

Safety and Efficacy Outcomes of Anterior Chamber Phakic Intraocular Lens Implantation and Dependency of Anterior Chamber Depth on Endothelial Cell Loss

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Abstract

Purpose: To evaluate the efficacy and safety of anterior chamber iris-supported phakic intraocular lens (AC-pIOL) implantation in patients with myopia, and compare endothelial cell loss (ECL) with a preoperative anterior chamber depth (ACD) between 2.4 to 3.0 and ≥ 3.0 mm.

Methods: Retrospective case series of sixty-two eyes who underwent an AC-pIOL implantation of non-foldable (Artisan/Verisyse[®]) and foldable lenses (Artiflex/Veriflex[®]) were analyzed. Outcome measures included corrected distance visual acuity (CDVA), intraocular pressure (IOP), spherical equivalent (SE), endothelial cell density (ECD) and ECL/year.

Two cohorts were established group 1: ACD between 2.4 and 3.0 mm and group 2: ACD ≥ 3.0 mm.

Statistical analysis included Student's t tests to evaluate the influence of ACD on ECD and differences between preoperative and postoperative continuous variables.

Results: A significant improvement of the SE ($-9.56 \pm 3.03D$ to $-0.35 \pm 0.43D$; $p < 0.001$) was reported. At the last follow-up visit, there was a significant decrease in ECD (2464.40 ± 246.15 cells/mm² to 2616.10 ± 275.14 cells/mm²; $p < 0.001$) and the mean ECL/year was $-2.09 \pm 2.34\%$. The mean ECL/year was higher in the non-foldable group ($-3.45 \pm 3.19\%$) compared with the foldable group ($-1.80 \pm 2.07\%$), without statistical significance ($p = 0.122$). The mean ECL/year in group 1 ($-2.16 \pm 2.54\%$) was slightly higher than that of the group 2 ($-2.04 \pm 2.26\%$), but this difference was not statistically significant ($p = 0.97$).

Conclusion: The AC-pIOL provided favourable outcomes in patients with myopia. Although the loss in ECD was considerable, a ACD with 2.4 mm cutoff appears to be safe for AC-pIOL implantation. Other studies should be carried out to establishing stricter criteria for ACD.

Keywords: Anterior Chamber Iris-Supported Phakic Intraocular Lens Implantation; Efficacy and Safety; Non-Foldable (Artisan/Verisyse[®]) and Foldable Lenses (Artiflex/Veriflex[®]); Endothelial Cell Loss with a Preoperative Anterior Chamber Depth (ACD) between 2.4 and 3.0 versus ≥ 3.0 mm

Abbreviations

pIOLs: Phakic Intraocular Lenses; AC-pIOL: Anterior Chamber Iris-Supported Phakic Intraocular Lens; ECD: endothelial cell density; ACD: Anterior-Chamber Depth; ECL: Endothelial Cell Loss; IOP: Intraocular Pressure; UDVA: Uncorrected Distance Visual Acuity; CDVA: Corrected Distance Visual Acuity; SE: Spherical Equivalent

Introduction

In 1978, Worst proposed the concept of iris-supported intraocular lenses for aphakic eyes under the name Iris Claw. In 1986, refractive surgeons began to implant the first iris-fixated phakic intraocular lenses (pIOLs) in phakic myopic eyes [1,2].

These lenses can correct medium to high myopia and astigmatism, allowing the patients to preserve accommodation and the original shape of the cornea. This technique is reversible with outcomes that are more predictable, with better quality of vision, since it maintains better coverage of the scotopic pupil and reduce the risk for halos and glare, with faster recovery than excimer surgery [2-8].

The anterior chamber iris-supported phakic intraocular lens (AC-pIOL) evolved to the non-foldable concave-convex lenses Artisan[®] (Ophtec BV) or Verisyse[®] (Abbott Medical Optics, Inc.), and the foldable Artiflex[®] and Veriflex[®] IOLs, that can be inserted through a smaller

incision which decreases surgically induced astigmatism. This led to less complications such as cataract, angle closure, glaucoma, pupil ovalization, uveitis, endophthalmitis and corneal decompensation caused by a postoperative decrease in endothelial cells [2,4,6,9]. The iris-fixated toric pIOL combines spherical and cylindrical correction [7,9,10].

Nevertheless, long-term reduction in endothelial cell density (ECD) after AC-pIOL implantation remains a concern, due to its close proximity to the cornea [1,8,11]. The anterior-chamber depth (ACD) and the ECD should be assessed before surgery [3,12]. A considerable range of ACD is described in the literature, that vary from 2.6 mm to 3.0 mm (to endothelium), with an endothelial cell density (ECD) equal or greater than 2000 cells/mm² [1,3].

Purpose of the Study

The purpose of this study was to evaluate the efficacy and safety of implantation of AC-pIOL in phakic myopic eyes. However, the main focus was the corneal endothelial cell loss (ECL) and to compare with preoperative ACD between 2.4 and 3.0 versus ≥ 3.0 mm (to endothelium).

Materials and Methods

This retrospective case series study, conducted at the Department of Ophthalmology, Centro Hospitalar de Leiria, analyzed myopic patients who underwent AC-pIOL implantation between May 2007 and February 2018, performed according to protocol by the same surgeon.

All patients were informed about the procedure, potential complications, and alternative refractive techniques with respective risks and benefits, and signed a detailed informed consent form in accordance with the Helsinki Declaration.

Four types of AC-pIOL were implanted: non-foldable iris-fixated (Artisan/Verisyse®; n = 10) and foldable iris-fixated (Artiflex/Veriflex®, n = 52).

The inclusion criteria were a stable refractive error for a minimum of 1 year, ACD 2.4 mm or greater (measured from the corneal endothelium to the anterior surface of the lens), ECD 2000 cells/mm² or greater, a normal topographic pattern and no additional ocular pathology.

Exclusion criteria were corneal, iris, or pupil abnormalities, uveitis, cataract, previous eye surgery, intraocular pressure (IOP) over 21 mmHg, glaucoma, retinal pathology, systemic disease, chronic treatment with corticosteroids, immunosuppressive treatment, and pregnancy.

Examinations were performed preoperatively and postoperatively at day 1, week 1 and months 1, 3 and 6. Subsequent examinations were performed annually. Many patients failed some of the postoperative evaluations, so, to avoid bias, data were analyzed on the first and last follow-up visits.

The examinations included uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA), both measured in Snellen lines and recorded in LogMAR units for subsequent statistical analysis, spherical equivalent (SE), slitlamp biomicroscopy, tonometry and indirect ophthalmoscopy with a peripheral retinal examination to rule out retinal tears, especially in highly myopic eyes.

ACD measurements were obtained with the Bausch and Lomb's Orbscan IIzTM and the evaluation of the central ECD with Nidek Specular Microscope CEM-530TM. Examinations were performed by different orthoptist technicians.

Perioperative and postoperative complications were also reported.

Eyes were put into two groups according to ACD, group 1 (ACD 2.4 to 3.0 mm): n = 23 eyes, and group 2 (ACD ≥ 3.0 mm): n = 39 eyes.

Visual and refractive outcomes and ECL were analyzed for the whole sample and for each group of ACD and AC-pIOL subtype. Annual ECL was calculated according to the following formula:

$$\text{ECL/year} = \frac{\text{ECCf} - \text{ECCi}}{\text{ECCi} \times \text{FU}} \times 100$$

where ECL/year is the mean percentage annual loss of endothelial cells, ECCf is the endothelial cell count at the last visit and ECCi the preoperative cell count, and FU is the time in years between the two endothelial cell count measurements.

Statistical analysis was performed using SPSS statistical software package, version 24.0 (SPSS Inc., IBM Corp., Armonk, NY, USA) and a p values less or equal than 0.050 were considered statistically significant.

The mean, standard deviation, and frequency were used in the statistical analysis of the sample’s demographics and clinical characteristics. The distributions of variables were determined with Kolmogorov-Smirnov tests. Independent and paired-sample Student’s t tests were used to test for differences between preoperative and postoperative continuous variables.

Results and Discussion

Sixty-two eyes of 33 patients, with equal percentage of right and left eyes, were included in this study. The mean age was 31.95 ± 6.40 years and 72,6% of the sample was composed by women and 27,4% by male.

Table 1 presents the preoperative characteristics of all eyes of the sample and table 2 separately for each group of ACD. Table 3 shows the number and percentage of each type of AC-pIOL.

Variable	Mean ± SD	Range
Age (years)	31.95 ± 6.40	20, 46
Sphere (D)	-8.95 ± 2.88	-3.25, -19.00
Cylinder (D)	-1.63 ± 1.04	-4.50, 1.00
SE (D)	-9.56 ± 3.03	-1.25, -20.37
CDVA (decimal/LogMAR)	0.85 ± 0.17/ 0.32 ± 0.42	0.4, 1.0/0.97, 0.0
IOP (mmHg)	13.38 ± 3.03	8.00, 21.00
ACD (mm)	3.05 ± 0.24	2.60, 3.82
ECD (cells/mm ²)	2616.10 ± 275.14	2053, 3630

Table 1: Population characteristics and preoperative data.

SE: Spherical Equivalent; CDVA: Corrected Distance Visual Acuity; IOP: Intraocular Pressure; ACD: Anterior Chamber Depth; ECD: Endothelial Cell Density.

Variable	Group 1 ACD 2.6 - 3.0 mm	Group 2 ACD ≥ 3.0 mm
Mean age ± SD (years)	35.35 ± 5.98	29.95 ± 5.83
Male/ female %	26.10/ 73,90	28.20/ 71.80
Eyes right/ left (n)	52.20/ 47.80	48.70/ 51.30
Mean sphere ± SD (D)	-9.34 ± 3.38	-8.72 ± 2.58
Mean cylinder ± SD (D)	-1.67 ± 1.24	-1.60 ± 0.90
Mean SE ± SD (D)	-9.77 ± 3.75	-9.44 ± 2.55
Mean CDVA ± SD (decimal/logMAR)	0.78 ± 0.18/ 0.46 ± 0.43	0.90 ± 0.15/ 0.23 ± 0.39
Mean IOP ± SD (mmHg)	14.29 ± 2.81	12.86 ± 3.06
Mean ACD ± SD (mm)	2.82 ± 0.11	3.19 ± 0.17
Mean ECD ± SD (cells/mm ²)	2599.65 ± 311.73	2625.79 ± 254.95

Table 2: Population characteristics and preoperative data of the 2 groups.

n: Number of Eyes; SE: Spherical Equivalent; CDVA: Corrected Distance Visual Acuity; IOP: Intraocular Pressure; ACD: Anterior Chamber Depth; ECD: Endothelial Cell Density.

pIOL type	Global	Group 1	Group 2
Nonfoldable n (%)	10 (16.1)	7 (30.4)	3 (7.7)
Foldable n (%)	52 (83.9)	16 (69.6)	36 (92.3)
Total n (%)	62 (100)	23 (37,10)	39 (62,90)

Table 3: Anterior chamber iris-fixated models for each type of pIOL.

n: Number of Eyes; pIOL: Phakic Intraocular Lens.

The mean follow-up period was 27.84 ± 26.45 months.

The mean preoperative SE had significantly improved from -9.56 ± 3.03D to -0.35 ± 0.43D (range: -1.87 to 0.25; p < 0.001) at the end of the follow-up (9,21D in absolute value).

The astigmatism significantly varied from $-1.60 \pm 0.90D$ to $-0.71 \pm 0.41D$ ($p < 0.001$), so the reduction in absolute astigmatism was 0.89D.

The difference between the mean preoperative value of CDVA 0.32 ± 0.42 LogMAR, and at the last visit 0.18 ± 0.36 LogMAR, was statistically significant ($p = 0.017$). UDVA at the last follow-up was 0.24 ± 0.41 LogMAR.

A loss of 1 Snellen line in CDVA occurred in 2 eyes (3.23%), there was no change in 36 eyes (58,06%) and 24 eyes (38,71%) gained 1 or more lines

There was no difference statistically significant between the mean preoperative IOP, 13.38 ± 3.03 , when compared with the mean IOP at the last visit, 13.28 ± 3.19 ($p = 0,870$).

We reported three patients with displacements of the AC-pIOL, with no need of surgery, two cases of pupillary block and one with iridocyclitis, with no further complications.

A significant decrease in mean ECD was found at the last follow-up visit: 2464.40 ± 246.15 cells/mm² compared with the baseline value of 2616.10 ± 275.14 cells/mm² ($p < 0.001$). The mean global calculated ECL/year was $-2.09 \pm 2.34\%$.

In the non-foldable group of AC-pIOL (Artisan/Verisyse®; $n = 10$), the mean ECD at the last visit was 2344.00 ± 220.67 cells/mm², a difference that was statistically significant ($p = 0.011$) when compared with the initial value 2738.70 ± 346.03 cells/mm².

The decrease in the mean ECD in the group of foldable lenses (Artiflex/Veriflex®; $n = 52$) was statistically significant ($p < 0.001$), when we compared the initial value 2592.52 ± 256.71 cells/mm², with the value at the last visit 2487.56 ± 245.95 cells/mm².

The mean ECL/year was higher in the non-foldable group ($-3.45 \pm 3.19\%$) compared with the foldable group (-1.80 ± 2.07 cells/mm²), without statistical significance ($p = 0.122$).

In group 1 the mean ECD measured at the last visit was 2422.91 ± 234.87 cells/mm², a difference that was statistically significant ($p = 0.030$) when compared with the initial value 2599.65 ± 311.73 cells/mm².

In group 2 a significant decrease at the last follow-up in mean ECD was also found ($p = 0.001$), whit a mean ECD of 2488.87 ± 252.33 cells/mm², compared to the initial value of 2625.79 ± 254.95 cells/mm².

The mean ECL/year in group 1: $-2.16 \pm 2.54\%$ was slightly higher than that of the group 2: $-2.04 \pm 2.26\%$, but this difference was not statistically significant ($p = 0.97$).

Many studies have reported the visual and safety outcomes and high quality of AC-pIOL in correcting moderate to high myopia [1,6,11,13-16].

In our department experience they were effective, with a statistical significant improvement of the SE (-9.56 ± 3.03 to -0.35 ± 0.43 D; $p < 0.001$), astigmatism (-1.60 ± 0.90 D to -0.71 ± 0.41 D; $p < 0.001$) and CDVA (0.32 ± 0.42 logMAR to 0.18 ± 0.36 logMAR). The mean UDVA at the last visit (0.24 ± 0.41 log-MAR), was very close to CDVA, with only 8 patients (12,9%) in whom visual acuity improved with correction.

Of the complications identified after AC-pIOL implantation, we had very few, listed on the results. However, decreases in ECD can be severe after pIOL implantation, and were the main focus of our study. After a mean follow-up period of 27.84 ± 26.45 months, our results shown a decrease in ECD (2616.10 ± 275.14 cells/mm² to 2464.40 ± 246.15 cells/mm²; $p < 0.001$). Although the statistically significant difference in the ECD loss, there were no cases of endothelial decompensation or need for IOL explantation.

A longitudinal study of unoperated eyes set the baseline of mean ECL at $0.6 \pm 0.5\%$ per year [17]. Other studies, reported an ECL from -3.8 to -12% in the first 2 years after implantation and from -0.5 to -1.8% per year in longer follow-up periods by Kohonen, *et al.* [18], Asseto, *et al.* report a 3.9% loss at 1 year and 5.4% loss at 2 years [17] and Menezo, *et al.* report a mean endothelial cell loss after placement of a pIOL of 3.9% at 6 months, 6.6% at 1 year, 9.2% at 2 years, 11.7% at 3 years, and 13.4% at 4 years [19].

The mean ECL/year of the eyes where we implanted a AC-pIOL, was within these values ($-2.08 \pm 2.34\%$), despite the decrease in ECD at the last follow-up visit being statistically significant with respect to the initial value.

Reports of ECL vary considerably from study to study for non-foldable and foldable anterior chamber iris-fixated lenses. Studies showed that for non-foldable lenses (Artisan/Verisyse®) the annual loss varies from -0.73 to -2.81% [1,13,15,16,20,24,25]. For foldable models Artiflex/Veriflex® an annual loss ranges from -0.54 to -2.65% [7,20-23].

Our study showed that de ECL/year for non-foldable lenses was $-3.45 \pm 3.19\%$ and $-1.80 \pm 2.07\%$ for foldable AC-pIOLs. These mean annual loss is lower for the non-foldable ones, as in the mentioned studies, but we didn't found a significant effect between the two types of lenses, which suggests that they have a similar safety profile.

According to Saxena, *et al.* a shallower ACD is a predictor of a greater ECD decrease, with a negative correlation between ACD and ECL after 3 years of follow-up, which remained significant up to a 7-year follow-up [1]. Menezo, *et al.* also found a significant negative correlation between ACD and ECL after 6 months [19]. However, in these studies, ACD measurements to endothelium or epithelium were not clearly defined [4].

We also analyzed the impact of ACD on ECD. The cutoff values were 2.4 and 3.0 mm. The mean annual ECL/year was higher for the shallower ACD group (mean annual ECL/year group 1: $2.16 \pm 2.54\%$ and group 2: $-2.04 \pm 2.26\%$), but could not find a significant effect. The absence of significant difference between the groups is in favor that probably this loss of endothelial cells occurs intraoperatively but the implant of these pIOL don't lead to a higher loss in eyes with a rather narrow ACD. However individual patients can have a critical ECL and therefore we recommend annual follow-up examinations with ECD measurement. It is also important emphasizing to patients, especially those with a rather narrow ACD, that a higher loss can mean a contact between the pIOL and corneal endothelium, such as when rubs the eye.

Our results showed that both non-foldable and foldable iris-fixated lenses and an ACD of 2.4 mm or greater (to endothelium), are safe for pIOL implantation procedure with a mean annual ECL/year within the values of other studies. Although the statistically significant decrease in ECD, it represents only a 5.80% decrease from the initial value after a mean follow-up of more than two years.

The irregular follow-up didn't allow to have the data of all patients in all follow-up visits, which is one of the major limitation of retrospective studies. Consequently, only a comparison of ECD in the first and last visits were possible and a mean annual ECL had to be estimated.

Conclusion

In conclusion, our study shows good refractive and safety outcomes with implantation of AC-pIOL. Few cases of postoperative complications were detected and resolved. Endothelial specular microscopy examinations before surgery and during regular intervals during the follow-up period are mandatory to monitor the long-term effect of the pIOL on the endothelium. The ACD should also be analyzed. However mean ECL/year was slightly greater in the group 1, according to our results the 2.4 mm (to endothelium) is a safe cutoff to the anterior chamber iris-fixated pIOL that we implanted.

Studies with a larger number of patients and a longer follow-up are needed to determine consensual ACD cutoff according to the type of lenses implanted.

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Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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