Long-term assessment of crystalline lens transparency in eyes implanted with a central-hole phakic collamer lens developing low postoperative vault

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Purpose: To assess long-term crystalline lens transparency in eyes implanted with phakic collamer intraocular lens (pIOL) with a central port and low postoperative vault for correction of myopia.

Setting: Clinica Baviera, Madrid, Spain.

Design: Retrospective cross-sectional single-center study.

Methods: Using a noninvasive Fourier-domain swept-source anterior segment optical coherence tomography system, shifts in myopic and astigmatic myopic eyes implanted with a pIOL with vaulting lower than 100 µm in miosis and more than 4 years of follow-up were dynamically evaluated. Main outcome measures were pIOL dynamic vault (vault interval and vault range [VR]), crystalline lens density, and anterior subcapsular lens opacities. Crystalline lenses were examined under slitlamp microscopy, and lens density was evaluated using quantitative Scheimpflug images. Scheimpflug images were compared with those of a control group comprising eyes that were candidates for pIOL implantation.

Results: The study population comprised 24 eyes from 16 patients previously implanted with a pIOL (5.82 ± 0.9 years) with central vault lower than 100 µm under photopically induced miosis. The mean vault value was 52 ± 19 µm under photopic light conditions and 113 ± 37 µm under scotopic conditions. The mean VR was 58 ± 24 µm. Anterior subcapsular lens opacities were found in only 1 eye (4.17%). The mean lens density was 7.94 ± 0.43, and no statistically significant differences were observed compared with the control group.

Conclusions: Long-term low vaulting in eyes implanted with a pIOL with a central port for correction of myopia was associated with a low risk for developing anterior crystalline lens opacities.

In 2011, the addition of a central port to the existing design of the Visian implantable collamer lens (ICL) (STAAR Surgical Company) represented a paradigm shift in posterior chamber phakic intraocular lens (pIOL) surgery. Pupillary block, the most feared early postoperative complication, has been eradicated, with the exception of isolated reports. Various studies have demonstrated good control of intraocular pressure in the short-term and medium-term.

However, we have yet to define the potential risk for developing early cataracts, mainly anterior subcapsular opacities. The main predisposing factor associated with the development of anterior subcapsular opacities with the older models is the low pIOL vaulting. Faced with this situation, refractive surgeons might sometimes be confronted with the dilemma of explanting vs observing, 2 potentially cataractogenic options. However, safety data from cohorts of patients implanted with central-hole pIOLs followed up in the long-term are remarkable. In the meta-analysis by Packer, published in 2016 and expanded in a later review, the author reported a zero incidence of anterior subcapsular opacities cataract formation. Indeed, since the central port was included in the ICL design, only a few articles have incidentally reported crystalline lens opacities or cataracts in eyes implanted with a hole pIOL.

This study aims to evaluate the risk for developing cataracts in the long-term (>4 years of follow-up) in eyes implanted with a pIOL developing low postoperative vault.
implanted with a central-hole PIOL and with a potential risk factor for cataractogenesis, that is, a low vaulting (<100 μm in miosis). Vaulting under light-induced maximum miosis was considered as selection criteria because it is during this status when the lowest vault is observed and, consequently, when there is a higher risk for contact between the PIOL and the crystalline lens. To achieve this objective, the study addressed 3 main goals. The first was to dynamically measure PIOL vaulting. The second was to describe the transparency status of the crystalline lens using the slitlamp. The third goal was to perform crystalline lens densitometry using Scheimpflug imaging and compare the results between a study and a control group.

METHODS

An observational, retrospective, nonrandomized single-center study with 2 different groups was designed. The study group comprised 24 nonconsecutive eyes (12 right) from 16 patients (10 women) who underwent unforeseen implantation of spherical (19) and toric (5) central-hole PIOLs (Visian ICL model V4c). All operations were performed at Clinica Baviera (Madrid, Spain) by the same experienced surgeon (F.G.-L.). As per the inclusion criteria, all eyes entering the study had a postoperative central vault in photopic induced miosis lower than 100 μm (52 ± 19 μm; range 9 to 94 μm)], and the PIOL had been in place in all eyes for more than 4 years (mean 5.82 ± 0.9 years; range 4.14 to 6.94 years) at the time of the investigation. All study procedures were in line with the recommendations of the Declaration of Helsinki. All patients provided their written informed consent for the surgical procedure and for the use of their personal data. Data collection fulfilled Spanish legal requirements, and the Medico-Legal Committee of Clinica Baviera approved the study.

The mean age of the patients at the time of the study was 38 ± 5 years (range 45 to 29 years). Sample eyes had a mean baseline preoperative spherical equivalent (SE) of −8.67 ± 0.71 diopters (D) (range −2.25 to −11.50 D). The sizes of PIOLs were distributed as follows: 12.1 mm in 2 eyes, 12.6 mm in 14 eyes, and 13.2 mm in 8 eyes. The mean implanted PIOL power was −9.50 ± 2.00 D (range −3.50 to −14.50 D). At the evaluation 3 months postoperatively, the mean SE was −0.10 ± 0.23 D (range +0.50 to −0.75 D), the mean postoperative uncorrected distance visual acuity was 0.01 ± 0.02 logarithm of the minimum angle of resolution (logMAR) (range 0.00 to 0.24 logMAR), and the mean corrected distance visual acuity (CDVA) was 0.01 ± 0.01 logMAR (range 0.00 to 0.17 logMAR). At the time of the study, the mean SE was −0.16 ± 0.20 D (range +0.25 to −1.25 D), the mean uncorrected distance visual acuity was 0.03 ± 0.05 logMAR (range 0.00 to 0.44 logMAR), and the mean CDVA was 0.00 ± 0.00 logMAR (range 0.00 to 0.17 logMAR).

A control group comprising unoperated healthy myopic eyes that were candidates for implantation of a PIOL was enrolled for Scheimpflug imaging assessment of the crystalline lens. The control group included 22 consecutive eyes from 17 patients. The mean age of the patients was 31 ± 6 years (range 22 to 43 years), and the mean SE was −10.23 ± 2.00 D (range −7.12 to −19.88 D). Scheimpflug imaging data were not available for 2 eyes of the study group, which were eventually excluded from this subanalysis.

Study Outcome Parameters

Vault Assessment by Anterior Segment Optical Coherence Tomography An anterior segment (AS) imaging examination was performed in all the eyes of the study group using Fourier-domain swept-source OCT with the CASIA2 instrument (Tomey Corp.). The study protocol with the CASIA device has been described elsewhere, although a more up-to-date unit with improved capabilities was used. For the purpose of this study, a dynamic analysis of the AS using a B version built-in software application to acquire an OCT video made up of a sequence of frames was performed. The video system of this new software runs at a very high scanning speed (20 frames per second), provides high-resolution images, and automatically controls the light that comes up in the AS movie mode to create differentiated brightness levels of light exposure. With this new methodology, the studied eye gaze is focused on an internal dot during imaging. This stage is followed by a 15-second video recording made under dark ambient illumination (0.5 lux, which is previously measured in the examination room using a light meter [PCE-MLM1, PCE Instruments]). The video comprises 3 consecutive sequences. First, a 5-second clip with dark ambient light; second, a 5-second clip during which the studied eye is exposed to an internal light of 990 lux; and third, once the internal light is automatically turned off, a new 5-second recording period under the initial scotopic ambient light conditions (Video 1, Vault dynamic assessment by AS-OCT in low vaulting phakic lens with central hole. available at http://links.lww.com/JRS/A204).

The images registered were then manually processed by freezing the OCT frame at the minimum and maximum pupil size. Biometric measurements of the PIOL vault, crystalline lens rise, anterior chamber depth from the corneal endothelium, angle-to-angle distance, and pupil size in the iris plane were taken in all selected OCT frames. The vault interval (VI), defined as the 2 central vault values measured in maximum mydriasis and miosis after the light-induced changes in pupil diameter was measured, and the vault range (VR), defined as the absolute difference between the 2 values comprising the VI, was calculated.

Lens Density Quantification Using Pentacam Imaging Analysis The high-resolution rotating Scheimpflug camera of the Pentacam device (HR version; OCULUS Optikgeräte GmbH) was used to acquire images of the crystalline lens under a consistent scotopic ambient light environment (0.5 lux) in the exploration room. Prior to any measurements, maximal eye pharmacological dilation was obtained. Scheimpflug images closest to the 0- to 180-degree meridian were chosen for analysis, and Pentacam Nucleus Staging (PNS) measurements were automatically calculated in the crystalline lens area studied. PNS is the built-in software that provides quantitative measurements of crystalline lens density based on a specific internal scale. The specific selected area drawn on the Scheimpflug image chosen for this study was obtained by matching the upper edge of the delimited area with the anterior capsule of the crystalline lens, centered on the apex of the cornea. The volume of the cylinder remained constant by keeping the width at 3 mm and the height at 0.6 mm and adjusting the lower limit of the area drawn until the same volume (3 mm³) was obtained in all the eyes (Figure 1, A and B).

Assessment of Lens Transparency by Slitlamp Examination An ophthalmologist evaluated crystalline lens transparency under slitlamp biomicroscopy and pupil dilation. Each feature of the crystalline lens was meticulously recorded.

Statistical Analysis

Eyes in the control group were chosen consecutively from patients who were candidates for implantation of an ICL; therefore, 1 eye or both eyes from each patient were included, depending on whether 1 eye or 2 eyes were to be operated on. The outcomes reported were entered into an Excel spreadsheet (Microsoft Corp.), and data were analyzed using R Core Team (R Foundation for Statistical Computing, https://www.R-project.org/).

After examining the distributions of the variables, a robust approach when describing data and testing the differences in mean values (Table 1) was adopted. Ranges and trimmed means with winsorized standard deviations were reported; 20% winsorization, as suggested by Wilcox, was used. To compare trimmed means, the Yuen test, again, as described by Wilcox, was performed. To control for the effect of age and SE, robust linear regression with M estimators was used. When comparing differences between measures in miosis and mydriasis, robust estimators were applied. The
differences between dependent samples were tested using the Yuen test. A P value less than 0.05 was considered statistically significant.

RESULTS

AS-OCT Assessment

The mean central vault value in the study group was 52 ± 19 µm (range 9 to 94 µm) under photopic light conditions and 113 ± 37 µm (range 45 to 183 µm) under scotopic light conditions. The mean VR was 58 ± 24 µm (range 1 to 133 µm). The mean pupil size in the iris plane was 2.99 ± 0.41 mm (range 2.34 to 4.05 mm) under photopic light conditions and 5.26 ± 0.46 mm (range 4.12 to 6.76 mm) under scotopic light conditions. Table 1 summarizes changes in vault and anterior chamber structures under different light conditions.

Pentacam Assessment

The PNS analysis works on a scale of 0 to 100 (0 = no cloudiness; 100 = completely opaque lens) for selected areas. It includes an automatically calculated mean, a

Table 1. Changes in vault and anterior chamber structures under different light conditions.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Miosis</th>
<th>Mydriasis</th>
<th>Miosis–Mydriasis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range (Min, Max)</td>
<td>Mean ± SD†</td>
<td>Range (Min, Max)</td>
</tr>
<tr>
<td>ACD (endo) (mm)</td>
<td>2.78, 3.57</td>
<td>3.14 ± 0.13</td>
<td>2.77, 3.57</td>
</tr>
<tr>
<td>ATA (mm)</td>
<td>11.14, 12.98</td>
<td>11.92 ± 0.34</td>
<td>11.22, 12.62</td>
</tr>
<tr>
<td>CLR (µm)</td>
<td>−5, 437</td>
<td>258 ± 126</td>
<td>−111, 438</td>
</tr>
<tr>
<td>Pupil size (iris plane) (mm)</td>
<td>2.34, 4.05</td>
<td>2.99 ± 0.41</td>
<td>4.12, 6.76</td>
</tr>
<tr>
<td>Vault (µm)</td>
<td>9, 94</td>
<td>52 ± 19</td>
<td>45, 183</td>
</tr>
</tbody>
</table>

ACD = anterior chamber depth; ATA = angle-to-angle distance; CLR = crystalline lens rise
†Yuen test for trimmed means (dependent samples).
‡Twenty percentage trimmed mean and winsorized SD.
maximum value, and the SD of lens density for these areas. The mean PNS density in the study group was 7.94 ± 0.43 vs 7.86 ± 0.21 in the control group. No statistically significant differences were found between the groups (\( P = .664 \)) (Table 2). Bivariate analysis revealed no statistically significant differences between the control and study eyes about mean and SD of the density (Figure 2).

**Slitlamp Assessment**

One left eye in the study group developed significant anterior subcapsular opacities, which were disclosed under slitlamp examination. The patient, a 45-year-old woman (age then) had undergone uneventful spherical pIOL surgery in both eyes 5.72 years before being enrolled in the study. The eye that developed the anterior subcapsular opacities had been implanted with a spherical ICL lens (size 12.6 mm, power \( /C0 = 11.50 \) D). CDVA was 0.18 logMAR before surgery and 0.17 logMAR 3 months postoperatively and remained at 0.17 logMAR when the patient entered the study. The anterior subcapsular cataract affected the visual axis, although the patient did not complain of visual loss (Figure 3, A–D).

The VI was 37 to 90 µm, and the VR was 53 µm (Figure 4, A and B). The right eye was implanted 5 days later than the left one with a pIOL 1 size larger (13.2 mm). At the time of the study, the VI was 236 to 200 µm, and VR was 36 µm. The crystalline lens in this eye was completely transparent. The remaining study eyes showed no signs of cataract or clinical or subclinical relevant crystalline lens opacities (Figure 5).

**DISCUSSION**

The Visian ICL designs preceding the current central-hole models were associated with a fairly high incidence of crystalline lens opacities and cataracts. In the trial by U.S. Food and Drug Administration, anterior subcapsular opacities were detected in 6% to 7% of eyes.\(^8\) In their large series of V4 ICL-implanted eyes, Alfonso et al. reported an explantation incidence due to cataract of 0.61%.\(^12\) The mean time between implantation of the pIOL and cataract surgery was 4.2 ± 1.8 years, and the mean vault distance was 103 ± 69 µm. In their 10-year follow-up study, Guber et al. observed lens opacity in 40.9% and 54.8% of patients at 5 years and 10 years after implantation, respectively, associating these opacities with a lower vault height.\(^14\) In other cohort reported by Gonvers et al., the incidence of ICL-induced anterior subcapsular cataracts was also high (27%), all cases with central vaulting equal to or less than 90 µm.\(^7\) Maeng et al. followed up 26 eyes with low pIOL vaulting (<250 µm) for up to 4 years and observed cataracts in 8 eyes (30.8%), mainly anterior subcapsular type, again one of the risk factors being a low vaulting (<52 µm).\(^11\)

Conversely, some researchers have reported cases of pIOLs without central hole with persistent low vaulting and no clinical evidence of crystalline lens opacities.\(^23,24\) Therefore, although there is clinical evidence of a relationship between low pIOL vaulting and formation of anterior subcapsular cataracts, it seems that other causes could also contribute.

In recent years, the rapidly growing clinical experience with central-hole pIOLs and the continued scarcity of reported cases of cataracts with these lens models suggest that the risk for developing cataracts could be significantly reduced due to the central port. In this regard, experimental data suggested that in porcine eyes implanted with central-hole pIOLs, the improved circulation of aqueous humor

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**Table 2. Pentacam Nucleus Staging assessment: descriptive and comparative data of study and control groups.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study (n = 22)</th>
<th>Control (n = 22)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>29, 45</td>
<td>22, 43</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sphere (D)</td>
<td>−10.5, −5.25</td>
<td>−19, 5.5</td>
<td>.004</td>
</tr>
<tr>
<td>Cylinder (D)</td>
<td>−5.5, 0</td>
<td>−5.25, 0</td>
<td>.550</td>
</tr>
<tr>
<td>SE (D)</td>
<td>−11.5, −5.75</td>
<td>−19.88, −7.12</td>
<td>.044</td>
</tr>
<tr>
<td>ALD</td>
<td>7.3, 9.6</td>
<td>7.1, 10.2</td>
<td>.664</td>
</tr>
<tr>
<td>SD LD</td>
<td>0.3, 1.2</td>
<td>0.2, 1.7</td>
<td>.590</td>
</tr>
</tbody>
</table>

ALD = average lens density; LD = lens density; SE = spherical equivalent

*Twenty percentage trimmed mean and winsorized SD.

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**Figure 2. Box plots of the mean and standard deviation of lens density in the control and study eyes measured using the Pentacam Nucleus Staging system.**
(AH) around the anterior surface of the crystalline lens prevents cataract formation. Several researchers have studied this AH flow using computational simulation patterns. Fernandez-Vigo et al. compared the dynamics of AH in 2 different types of ICL design, namely, V4b (tritomy) and V4c (central hole), concluding that AH flow was more physiological with the central-hole model. Kawamorita et al. had previously suggested same conception, and in their more recent research, these investigators theorized that the central hole size of 0.36 mm available in current models was close to ideal from the standpoint of AH fluid dynamics. In a more clinical perspective, various authors showed a reduced incidence of cataracts and lens opacities with the central-hole pIOLs. It remained unclear, however, whether this potential benefit of the central port might be protective against developing cataracts, even in eyes with low vault.

In our series, 24 eyes with a very low vault implanted with central-hole pIOLs were followed up than a mean period of 5.82 ± 0.9 years. According to existing literature, these eyes should be deemed at high risk for developing cataracts, although only 1 eye (4.17%) developed anterior subcapsular opacities. Compared with the series by Maeng et al., very similar in number of eyes and follow-up period, the incidence of clinically significant cataracts was much lower in our cases implanted with central-hole pIOLs (4.17% vs 30.8%). This finding strongly suggests that the presence of the central port might be protective against developing cataracts, even in eyes with low vault.

One relevant aspect of our methodology is the dynamic approach to pIOL vaulting measurement, as described in our previous articles. In miosis, the pIOL approaches the crystalline lens because of the foremost movement of the iris thrust on the upper face of the pIOL, whereas, simultaneously, the crystalline lens rise increases. Our hypothesis is that the continuous turnover of AH through the central port caused by the dynamic bellows movement of both the iris and the crystalline lens keeps continually renewed the AH between the pIOL and the crystalline lens, especially in the central area. The dynamic AS-OCT images suggest that there is no other way out of the AH except through the central port. This streamlined clearance might likely facilitate a more physiologic metabolism for the crystalline lens in pIOL-implanted eyes, thus potentially explaining the low prevalence of anterior subcapsular lens opacities found in our series. It is remarkable that none of the studies that have addressed this topic previously have taken into account the dynamics of AH flow.
account the unquestionable dynamic nature of pIOL lens vaulting, whereas the authors provided limited or no information about pupil sizes or the lighting conditions under which vaulting measurements were taken.

It is also interesting to note, according to our literature review, that, to our knowledge, this is the only study to use a completely objective tool to assess the clarity of the crystalline lens. The Pentacam PNS tool has been validated in previous studies and has high interobserver and intraobserver repeatability and reliability.32,33

Our study is subject to a series of limitations. Ideally, it would have been more appropriate to assess the transparency of the crystalline lens by comparing Scheimpflug images in the implanted eyes both preoperatively and postoperatively. Unfortunately, the Pentacam device was unavailable to us when the procedures were performed. For similar reasons, a dynamic evaluation of the vault could not be performed in the early postoperative period. Another limitation is that we only performed a dynamic assessment for the central vault. However, many of the anterior subcapsular cataracts seen with the nonhole pIOL models, especially in very high myopia, are not directly associated with low central vaulting but with a peripheral contact. In these areas, the thickest section of a high-minus-power pIOL (i.e., the external meniscus of the optic zone) might be in contact with the anterior lens capsule. In our series, however, we did not observe any significant peripheral vault reduction or any pIOL–crystalline lens contact, probably because the pIOL power in our sample was not very high (maximum value implanted below −15 D).

In conclusion, this study demonstrates the good long-term tolerance of the crystalline lens to low vaulting in eyes implanted with a pIOL provided with a central port, by contrast to previous models without a central hole. Because the risk for cataract seems to be reduced, the minimum postoperative central vault value for a central-hole pIOL should be defined from this safety perspective. Further investigations, ideally with a prospective, longitudinal design and long-term clinical outcomes in larger series and including dynamic measurements, might provide more accurate data about the real risk for developing cataracts with central-hole pIOLS and the best approach to consider in eyes with low vault. Until then and based on the results of this study and existing evidence, low central vault of 100 μm or less in miosis could be safely monitored without initially exchanging the central-hole pIOL.

WHAT WAS KNOWN

• Low postoperative vaulting after implantation of a phakic collamer intracorneal lens without a central hole is the main predisposing factor to develop anterior subcapsular crystalline lens opacities.

WHAT THIS PAPER ADDS

• Eyes implanted with a phakic collamer intracorneal lens provided with a central port showed a low risk for developing anterior crystalline lens opacities.

REFERENCES


Disclosures: None of the authors has a financial or proprietary interest in any material or method mentioned.