Literature Review to Better Determine Risk for Cataract With Collagen Copolymer IOLs

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Purpose

- The scholarly literature reports cataract associated with ICL implantation can range from a low of 2.5% all the way up to 33%.
- A range of such magnitude suggests low reproducibility of ICL results or inconsistency in the literature.
- The rates in my practice have been stable and lower than 2.5%.
- We suspected inconsistency in the literature and investigated to find out what could be amiss.

Methods

- 22 articles were analyzed to gain a thorough understanding of the data, cohorts, study methods, computation of percentages, and results.
- We defined “cataract” as clinically significant cataract resulting in loss of BSCVA and leading to replacement with an IOL.

Results: the real rate of clinically significant cataract

- The incidence of clinically significant cataract reported in the 22 studies ranged from 0% to 30%.

BUT….

- 3 articles reported cataract incidence >10%.
- 19 articles reported cataract from 0 – 6.9%.
  - And, when the V3 model results from the ITM study were dropped, the range of cataract dipped to 0 – 5%.

Incidence of reported cataract in 22 articles. Articles highlighted in yellow were identified as outliers.

Year	Author and Article♦	Rate of cataract
2004	US ITM study 3-year follow up[2]	0.6% (3 of 525 eyes)
2010	Alfonso–1-year follow-up[3]	0% (50 eyes)
2011	Alfonso–5-year follow-up[4]	.05% (1 of 188 eyes)
2007	Chang–High Myopic Asian Eyes[5]	1.6% (1 of 161 eyes)
2011	Fernandes Review of ICL complications[6]	1.5% (2592 eyes)
2003	Gonvers–Relationship of vaulting to cataract[7] *	27% (20 of 75 eyes)
2009	Kamiya –Changes in vaulting[8]	4% (3 of 75 eyes)
2009	Kamiya –Four year follow-up[9]	1.8% (1 of 56 eyes)
2010	Kojima–Changes in vault during one year[10]	0% (36 eyes)
2011	Kojima–Lens sizing Method[11]	0% (47 eyes)
2003	Lackner–Outcome after treatment[12]	10.7% (8 of 76 eyes)
2004	Lackner–Long-term results[13]	3.9% (3 of 76 eyes)
2011	Maeng–Risk factor for cataract development[14]**	30.8% (8 of 26 eyes)
2011	Parkhurst–ICLs in US Military Warfighters[15]	0% (135 eyes)
2012	Reinstein–Comparison of vault predictability[16]	0% (50 eyes)
2003	Sanchez-Galeana–Lens opacities[17]	1% (2 of 170 eyes)
2006	Sanders–ICL/LASIK comparison for low myopia[18]	0% (144 eyes)
2002	Sanders–Incidence of lens opacities (V3 vs. V4)[19]	V3:6.9% (6 of 87 eyes) V4: 0.2% (1 of 523 eyes)
2008	Sanders–ASCC 5 years after ICLs in FDA trial[20]	1.3% (7 of 526 eyes)
2007	Sanders–Matched population ICL vs. LASIK[21]	0% (164 eyes)
2010	Schmidinger–Long-term changes in vaulting[1] ***	5% (4 of 84 eyes)
2012	Zhou–Mid-long term follow-up[22] †	0.5% (5 of 993 eyes)

♦See slide 10 for full citation
*Did not distinguish clinically significant from not significant.
**Cross section of patients with low vault identified
***Only percentages of cataract were reported. We had to calculate the number of eyes
†Not clear how many were clinically significant

Results: 3 articles appear to be outliers

- Maeng: 30%. x-sectional study patients selected *because* they were more likely to develop cataract.
- Gonvers: 27% included all opacities. Clinically significant was only 2.7%. Obsolete models of ICL included. Small sample probably caused Type II statistical errors. Incorrect sizing technique. Cohort age too high.
- Lackner: 33% (all opacities). 10.7% (clinically significant) Used 6 models of ICL, including prototypes. Probably includes Type II statistical errors. Incomplete Methods lacks sizing technique, some demographic data. Older cohort, high average refractive error

Results: Variables and rate inflation

- Definition of “cataract” includes all opacities, not just clinically significant.
- Repeated citations of obsolete studies, esp. Gonvers and Lackner.
- Convoluted computations
  - Percentages with no “n”
  - Percentages of percentages
- Poor writing and lack of editing

Results (example of convoluted computations combined with poor writing)

- *Original: "In this trial, ASCC developed in 28% of eyes in the ICM-V4 group …. An ICL removal with cataract extraction had to be performed in 17% of eyes with an ICM-V4 at 43 ± 34 months (range, 9–103 months) after the first appearance of an ASCC."*[1]

- *Edited: ASCC developed in 24 (28%) of 84 eyes in the ICM-V4 group. Of those 24 eyes, an ICL removal with cataract extraction had to be performed in 4 …after the first appearance of an ASCC.*

Conclusions

- The often quoted range of 2.9%–33% ICL-associated cataract is incorrect.
- Obsolete study results should not be cited by authors reporting ICL results.
- 0%–5%, as reported in 19 studies, is far more reflective of clinical experience with ICLs, and is a much more realistic statistic upon which to make the decision to implant ICLs.

Literature Review to Better Determine Risk for Cataract with Collagen Copolymer IOLs

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PURPOSE

The scholarly literature regularly reports that cataract associated with ICL implantation can range from a low of 2.5% all the way up to 33%.[1] A range of such magnitude suggests either low reproducibility of ICL results or inconsistency in the way results are reported in the literature.

In clinical practice we do not see this inconsistency with ICL implantation. The rates of ICL-associated cataract in my own practice have remained extremely low and stable over the six and a half years that I have been implanting them. Additionally, the rates in my practice are lower than the 2.5% that is often the reported as the lower end of the range. Therefore, we suspected that the inconsistency originates in the reporting of results.

The repeated publication of this statistic may well be hindering wider adoption of the ICL among ophthalmologists in the United States. We undertook an investigation of the literature to find out what, if anything, was amiss.

METHODS

Our starting point was a collection of peer reviewed articles that had been pulled for an earlier study of ICLs, as these papers represented a good cross-section that spanned about 10 years. We also mined the reference lists of the original articles and added several studies based on repeated citations of those articles. We eliminated articles that did not report on incidence of cataract. Only articles published in the peer reviewed literature were used in this study.

Twenty-two articles[1–22] were identified for inclusion in the study. Each article was analyzed, paragraph by paragraph, to gain a thorough understanding of the data, cohorts, study methods, computation of percentages, and results.

For the current study, we defined "cataract" as clinically significant cataract resulting in loss of BSCVA and leading to phacoemulsification and replacement with an IOL.

RESULTS

Table 1 shows that the incidence of clinically significant cataract reported in the 22 studies ranged from 0% to 30%. The three articles highlighted in yellow reported cataract incidence over 10%. The 19 remaining articles reported cataract from 0 – 6.9%. When the V3 model results from the ITM study were dropped, the range of cataract dipped to 0 – 5%.[7,12,14]

Analysis of articles reporting percentages higher than 5%

Maeng[14]

The 30% cataract rate reported in the article by Maeng is explained by the study cohort (n=26 eyes), which is a cross section of patients from a larger study (n=233 eyes) identified as having risk factors for cataract development. The risk factors were: lower vaulting (mean, 42.4 ± 34.0 µm vs. 141.4 ± 82.2 µm); greater age (mean, 42.6 ± 7.3 vs. 34.9± 6.9 years); and higher pre-operative SE (mean, -17.1 ± 4.4 D vs. -10.7 ± 2.7 D) than the rest of the cohort. Additionally, the 30% refers to all opacities. Actual clinically significant rate was 19.2%.[14]

Gonvers[7]

The 27% rate given in the abstract refers to all opacities. Digging deeper into the study revealed that only 2 (2.7%) met our criteria for clinically significant. The 27% rate is repeated here because that is the rate printed in the abstract , and that rate tends to be cited everywhere. This study included V3 and V4 models, and results were not stratified by model. Gonvers found no statistical difference between V3 and V4 model results or vault size, which Sanders states is probably a Type II statistical error (false negative).[20] Gonvers routinely implanted lenses that were 0.5 mm smaller than would have been implanted in the US, which results in smaller vault.[20] Additionally, patients as old as 62 years (mean age 42) were implanted.

Lackner[12]

The body of this article is the source of the 33% statistic that is often quoted as the high end of the range. According to Lackner, 25 of 75 eyes developed lens opacifications. Cataract surgery was performed on 8 eyes (10.7% of all cases) which is lower, but still a much higher incidence of cataract than is normally seen in clinical experience. Six different models, including the V3, were implanted in this cohort. Four of them were discontinued and two were prototypes.[20] Lackner found no statistical difference in results by model, but this was probably also a Type II statistical error because of the small sample size.[20] How the ICL length was determined is not reported. Mean patient age was 38.3 ± 11.5 (range 21.7 – 60.6). Average myopia was -16.23. Demographic information on the patients who had cataract surgery was not reported, nor was the model of ICL disclosed.

RESULTS *(continued)*

Table 1. Incidence of reported cataract in 22 articles
Articles highlighted in yellow were identified as outliers

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** Cross section of patients with low vault identified

*** Only percentages of cataract were reported. We had to calculate the number of eyes

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A) *Unedited version: "In this trial, ASCC developed in **28% of eyes in the ICM-V4 group**… An ICL removal with cataract extraction had to be performed in 17% of eyes with an ICM-V4 at 43 ± 34 months (range, 9–103 months) **after the first** appearance of an ASCC."*[1]

B) *Proposed edit: In this trial, ASCC developed in 28% **(24 of 84)** of eyes in the ICM-V4 group… Of those 24 eyes, an ICL removal with cataract extraction had to be performed in 4 **(5% of eyes in the ICM-V4 group)** at 43 ± 34 months (range, 9–103 months) after the first appearance of an ASCC.*

Figure 1 shows how editorial presentation of data can be misleading. A) It appears that 17% of all V4 recipients (17% of 84=14) had to have the extraction procedure. Note that the author says cataract extraction was performed in 17% of eyes with the V4…**AFTER the first appearance of ASCC.** Additionally, the author does not give numbers of eyes. Therefore the 17% applies only to eyes with ASCC, not to all eyes with the V4. B) A rewritten version of the sentence shows how the data could have been made easier to grasp.

Sanders[20]

This study explains why the V3 lens was discontinued. The V3 results account for the 6.9% rate of cataract. The differences in results between the V3 and V4 models are dramatic and statistically significant. In his 2008 follow-up article, Sanders directly addresses Lackner's and Gonvers' assertions that there are no statistical differences between the V3 and V4 results. He attributes their findings to Type II statistical errors (false negatives) caused by small sample size.[20]

Variables that lead to rate inflation

Definition of cataract

It is important to distinguish what the author means by incidence of cataract. The percentage given in the abstract is not always the percentage of clinically significant cataract. It may encompass all opacities, whether or not they have potential to threaten sight. The most important percentage is the percentage of eyes that lose 2 or more lines of BSCVA and that have to have cataract surgery. The reader may have to do some calculations to unearth that rate.

Reliance on and continued repetition of studies reporting obsolete and/or incorrect data

We found that two studies, one by Gonvers[7] and the other by Lackner[12] are virtually institutionalized, even though many of their findings are demonstrably outdated. Their data are based on obsolete models of the ICL. Their sizing methods were either questionable or not described. Their statistical findings are probably due to type II false negative errors.[20] Remarkably, they found no statistical difference in vaulting between V3 and V4 models; and no statistical difference in occurrence of cataract among different models.[7, 12] Lackner found no statistically significant correlation between low vault and cataract.[12] Sanders rebutted the Gonvers and Lackner articles in 2008,[20] but the findings of these papers continue to be repeated by other authors. One or both of the Gonvers and Lackner articles were cited in 13 of the 18 papers in this study that were published subsequent to their release.[1,3–6, 8–15]

Convoluted computations and poor editing

Figure 1 shows how using percentages without including the number of eyes, along with imprecise wording creates incorrect perceptions. The actual incidence of clinically significant cataract in this study was 5%,[1] but it was not reported as such, and it was difficult to figure it out. It required a half an hour of scrutinizing the methods and results sections to uncover it. Even Fernandes, in his well thought out and well written review of ICL complications,[6] is guilty of forcing the reader to perform calculations to find that 1.5% of all eyes in his review developed clinically significant cataract. The abstract first states that 136 (5.2%) cases of some form of cataract were reported. It goes on to say that "cataract surgery was carried out in 27.9% (38) of eyes," —implying all the eyes in all the articles. Fernandes does present the n, so it only takes a few seconds to figure out that 38 is 1.5% of 2592 eyes. Still, 27.9% is a figure that is likely to be repeated because it is in the abstract.

CONCLUSIONS

As authors and researchers, it is important to be thorough and precise in our definitions. As readers and physicians, it is important to dig deeper than the percentages reported in the abstract to understand how the data are presented and what they really mean.

The wide range of ICL associated cataract (2.9% – 33%) that is often reported in the literature does not reflect clinical experience. When the cross sectional and obsolete study results are removed from this collection of studies, the range of clinically significant cataract contracts dramatically to 0% – 5%, which is far more reflective of current clinical experience. This is a much more realistic statistic upon which to make the decision to implant ICLs.

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