Late in-the-bag intraocular lens dislocation

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This review aimed to evaluate the cumulative incidence, patient characteristics, predisposing conditions, and treatment outcomes for late intraocular lens (IOL) dislocation. Literature searches in PubMed (MEDLINE), Embase, and Cochrane Library Central database identified 1 randomized clinical trial, 1 prospective case series, 2 prospective cohort studies, and 36 retrospective studies of this condition, which showed that the cumulative incidence was 0.5% to 3%, it occurred on average 6 to 12 years after cataract surgery, and mean patient age was 65 to 85 years. Pseudoxfoliation syndrome, myopia, and previous vitrectomies were the most common predisposing conditions.

Studies indicated that IOL repositioning and IOL exchange provided similar visual outcomes and were equally safe. The long-term visual outcome seemed satisfactory. However, the quality of evidence regarding treatment was in general quite low. More studies of late in-the-bag IOL dislocation are needed, and in particular, different surgical techniques should be included in high-quality clinical trials.

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More than 50% of the population experience cataracts by the age of 75 years, and in many countries, cataract surgery is the most frequently performed operation in the healthcare system. Still, surgical rates are too low in developing countries, and globally, cataracts remain a leading cause of blindness. The demand for surgery is therefore expected to rise further in the years to come as a result of wider access to affordable surgical care, as well as increased life expectancy and changing indications for surgery, especially in terms of refractive care, as well as increased life expectancy and changing indications for surgery, especially in terms of refractive change or lowering of the intraocular pressure (IOP).

Cataract surgery represents a success story in medicine. The surgical technique has evolved over the years, followed by improvements in outcome. One of the successful changes was the introduction of the continuous curvilinear capsulorhexis (CCC) technique in the 1980s. A CCC with implantation of the intraocular lens (IOL) inside the capsular bag is considered to be beneficial to achieve a stable, well-centered lens with less iris friction and reduced inflammation. The risk of complications from today’s standard cataract surgery is minor, and the visual outcome is usually excellent if the patient has no other eye diseases.

However, adverse events may occur, and among the most serious are loosening and dislocation of the IOL. These dislocations are classified according to the position of the IOL, which can be partly or completely outside the capsule (out of the bag) or inside the capsule (in the bag) representing a dislocation of the whole IOL–capsule complex. Out-of-the-bag IOL dislocation occurs usually in the early postoperative period and is often associated with rupture of the posterior capsule. In-the-bag IOL dislocation usually occurs at a much later stage after cataract surgery as a result of zonular weakening and loosening, sometimes associated with pronounced contraction of the anterior lens capsule. Late in-the-bag IOL dislocation was first reported by Davison in 1993 and has been described as almost nonexistent until the advent of CCC. The term “late” refers to the fact that most cases occur months to years after cataract surgery (usually defined as more than 3, 6, or 12 months). In some cases, the term “spontaneous” is used; however, a considerable number of these patients have preexistent loose zonular fibers at the time of cataract surgery, and furthermore, trauma is considered a contributing factor in some patients, even low-energy blunt trauma or light head injuries. Therefore, not all cases are obviously spontaneous, and to encompass even these cases, the term “late in-the-bag IOL dislocation” seems appropriate.

Although the number of out-of-the-bag IOL dislocations seems to have decreased over recent decades, several articles have reported a rising trend of late in-the-bag IOL dislocation. Accordingly, research focus on this condition has increased. A thorough review was published by Gimbel et al. in 2005, which noted that the choice of operation method to treat late in-the-bag IOL dislocation has traditionally depended on the surgeon’s preference. Since then, several clinical studies have been performed, and more available knowledge now seems to suggest at least
some clinical recommendations. The aim of this review was to provide an update of the literature on late in-the-bag IOL dislocation, in particular by describing the cumulative incidence, patient characteristics, predisposing conditions, main surgical treatments, possible surgical complications, and expected outcomes.

**METHODS**

**Eligibility Criteria**

In this review, we searched for published articles on late in-the-bag IOL dislocation. We aimed to identify all randomized clinical trials involving the surgical treatment and, if several trials were identified, include them in a standardized risk-of-bias evaluation and meta-analysis. Secondarily, we searched for other clinical studies where more than 50% of patients—and at least 10—had late in-the-bag IOL dislocation. From these studies, we aimed to evaluate the incidence, patient characteristics, predisposing conditions, surgical treatments, and expected visual outcomes, surgically induced astigmatism, and complications. For surgical treatments, we focused on the comparison of the 2 main operation methods: IOL repositioning and IOL exchange; specific surgical techniques have not been discussed in much detail. This review has been reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. A Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram is presented as online Supplement 1 (see Supplemental Digital Content 1, available at http://links.lww.com/JRS/A338). The research adhered to the Declaration of Helsinki.

**Search Methods**

Because several terms have been used for this condition, and many IOL dislocation studies include a mixture of conditions and patient groups, we wanted to conduct a broad search to identify even articles where not all patients had late in-the-bag IOL dislocation. A search strategy was developed in collaboration with the Medical Library at Oslo University Hospital/University of Oslo. The search was restricted to English language with no time restriction. It was finished in June 2020 and was performed in the following electronic databases: PubMed (MEDLINE), Cochrane Database of Systematic Reviews, and Embase. In PubMed, we performed a search using Medical Subject Headings and text words including Late-in-the-bag, Intraocular lens dislocation, Artificial Lens Implant Migration, Intraocular Lenses, Cataract Extraction, and Prosthesis Failure. A detailed search strategy is presented as an online Supplement 2 (see Supplemental Digital Content 2, available at http://links.lww.com/JRS/A339).

**Study Selection**

One of the authors (O.K.) went through all abstracts to screen for articles that could potentially contain information about IOL dislocations. This author read the articles in full and evaluated whether patients with late in-the-bag IOL dislocation were included, which were the relevant articles for this review, and, if so, the proportion with this condition. Relevant articles were further categorized according to study design and whether they presented results related to the following topics: incidence, predisposing conditions, baseline characteristics, association with glaucoma, description/comparison of surgical techniques, and comparison of IOL repositioning vs IOL exchange. The reference lists of these articles were further screened for relevant articles that had not been identified by the systematic search. No efforts were made to identify unpublished results.

**Risk-of-Bias Assessment**

The literature search identified only 1 randomized clinical trial (by the authors of this review). For this reason, and because intervention outcomes were not the only focus of the review, we did not perform any meta-analysis, nor did we evaluate the studies strictly according to a specific risk-of-bias tool. However, the quality of evidence was evaluated in accordance with the main aspects of the revised Cochrane risk-of-bias tool in randomized trials (RoB 2.0) and the Cochrane Risk of Bias in Non-randomized Studies of Interventions tool. This included assessing the risk of bias in selection of study participants; in selection and classification of interventions; in measurement of the outcomes; due to missing data; and in selection of the reported results.

**RESULTS**

The search identified a total of 1000 references (1070 before removing duplicates). Most were not considered relevant as they described other conditions (such as subluxation or dislocation of the crystalline lens; dislocation of a phakic IOL; out-of-the-bag IOL dislocation only; surgical techniques of cataract surgery; IOL types; symptoms and complications after cataract surgery such as IOL tilt; calcification or opacification of the IOL; and different adverse outcomes related to the lens capsule). The presented overview also excluded letters to the editor and case reports of fewer than 10 patients with late in-the-bag IOL dislocation. Of the included articles, 29 had only late in-the-bag IOL dislocation patients, with 1 randomized clinical trial, 1 prospective case series, 1 cohort study, and 4 histopathologic studies of dislocated in-the-bag IOL complexes either in general or with capsular tension ring (CTR) specifically; the remaining were retrospective clinical studies. In another 11 articles, at least 50% of the patients had late in-the-bag IOL dislocation, of which 1 was a prospective cohort study and the remaining were retrospective studies. Further 2 articles mentioned in-the-bag IOL dislocation as part of a population study. In addition, 4 editorials and 10 reviews mainly or partly discussed late in-the-bag IOL dislocation. A number of articles were excluded because they contained less than 50% or an unknown proportion with the condition, although 1 of these articles reported some results separately for in-the-bag IOL dislocation.

**Quality of Evidence**

Most studies in this review were observational and retrospective, and many of them included fewer than 50 patients with late in-the-bag IOL dislocation. The articles varied in terms of whether they reported specific inclusion criteria in detail, and even if so, most articles did not indicate whether the criteria were defined before or after the data were gathered, or who performed the review of the medical records. In a few studies, some of the results were based on reporting forms filled out by the surgeons; a few others used standardized forms for obtaining information from medical records. Several studies included only patients with pseudoexfoliation syndrome (PEX), and a few included only patients with previous vitrectomy, whereas some studies excluded all cases with zonular deficiencies noticed during cataract surgery or cases with ocular trauma or previous vitrectomy. These restrictions greatly influence the patient characteristics and predisposing conditions.
conditions. Wide variation was also seen in follow-up time, both within studies and between them. In addition, many studies included a mixture of conditions, which affects the results. We have tried to adjust for this fact by including only studies with at least 50% of the patients having in-the-bag IOL dislocation, and we have tried to indicate which studies had less than 100% of this patient group (Tables 1 and 2). Only in very few studies was the evaluation of patient characteristics and predisposing conditions compared with a nonaffected matched control group or to the fellow eye. 25,27

Three prospective studies compared surgical interventions, of which only 1 randomly assigned patients to interventions. 20,48,54 In this trial that we performed, 1 surgeon performed all the operations, which may be both a strength and a limitation regarding interpretation of the results. In most studies, the choice of operation method was based on the surgeon’s preference, and the surgeons were usually part of the study group. Because of the retrospective nature of most studies, main outcome variables like corrected distance visual acuity (CDVA) were often not measured in a standardized way. This is particularly problematic if studies emphasize the postoperative change in CDVA in evaluation of treatment effect, rather than simply examine the postoperative CDVA. 15,23,41,47,55

The lack of standardized measurement protocols—both regarding length of follow-up and instruments used—also affects the reporting of complications like cystoid macular edema (CME). Missing data were often not commented on in included articles or were an exclusion criterion. 37,38

Our randomized clinical trial had a quite high number of included patients randomly assigned to interventions. Furthermore, it had a detailed description of inclusion criteria and outcome measurements, 1 surgeon who performed all operations, and the results were reported in accordance with the Consolidated Standards of Reporting Trials statement. 20,32–37,78 However, even in this study, there were some concerns of bias, as the baseline characteristics differed to some extent between the groups, masking was mostly not performed, and multiple analyses were performed. In addition, missing data turned out to be a considerable issue in this patient population, largely explained by the association with higher age. Still, missing data were presented in detail and accounted for in sensitivity analyses. 20,32–37 The other studies included in this review were judged to be at high risk of bias, based on the discussed aspects; furthermore, they did not seem to have used guidelines for reporting their study results, and many articles did not explicitly discuss their own limitations. A quite high proportion of studies, even those published in recent years, had very small sample sizes (Tables 1 and 2).

**DISCUSSION**

**Frequency of Condition**

A few studies have evaluated the frequency of IOL dislocation after cataract surgery and estimated an annual incidence rate of 0.0% to 0.05% and a cumulative incidence of 0.1% to 3% over 10 to 25 years. 22,23,26–29,42,53,64,79 In 1 of these studies (a prospective cohort in Sweden), 1.2% had late IOL dislocation requiring surgical attention at some point within 20 years after cataract surgery, and the study estimated a cumulative 20-year incidence of 3%, and 6% in patients with PEX. 42 The wide variation in reported incidence rates has been suggested as resulting from unequal distribution of predisposing conditions across various populations. 63 Furthermore, the follow-up length varies, and the incidence is calculated differently to some extent, particularly in terms of whether the reported rates included all dislocations, late dislocations, or specifically late in-the-bag dislocations, as well as whether the incidence was calculated for pseudophakic eyes or patients with pseudophakia. 22,26,27,29,42,63,64,79

An increasing trend for the occurrence of in-the-bag IOL dislocation has been reported. 16,21,27,28,30 This may possibly reflect a real increased incidence, or it could rather be the result of more cases due to a larger pseudophakic population, potentially in combination with an increased focus and awareness of this condition. 26,65 Furthermore, it is uncertain whether the trend is caused primarily by increased life expectancy, by other factors such as change in surgical technique, or both. Today, many younger cataract surgeons have minimal experience with extracapsular and intracapsular cataract extraction, and thus perform CCC and phacoemulsification in almost all cases, also complicated, high-risk cases with loose zonular fibers and/or mature cataract. This have likely resulted in a higher number of surgeries with CCC and in-the-bag IOL placement. For retinal pathology, it seems reasonable to assume that the use of vitrectomy has increased considerably in many countries in recent decades, which may have contributed to the increase of late in-the-bag IOL dislocation, because vitrectomy is an important predisposing condition. 14,16,20,23,24,42

A population study from Olmsted County, Minnesota, found an increased number of cases, but a stable incidence of late IOL dislocations over a 20-year period. 63 The authors assumed that this could be explained by more people with an IOL and thus more people at risk. This view is in line with similar findings over a much shorter time span in a study from southern Sweden, whereas a population study from western Australia found an increased incidence of IOL dislocation over a period of 22 years. 26,79 However, none of these studies reported trends for late in-the-bag IOL dislocations specifically. This was investigated in a cohort study from Värmland, Sweden, which found that the incidence of late in-the-bag IOL dislocation increased over a 20-year period, even after adjusting for the growing pseudophakic population. 27 Proposed explanations included a longer mean duration of pseudophakia in the population (years at risk) and potentially a lower threshold in recent years for performing phacoemulsification cataract surgery on more challenging cases that have a higher risk for dislocation.

**Patient Characteristics**

Typical characteristics of patients with late in-the-bag IOL dislocation are presented in Table 1. Late in-the-bag IOL dislocation occurs on average 6 to 12 years after cataract
surgery, and the mean patient age varies between 65 and 85 years.\textsuperscript{13–16,20,21,23–27,29,40–42,44–49,54,55} Some studies report a predominance of men, with proposed explanations suggesting that they have weaker zonular fibers and/or more frequently experience trauma.\textsuperscript{13,15,22,23,29,41,47,80} Other studies have shown no difference or have found a small predominance of women, suggesting that this reflects their likely higher prevalence of PEX and/or the sex difference for pseudophakia (with more women having cataract surgery), in addition to their higher life expectancy.\textsuperscript{20,21,24–26,48,54,55,80–84} The greater proportion of women seems to be especially high in groups where PEX is a common predisposing factor.\textsuperscript{16,23} Based on the inconsistent findings of the gender distribution for late-in-the-bag IOL dislocation, it appears uncertain whether sex is an individual risk factor.

### Predisposing Factors

Different conditions are associated with late in-the-bag IOL dislocation. PEX has been established as 1 of the most important predisposing factors (Table 1), being present in 31% to 83% of cases (except a few studies showing proportions of 16% to 17%).\textsuperscript{13,15,16,20,22–25,40,41,46–48} Furthermore, some studies have only included patients with PEX.\textsuperscript{14,21,25,55} Varying proportions of PEX may be related to differences in study inclusion criteria, patient ages, or geographical variation.\textsuperscript{85} In addition, signs of PEX can be overlooked, especially in patients with pseudophakia, as

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**Table 1. Patient Characteristics.**

<table>
<thead>
<tr>
<th>Study</th>
<th>ITBD (%)</th>
<th>Design</th>
<th>n*</th>
<th>Mean age (y)</th>
<th>Sex (M) (%)</th>
<th>Time to disl (y)</th>
<th>Predisposing (most frequent) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jehan et al.\textsuperscript{14}</td>
<td>100</td>
<td>RCS</td>
<td>8</td>
<td>77</td>
<td>43</td>
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<td>—</td>
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<td>RCS</td>
<td>25</td>
<td>75</td>
<td>68</td>
<td>6.9</td>
<td>PEX 44</td>
</tr>
<tr>
<td>Chan et al.\textsuperscript{56}</td>
<td>50</td>
<td>RCS</td>
<td>15</td>
<td>63</td>
<td>50</td>
<td>3.4</td>
<td>PEX 20</td>
</tr>
<tr>
<td>Hayashi et al.\textsuperscript{15}</td>
<td>61</td>
<td>RCS</td>
<td>38</td>
<td>71</td>
<td>71</td>
<td>8.3</td>
<td>PEX 45</td>
</tr>
<tr>
<td>Davis et al.\textsuperscript{16}</td>
<td>100</td>
<td>RCS</td>
<td>86</td>
<td>75</td>
<td>54</td>
<td>8.9</td>
<td>PEX 50</td>
</tr>
<tr>
<td>Lorente et al.\textsuperscript{51}</td>
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<td>45</td>
<td>81</td>
<td>57</td>
<td>8.0</td>
<td>PEX 67</td>
</tr>
<tr>
<td>Jakobsson et al.\textsuperscript{26}</td>
<td>75</td>
<td>RCS</td>
<td>63</td>
<td>79</td>
<td>44</td>
<td>6.8</td>
<td>PEX 60</td>
</tr>
<tr>
<td>Matsumoto et al.\textsuperscript{51}</td>
<td>100</td>
<td>RCS</td>
<td>21</td>
<td>68</td>
<td>57</td>
<td>7.9</td>
<td>Vitrectomy 40</td>
</tr>
<tr>
<td>Fernandez-Buenaga et al.\textsuperscript{29}</td>
<td>100</td>
<td>RCS</td>
<td>61</td>
<td>71</td>
<td>69</td>
<td>7.5</td>
<td>Myopia 20</td>
</tr>
<tr>
<td>Shingleton et al.\textsuperscript{55,c}</td>
<td>91</td>
<td>RCS</td>
<td>74</td>
<td>84</td>
<td>35</td>
<td>8.5</td>
<td>—</td>
</tr>
<tr>
<td>Jakobsson et al.\textsuperscript{26}</td>
<td>88</td>
<td>Prosp cohort</td>
<td>80</td>
<td>90</td>
<td>40</td>
<td>8.1</td>
<td>PEX 59</td>
</tr>
<tr>
<td>Krépilite et al.\textsuperscript{81}</td>
<td>88</td>
<td>RCS</td>
<td>51</td>
<td>72</td>
<td>67</td>
<td>5.3</td>
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<tr>
<td>Ostern et al.\textsuperscript{21,4}</td>
<td>100</td>
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<td>82</td>
<td>42</td>
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<tr>
<td>Dabrowska-Klodka et al.\textsuperscript{27,4}</td>
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<td>Retrosp cohort and nested case-control</td>
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<td>—</td>
<td>—</td>
<td>8.0</td>
<td>PEX 68</td>
</tr>
<tr>
<td>Leung et al.\textsuperscript{25,a}</td>
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<td>Retrosp matched case-control</td>
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<td>90</td>
<td>41</td>
<td>7.7</td>
<td>—</td>
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<tr>
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<td>RCS</td>
<td>83</td>
<td>72</td>
<td>44</td>
<td>10.9</td>
<td>Myopia 40</td>
</tr>
<tr>
<td>Kristianslund et al.\textsuperscript{20}</td>
<td>100</td>
<td>Prosp RCT</td>
<td>104</td>
<td>82</td>
<td>39</td>
<td>10.3</td>
<td>PEX 83</td>
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<tr>
<td>Torres et al.\textsuperscript{49}</td>
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<td>RCS</td>
<td>11</td>
<td>83</td>
<td>—</td>
<td>9.0</td>
<td>—</td>
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<tr>
<td>Bande et al.\textsuperscript{50}</td>
<td>100</td>
<td>RCS</td>
<td>36</td>
<td>69</td>
<td>75</td>
<td>11.5</td>
<td>PEX 39</td>
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<tr>
<td>Koike et al.\textsuperscript{50}</td>
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<td>RCS</td>
<td>14</td>
<td>70</td>
<td>93</td>
<td>6.2</td>
<td>—</td>
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<tr>
<td>Fujikawa et al.\textsuperscript{60}</td>
<td>69</td>
<td>RCS</td>
<td>36</td>
<td>69</td>
<td>78</td>
<td>10.0</td>
<td>Vitrectomy 33</td>
</tr>
<tr>
<td>Baba et al.\textsuperscript{46}</td>
<td>100</td>
<td>RCS</td>
<td>15</td>
<td>66</td>
<td>—</td>
<td>8.3</td>
<td>—</td>
</tr>
<tr>
<td>Ragam et al.\textsuperscript{54,4}</td>
<td>75</td>
<td>RCS</td>
<td>21</td>
<td>79</td>
<td>50</td>
<td>11.9</td>
<td>—</td>
</tr>
<tr>
<td>Giarsanti et al.\textsuperscript{59}</td>
<td>71</td>
<td>RCS</td>
<td>22</td>
<td>76</td>
<td>—</td>
<td>—</td>
<td>PEX 48</td>
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<td>Faramarzi et al.\textsuperscript{46}</td>
<td>100</td>
<td>RCS</td>
<td>11</td>
<td>67</td>
<td>—</td>
<td>—</td>
<td>PEX 64</td>
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<td>Subasi et al.\textsuperscript{47}</td>
<td>100</td>
<td>RCS</td>
<td>39</td>
<td>70</td>
<td>67</td>
<td>7.2</td>
<td>PEX 31</td>
</tr>
<tr>
<td>Buines et al.\textsuperscript{48}</td>
<td>100</td>
<td>RCS</td>
<td>134</td>
<td>82</td>
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<td>8.2</td>
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<tr>
<td>Artzen et al.\textsuperscript{48}</td>
<td>100</td>
<td>Prosp case series</td>
<td>165</td>
<td>79</td>
<td>43</td>
<td>9.3</td>
<td>PEX 80</td>
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<tr>
<td>Mönestam\textsuperscript{42,h}</td>
<td>100</td>
<td>Prosp RCT</td>
<td>104</td>
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<td>Vounotrypidis et al.\textsuperscript{57}</td>
<td>62</td>
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<td>18</td>
<td>81</td>
<td>44</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

— = PEX and/or glaucoma and/or previous vitrectomy were inclusion criteria (or predisposing factor not reported); disl = dislocation; ITBD = in-the-bag dislocation; PEX = pseudoexfoliation syndrome; Prosp = prospective; Retrosp = retrospective; RCS = retrospective case series; RCT = randomized clinical trial

\textsuperscript{a}Clinical studies with at least 50%, and at least 10 patients with this condition included (case reports, basal studies, and reviews excluded). Sorted after publication year.

\textsuperscript{b}No. of eyes with in-the-bag IOL dislocation.

\textsuperscript{c}Only examined PEX patients.

\textsuperscript{d}One hundred forty eyes with IOL dislocation (retrospective cohort), of whom 123 were compared with a control group without dislocation.

\textsuperscript{e}Seventy-one dislocation eyes and 71 fellow eyes.

\textsuperscript{f}Median age.

\textsuperscript{g}Presented for 156 patients. Some excluded before further analysis.

\textsuperscript{h}Cohort of 800 patients; also described in Mönestam 2009.\textsuperscript{29}
special attention is needed to detect the presence of pseudoexfoliative material on the pupillary edge. A histopathologic study found that although 33% of patients with in-the-bag IOL dislocation were clinically evaluated as having PEX, the proportion increased to 65% when the dislocated complexes were examined microscopically after explantation.43

Other associated conditions include previous vitreoretinal surgery (reported as high as 10% to 25% in some studies), myopia/increased axial length (reported as high as 10%–40% in some studies), uveitis, retinitis pigmentosa, certain connective tissue disorders, and trauma—both direct blunt trauma and indirect, the latter in the form of head injuries or working with vibrating machines.13–16,20,22–24,41–43,46,87 It is assumed that these conditions predispose through weakening and loosening of the zonular fibers.13–17,88 In several eyes, this process likely already started before implantation of the IOL, as shown in 1 study in which 38% of the eyes with in-the-bag IOL dislocation had zonular dehiscence at the time of cataract surgery.26,27,89

Other Factors

Some reports have indicated a possible association between dislocation of the IOL–capsule complex and certain IOL designs and materials. However, the results are inconsistent, and in the studies that have found an association, they likely reflected the IOL types used most frequently some years previously.13–16,26,28,41 Still, plate–haptic silicone IOLs have been associated with an increased risk for anterior capsule opacification with secondary capsule contraction, which may subsequently increase the risk for dislocation.17,90–92

A possible preventive role of a CTR has been discussed; however, no prospective comparative studies specifically addressing this issue seem to have been published.16,28,41,43,44,55,86 One prospective case series reported a shorter time since cataract surgery in dislocation eyes with CTR, and a prospective cohort study found a higher proportion of late dislocation in eyes with CTR.42,48 However, all existing studies examining this aspect are probably complicated by the selection bias of which patients receive a CTR. In addition, there is reason to believe that the perioperative implantation of the CTR induces some damage to the zonular fibers, which may increase the vulnerability for later dislocation.93 Thus, no final conclusion regarding a possible preventive role of CTR has been reached so far.

### Table 2. Visual Outcomes After Late in-the-Bag IOL Dislocation Surgery: Repositioning and Exchange.

<table>
<thead>
<tr>
<th>Study</th>
<th>ITBD (%)</th>
<th>n*</th>
<th>Reposition (%)</th>
<th>Exchange (%)</th>
<th>VA &gt; 20/40 (%)</th>
<th>Mean VA</th>
<th>Compared repositioning vs exchange</th>
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<tr>
<td>Chan et al.56</td>
<td>50</td>
<td>15</td>
<td>100</td>
<td>0</td>
<td>83</td>
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<td>Hayashi et al.15</td>
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<td>51</td>
<td>62.2</td>
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<td>Jakobsson et al.26</td>
<td>75</td>
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<td>6</td>
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<td>47.5</td>
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<td>Shingleton et al.35,42</td>
<td>88</td>
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<td>100</td>
<td>0</td>
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<td>100</td>
<td>39</td>
<td>51</td>
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<td>Subasi et al.47</td>
<td>100</td>
<td>134</td>
<td>50</td>
<td>48</td>
<td>67</td>
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<td>62</td>
<td>112</td>
<td>0</td>
<td>100</td>
<td>NR</td>
<td>0.42</td>
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</table>

ITBD = in-the-bag dislocation; NR = not reported; randomz = randomized; signif diff = significant difference; VA = visual acuity

*aNumber of eyes with in-the-bag IOL dislocation.

*bLogarithm of the minimum angle of resolution (except Hayashi et al. 2007 and Rey et al. 2016).

*cOnly compared increase in corrected distance VA.

*dOnly examined pseudoexfoliation syndrome-patients.

*eCompared VA for those with and without combined IOL dislocation/glaucoma surgery.

*fVA 0.33 for those without combined repositioning and Ahmed glaucoma drainage device.

*gApproximate VA; not reported for all patients in the article. Capsule removed in the repositioning group. No significant difference, but few total number of eyes (n = 15).

*hFocused on comparison between preoperative and postoperative values.
Posterior capsulotomy with Nd:YAG laser has also been mentioned as a possible risk factor; however, study results are ambiguous.14,16,21,26 Even if an association exists, it might be difficult to conclude whether Nd:YAG laser capsulotomy is a risk factor itself or instead a consequence of a common factor that leads to both posterior capsule opacification and anterior capsule contraction, which may contribute to progressive loosening of the IOL–capsule complex. The latter view is partly supported by a population study, which showed a decreased risk for IOL dislocation if posterior capsulotomy was performed within 1 year after cataract surgery (in-the-bag dislocations specifically were not reported).64

Association With Glaucoma

An association between late in-the-bag IOL dislocation and glaucoma and/or increased IOP has been found in several studies.14,20,21,25–27,37,41,48,54,55 In our study, 38% of patients with late in-the-bag IOL dislocation had preexisting glaucoma, of whom 44% had a high IOP; in addition, 22% had a high IOP (≥22 mm Hg) before surgery without known glaucoma.20,37 It has been discussed whether the increased IOP is caused by the IOL dislocation—and thus can be resolved by dislocation surgery—or if both conditions are the results of another common causal factor.25,37,41,54,55 The association with increased IOP seems especially prominent in studies with a high proportion of patients with PEX, and it has been suggested that in many cases, the IOL dislocation and the simultaneous increased IOP are both linked to advanced-stage PEX.25,37 Some studies have found that these patients usually require treatment for both the high IOP and the IOL dislocation in parallel and further, that high IOP is a frequent postoperative event, indicating that it may be related to underlying glaucoma.15,20,23,32,37,41,49,54,55 However, a few studies have reported an improvement in the IOP after dislocation surgery and even discontinuation of glaucoma medication in the postoperative period, indicating that the dislocation itself was a contributing factor. Still, other studies had more ambiguous results.25,32,41,54,55 It has also been discussed whether the increased IOP is related to the grade of dislocation, possibly resembling uveitis–glaucoma–hyphema (UGH) syndrome.34,40,94 Studies with a lower proportion of PEX reported no cases of high IOP before surgery.24,51,57,60,75 This may indicate that high IOP is rare in these eyes; however, it may also be because these aspects were omitted from their results. Although PEX is an important factor in many areas, no published studies seem to have been designed to specifically evaluate the reason for the associated increased IOP, or whether PEX glaucoma is preexistent or develops after the dislocation. Therefore, definite answers to these questions remain uncertain.

SURGICAL TREATMENT

The surgeon’s preference has traditionally determined the choice of surgical technique for patients with late in-the-bag IOL dislocation, and numerous surgical methods have been described. Although comparative treatment studies within this field were lacking previously—in particular prospective intervention studies—this review has identified several relevant articles published in recent years, in addition to some earlier publications (Table 2).28 One prospective intervention study and numerous observational case series have described and to some extent compared visual outcome and safety in terms of complications for the main operation methods: IOL repositioning and IOL exchange.15,20,21,23–26,32,41,54,55 However, the clinicians are first faced with the question of surgical indication and the timing of surgery.

Symptoms and Grading

Late in-the-bag IOL dislocation occurs on a continuum from pseudophacodonesis, through subluxation, to dislocation of the IOL–capsule complex into the vitreous cavity (total dislocation). Some patients have acute vision loss, whereas others experience more subtle symptoms, such as glare, halos, diplopia, or oscillating vision over a longer period of time, as well as gradual visual impairment (dependent on the degree of dislocation).

Several studies have graded the dislocation according to the position of the IOL optic, usually as grades 1 to 4, from mild to total dislocation.20,32,34,40,41,61 When patients with late in-the-bag IOL dislocation are evaluated, it is essential for surgical planning to also examine them in the supine position, especially in dislocation grade 3. This is to determine whether the IOL–capsule complex remains in this position, accessible to operation with an anterior approach, or if it dislocates posteriorly away from the pupillary plane, which in our experience is often the case in previously vitrectomized eyes. In a few other cases, the superior haptic of an almost totally dislocated IOL may become more visible in the supine position, indicating that operation with an anterior approach is possible.

Timing of Surgery and Surgical Access

Indication for surgery is usually determined by whether disturbing symptoms are present and confirmation of the dislocation by the slitlamp examination.28 However, an optimal timing of surgery has not been fully clarified. In a retrospective case series, Østern et al.21 found that although only 4% of late in-the-bag IOL dislocations deteriorated in the first month after referral, that number was approximately 40% when the operation was delayed for 1 to 6 months. Thus, it seems advantageous to perform the operation within a few months after the diagnosis, assuming that surgery is easier to perform and has fewer serious complications when the IOL is not completely dislocated preoperatively.21,28 In our prospective study, we found no significant association among dislocation grades 1 to 3 in terms of postoperative visual outcome.62 However, the study did not include grade 4. We have not identified any large, prospective studies that have described the natural progression of the dislocation in various subgroups of patients, nor that have compared the postoperative outcome of surgeries for dislocation grades 1

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to 3 vs total dislocation (grade 4). Our clinical impression is that surgery is quite urgent if there is sudden debut of symptoms, pronounced pseudofakodonesis, and/or dislocation grade 3.

Comparisons of the surgical approach are lacking. In some eye clinics, vitreoretinal surgeons are responsible for all IOL dislocations, whereas in other clinics, anterior segment surgeons manage these cases if surgery can be performed with an anterior access. In cases with total dislocation of the IOL—capsule complex, vitreoretinal surgery with a pars plana approach is always required. The potential advantages of this approach are the opportunity for complete vitrectomy, easier management of preexisting complications associated with pars plana vitrectomy. 

A nonrandomized study by Jakobsson et al. showed more postoperative events in general associated with the anterior approach compared with pars plana vitrectomy; however, the study was not designed for such a comparison, and few patients were operated on with the anterior approach, thus, a potential selection bias may have been present. A study by Artenz et al. showed similar results for the 2 approaches; however, the surgical techniques were different in the 2 groups (repositioning and exchange, respectively), making the interpretation somewhat difficult. Because we have not identified any other studies that have made such comparisons, the matter of which approach is superior remains inconclusive. Nevertheless, it has been shown prospectively that both IOL repositioning and IOL exchange performed with an anterior surgical access provide highly satisfactory visual outcomes in most patients. It seems reasonable to assume that such surgery is less resource demanding and more available than pars plana vitrectomy. Furthermore, these patients are often referred to anterior segment surgeons, as the condition is related to the IOL placement, which is considered to be their domain. Experience is often required in preoperative planning for carefully assessing whether the IOL with haptics is totally inside the capsular bag, as well as for evaluating the often-associated high IOP and possible need for glaucoma surgery.

Surgical Techniques

Intraocular Lens Repositioning Scleral suturing is the most common surgical technique for IOL repositioning, whereas suturing of a dislocated complex to iris appears to be rarely used in clinical practice. Sutureless scleral fixation techniques seem to be applied only for fixation of the IOL without the capsule, either by IOL exchange or by repositioning of the dislocated IOL after removal of the capsule. Not all dislocated IOLs have a design that allows for repositioning by scleral suturing, such as plate–haptic IOLs without peripheral holes or without closed haptics. Furthermore, some cases with a pronounced amount of lens regenerates in the periphery of the capsule may neither be ideal candidates for repositioning by scleral suturing. In addition, some surgeons have advocated that 1-piece acrylic IOLs with thick haptics should not be repositioned because of the risk for iris chafing and UGH syndrome. This seems sensible if a dislocated IOL is outside the lens capsule (out of the bag), as these IOLs are not designed for sulcus placement and may subsequently rub against the iris. However, the literature does not seem to support a contraindication of this technique when the dislocated 1-piece IOL remains inside the capsule (in the bag). Still, opinions on this matter vary to some extent, and it has been claimed that pseudophacodonesis and mild dislocation of an IOL—capsule complex may induce UGH syndrome, possibly related to large Soemmering ring in some cases.

Suture erosions and suture breakage have occurred with the 10-0 polypropylene suture often used for scleral fixation: a few studies have reported rates as high as 18% to 28% in the longer term. Thus, some surgeons have recommended using the 9-0 polypropylene suture or a Gore-Tex suture instead. These high rates of broken suture were seen in studies on scleral suturing of only the IOL (not the capsule); in addition, other studies on the same type of surgery have not confirmed these findings. Furthermore, suture breakage seems to occur in younger patients in particular, whereas it appears to be more seldom in elderly patients who are operated on for late in-the-bag IOL dislocation, possibly due to the preventive effect of the capsule avoiding direct friction between the suture and the (sharp) haptic edge.

Intraocular Lens Exchange A number of IOL types can be considered in IOL exchange. In 2003, Wagoner et al. published a review of secondary IOL implantation in eyes that lacked adequate capsular support for various reasons (eg, other surgical indications than IOL dislocation, as well), including open-loop anterior chamber IOLs, scleral-sutured IOLs, and iris-sutured IOLs. They concluded, in accordance with others, that no clear evidence indicates that any of these IOLs are superior to the others. However, the review did not consider iris-claw IOLs or sutureless scleral fixation techniques, both of which seem to be increasingly used on various indications, with good results.

Studies on IOL dislocation surgery have also reported promising results with the iris-claw lens. Although the original recommended placement for the iris-claw IOL is in the anterior chamber, a number of studies have enclavated this IOL retropupillary. A retrospective study of aphakic cases with inadequate capsular support found that the 2 positions were equally effective and safe. No clinical trial seems to have made such a comparison strictly in IOL dislocation eyes. In our randomized clinical trial on late in-the-bag IOL dislocation, IOL exchange with a retropupillary iris-claw IOL was compared with IOL repositioning by scleral suturing; the study showed that the 2 methods provided similar efficacy in terms of postoperative visual outcome, and they were considered equally safe, with similar 2-year postoperative corneal endothelial cell loss.
In recent years, different techniques for sutureless scleral fixation of the IOL have emerged as options for treatment in aphakic eyes, with fixation of the IOL haptics using fibrin glue and scleral tunnels alone or in combination, with the use of needle-guided scleral fixation combined with cauterization of the haptic end to make a flange, or using a scleral-fixated IOL with anchor haptics.97,102,123 These techniques may probably be suitable for IOL exchange surgery as well; however, we have not identified any comparative clinical trials using these techniques in 1 of the treatment groups for late in-the-bag IOL dislocation surgery.103

**Treatment Outcomes**

**Intraocular Lens Repositioning or Exchange** A dislocated IOL can be either repositioned or exchanged, and as described, various surgical techniques for these methods exist and have been evaluated. However, several studies include different types of IOL dislocation in their comparisons of operation methods, and in some studies even aphakic eyes and dislocation of crystalline lenses, often without subgroup analysis of each condition despite the obvious differences. The purpose of the present review was to report results only for late in-the-bag IOL dislocation.15,30,54,80,103

IOL repositioning by scleral suturing is mentioned in a number of articles as the recommended operation method for this specific condition, whereas only a few publications have argued that IOL exchange is preferable.21,23,24,26,56,95 Arguments in favor of IOL repositioning have been that it is less traumatizing (in particular for the corneal endothelium) and that hypotony during surgery is easier to avoid with the smaller incisions, thus reducing the risk for serious complications like choroidal expulsive hemorrhage.13,23,26,56,95

Small incisions may also be beneficial in terms of surgically induced astigmatism.28 The potential relevant factors that have been put forth in favor of IOL exchange surgery include IOL centration, stability, and better fundus visualization after removal of the capsule, as well as a predictable postoperative refraction.24,36 In addition, for some exchange techniques, operation time may be shorter, and the surgery technically easier, than IOL repositioning by scleral suturing.25 Finally, IOL exchange is the only option in the case of IOL designs that cannot be sutured, damaged IOLs, or if refractive change is required.20,23,55

However, many of the arguments in favor of one or the other method do not seem to be sufficiently supported by large, well-designed clinical trials. Several studies on late in-the-bag IOL dislocation surgery have described—and to some extent compared—different operation methods and placements of the IOL; however, some of these included both in-the-bag and out-of-the-bag IOL dislocations, and moreover, many of them applied a retrospective observational research design without statistical comparison, and/or included few patients.13–15,20,21,23–26,30,32,35–37,41,54–56,80,124 Therefore, previously, no definite clinical recommendations have been made in terms of the choice between IOL repositioning and IOL exchange. A few retrospective case series have indicated that these 2 main operation methods seem to provide similar visual outcomes, but in terms of complications, the findings have been more ambiguous.21,23,30,41,55,124 We identified only 1 randomized clinical trial that specifically compared IOL repositioning and IOL exchange for late in-the-bag IOL dislocation.20,23,30,35–37 In this study, IOL repositioning by scleral suturing was compared with IOL exchange with an iris-claw IOL. The results showed a similar efficacy in terms of visual outcome after 6 months and 2 years, in line with previous retrospective studies.20,21,23,30,41,55 The mean 6-month postoperative CDVA was 0.3 logarithm of the minimum angle of resolution (logMAR) for all study patients, improving to 0.2 logMAR after 2 years.20,32 Based on the proportion with CDVA ≥ 20/40, it seems that the visual outcome almost approaches the level seen in similar-aged people in the general population.32,125 Also, a prospective case series found similar results for IOL repositioning and IOL exchange.48 As shown in Table 2, other studies on late in-the-bag IOL dislocation have reported a mean of 0.26 to 0.64 logMAR after various times of follow-up intervals.15,21,23–25,41,48,54,55

Many studies on IOL dislocation have emphasized the CDVA change/improvement following surgery, rather than the postoperative CDVA, when reporting the results.15,23,41,55 Although the change is intuitively important (not least for the patients), it is not necessarily the best parameter to evaluate efficacy, as it is highly dependent on the position of the dislocated IOL–capsule complex at the preoperative examination (ie, whether the complex is disturbing the center of the visual axis). It should further be mentioned that the postoperative improvement in visual acuity may be greatly affected by whether an aphakic correction is used in eyes with dislocation grades 3 and 4.

**Surgically Induced Astigmatism and Refractive Outcome** Surgically induced astigmatism has been mentioned as a possible disadvantage of IOL exchange; however, very few studies have actually investigated this aspect in relation to late in-the-bag IOL dislocation surgery.15,23,126 A few retrospective case series of IOL dislocation surgery have indicated that IOL exchange with a large incision may lead to more induced astigmatism.15,24,103,126 A large incision is necessary when an unfoldable IOL is implanted (such as an iris-claw IOL or anterior chamber IOLs), whereas a smaller incision may be applied if a foldable scleral-fixated IOL is implanted. In our randomized clinical trial on late in-the-bag IOL dislocation that compared IOL repositioning by scleral suturing vs IOL exchange with an iris-claw lens, it was shown by vector analysis a tendency for more induced astigmatism with IOL exchange.36 However, this difference was only modest, and probably explained by the advantages of the frown scleral tunnel incision, as previously shown in cataract surgery.127,128

Furthermore, only a few studies on late in-the-bag IOL dislocation surgery have reported refractive outcomes.15,24,32,36 In our study, we found a myopic shift in eyes operated with IOL repositioning by scleral suturing, a tendency also shown in other studies.36,56 This is probably explained by a forward shift of the IOL–capsule complex after scleral fixation compared with what was seen before the
dislocation. Several studies with various indications for scleral suturing have advocated a suture placement of approximately 1.5 to 2.0 mm behind limbus; however, for late in-the-bag IOL dislocation, it seems that more than 2.0 mm is necessary to restore the preoperative position of the IOL–capsule complex and thus achieve a refraction similar to that before the dislocation.36,56,80

For IOL exchange in late in-the-bag IOL dislocation eyes, iris-claw IOLs have shown a good refractive predictability, whereas refractive results for other exchange techniques seem to be lacking. The A-constant (SRK/T) given by the manufacturer for the iris-claw IOLs Artisan (Artisan Aphaikia Model 205, Ophtec BV) or Verisyse (VRSA54, Abbott Laboratories, Inc.) is 115.7 for prepupillary placement and 116.9 for retropupillary placement.36 Our prospective intervention study of late in-the-bag IOL dislocation surgery calculated that an A-constant of 117.3 for retropupillary placement might be even better.36 The A-constant for the iris-claw IOL (several indications) has also been discussed in a short review.73

Surgical Complications This review did not aim to describe all possible complications of late in-the-bag IOL dislocation surgery. As previously mentioned, only a few studies with prospective follow-up have been conducted in this field, which limits the ability to provide such an overview. Furthermore, single studies often have too small sample sizes to evaluate the occurrence of rare complications. Still, some potentially relevant aspects were identified in the included articles. In terms of the comparison of operation methods for late in-the-bag IOL dislocation, 2 retrospective case series have indicated that IOL exchange is associated with more complications overall or at least during surgery than IOL repositioning.21,55 In a randomized clinical trial, it was shown that IOL exchange had more vitreous loss to the anterior chamber and more (minor) iris injuries during surgery.20 These are both likely to be sometimes inevitable due to the manipulation when removing the whole IOL–capsule complex from behind the iris, which risks disturbing the anterior vitreous membrane and damaging the sphincter, especially in poorly dilated pupils.20 This randomized trial also discussed other possible perioperative differences between the methods, such as a tendency of more intraocular hemorrhage with scleral suturing; however, overall, few differences seem to have been observed between these methods in perioperative complications.20

High IOP High IOP is often mentioned as a common postoperative complication of IOL dislocation surgery.15,20,25,32,37,41,54,55 However, studies do not always mention time after surgery at which it occurred, and it often seems to be related to underlying glaucoma, as previously discussed. Therefore, the term “complication” should be used carefully. Large studies with standardized follow-up in the early postoperative period are needed to evaluate this aspect further.

Cystoid Macular Edema CME has been identified as one of the most frequent postoperative complications in these eyes. Studies have reported CME in 0% to 24% of patients following surgery for IOL dislocation.13,20,21,30,41,54,55,80,124 Although this wide variation is probably related to surgical techniques, it likely also reflects various other factors, such as: the different time points for postoperative examinations, the considerable variation in follow-up intervals, differences in sample size, weak study designs, and other surgical indications than late in-the-bag IOL dislocation. In addition, many studies have relied on clinical examination to detect CME or at least not included standardized image analysis. Recent literature has not demonstrated any statistically significant difference for the risk for CME between IOL repositioning and IOL exchange in patients with late in-the-bag IOL dislocation.20,32 Nevertheless, it may be hypothesized that the sometimes inevitable vitreous prolapse with IOL exchange may increase the risk for CME, especially in younger patients without posterior vitreous detachment. Thus, the surgeon should conduct careful evaluations to avoid vitreous to the incisions, possibly also in the fixation site for the new IOL.

Retinal Detachment Another feared postoperative complication is retinal detachment, which has been reported in the range of 3% to 8% in some studies.13,15,21,54,56,75 However, several other studies have reported no cases. The risk for retinal detachment may theoretically be higher after IOL exchange compared with IOL repositioning, although this has not been shown in various studies.13,20,23,32,54 When high numbers are reported, this may possibly be explained by inclusion of other types of IOL dislocation.15 It also seems likely that the risk for retinal detachment is related to the predisposing factor(s) for the dislocation—ie, in myopic eyes or after trauma. However, to demonstrate such associations would require very large patient samples, which so far has not been the case.

Late Endophthalmitis In the studies of late in-the-bag IOL dislocation, no cases of late endophthalmitis have been reported.

Redislocation The concern for redislocations after IOL dislocation surgery, in particular after scleral suturing, has also been discussed.36,111 However, the risk for suture breakage seems to be quite minor after late in-the-bag IOL dislocation surgery, at least in elderly patients, even with use of 10-0 polypropylene suture. Suture slippage, with loosening of the sutures from the haptic, also seems less likely when the suture passes through the lens capsule.20,21,32,55,111 Other surgical techniques may also have redislocation; for example, there have been cases with loosening of the enclavation of the iris-claw IOL.20 It can be hypothesized that this risk increases when there is an atrophic iris; however, little knowledge on this aspect is available. In our prospective trial of late in-the-bag IOL dislocation, we identified only 2 cases (3%) of redislocation after a 2-year follow-up, 1 each in IOL repositioning and IOL exchange.52 This seems to be in accordance with, or lower, than results for sutureless scleral fixation or iris-claw IOLs for other surgical indications.116,129–131

Corneal Endothelial Cell Loss Another concern with late in-the-bag IOL dislocation surgery has been corneal endothelial cell loss, particularly after IOL exchange. This is
related to the surgical trauma when removing the dislocated IOL–capsule complex and to some of the specific IOLs used in exchange surgery, such as angle-supported anterior chamber IOLs and iris-claw IOLs used in a pupillary position.\textsuperscript{28} Several factors can theoretically lead to a rather pronounced endothelial cell loss after IOL exchange in late in-the-bag IOL dislocation eyes. These factors include the large corneal wound (if a corneal incision is chosen); surgical manipulation near the corneal endothelium, particularly when the IOL–capsule complex is removed; frequent need for anterior vitrectomy; and increased inflammation following explantation of the dislocated complex through the pupil and/or in relation to possible iris fixation of a new IOL. However, few evaluations have been made of these factors in studies on late in-the-bag IOL dislocation. One study found a tendency of greater endothelial cell loss following IOL exchange surgery compared with IOL repositioning after 6 months but not after 2 years.\textsuperscript{29,31} From this result, one could speculate that perioperative factors lead to a larger short-term endothelial cell loss for IOL exchange that tends to even out after some time. Otherwise, few studies have evaluated the corneal endothelium after IOL dislocation surgery. One study found an endothelial cell loss of 11% and 13% after repositioning by scleral and iris suture fixation, respectively, whereas 2 other studies reported no statistically significant difference in endothelial cell loss between IOL repositioning and IOL exchange; however, all these studies had less than 50% or an unknown proportion of late in-the-bag IOL dislocation.\textsuperscript{80,103,126} To reach more certain conclusions regarding endothelial cell loss after IOL dislocation surgery, more prospective studies and long follow-up intervals are needed.

In conclusion, this review revealed that late in-the-bag IOL dislocation occurs on average almost 10 years after cataract surgery with a cumulative incidence of 0.5% to 3%. PEX, myopia, and previous vitreoretinal surgery are important predisposing conditions, and several studies have found an association with glaucoma. In terms of treatment, some literature seems to indicate that IOL repositioning and IOL exchange have comparable efficacy in terms of visual outcome and that both have acceptable safety with few serious surgical complications (at least for the surgical techniques compared in the existing literature). However, only 1 randomized clinical trial was identified, and the remaining studies were in general judged to be at high risk of bias. Furthermore, the results from existing studies may not necessarily be generalizable to other populations, age groups, and settings. Based on the existing literature, none of the operation methods seem superior to the others in all aspects and thus the best choice for all patients with late in-the-bag IOL dislocation. However, increased knowledge is required before specific recommendations can be given.

REFERENCES


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