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Risk factors for explantation of iris-fixated phakic intraocular lenses

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Purpose: To determine risk factors for explantation of iris-fixated phakic intraocular lenses (pIOLs) with a maximum 17-year follow-up.

Setting: University Eye Clinic Maastricht, Maastricht UMC+, the Netherlands.

Design: Prospective case series.

Methods: Eyes that had implantation of 1 of various iris-fixated pIOL models from 1998 to 2016 were evaluated. Primary outcome measures were the rate and proportion of pIOL explantations and the survival time (ie, time to pIOL explantation) in general and specifically as a result of cataract formation or endothelial cell loss (ECL).

Results: The study comprised 1037 eyes. The mean follow-up was 69.3 months ± 52.8 (SD) and the mean preoperative age, 40.2 ± 10.9 years. The overall explantation rate was 12% after a mean of 166.1 months ± 3.0 (standard error). Phakic IOL explantations were performed in 59% of eyes because of cataract formation and in 32% because of ECL. Shorter survival was seen with a higher preoperative age (hazard ratio [HR], 1.07/y; P < .001), longer axial length (AL) (HR, 1.10/mm; P = .009), and smaller anterior chamber depth (ACD) (HR, 4.47/mm; P < .001). Factors for shorter survival resulting from cataract were older preoperative age, longer AL, and larger ACD. Risk factors contributing to shorter survival resulting from ECL were a smaller ACD, lower endothelial cell density, and implantation with an Artisan hyperopia (toric) or Artiflex myopia (toric) IOL.

Conclusions: The explantation rate of iris-fixated pIOLs was 12% after almost 14 years of follow-up, with 59% of pIOL explantations caused by cataract formation and 32% caused by ECL. An older preoperative age, longer AL, and smaller ACD were risk factors for a shorter survival.
Implantation Criteria

Before pIOL implantation, patients had to be 18 years or older and have a stable refraction for at least 2 years. The anterior chamber depth (ACD) from the corneal endothelium to the anterior plane of the crystalline lens had to be at least 2.8 mm with a maximum clear lens rise of 600 μm. The criteria for the minimum preoperative ECD depended on age, with more than 2800 cells/mm² required for patients from 21 to 25 years old, more than 2650 cells/mm² for patients from 26 to 30 years old, more than 2400 cells/mm² for patients from 31 to 35 years old, more than 2200 cells/mm² for patients from 36 to 45 years old, and more than 2000 cells/mm² in patients older than 45 years.

Phakic Intraocular Lenses

The Artisan myopia pIOL is a 1-piece poly(methyl methacrylate) (PMMA) rigid lens with a convex–concave optic and a total diameter of 8.5 mm. The optic diameter is variable and depends on the required refractive correction; pIOLs with a power from −1.0 to −15.5 diopters (D) are available in a 6.0 mm optic diameter and powers from −1.0 to −23.5 D in a 5.0 mm optic diameter.

The Artisan hyperopia pIOL is a 1-piece PMMA rigid lens with a convex–concave optic and a spherical power ranging from −1.0 D to +12.0 D. The total diameter is 8.5 mm and the optic diameter, 5.0 mm.

The Artisan toric pIOL is a 1-piece PMMA rigid lens with a convex–concave optic, a spherical power ranging from +14.0 to −22.0 D, and a cylindrical power up to −7.5 D. The total diameter is 8.5 mm and the optic diameter, 5.0 mm.

The Artilex myopia pIOL is a 3-piece IOL with a polysiloxane optic and PMMA haptics. It is a foldable with a convex–concave optic and spherical power ranging from −2.0 to −14.5 D. The total diameter is 8.5 mm and the optic diameter, 6.0 mm.

Surgical Technique

All surgeries were performed by the same surgeon (R.N.) at the University Eye Clinic Maastricht under general or local anesthesia. All surgeries were performed by the same surgeon (R.N.) at the University Eye Clinic Maastricht under general or local anesthesia.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows software (version 23, IBM Corp.). Descriptive analyses were performed to compute mean ± SD of the preoperative characteristics, and analysis of variance was used to test for preoperative differences. Kaplan-Meier analyses were performed to assess the number of explantations as well as to assess the median, 75%, and median survival. Additional univariate and multivariate Cox regression analyses were performed to identify risk factors for a shorter survival. A P value less than 0.05 was considered statistically significant in all analyses.

Outcome Measures

The primary outcome measures were the rate of explantation of the each pIOL model and the proportion of eyes that had pIOL explantation because of cataract formation or ECL. Survival analyses were performed to assess how long it took until the pIOL was explanted in 50% of eyes (ie, median survival). The secondary outcome measures were the mean survival and time until 25% of pIOLs were explanted (ie, 75% survival). Survival analyses were performed with the following 3 endpoints: explantation in general, explanation because of cataract formation, and explanation because of ECL.

The preoperative patient age, axial length (AL), ACD, and endothelial cell density (ECD) were evaluated as possible contributors to survival, as were the intraocular pressure (IOP), patient sex, pIOL type, and refractive error (myopia versus hyperopia). To assess the effect of the different pIOL models, the following 3 subgroups were created: rigid myopia (toric), consisting of rigid myopia pIOLs (ie, Artisan myopia and Artisan myopia toric), rigid hyperopia (toric), consisting of rigid hyperopia pIOLs (ie, Artisan hyperopia and Artisan hyperopia toric); and foldable myopia (toric), consisting of foldable myopia pIOLs.

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The study evaluated 1037 eyes. An Artisan myopia pIOL was implanted in 381 eyes, an Artisan hyperopia pIOL in 38 eyes, an Artisan toric pIOL in 130 eyes, an Artiflex myopia pIOL in 299 eyes, and an Artiflex toric pIOL in 199 eyes. Table 1 shows the preoperative characteristics, including age, sex, AL, ACD, IOP, ECD, and MRSE, in the entire cohort and in each pIOL subgroup.

Overall, explantation was performed in 12% of eyes (120/1037). The main reasons for explantation were cataract formation and ECL (Table 2). Explantation was performed for other reasons in 11 eyes (9%) as follows: high IOP (5 eyes), pIOL decentration after a blunt trauma (1 eye), after transpars plana vitrectomy and phacoemulsification for retinal detachment repair (1 eye), visual loss unrelated to cataract formation (1 eye), pIOL decentration and visual impairment (1 eye), diplopia caused by anisometropia (1 eye), and pigment depositions on the optic (1 eye). Figure 1 shows the proportion of eyes requiring pIOL explantation because of cataract formation or ECL in the total cohort and in each pIOL subgroup. Table 2 shows the number of pIOL explantations and the mean (i.e., 50%), 75%, and median survival in the total cohort and in each subgroup.

### RESULTS

The study evaluated 1037 eyes. An Artisan myopia pIOL was implanted in 381 eyes, an Artisan hyperopia pIOL in 38 eyes, an Artisan toric pIOL in 130 eyes, an Artiflex myopia pIOL in 299 eyes, and an Artiflex toric pIOL in 199 eyes. Table 1 shows the preoperative characteristics, including age, sex, AL, ACD, IOP, ECD, and MRSE, in the entire cohort and in each pIOL subgroup.

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### Risk Factors for Explantation

The mean patient age at IOL explantation was 54.6 ± 8.3 years, with a mean of 166.1 months until explantation (Table 2). Univariate risk factors for a shorter

### Table 1. Preoperative characteristics in patients with iris-fixated phakic intraocular lenses.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total Cohort</th>
<th>Artisan Myopia (Toric)</th>
<th>Artisan Hyperopia (Toric)</th>
<th>Artiflex Myopia (Toric)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implants/patients (n)</td>
<td>1037/522</td>
<td>466/255</td>
<td>77/45</td>
<td>494/270</td>
<td>—</td>
</tr>
<tr>
<td>Mean age (y)</td>
<td>40.2 ± 10.9</td>
<td>41.1 ± 10.8</td>
<td>37.3 ± 11.7</td>
<td>39.7 ± 10.9</td>
<td>.007*</td>
</tr>
<tr>
<td>Males/females (%)</td>
<td>38/62</td>
<td>38/62</td>
<td>53/47</td>
<td>36/64</td>
<td>—</td>
</tr>
<tr>
<td>Mean AL (mm)</td>
<td>27.0 ± 2.27</td>
<td>28.0 ± 2.28</td>
<td>21.8 ± 1.53</td>
<td>26.8 ± 1.31</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Mean ACD (mm)</td>
<td>3.6 ± 0.35</td>
<td>3.67 ± 0.35</td>
<td>3.39 ± 0.35</td>
<td>3.63 ± 0.33</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Mean IOP (mm Hg)</td>
<td>15.1 ± 3.1</td>
<td>14.7 ± 3.0</td>
<td>14.8 ± 3.1</td>
<td>15.4 ± 2.9</td>
<td>.008*</td>
</tr>
<tr>
<td>Mean ECD (cells/mm²)</td>
<td>2713 ± 350</td>
<td>2669 ± 367</td>
<td>2739 ± 401</td>
<td>2748 ± 322</td>
<td>.002*</td>
</tr>
<tr>
<td>Mean MRSE (D)</td>
<td>−9.63 ± 5.87</td>
<td>−12.50 ± 5.04</td>
<td>3.80 ± 2.03</td>
<td>−9.13 ± 2.84</td>
<td>&lt;.001*</td>
</tr>
</tbody>
</table>

Means ± SD

ACD = anterior chamber depth; AL = axial length; ECD = endothelial cell density; IOP = intraocular pressure; MRSE = manifest refraction spherical equivalent

*Statistically significant difference
survival in general were a higher preoperative age ($P < .001$), longer AL ($P = .023$), smaller preoperative ACD ($P < .001$), and lower preoperative ECD ($P < .001$). After insignificant ($P > .05$) risk factors were removed using multivariate Cox regression analysis, the final model identified a higher preoperative age (HR, 1.07/y; 95% confidence interval [CI]; 1.04-1.09; $P < .001$), longer AL (HR, 1.10/mm; 95% CI, 1.02-1.18; $P = .009$), and smaller ACD (HR, 4.47/mm; 95% CI, 2.43-8.22; $P < .001$) as risk factors for a shorter survival. Figure 2 shows the survival curve for pIOL explantation in general.

**Risk Factors for Explantation Resulting from Cataract Formation**

The mean survival until pIOL explantation resulting from cataract formation was 181.4 months (Table 2); explantation was performed at a mean age of 56.2 ± 8.0 years. A higher preoperative age ($P < .001$), longer AL ($P < .001$), larger preoperative ACD ($P = .004$), and lower ECD ($P = .008$) were identified as significant risk factors for a shorter survival in univariate Cox regression analyses. The final multivariate Cox regression analysis pointed toward a higher preoperative age (HR, 1.09/y; 95% CI, 1.06-1.13; $P < .001$), longer AL (HR, 1.79/mm; 95% CI, 1.49-2.15; $P < .001$), and larger ACD (HR, 5.29/mm; 95% CI, 2.265-12.38; $P < .001$) as risk factors for a shorter survival. Figure 3 shows the survival curve for pIOL explantation because of cataract formation.

**Risk Factors for Explantation Resulting from Endothelial Cell Loss**

Explantation related to ECL was performed at a mean age of 53.7 ± 7.8 years, with a mean survival of 187.0 months (Table 2). The mean ACD and ECD at the time of explantation were 3.20 ± 0.28 mm and 1254 ± 371 cells/mm², respectively.

Univariate Cox regression analyses identified a higher preoperative age ($P = .008$), female sex ($P = .003$), shorter AL ($P = .004$), smaller preoperative ACD ($P < .001$), lower ECD ($P < .001$), and hyperopic refractive error ($P = .008$) as risk factors for a shorter survival. Subsequently, the influence of the pIOL group was evaluated, showing an increased risk for a shorter survival after implantation of a rigid hyperopic (toric) or foldable myopic (toric) pIOL compared with implantation of a rigid myopic (toric) pIOL ($P = .002$). The final multivariate analyses identified a smaller preoperative ACD (HR, 9.62/mm; 95% CI, 2.97-31.17; $P < .001$) and lower ECD (HR, 1.002/cells/mm²; 95% CI, 1.001-1.002; $P < .001$) as factors increasing survival.
the risk for a shorter survival and identified implantation of a rigid hyperopic (toric) (HR, 3.09; 95% CI, 1.09-8.77, \( P < .034 \)) or foldable myopic (toric) pIOL (HR 4.45, 95% CI, 1.70-11.69, \( P = .002 \)) as a risk factor compared with implantation of a rigid myopic (toric) pIOL. There was no significant difference in risk for ECL-related pIOL explantation between eyes with a rigid hyperopic (toric) or foldable myopic (toric) pIOL. \( \text{Figure 4 shows the 3 survival curves corresponding to ECL-related explantation in all subgroups.} \)

**DISCUSSION**

To our knowledge, this prospective study is the first to use survival analyses to evaluate the explantation rate, time to explantation (ie, survival), and risk factors for explantation of iris-fixated pIOLs in a single-center single-surgeon setting.

The mean follow-up in this study ranged from 90 months in the rigid myopic (toric) (Artisan) group to 50 months in the foldable myopic (toric) (Artiflex) group, which is longer than in most previous studies of iris-fixated pIOLs; the follow-up was 50 months or less in the vast majority of these studies. Only 9 of these studies reported pIOL explantations as well as the reason for pIOL explantation (Table 3). In this study, the explantation rate was 12% (17% rigid myopic [toric] pIOLs after a mean of 168 months; 12% rigid hyperopic [toric] pIOLs after a mean of 110 months; 6% foldable myopic [toric] pIOLs after a mean of 127 months).

Explantation rates have been reported only in studies of rigid pIOLs. The explantation rate in these studies was highly variable (0.2% after 4 months; 1.1 to 2.8% after 3 years; 1.2% to 7.6% after 5 to 6 years; 2.3% after 10 years). In the current study, all 3 groups had explantation rates similar to the rates in these previous papers after 5 years; however, explantation rates after 10 years were slightly higher in our groups than in a previous study.

The median survival in all groups combined was 183 months, similar to the median survival in the rigid myopic (toric) group. The median survival could not be computed in the rigid hyperopic (toric) and foldable myopic (toric) groups because of too few explantations. There were no significant differences in the mean follow-up between pIOL groups, even though the successive launch dates of the different pIOL types resulted in fewer rigid hyperopic (toric) pIOLs and foldable myopic (toric) pIOLs reaching a 10-year follow-up.

**Table 3. Previous studies reporting explantation rates in eyes with iris-fixated pIOL.**

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>pIOL Type</th>
<th>Eyes (n)</th>
<th>Pts (n)</th>
<th>Follow-up (Y)</th>
<th>Total</th>
<th>Cataract</th>
<th>ECL</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budo/2000</td>
<td>Artisan myopia</td>
<td>249</td>
<td>NR</td>
<td>3</td>
<td>2.80</td>
<td>1.20</td>
<td>0.40</td>
<td>Other reasons for explantation not reported</td>
</tr>
<tr>
<td>Tahzib/2007</td>
<td>Artisan myopia</td>
<td>89</td>
<td>49</td>
<td>10</td>
<td>2.25</td>
<td>2.25</td>
<td>NA</td>
<td>Two explanted after 3 years due to cataract; 2 explanted due to ECL after 3 y, 1 after 5 y</td>
</tr>
<tr>
<td>Guell/2008</td>
<td>Artisan myopia</td>
<td>101</td>
<td>61</td>
<td>5</td>
<td>1.25</td>
<td>0.50</td>
<td>0.75</td>
<td>—</td>
</tr>
<tr>
<td>Saxena/2008</td>
<td>Artisan myopia (toric), Artiflex myopia</td>
<td>318</td>
<td>NR</td>
<td>2.9†</td>
<td>1.26</td>
<td>1.26</td>
<td>NA</td>
<td>—</td>
</tr>
<tr>
<td>Silva/2008</td>
<td>Artisan myopia</td>
<td>19</td>
<td>NR</td>
<td>5</td>
<td>7.60</td>
<td>3.80</td>
<td>NA</td>
<td>One explantation due to bothersome glare and halos</td>
</tr>
<tr>
<td>Stulting/2008</td>
<td>Artisan myopia</td>
<td>1179</td>
<td>662</td>
<td>3</td>
<td>1.10</td>
<td>0.25</td>
<td>NR</td>
<td>Other reasons for explantation not reported</td>
</tr>
<tr>
<td>Titiyal/2012</td>
<td>Artisan myopia</td>
<td>85</td>
<td>44</td>
<td>5</td>
<td>1.17</td>
<td>NA</td>
<td>1.17</td>
<td>Explantation caused by early corneal decompensation after dislocation due to insufficient enclavation</td>
</tr>
<tr>
<td>Moshirfar/2014</td>
<td>Artisan myopia</td>
<td>213</td>
<td>NR</td>
<td>5.6†</td>
<td>2.76</td>
<td>2.30</td>
<td>0.92</td>
<td>Median time to explantation 9.3 years; both cataract and ECL in 1 eye</td>
</tr>
<tr>
<td>Kamiya/2017</td>
<td>NR (iris-fixated)</td>
<td>50</td>
<td>NR</td>
<td>0.33</td>
<td>0.20</td>
<td>NA</td>
<td>NA</td>
<td>One explantation because of bothersome halos</td>
</tr>
</tbody>
</table>

ECL = endothelial cell loss; NA = not applicable; NR = not reported; pIOL = phakic intraocular lens; Pts = patients

*First author
†Mean
To aid clinicians in their preoperative counseling, we performed supplementary analyses computing how long it would take until pIOL explantation is performed in 25% of patients. Referred to as 75% survival in this paper, it took 119 to 138 months until 25% of pIOLs would be explanted depending on the subgroup. In the rigid hyperopic (toric) group, the 25% pIOL explantation threshold resulting from ECL was reached after a significantly shorter follow-up than in the rigid myopic (toric) group (122 months versus 180 months). Unfortunately, because of the small number of explantations, it was not possible to compute this value for cataract formation as an indication for explantation. No previous study performed any of these analyses for angle-supported or iris-fixated pIOLs, and only 1 study reported survival for posterior chamber pIOLs. In the latter study, cataract-related explantation rates after implantation of an ICL V4 posterior chamber pIOL (STAAR Surgical Co.) were 4.9% at 5 years and 18.3% at 10 years. Neither the 75% survival nor the median survival was computed in this paper; however, the reported survival curve shows a trend similar to that in our study, with slightly higher rates of explantation 10 years after pIOL implantation. As reflected in the median survival, a large number of explantations in our study took place after more than 10 years, which we attribute to the steepened decrease in survival in the final years of follow-up (Figure 4).

The main reason for explantation in the current study was cataract formation in the myopic (toric) groups and ECL in the hyperopic (toric) group. The results in the myopic groups are in line with earlier findings in the literature describing cataract formation as an age-related process occurring at a younger age in a highly myopic (ie, longer AL, larger ACD) target group. Cataract formation was not related to the iris fixation of the pIOL per se, given that early postoperative cataract formation was not detected. The etiology of ECL in eyes with a pIOL is not completely understood; however, consensus has been reached regarding the importance of an adequate preoperative ECD and sufficient distance between the pIOL and the corneal endothelium as potentially protecting against increased ECL. A shallow anterior chamber, as in hyperopic eyes, will bring the iris-fixated pIOL closer to the endothelium. Hypotheses suggest that intermittent contact between the edges of the pIOL and the endothelium result in exaggerated ECL. However, dynamic studies showing minimal movement of the iris-fixated pIOL during accommodation and taking into account that patients are strictly forbidden to rub their eyes postoperatively seem to contradict this theory. Also, application of strict preoperative safety margins for the distance between the pIOL and the central and peripheral corneal endothelium, as performed in this study, is believed to protect the patient against increased ECL. Other etiologies of ECL might be subclinical inflammation and changes in aqueous humor flow that disturb the supply of nutrients or the disposal of waste material, creating a cytotoxic environment in which endothelial cell death increases. Most likely, a combination of the above is responsible for the differences in ECL, as shown in the current study and a previous paper.

In summary, the current study assessed the survival of 3 subgroups of iris-fixated pIOLs. Because pIOLs are implanted in relatively young, healthy, phakic eyes, it is important to analyze the long-term safety of these IOLs. Our results can aid surgeons during preoperative counseling and inform patients about the survival profile of iris-fixated pIOLs. Because we detected a steep decline in survival in the final years of follow-up, we recommend that patients having implantation of iris-fixated pIOLs be informed preoperatively and actively approached postoperatively to comply with a strict long-term follow-up regimen including ECD measurements on a regular (bi) annual basis to detect and monitor ECL at an early stage.

WHAT WAS KNOWN
- The presence of a phakic intraocular lens (pIOL) increases annual endothelial cell loss (ECL).
- A known risk factor for increased ECL after pIOL implantation is a smaller anterior chamber depth.
- Cataract formation occurs at an earlier age in highly myopic patients.

WHAT THIS PAPER ADDS
- Explantation rates of iris-fixated pIOLs increased after 10 years of follow-up.
- Long-term follow-up of iris-fixated pIOLs is mandatory because cataract formation and ECL were reasons for explantation in one third and two thirds of cases, respectively.

REFERENCES


OTHER CITED MATERIAL


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