 7.4 years follow-up. The
mean preoperative ECD fell from 2,803 ± 423 cells/mm² preoperatively to 2,580 ± 357 cells/mm² after surgery (Wilcoxon test; p = 0.007). We also found lower ECD in the non-operated eye over the 7.4 years follow-up. Mean ECD decreased from 2,690 ± 440 cells/mm² at baseline to 2,628 ± 400 cells/mm² after 7.4 years, although these differences were not statistically significant (Wilcoxon test; p = 0.16). The endothelial cell loss between baseline and 7.4 years was 10.8 ± 18.6% in the operated eyes and 3.1 ± 13.5% in non-operative eyes (Figure 3). The lower ECD over time found in non-operative eyes could be attributed to natural physiological losses and aging. Endothelial cell loss due to pIOL surgery was 7.7% at 7.4 years follow-up.

Table 1. Preoperative patient demographics and pIOL characteristics.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mean ± SD</th>
<th>Range [Min, Max]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>33.78 ± 6.99</td>
<td>24 to 49</td>
</tr>
<tr>
<td>Gender (% female)</td>
<td>86%</td>
<td></td>
</tr>
<tr>
<td>Spherical equivalent (D)</td>
<td>-13.65 ± 5.40</td>
<td>-25.25 to -0.75</td>
</tr>
<tr>
<td>Endothelial cell density (cells/mm²)</td>
<td>2,730.23 ± 434.22</td>
<td>2,000 to 3,784</td>
</tr>
<tr>
<td>Anterior chamber depth (mm)</td>
<td>3.21 ± 0.28</td>
<td>2.80 to 3.72</td>
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D: diopters; SD: standard deviation

DISCUSSION

The aim of this study was to evaluate ECD after pIOL implantation in one eye to correct anisometropia and in the non-operated contralateral eye during long-term follow-up, and to determine the percentage loss due to lens implantation. Mean endothelial cell loss between preoperative evaluation and follow-up after pIOL implantation was 10.8%. In contrast, mean endothelial cell loss between baseline and after 7.4 years in non-operated eyes was 3.1%, so endothelial cell loss due to pIOL implantation was 7.7%. In both eyes, residual densities after follow-up were well above the commonly accepted safety limit for explantation, i.e. > 2,000 cells (see Figure 2).

Previous studies have evaluated corneal endothelial cell loss due to aging, disease or intraocular surgery. Normal aging endothelial cell loss is estimated to be 0.5%-0.6% per year. In our study, we found 3.1% physiological ECD loss over 7.4 years, which...
corresponds to 0.42% ECD loss per year. Several authors have studied long-term ECD after ICL implantation. Jiménez-Alfaro et al.14 assessed safety in 20 high myopic eyes undergoing ICL surgery over a 2-year follow-up. The percentages of cell loss after 3, 6, 12, 18 and 24 months were 4.41%, 4.83%, 5.17%, 5.46% and 6.57%, respectively. No statistically significant differences were found between visits, except for the comparison between 3 and 24 months and 6 and 24 months, so losses were thought to be non-progressive. Dejaco et al.15 evaluated long-term endothelial cell changes in phakic eyes after ICL implantation to correct high levels of myopia and hyperopia. Mean endothelial cell loss compared to the preoperative evaluation was 1.8% at 3 months, 4.2% at 6 months, 5.5% at 12 months, 7.9% at 2 years, 12.9% at 3 years, and 12.3% at 4 years. These authors observed rapid cell loss during the first postoperative year, but no statistical significant changes were observed at 2, 3 and 4 years post-surgery. Again, these results indicate stabilization of cell loss 2 years after ICL implantation. Ravalico et al.16 studied the relationship between corneal endothelial damage and anterior chamber intraocular lenses over 5 years of follow-up, concluding that the pIOL did not appear to alter corneal endothelial function. Endothelial cell loss was more closely related to surgical trauma than the presence of IOL in the anterior chamber. Lackner et al.13 found a correlation between endothelial cell loss and lens opacification after ICL implantation in 76 myopic eyes over 3 years. This fact suggests that surgical trauma triggers long-term inflammatory reactions. Edelhauser et al.17 found that cell loss between baseline and 3 months was 2.1%; 3 months and 1 year, 0.9%; 1 year and 2 years, 2.3%; 2 year and 3 years, 3.2%; and 3 years and 4 years, 0.1% after ICL implantation in 526 myopic eyes. The authors suggest that cell loss between 1 and 3 years is explained by prolonged corneal remodeling following the surgical procedure, while cell loss between 3 and 4 years was negligible. Thus, regardless of the cause of endothelial cell loss over the first 3 years, 4-year outcomes suggest that chronic loss was not sustained. Recently, Igarashi et al.18 evaluated clinical outcomes of ICL implantation for moderate to high myopia over an 8-year follow-up. They reported that ECD fell significantly; the mean percentage of endothelial cell loss was 4.3%, 2.2%, 3.8% and 6.2% after 6 months, 1 year, 4 years and 8 years post-surgery, respectively. Some discrepancies between those studies and ours could be attributed to different follow-up periods, sample size, patient age and preoperative refraction, surgeon’s skill, ICL model implanted and the device used for ECD measurements.

Causes of endothelial cell loss after refractive surgery are numerous. After any intraocular surgery, ECD decreases depending on time of surgery and the type of procedure. For instance, 10 years after cataract surgery with posterior chamber intraocular lens implantation, eyes continue to lose endothelial cells at a rate of 2.5% per year23. Other studies reported losses of 14% in phakic eyes after phacoemulsification over a 2-year follow-up24. In contrast, no significant changes in central corneal ECD have been found after laser in situ keratomileusis at 3 years25,26. Tehrani et al.27 studied endothelial cell loss after implantation of a toric iris-fixated pIOL. They reported that annual cell loss was 1.9% for the myopic group and 1.6% for the hyperopic group. Thus, endothelial cell loss after pIOL implantation could be mainly attributed to the surgical procedure. It also has been suggested that endothelial cell loss could be due to chronic subclinical inflammation lasting between 1 and 2 years after an iris-claw and angle-supported pIOLs implantation28.

In conclusion, although there is significant endothelial cell loss after ICL implantation, residual ECD after the follow-up period was greater than 2,000 cells, so ICL surgery can be considered a safe procedure for the correction of low to high levels of anisometropia. Moreover, the outcomes also showed a loss of ECD in the non-operated eyes after 7.4 years, which might be due to natural physiological changes and aging.

REFERENCES


