UNIVERSITY OF GOTHENBURG

THE SAHLGRENSKA ACADEMY

Degree Project

Comparison of a Hydrophobic and Hydrophilic Acrylic Intraocular Lens regarding Posterior Capsule Opacification in Patients with and without Uveitis

Jasmin Khalaj Samadi

Department of Ophthalmology, Institute of Neuroscience and Physiology,

Sahlgrenska University Hospital

Gothenburg, Sweden

Degree project:	30 credits
Program:	Program in Medicine
Year:	2021
Supervisor:	Madeleine Zetterberg, MD, PhD

Table of Contents

List of Abbreviations

AQUA – Automated Quantification of After-Cataract
EPCO – Evaluation of Posterior Capsule Opacification
IOL – Intraocular lens
LEC – Lens epithelial cell
Nd:YAG-laser – Neodymium:yttrium aluminium garnet laser
PCO – Posterior Capsule Opacification
POCO system – Posterior Capsule Opacity system

Abstract

Comparison of a Hydrophobic and Hydrophilic Acrylic Intraocular Lens regarding Posterior Capsule Opacification in Patients with and without Uveitis

Introduction: Posterior capsule opacification (PCO) is the most common complication after cataract surgery. PCO rates vary between intraocular lenses (IOLs) implanted. Hydrophobic and hydrophilic lenses are widely used, and it is important to investigate which lens has less PCO development, not least in patients with uveitis, who have higher risk of developing PCO.

Aim: To compare PCO after cataract surgery with a hydrophobic or hydrophilic sharp edged IOL in patients with and without uveitis.

Methods: In this randomized controlled study, patients with and without uveitis eligible for bilateral cataract surgery with a hydrophobic and hydrophilic IOL between 2017-2020 were included. PCO incidence and proportion of PCO on the posterior capsule after 1 year was assessed by two graders.

Results: 20 patients **(**40 eyes) were included. Most eyes in in the study did not develop PCO. PCO occurred in 7 eyes (38.9 %) with uveitis and 7 eyes (31.8 %) without uveitis ($p = 0.641$). PCO developed in 6 eyes (30 %) with the hydrophobic IOL and 8 eyes (40 %) with the hydrophilic IOL ($p = 0.507$). The median of the proportion of the posterior capsule covered with PCO was 43 % in the uveitic group and 36 % in the non-uveitic group ($p = 0.522$). The median of the proportion of the posterior capsule covered with PCO was 35 % for the hydrophobic IOL and 39.5 % for the hydrophilic IOL ($p = 0.332$).

Conclusions: No significant difference in PCO development between patient groups nor IOL types were seen. The higher incidence in uveitic eyes could indicate higher risk for uveitic patients of developing PCO. The lower PCO incidence in hydrophobic IOLs could suggest that hydrophobic IOLs are valuable for minimizing PCO development. These findings should be confirmed in larger studies.

Key words: Posterior capsule opacification, intraocular lens, uveitis

1. Introduction

A cataract is opacification or clouding of the lens of the eye to the point that the patient's vision is impaired. Cataract surgery is currently the most performed surgical procedure in Sweden [1] and one of the most common procedures in the Western world. During the procedure, the patient's own lens is removed and a new artificial lens, an intraocular lens (IOL), is put into place. The patient's eyesight is thus restored. There are several intraocular lenses on the market with different qualities, such as different materials and design. The intraocular lenses differ regarding various outcomes, such as the frequency of postoperative complications. The most common postoperative complication after cataract surgery is posterior capsule opacification (PCO), where epithelial lens fibres proliferate and migrate to the posterior lens capsule and the patient might once again experience visual impairment. As the qualities of the different IOLs, such as their material and their design, can play an important role for PCO development, it is important to investigate which IOL is best for the patients. For instance, patients with uveitis, inflammation of the ocular uvea (iris, ciliary body and choroid), have a higher risk of developing cataract, and inflammation has been associated with higher risk for posterior capsule opacification. For these patients, the right choice of intraocular lens is presumably of vast importance in order to prevent the complication. However, there is at the moment no consensus regarding which IOL is the best choice for patients with and without uveitis for preventing posterior capsule opacification, which indicates a need for studies that evaluate PCO development for different IOLs.

1.1. The lens of the eye

The lens of the eye refracts ⅓ of the light that enters the eye and with its elastic capacity helps focus the sight on the desired distance and object. As the lens is an avascular structure, oxygen and important nutrients are transported to the lens from the aqueous humour. It is the lens epithelium that permits the transportation into the lens. The lens does not have any nerve fibres. [2, 3]

The lens is attached to zonular fibres that connect the lens to the ciliary body and can help the lens change shape and thus focus on various distances. The zonular fibres help stretch out the lens, making it possible to see objects far away. During accommodation, the zonular fibres relax and the lens becomes more round, making it possible to focus on objects that are close. The lens capsule is a transparent basement membrane that surrounds the lens and helps maintain the shape of the lens. With time it becomes the thickest basement membrane in the

body. The capsule mainly consists of collagen IV and is thickest anteriorly and thinnest posteriorly.

The lens epithelial cells differentiate into lens fibres, which do not contain a nucleus or organelles. These lens fibres are regularly arranged, creating transparency and enabling light to flow through the eye to the retina. If this regular arrangement is disrupted, opacification of the lens, also known as cataract, will occur, leading to visual impairment. Throughout life the lens continues to produce new cells, with the old cells remaining in the nucleus of the lens and the new cells being found in the cortex of the lens. [3, 4]

1.2. Cataract

Cataract is an opacification of the lens. Lens proteins oxidize and agglutinate, resulting in loss of transparency in the lens and a gradual increase in visual impairment. The patient can experience symptoms such as monocular diplopia, reduced vision in dim light and glare (discomfort in the presence of bright light) [4, 5]. If the cataract is advanced it can result in blindness, which is reversible through surgery.

There are several risk factors for developing cataract, with high age being the most common factor. A high proportion of the older population suffer from cataract and over 90 % of all cataracts are senile, meaning they are acquired due to high age [2]. One study from the community of Tierp in Sweden estimated the prevalence to ⅓ of the patients in the age group 65-74 [6]. However, cataract can develop in all ages and can even be seen in newborns. Other risk factors for cataract development are ultraviolet radiation, corticosteroids and metabolic diseases such as diabetes. Uveitis, inflammation in the uveal layer of the eye, is another known risk factor for cataract [5]. The higher risk for cataract in patients with uveitis is in part due to the inflammation, and in part due to the treatment with corticosteroids.

The only way to remove cataract is through surgery. In Sweden, cataract surgery is the most common surgical procedure [1]. In 2019, the number of surgeries performed in Sweden amounted to 139 665, and the average age for cataract surgery in Sweden is 74 years for both men and women [1]. Historically, cataract surgery has been performed since 1000 B.C in various forms. The surgical methods have become more advanced and refined over the centuries and in the 1980s, the method of extracapsular lens extraction (ECCE) was widely used [2, 7]. During ECCE, capsulorhexis is performed, where the anterior lens capsule is

opened and the lens is removed. The posterior capsule remains intact. Phacoemulsification, an advancement of ECCE, is the standard method used today in developed countries. The patient receives local anesthesia, a small incision of 2-3 mm is made and the opacified lens is fractionated with an ultrasound probe and aspirated through a needle. Afterwards, the posterior lens capsule is polished and an intraocular lens is inserted into the capsular bag, i.e. the space in front of the posterior lens capsule and behind the iris [3].

Serious postoperative complications after cataract surgery, such as endophthalmitis and retinal detachment, are rare [8, 9]. More common, however, is the postoperative complication of posterior capsule opacification.

1.3. Posterior Capsule Opacification

Posterior capsule opacification (PCO) is the most common postoperative complication after cataract surgery, with an incidence reported to range from < 5 % to as high as 50 % [10]. It is not possible to remove all lens epithelial cells during cataract surgery. Remaining lens epithelial cells proliferate and can migrate to the posterior lens capsule, leading to an opacification of the structure. Several symptoms of PCO are the same as the symptoms of cataract, such as reduced visual acuity, glare, and monocular diplopia [8]. There are two types of posterior capsule opacification: fibrosis-type PCO and pearl type, or vacuolated, PCO. Fibrosis-type PCO is believed to develop because of a fibroblastic metaplasia of lens epithelial cells, where they express α-smooth muscle actin that is not detected in normal lens cells. This leads to wrinkles and folds in the posterior lens capsule [8, 11]. Pearl-type PCO develops due to proliferation of swollen lens epithelial cells and stands for the majority of cases of decrease in visual function related to PCO [8, 12].

The main indication for treatment of posterior capsule opacification is reduced visual acuity that prevents or complicates the patient's daily activities. PCO is treated with neodymium:yttrium aluminium garnet (nd:YAG) laser. The nd:YAG laser creates a central opening in the opacified posterior lens capsule, a capsulotomy, which immediately improves the patient's vision by enabling light to once again flow through the eye. Most often, the nd:YAG laser is successful but there are certain risks associated with the treatment such as cystoid macular edema and retinal detachment [3].

Several PCO evaluation systems have been used throughout the years for evaluating posterior capsule opacification. In 1997, Tetz et al [13] introduced the Evaluation of Posterior Capsule Opacification (EPCO) software, which clinically grades PCO in eye images from 0-4 based on severity. A PCO score is calculated by multiplying the severity grade by the fraction of the area of the capsule that is involved behind the optic of the intraocular lens. The EPCO software is subjective as a grader is needed to select the areas of opacification and grade them. Another PCO evaluation system is the POCO system, developed by researchers at St. Thomas's Hospital in London, which soon progressed to the POCO-man system [14]. The system is semiobjective as it evaluates images by having a grader identify areas of PCO, and then automatically calculate the areas of PCO, giving a result in percentage. Furthermore, the PCO evaluation system Automated Quantification of After-Cataract (AQUA) was developed by Buehl et al in 2002 [15]. The AQUA software is automated, and the program detects the grade of PCO without any subjectivity in its measurement. The aforementioned PCO evaluation systems have not been updated for several years and are therefore currently not in use. Recent studies on PCO have used ImageJ (NIH, Bethesda, MD, USA), a biomedical imaging software for scientific image analysis which is available for free on an open platform.

As PCO causes complications for the patients and the treatment of PCO is associated with risks, there has been extensive research over the years to strive to eliminate PCO, with various strategies put in place. Among the strategies are better surgical techniques [16], as well as improved material and design of intraocular lenses [17, 18]. These are ways to delay the onset and minimize PCO but have, however, not fully eliminated the issue.

1.4. Intraocular Lenses

An intraocular lens (IOL) is a lens implanted during cataract surgery. Today, a vast number of intraocular lenses exist on the market, with different materials and designs. Previous studies have identified the optic edge design as well as the biomaterial of IOLs as potential important factors in the development of posterior capsule opacification.

In terms of IOL design, the IOL has a central part called the optic, which contains the refracting element of the lens. The other part of the IOLs is called haptics, which are the structures that stabilize and support the IOL, keeping the IOL in place by anchoring it to peripheral ocular structures. IOLs where the optic and the haptics are made of the same

material are called 1-piece IOLs and IOLs with different materials of the optic and the haptics are called 3-piece IOLs. Both 1-piece and 3-piece IOLs are used today with good clinical results.

The optic edge design of the IOL has been shown to play an important role in the prevention of PCO progression. The optic edge of the IOL can have different forms, namely round or sharp/square. IOLs with a round optic edge have a right angle between the lateral edge and the posterior surface of the IOL. IOLs with a sharp or square optic edge create a firm linear contact between the lens and the posterior capsule. The design of the sharp or square edges creates a mechanical barrier to lens epithelial cells that migrate toward the center of the posterior capsule, and thus limits posterior capsule opacification. Prior to the work of Nagata and Watanabe [19] the role of the optic edge for preventing PCO was largely unknown. Their study demonstrated the significance of a sharp optic edge in order to limit posterior capsule opacification, and several studies have since shown a significantly lower rate of PCO in sharp- or square-edged optics in comparison to round-edged optics [20-23]. Sharp- and square-edged optics are the predominant optic edge design today.

The majority of the intraocular lenses used today are flexible IOLs. Using an injector, a folded IOL is implanted and unfolds inside the eye. This requires only a very small incision and decreases the risk of bacterial infection as the intraocular lens avoids contact with the ocular surface. Flexible IOL biomaterials can be divided into two main groups: silicone lenses and acrylic lenses. Acrylic intraocular lenses have a long history in clinical practice and can further be divided into hydrophobic and hydrophilic acrylic lenses, depending on the degree to which a drop of water makes an angle to the lens surface. If the angle is larger, the material is more hydrophilic and vice versa [24]. Hydrophobic acrylic lenses consist of chains of copolymers of acrylate and methacrylate, making them foldable and durable. They contain less water than 1 % and have a high refractive index. Hydrophilic acrylic lenses consist of the materials hydrophilic acrylic monomer and hydroxyethylmethacrylate (poly-HEMA) and have a higher water content.

Previous studies have explored the role of hydrophobic and hydrophilic IOLs in regard to PCO development. In a meta-analysis by Li et al [25], data from 9 prospective randomized controlled trials were analyzed with a total of 861 eyes in patients that went through cataract surgery with phacoemulsification that included either a hydrophobic or hydrophilic

intraocular lens, with a follow-up time of at least 1 year. They concluded that hydrophobic acrylic lenses have a lower rate of posterior capsule opacification. Furthermore, Vasavada et al [26] compared PCO rates between 1 hydrophobic lens and 2 hydrophilic lenses and could see significantly less development of PCO in the hydrophobic acrylic group after 3 years. In contrast, Findl et al found no statistically significant difference between hydrophilic and hydrophobic lens materials and the rate of posterior capsule opacification in their review including 66 prospective, randomized and controlled studies, with a follow-up time of at least 1 year [27]. This view was supported by Koshy et al [28], who compared a hydrophilic and a hydrophobic acrylic lens with sharp edges and did not find any statistically significant difference in development of posterior capsule opacification. Overall, these studies display an uncertainty regarding which IOL type is the best in regard to PCO development and highlight the need for further research.

1.5. Uveitis

Uveitis is inflammation in the uvea, the layer of the eye that consists of the iris, the ciliary body and the choroid. Some of the prime functions of the uvea are regulation of the light that reaches the retina, producing aqueous humour and providing the outer layer of the retina with nourishment. A study by González et al [29] estimated the prevalence of uveitis to 540 per 100 000 in the United States. It is a major cause of blindness in the Western world as well as in developing countries. Uveitis is most often idiopathic but may also be part of a systemic autoimmune disease, such as sarcoidosis, Mb Bechterew and systemic lupus erythematosus.

Uveitis can be categorized based on anatomy. The Standardization of Uveitis Nomenclature (SUN) Working Group [30] categorizes uveitis anatomically into anterior, intermediate and posterior uveitis. Anterior uveitis affects the iris or the anterior part of the ciliary body. This is the most common type of uveitis. Intermediate uveitis is primarily vitreous inflammation and includes pars planitis. Posterior uveitis involves the choroid or the retina. Panuveitis involves all parts of the uvea. Furthermore, uveitis can be divided into acute or chronic uveitis. Acute uveitis has a sudden debut and is active during a limited period of time. Chronic uveitis is persistent and returns in less than 3 months if treatment is ended. Patients with acute anterior uveitis may experience unilateral pain, watery discharge and photophobia. For patients with chronic uveitis, the most important symptom is impaired visual acuity.

Patients with uveitis have a higher risk of developing cataract, due to both the inflammation as well as the topical and systemic steroids that are used in the treatment of uveitis. Moreover, the inflammation may lead to a potentially higher risk for posterior capsule opacification. Different factors of IOLs have previously been explored regarding PCO development in patients with uveitis, such as the biocompatibility of the IOLs. The biomaterial of the IOLs vary in biocompatibility. Uveal biocompatibility refers to the inflammatory reaction induced by different IOL types, where hydrophilic IOLs have shown better uveal biocompatibility in studies, meaning they might lead to a milder inflammatory reaction [31]. Capsular biocompatibility refers to proliferation of remaining lens epithelial cells. Hydrophilic IOLs have shown possibly less capsular biocompatibility, with an increased risk of developing PCO [31]. However, there is uncertainty in the field regarding the role of hydrophobic and hydrophilic lenses for PCO in patients with uveitis. Abela-Formanek et al [32] found that the incidence of PCO was lower in the hydrophobic IOL groups than in the hydrophilic IOL groups. This view was supported by Richter-Mueksch et al [33], who found that the PCO rate was significantly higher in the hydrophilic IOL group. However, Roesel et al [34] in their study found that no difference in PCO development could be seen between hydrophilic and hydrophobic acrylic IOLs six months after cataract surgery in patients with uveitis. Nor could any difference between the biomaterials regarding PCO be found in a study of Rauz et al [35], who evaluated PCO development in various IOL biomaterials. The contradictory findings indicate a need for further research for determining which intraocular lens type is the best for patients with uveitis in order to avoid PCO.

2. Aim and Research Questions

The aim of this study was to compare the postoperative complication PCO after cataract surgery with a hydrophobic or a hydrophilic sharp edged IOL in patients with and without uveitis at 1-year follow-up. This could contribute to a greater understanding of whether hydrophobic or hydrophilic lenses are best suited for uveitic and non-uveitic patients in order to minimize PCO.

Specific research questions were:
Is there a difference regarding development of posterior capsule opacification after cataract surgery with the hydrophobic or hydrophilic acrylic lenses?

Do patients with uveitis differ from patients without uveitis in regard to development of posterior capsule opacification?

The hypotheses are stated as follows:
H0 (Null hypothesis): There is no difference regarding PCO between the hydrophilic lens type and the hydrophobic lens type at 1 year-follow-up.

H0: There is no difference regarding PCO between the two patient groups at 1 year-follow-up.

3. Material and Methods

This study was part of an ongoing, not yet published randomized controlled study by Pålsson et al that aims to evaluate complications after cataract surgery with a hydrophobic and hydrophilic IOL in patients with and without uveitis. The IOLs were implanted between the years of 2017-2020 at the Eye Clinic, Sahlgrenska University Hospital, Mölndal. This study focuses on the complication of PCO and includes the patients with and without uveitis that had bilateral cataract surgery and complete data at 1-year follow-up. All patients planned for surgery received written as well as oral information about the study and gave written consent. The study included both patients with uveitis and without uveitis. Patients with complete data at 1-year follow-up were included. Exclusion criteria were not being able to participate in follow-up exams, surgery performed by another surgeon than the two study surgeons or too poor quality of the eye images.

34 patients were recruited for this study, which is a common sample size in randomized, controlled studies regarding complications after cataract surgeries such as PCO in patients with uveitis. The recruitment of patients to these types of studies is often arduous, leading to smaller study samples. Furthermore, uveitic patients only constitute a small number of patients undergoing cataract surgery. In the eye clinic at Sahlgrenska University Hospital, Mölndal, uveitic patients only constitute 1-2 % of all cataract patients. Bilateral surgeries were chosen in order to be able to compare paired data, which leads to safer conclusions, albeit with the result of fewer cases.

To randomize the patient's eyes to either the hydrophilic or the hydrophobic IOL, a web-based online randomization system was used. The first eye to undergo cataract surgery in both the uveitic and the non-uveitic group was randomized to either the hydrophilic or the hydrophobic IOL. The second eye had the other type of IOL implanted.

The patients and the eye photograph graders were masked to the IOL type implanted. When it was time for the statistical analysis, the subject’s implanted IOLs were unmasked to the graders. The surgeons were not masked to the patients IOL type and read about the lens type they were to implant prior to the surgery, which is standard in cataract surgery. Two experienced cataract surgeons (M.Z, C.S) performed the cataract surgeries with the same technique and procedure between the years 2017-2020. Topical anesthesia was used and an anterior continuous curvilinear capsulorhexis (ACCC) was created. Hydrodissection, a

technique used to separate the lens from the capsular bag, was performed, followed by phacoemulsification and IOL implantation. The 1-piece hydrophilic intraocular lens Incise (Bausch & Lomb, Rochester, N.Y., USA) used in the study is an IOL with a sharp optic edge of 360°, with an optic diameter of 6.00 mm and an overall length of 11.00 mm. The hydrophobic intraocular lens Vivinex iSert XC1 (Hoya surgical optics, Tokyo, Japan) is a 1-piece IOL with a sharp optic edge of 360°, with an optic diameter of 6.00 mm and an overall length of 13.00 mm.

For the uveitic patients, the inflammation was graded following the criteria of the Standardization of Uveitis Nomenclature (SUN) Working group. Before surgery, a minimum of 3 months of non-existing or stable inflammation was confirmed. 7-14 days prior to surgery, the uveitic patients were examined in order to determine that the inflammation had not deteriorated. One week before surgery, standard anti-inflammatory treatment was initiated with Dexamethasone (Isopto-Maxidex®) 1mg/ml, three times daily, and Nepafenak (Nevanac®) 3 mg/ml, once daily, and treatment was ended 6 weeks after surgery. Patients without uveitis began the same anti-inflammatory treatment postoperatively and ended the treatment 3 weeks after surgery.

The patients were scheduled for follow-up examinations for PCO after 6 months, 1 year and 2 years after cataract surgery. The data from the 1-year follow-up was included and analyzed in this study. The reason for choosing 1-year follow-ups was that a long follow-up is valuable for evaluating if PCO has developed. However, the 2-year follow-ups for the patients are currently ongoing and several follow-ups have not been performed yet. Therefore, the 1-year follow-ups were chosen. Retroillumination was used for the photographs, which is a way to examine structures of the eye such as the lens and the posterior capsule that uses the red reflex from the retina to highlight opacifications. Retroillumination photographs were taken with a slit lamp biomicroscope in order to detect PCO.

The independent variables of the study were age at surgery, gender (male or female), uveitis, uveitic etiology, uveitic anatomical localization and type of IOL. The dependent variables were PCO noted as yes or no, and the proportion of PCO covering the posterior capsule. PCO was assessed subjectively in the image analysis system ImageJ (NIH, Bethesda, MD, USA). ImageJ was selected for its availability and updated settings. The patient's eye photographs were imported to ImageJ from their medical journal. Two graders independently evaluated

and graded the images while being masked to the type of implanted IOL and all other patient data. One grader (K.S) is an experienced ophthalmologist and has long experience in interpretation of PCO in eye images. The other grader (J.K) is a medical student and was trained in PCO assessment and grading for this study. If there was any disagreement among graders, it was settled through consensus, which is in line with previous studies including several graders [36].

4. Data collection procedures/ Variable analyses/ Statistical methods

In ImageJ, it was first determined whether the patient had PCO or not, and this was noted as yes or no. All areas of continuous opacification were considered. On the eye images with PCO, the number of quadrants (1-4) with PCO were noted. Thereafter, the area of the capsulorhexis and the areas with PCO were drawn out with a computer mouse. The program then measured the areas. The proportion of PCO was measured as the area of PCO divided by the area of the capsulorhexis. If the eye image was assessed to be of too poor quality for assessment by both graders, the patient was excluded.

Based on power calculations regarding clinically relevant differences in the complications flare level and cystic macular edema, a study sample of at least 100 uveitic eyes and 100 non-uveitic eyes was calculated to be needed to receive a power of 80 % with a 2-sided α level of 5%.

The statistical program used for the study was SPSS statistical software (version 26.0, International Business Machines). For descriptive statistics, the mean value ± standard deviation or median with range was used, depending on the distribution of the data. The categorical outcome variable PCO yes/no was compared between the two patient groups and the two IOL types using Chi2-test. To compare the continuous outcome variable proportion of PCO covering the posterior capsule surface, the non-parametric Mann-Whitney U-test was used, as the data was not normally distributed. To investigate a potential relationship between the independent and dependent variables, binary logistic regression was performed, with PCO as the dependent variable and age at surgery, sex, uveitis and IOL type as covariates. A p-value of < 0.05 was regarded as statistically significant. To test interrater reliability, Kappa statistics with 95% confidence intervals, including the percentage of agreement between graders, was calculated by a statistician linked to the Department of Ophthalmology.

5. Student's contribution

The work included collecting data from the patient journals. Eye images were extracted from the journals, anonymized, and imported to the image analysis system ImageJ. In ImageJ, PCO was measured and graded on each photograph. Moreover, statistical analyzes were performed on the patient data and interpreted with the help of the supervisor of the degree project. Kappa statistics was performed by a statistician connected to the Department of Ophthalmology. Literature relevant for the study was gathered in order to write the thesis.

6. Ethics

The study was approved by the Regional Ethical Board, University of Gothenburg, registration number 031-16. Furthermore, this study has complied with the tenets of the Declaration of Helsinki. Patients were provided information about the study in both written and oral form, as well as information that they can withdraw from the study at any time. They were then asked to participate. Furthermore, written patient consent was acquired from all patients. To be allowed to read patient journals for the study, a form for accessing journals was signed by the Head of the Department of Ophthalmology. The patient data was anonymized and coded. Only non-invasive eye examinations were performed. Most of the examinations are routine after cataract surgery, and they do not cause discomfort or pain for the patient. The two lens types used in the study are routinely used for cataract surgery at the clinic today and it has not been shown that one lens is more beneficial than the other for patients.

7. Results

20 patients (40 eyes) were analyzed. 9 patients (45 %) were uveitic patients and 11 patients (55 %) were in the non-uveitic group. Figure 1 demonstrates the steps in the process of selecting the study patients.

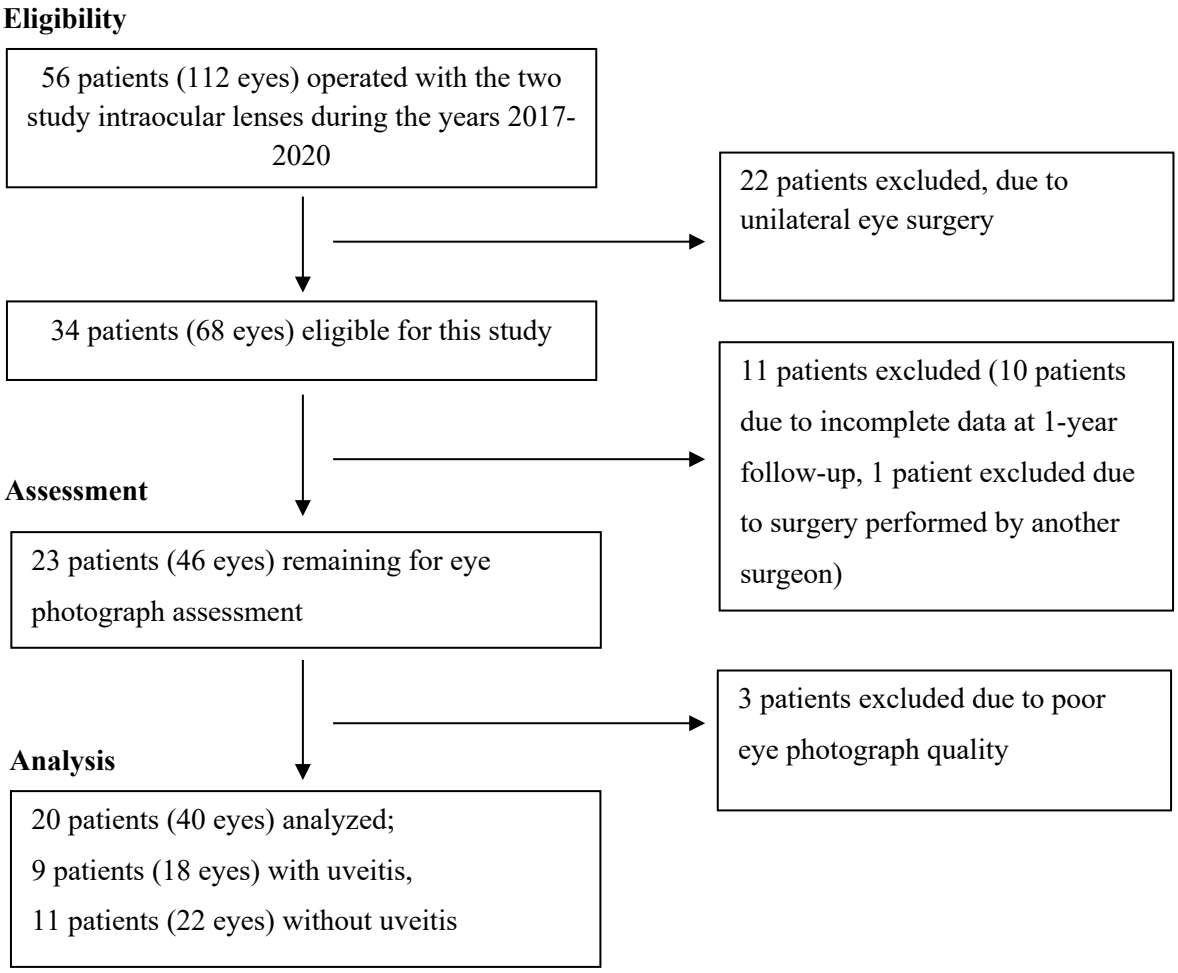


Figure 1. Flow chart of the steps in the process of selecting patients for the study.

Clinical characteristics are shown in Table 1. Regarding distribution in gender, there were more women in both groups with 6 (67 %) female patients in the uveitic patient group and 9 (82 %) female patients in the non-uveitic group. The median age at surgery was 68.5 years (range 55-77 years) in the uveitic group and 75 years (range 59-88 years) in the non-uveitic patient group. All patients with uveitis had anterior uveitis. 5 patients (56 %) in the uveitic group had idiopathic uveitis whereas the other patients (44 %) had a systemic disease associated with uveitis.

Table 1. Clinical characteristics of patients with and without uveitis
Characteristics of the uveitic (n = 9) and the non-uveitic (n = 11) patient group.
Gender, age at surgery and etiology of uveitis of the study patients are presented.

Parameter	**Uveitis (n = 9)**	**No uveitis (n = 11)**
Sex, n (%)		
Female	6 (67 %)	9 (82 %)
Male	3 (33 %)	2 (18 %)
Age at surgery, years		
Mean (± SD)	66.3 (± 6)	74.9 (± 7.2)
Median (range)	68.5 (55–77)	75.0 (59–88)
Uveitis etiology/associated systemic disease, n (%)		
Idiopathic uveitis	5 (56 %)	
Morbus Bechterew	1 (11 %)	
Sarcoidosis	1 (11 %)	
Crohn's disease	1 (11 %)	
TINU	1 (11 %)	

n, number of patients; %, percentage of the entire group.
Abbreviations: SD, standard deviation; TINU, Tubulointerstitial Nephritis and Uveitis Syndrome.

Calculations of interrater reliability resulted in a percent agreement of 0.9487, meaning that in over 94 % of the assessments, the two graders were in complete agreement. Furthermore, the calculations resulted in a Kappa value of 0.8971 (95% CI 0.76-1.00), which is considered to represent a high level of agreement [37].

Table 2 shows the number of eyes affected by PCO in the two patient groups and with the two IOL types. Most eyes in both patient groups and with both IOL types had not developed PCO at 1-year follow-up. PCO occurred in 7 eyes (38.9 %) with uveitis and in 7 eyes (31.8 %) without uveitis (p = 0.641). Regarding the two IOL types, PCO developed in 6 eyes (30 %) with the hydrophobic IOL and 8 eyes (40 %) with the hydrophilic IOL (p = 0.507).

Table 2. Posterior capsule opacification (PCO) in eyes with and without uveitis and in eyes with the hydrophobic and hydrophilic intraocular lens (IOL)

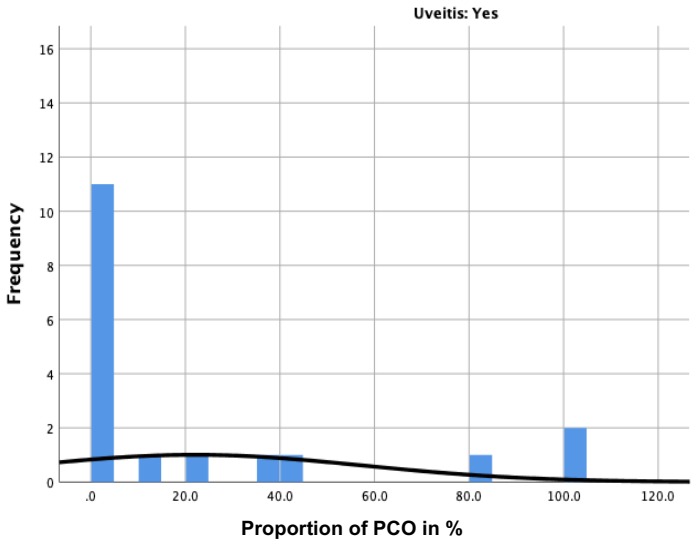
The table represents the number of eyes that have developed posterior capsule opacification (PCO) at the 1-year follow-up. The number of eyes in the two patient groups as well as with the two intraocular lens types are displayed. Though a slightly higher incidence of PCO can be seen in the uveitic patient group and with the hydrophilic IOL, no significant difference could be detected.

Parameters	Eyes with PCO, n (%)	Eyes without PCO, n (%)	p-value
Patient group			
Uveitis	7 (38.9 %)	11 (61.1 %)	0.641[a]
No uveitis	7 (31.8 %)	15 (68.2 %)	-
IOL type			
Hydrophobic IOL	6 (30 %)	14 (70 %)	0.507[a]
Hydrophilic IOL	8 (40 %)	12 (60 %)	-

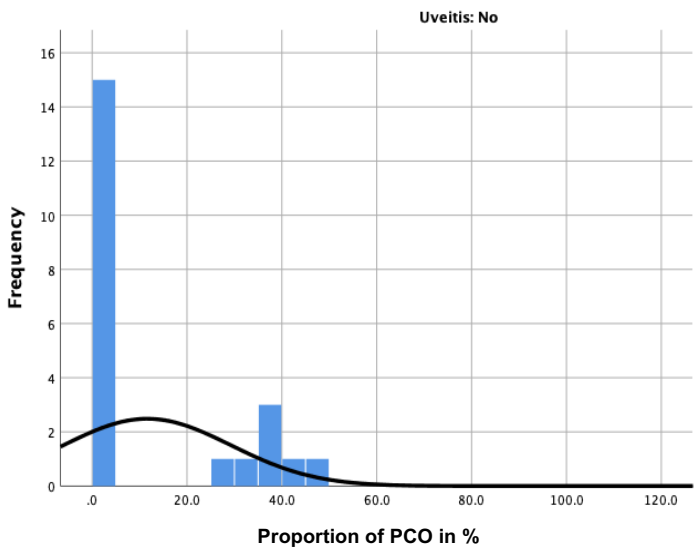
Note: [a]Pearson Chi-Square test
n, number of patients; %, percentage of the entire group.
Abbreviations: PCO, posterior capsule opacification; IOL, intraocular lens.

For eyes that had developed PCO at 1-year follow-up, the median of the proportion of the posterior capsule surface covered with PCO was 43 % (range, 12-100) in the uveitic group and 36 % (range, 28-46) in the non-uveitic group (p = 0.522). Figures 2.a and 2.b show the frequency of the proportion of the posterior lens capsule covered by PCO in the two patient groups. The figures show that a high number of the eyes did not have PCO at the 1-year follow-up. When looking at the eyes that developed PCO, uveitic eyes had a wider range in values, and a number of uveitic eyes presented with a higher proportion of the lens capsule covered in PCO compared to eyes in the non-uveitic group (figure 2.c.).

2.a.



2.b.



2.c.

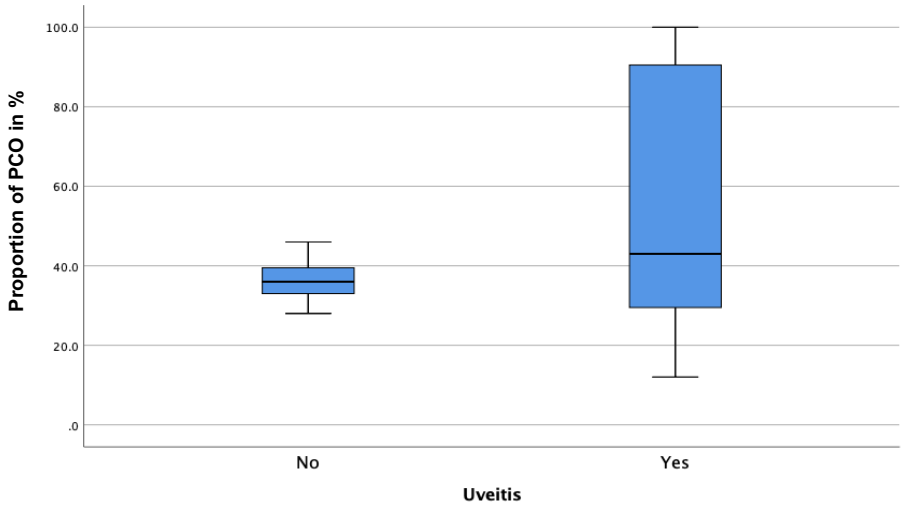
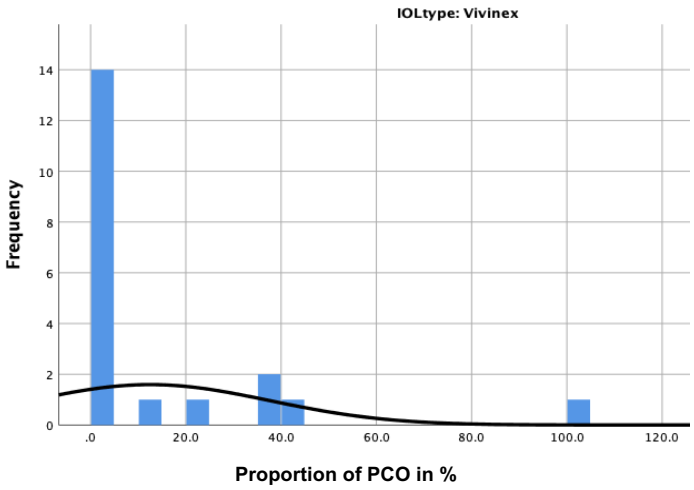


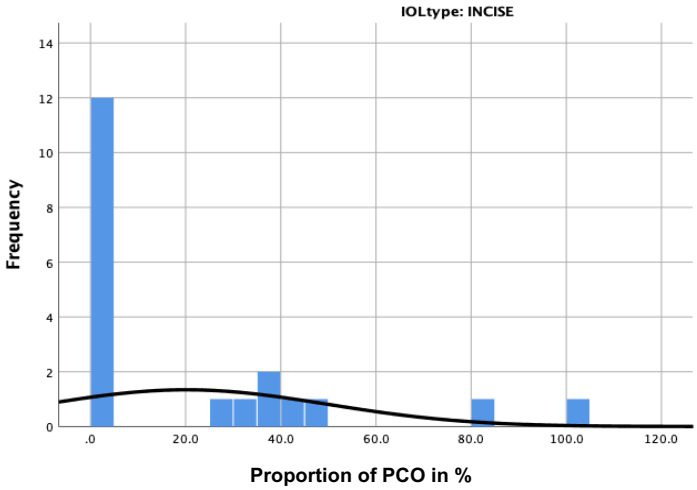
Figure 2. Distribution of the proportion of the posterior capsule surface covered with posterior capsule opacification (PCO) divided by patient groups.
The frequency of the proportions of the posterior capsule surface covered with PCO in the uveitic group is displayed in figure 2.a. and in the non-uveitic patient group in figure 2.b. Most of the eyes in both patient groups had not developed PCO at 1-year follow-up. Figure 2.c. shows a box-and-whiskers plot of the proportion of the posterior capsule surface covered with PCO in eyes that developed PCO, divided into the two patient groups. The boxes represent the interquartile range and whiskers represent the minimum and maximum value. The solid horizontal line is the median value. Uveitic eyes presented a greater range of values, with some uveitic eyes presenting a higher proportion of the lens capsule covered in PCO compared to eyes in the non-uveitic group. Abbreviations: PCO, posterior capsule opacification.

The median of the proportion of the posterior capsule surface covered with PCO in the eyes that had developed PCO at 1-year follow-up was 35 % (range, 12-100) for the hydrophobic Vivinex IOL and 39.5 % (range, 28-100) for the hydrophilic Incise IOL (p = 0.332). The frequency of the proportion of the posterior lens capsule covered by PCO is shown in figures 3.a. and 3.b. They show that a high number of eyes had not developed PCO at 1-year follow-up. Regarding the eyes that developed PCO, the eyes with the hydrophilic Incise IOL showed a slightly wider range of values and a number of eyes with the hydrophilic IOL presented with a higher proportion of the posterior capsule being covered in PCO compared to eyes in the hydrophobic Vivinex group (figure 3.c.).

3.a.



3.b.



3.c.

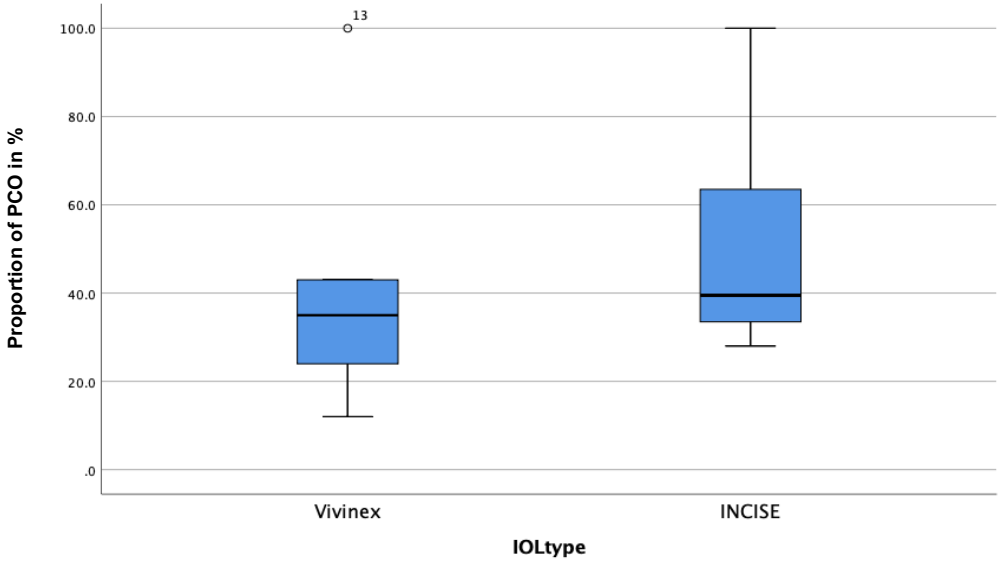


Figure 3. Distribution of the proportion of the posterior capsule surface covered with posterior capsule opacification (PCO), divided by intraocular (IOL) lens type.
Figure 3.a. shows the frequency of the proportion of PCO covering the posterior capsule in eyes with the hydrophobic lens Vivinex, and figure 3.b. shows the frequency in eyes with the hydrophilic lens Incise. Figure 3.c. demonstrates a box-and-whiskers plot of the proportion of the posterior capsule surface covered with PCO in eyes that developed PCO, divided into the two IOL types. The boxes represent the interquartile range and whiskers represent the minimum and maximum value. Eyes with the hydrophilic Incise IOL presented a slightly wider range of values, and a number of eyes with the hydrophilic Incise IOL showed a higher proportion of the posterior capsule being covered in PCO compared to eyes in the hydrophobic Vivinex IOL group.
Abbreviations: PCO, posterior capsule opacification. IOL, intraocular lens.

Binary logistic regression was performed to evaluate potential associations between PCO and other variables studied. The following variables were selected as independent variables: age, gender, uveitis and IOL type. The results are displayed in table 3. A statistically significant positive association was shown between PCO and age at surgery ($p = 0.023$).

Table 3. Binary logistic regression, evaluating potential factors associated to posterior capsule opacification (PCO)

The covariates analyzed include age at surgery, intraocular lens type, gender and uveitis. Age at surgery was found to have a statistically significant positive association to posterior capsule opacification, meaning a lower age at surgery was associated with an increased risk of developing PCO.

Covariates	B	SE	OR	95% CI	p-value
Higher age at surgery	-0.168	0.074	0.845	0.731-0.977	0.023
No uveitis	-1.857	1.009	0.156	0.022-1.127	0.066
Hydrophobic IOL	-0.255	0.368	0.489	0.377-1.594	0.489
Male	-0.323	0.827	1.382	0.273-6.984	0.696

Abbreviation: PCO, posterior capsule opacification; IOL, intraocular lens; B, unstandardized regression weight; SE, standard error; OR, odds ratio; CI, confidence interval.

8. Discussion

In this study, the majority of eyes did not develop PCO at 1-year follow-up. Regarding our research question on whether there was a difference in PCO development between patients with and without uveitis, there was no statistically significant difference in the number of eyes developing PCO between the patient groups, with 7 (38.9 %) uveitic eyes and 7 (31.8 %) non-uveitic eyes developing PCO ($p = 0.641$). Furthermore, when viewing the proportion of the lens capsule covered in PCO, the uveitic eyes with PCO presented a greater range in values, where a number of uveitic eyes showed a higher proportion of the lens capsule covered in PCO compared to eyes in the non-uveitic group. However, the difference between the patient groups of the proportion of the posterior capsule covered in PCO was not statistically significant ($p = 0.522$). Although the difference between the patient groups was not significant, the higher incidence of PCO in the uveitis group as well as the higher proportion of the lens capsule covered in PCO in a number of uveitic eyes is in accordance with previous research presenting a higher risk for PCO in uveitic patients [32, 38]. For example, Abela-Formanek et al compared PCO development 1 year after cataract surgery and found a statistically significant higher development of PCO in the uveitic patient group compared to a control group [39]. A possible explanation for this study's non-significant results could be that this study had a small uveitic patient group. It may be speculated that a larger patient group could present statistically significant results and provide better answers to this study's hypotheses regarding whether there is a difference in PCO development between the patient groups with the two IOLs.

In our study, the most common etiology of uveitis was idiopathic uveitis ($n = 5$, 56 %), which is the most common uveitic etiology in general. The only anatomical localization of uveitis presented was anterior uveitis. Previous studies have shown a more heterogeneous distribution of anatomical localization of uveitis, such as a study conducted in a referral center in Italy by Cimino et al [40] which showed an anatomical distribution of 51.2% of patients with anterior uveitis, followed by posterior uveitis at 23.4%. The reason that our study only had patients with anterior uveitis is uncertain and could perhaps be described by the small uveitic patient group in the study. However, anterior uveitis is the most common form of uveitis and accounts for over 50% of all cases in the western world [41, 42]. Furthermore, posterior uveitis is often the most severe type of uveitis, with possible impact on the retina and the choroid which might lead to permanent loss of vision. It is possible to assume that fewer patients with severe cases of uveitis were eligible for cataract surgery

during the recruitment period of the study, which could have led to the final distribution of the study. In addition, the fact that only anterior uveitis was presented in our study makes conclusions of this study regarding uveitic patients only applicable to patients with anterior uveitis.

As for the study's research question regarding whether there is a difference in PCO development between the IOLs, there was no statistically significant difference in the number of eyes developing PCO between the hydrophilic and the hydrophobic IOL types. A slightly higher number of eyes with the hydrophilic Incise IOL developed PCO at 1-year follow-up. Furthermore, some eyes with the hydrophilic IOL had a higher proportion of the posterior capsule being covered in PCO compared to eyes with the hydrophobic IOL, and the hydrophilic group presented a wider range of values. However, the difference between the proportion of PCO in the IOL types was not statistically significant. To the authors knowledge, no previous studies have compared the PCO development between the two study IOLs Vivinex and Incise. Previous studies have compared the PCO development between other hydrophobic and hydrophilic IOLs. Furthermore, previous studies have used other software to evaluate PCO. Thus, the results of previous studies cannot fully be extrapolated to our study, and it is important to bear this in mind as conclusions are drawn of our study.

There are previous studies that have reported higher PCO rates in hydrophilic acrylic IOLs compared to hydrophobic IOLs [43-46]. In a meta-analysis by Zhao et al [47], data from 11 randomized controlled studies were analyzed with a total of 889 eyes in patients that went through cataract surgery including either a hydrophobic or hydrophilic intraocular lens. They concluded that hydrophobic acrylic lenses have a lower rate of posterior capsule opacification. Zhao et al describe that this could in part be due to the ability of the hydrophobic lens to increase adhesiveness between the intraocular lens and the posterior capsule, which leads to less space between the IOL and the posterior lens capsule where lens epithelial cells can migrate. This was first described by Linnola in 1997 in his “sandwich theory” [48], which states that a single layer of lens epithelial cells (LECs) binds to both the intraocular lens and the posterior lens capsule. This creates less space for the LECs to migrate, which prevents further posterior capsule opacification. Furthermore, Linnola et al found that proteins such as fibronectin and laminin give better adhesiveness between the IOL and the posterior capsule, leading to less LEC migration and lower PCO rates, and found that fibronectin and laminin binds best to hydrophobic intraocular lenses [49]. These properties of

hydrophobic IOLs could be a reason that our study found a lower number of eyes with PCO, as well as fewer eyes with a high proportion of PCO covering the lens capsule, in the hydrophobic group.

In addition to the material of the IOL, another factor that may be important for the prevention of PCO is the posterior optic edge design of the IOLs. The importance of a sharp posterior optic edge for preventing PCO has been pointed out in several studies [21, 50, 51]. Nishi et al studied this effect in rabbits and stated that a sharp optic edge seems to create a barrier and induce contact inhibition for migrating lens epithelial cells, thus preventing PCO [52]. Although the lenses in our study differ in material, the posterior optic edges of the Vivinex and the Incise IOL are similar. Both IOLs have a 360° sharp posterior optic edge. Furthermore, the posterior optic edge radius of curvature of the hydrophobic Vivinex lens is 7.6 μm and is 7.7 μm for the hydrophilic Incise lens. In a study by Nanavaty et al [53], the sharpness and thickness of several IOLs were measured, including the Incise and Vivinex IOLs. The authors concluded that intraocular lenses that have a radius of curvature < 10 μm seem to have lower PCO rates, as this radius of curvature gives an effective barrier effect. Both the Vivinex and the Incise lens have a radius curvature of < 10 μm, and the Incise lens was the only hydrophilic IOL to show this in the study by Nanavaty et al. The similarities between the study IOLs in optic edge design and radius of curvature could be a reason that this study did not find a vast difference between the IOLs regarding PCO development.

As aforementioned, no previous studies have, to the authors knowledge, been conducted comparing PCO development between the study's two IOLs. For the Vivinex lens, one long-term prospective randomized controlled study has been made, by Leydolt et al [54]. However, the study compared PCO development in the Vivinex lens to another hydrophobic IOL. The authors showed that the Vivinex lens had lower rates of PCO 3 years after cataract surgery and suggested that the sharper posterior edge as well as the higher hydrophobicity of the Vivinex IOL are potential factors for the lower PCO rates seen with the intraocular lens. Regarding the Incise lens, a study by Lubiński et al [55] evaluated postoperative outcomes with the Incise lens and found low PCO-incidence 1 year after cataract surgery and suggested that the reason was the 360° sharp-edge profile of the IOL, which prevents PCO formation. Another study by Toygar et al [56] presented the outcome of PCO with the Incise lens after 6 months and found that 9 eyes (14.7 %) had mild PCO, and no eyes required treatment with nd:YAG laser. They also attribute the findings to the fact that the Incise lens has a 360° sharp

edge as well as a small radius, which prevents PCO. These previous findings as well as the results of this study of the two IOLs imply that a variety of factors of the two IOLs, such as their optic edge design and their IOL material, play an important role in PCO development. However, more studies on the two study IOLs are needed to further evaluate their ability to prevent PCO development compared to each other as well as to other IOLs in the field.

A statistically significant positive association was found between PCO and age at surgery ($p = 0.023$). A lower age at cataract surgery was associated with an increased risk of developing PCO. This is in agreement with the well-established notion in the field that PCO development is age dependent, with lower rates of PCO seen in older patients and higher rates in younger patients. Several studies have found lower age to be a risk factor for PCO [57-59]. In this study, the uveitic patients had cataract surgery at a younger age (mean 66.3 years) compared to the patients without uveitis (mean 74.9 years). This result matches those observed in earlier studies [60]. The incidence of PCO as well as the proportion of PCO covering the posterior capsule was higher in the uveitic group. Although these results were not statistically significant, they support the view that young age is a risk factor for PCO.

In this study, the eye images were assessed by two graders independently, and interrater reliability resulted in a percent agreement of 0.9487 and in a Kappa value of 0.8971 (95% CI 0.76-1.00), showing a high level of agreement between graders. It is often of value to evaluate the agreement of several graders to see if a method or study can be replicated by future researchers with consistent estimates, and therefore it could be considered a strength that our study had two graders. The high agreement could indicate that ImageJ has potential as a PCO evaluation software. However, this study is small and very few studies have been made that evaluate the agreement of graders during PCO evaluation with ImageJ. In a study by Almenara et al [61], ImageJ was used to compare PCO in two hydrophobic IOLs. Three ophthalmologists graded the eye photographs and interobserver agreement was calculated using intraclass correlation coefficient (ICC) and indicated good reliability. However, as our study has used a different statistical approach for evaluating interobserver agreement, the results of the study by Almenara cannot be extrapolated to our study. To reach valid conclusions on whether ImageJ is a valuable software for future PCO studies, more studies are needed with assessment of interrater reliability when using ImageJ as a PCO software.

The results of this study suggest an important role of the IOL material and design in the study's IOLs for PCO development in patients with and without uveitis. As this study did not provide statistically significant values, and this is the first study comparing the Vivinex and Incise IOLs, the question remains as to which of the two study IOLs are better for the patient groups. This indicates a need for future studies that evaluate and compare the IOLs. To improve the experiment and thus better test the study's hypotheses in future studies, it is desirable that these future studies include larger patient groups, with more uveitic etiologies and anatomical localizations in the uveitic patient group, so that results and conclusions can be applicable to more patients with uveitis. Furthermore, a longer follow-up time than 1 year could be of value, as significant differences in PCO development could be shown at a longer time after surgery. In addition, an evaluation of the ImageJ software for PCO measuring should be included in future studies. These factors will be further discussed in the methodological discussion.

8.1. Methodological considerations/Strengths and Weaknesses

Two experienced surgeons performed cataract surgery in this study, with the same surgical technique. The technique of phacoemulsification was used, as it is the routine method for cataract surgery today. Previous studies have investigated the role of phacoemulsification for PCO prevention in comparison to previous surgical techniques and have found that phacoemulsification is associated with less PCO development [62, 63]. The use of the same surgical technique, and it being the established phacoemulsification technique, is considered a strength of the study. Even though the same technique has been used for the cataract surgeries, one could argue that it could be better to use only one surgeon for all surgeries, as potential differences in surgery would then be eliminated, and that using two surgeons is a potential weakness of the study. However, to the authors knowledge, no study has been made to evaluate the difference between individual surgeons for the development of PCO, and similar to our study, previous studies often investigate PCO incidence after cataract surgery by more than 1 surgeon [43, 64-66].

In this study, the importance of good eye photograph quality became evident. Certain eye photographs could be assessed but were, however, not of optimal quality. This made the assessment more difficult. Other photographs were blurry or out of focus, despite the photographer's best efforts to take a good photograph and had to be excluded. The assessment of PCO in eye photographs improves with better eye photograph quality and vice versa. It is

important to optimize the photographs, for instance by using experienced photographers and ensuring the patients full cooperation, so that the assessments become as good as possible, and no exclusions have to be made. This is not least important as the group of uveitic patients undergoing cataract surgery often is very small to begin with, as was the case in our study.

Regarding the study design, this study was part of a randomized controlled study. This is a strength of the study, as randomized controlled studies are considered the golden standard to establish causal conclusions, and they reduce bias. As for the patient groups, the study consisted of 2 independent groups, one group with uveitis and one without uveitis, in order to answer the study's research questions regarding whether there is a difference in PCO development in eyes with two IOLs between patients with and without uveitis. As the distinction between patients with and without uveitis is clear, the allocation of our study sample into two groups was uncomplicated. This allocation was a clear choice in order to address the hypotheses in the best possible way. Unfortunately, both the uveitic and the non-uveitic patient groups in the study were small. The small group sizes can be explained in part by the covid-19 pandemic; due to the pandemic, several patients did not come to their scheduled 1-year follow-up. This led to loss of important patient data for this study and a smaller patient group. Furthermore, patients with uveitis that undergo cataract surgery are in general a small group. The small study sample is a weakness of this study and to properly evaluate the hypotheses of the study, future studies should be performed with larger study groups.

The layout of the experiment of using patients with bilateral surgeries meant that the left and right eye of patients could be compared, which is an advantage as it eliminates the difference between individuals. Intraindividual differences are observed and interindividual differences are eliminated. Regarding PCO-development, it is common that both eyes of a patient develop PCO but to varying degrees. The PCO degree can vary even if there is no difference between the eyes regarding other factors. Furthermore, the degree of uveitis can vary between eyes and can affect how much PCO will develop. However, neither the asymmetry in presence of uveitis nor development of PCO is systematical. This means that there is no bias involved that could affect the outcome of the experiment in regard to how the eyes are related to each other.

This study examined PCO development 1 year after cataract surgery. The follow-up time of 1 year can both be considered both a strength and a limitation; other studies have evaluated PCO development in IOLs after 1 year follow-up [43, 45, 67, 68] with significant results. However, to further evaluate PCO development in the IOLs, it could be valuable with longer follow-up time, as longer time after surgery might be needed to see a significant result of PCO development in the IOL-types. In a study from Nanavaty et al [69], the PCO rate in 2 hydrophilic IOLs was compared to a hydrophobic IOL, and the authors found a higher PCO rate in the hydrophilic lens after 2 years. Furthermore, Vasavada et al [26] compared a hydrophobic and two hydrophilic IOLs with sharp 360° edges and concluded that the hydrophilic IOLs were effective in retarding PCO until the 1-year follow-up but not up to 3 years, unlike the hydrophobic IOL. A longer follow-up than 1 year might be needed to see significant results regarding PCO, and further research with longer follow-up time could therefore be of value for observing PCO development in the hydrophilic and the hydrophobic study IOLs. For the study patients, a 2-year follow-up is scheduled and, in the future, it could be of interest to schedule an even longer follow-up time.

As previously stated, this study did not find significant results, and the lack of significance and the potential clinical relevance of the findings will be discussed in this section. As uveitic patients constitute a small group of patients undergoing cataract surgery, and recruitment for studies implanting different intraocular lenses in cataract surgery are difficult in general, it could cause smaller study samples and less significance. Calculations of power post-hoc were performed regarding the result of the IOL types, to evaluate the power of the study with the study's sample size. It was shown that with the difference detected of 30 % developing PCO with the hydrophobic IOL and 40 % with the hydrophilic IOL with the study sample of 40 eyes, the statistical power is only 6 %. This demonstrates that the number of patients in the study is far too small to gain a power of 80 %, which is the usual desired power for studies. Another factor to consider is the effect size; if the difference in PCO development between the IOL types would have been large, a small sample size could have been sufficient, and the acquired sample size could have sufficed. However, the result of 30 % developing PCO in the hydrophobic group and 40 % developing PCO in the hydrophilic group did not present a vast enough difference. An analysis of effect size after the experiment showed that in order to achieve a large enough effect size, with a power of 80 % and an α level of 5 %, the difference between the hydrophilic and hydrophobic group would have had to be 40 % vs 3 %, with our achieved sample size of 40 eyes. In this study, the first study to compare the two lenses Incise

and Vivinex, the two IOLs did not present a vast difference in PCO development. This demonstrates that to better compare the lenses and gain higher study power, a larger study sample is needed, which would result in more clinically relevant results.

For this study, a long and extensive search was made in order to find an updated, useful software for evaluation of PCO in eye images. As stated in the introduction of this paper, several analysis software's have been used throughout the years for evaluating PCO but have not been updated for several years and are therefore currently not in use, such as the software Automated Quantification of After-Cataract (AQUA), and the Evaluation of Posterior Capsule Opacification (EPCO) software. A few recent studies on PCO, like our study, have used ImageJ (NIH, Bethesda, MD, USA) [61, 70, 71], a software for scientific image analysis which is available for free on an open platform. ImageJ is subjective in evaluating PCO, unlike for instance the AQUA software which is automated and does not have subjectivity in its measurement of PCO, meaning no risk for subjective bias. Other softwares such as the EPCO software are, however, also subjective and have proved to work well for evaluating PCO. This study showed a high level of agreement between the two graders, indicating that ImageJ might be appropriate for measuring PCO. However, as only a few studies have been made using ImageJ as a PCO evaluation software, and these studies do not evaluate the effectiveness of ImageJ, the benefits of the software for PCO evaluation remains uncertain. The effectiveness of ImageJ for PCO evaluation should be investigated in further studies, as ImageJ could be a valuable method and the field could benefit from using one standardized software for PCO measurement.

9. Conclusions and Implications

This study was the first to compare development of PCO, the most common postoperative complication after cataract surgery, in the IOLs Vivinex and Incise. The results shown in this study could be important for future studies comparing the two IOLs, as well as studies comparing other hydrophobic and hydrophilic IOLs. In conclusion, no significant differences in PCO development were seen between the IOLs. Although not significant, the result of this study of a lower incidence of PCO, as well as fewer eyes with a high proportion of PCO covering the lens capsule, in eyes with the hydrophobic Vivinex IOL is similar to previous studies in the field. This result could bear clinical relevance as it could indicate that hydrophobic lenses are a better option for reducing PCO, and thus, it could be of value to use hydrophobic IOLs to minimize PCO. Furthermore, the optic edge sharpness and similarities of the two study IOLs could be a reason that no vast difference in PCO development between the IOLs could be found and a reason most patients in the study did not develop PCO. This result could imply that the two IOLs could be of value in the clinic for minimizing PCO, and it is therefore of interest to further evaluate them in future studies.

Regarding patients with and without uveitis, this study could not find a significant difference of PCO development between the two patient groups. However, the incidence of PCO was higher in the uveitic group compared to the non-uveitic group, and a higher proportion of the lens capsule covered in PCO was found in a number of uveitic eyes. It could therefore be speculated that uveitis can lead to more PCO development, similar to results seen in earlier studies. As PCO is the most common postoperative complication after cataract surgery, with several problematic symptoms, further research is valuable for determining which of the two study IOLs is better to use in the clinic for reducing PCO development in the patient groups. Patients with uveitis are important to consider as a higher incidence of PCO previously has been associated with inflammation. As many uveitic eyes did not develop PCO in this study, the study IOLs could be of use for the patient group and evaluating the Vivinex and Incise IOL further could determine which IOL is best for uveitic patients.

The evaluation of interrater reliability of eye photograph grading in this study showed a high level of agreement between the two graders. This study's result of a strong interrater reliability could suggest that ImageJ has potential value for use as a PCO evaluation system. This knowledge could be useful in the clinic as well as in future research, as a good PCO evaluation system with good reproducibility between graders is important for measuring PCO

and to better compare results from different studies. This would benefit the group of patients at risk of suffering from PCO, as more accurate conclusions could be drawn on how to minimize the complication. However, this study was small and is one of few studies evaluating the interrater reliability of ImageJ. As there is a need in the field for an updated and available PCO evaluation software, future studies should be conducted, further evaluating the effectiveness of ImageJ as a software for measuring PCO. This could provide the field with a much needed standardized, systematic PCO evaluation system.

PCO is a treatable complication that has declined in incidence, owing to progress in surgical technique and development of intraocular lenses. However, PCO is still the most common complication after cataract surgery. As a vast number of patients are affected by cataract each year, consequently, thousands of patients in Sweden gain PCO, as well as millions throughout the world. The complication presents impaired visual acuity and symptoms that negatively affect the patient's everyday life, with a neglect in quality of life. Therefore, eradication of PCO is desirable and studies such as this study, which evaluates IOLs in order to see which IOLs are best for preventing PCO development in various patient groups, are needed to reach this goal. The results of this study regarding the development of PCO with the Incise and Vivinex IOL in patient groups, as well as the assessment of the system ImageJ for PCO evaluation, could be meaningful in the work of reducing PCO. Moreover, although an established treatment for PCO, the nd:YAG laser capsulotomy, now exists, there are several factors to keep in mind regarding the treatment. First, the laser treatment is not entirely without risk. Though rare, complications such as damage to the IOL, cystoid macular edema and retinal detachment can arise, with the latter being sight-threatening. Second, the treatment of the vast number of patients takes up valuable time and presents a considerable cost for the health care system. Third, in a global perspective, the access to nd:YAG laser treatment varies throughout the world, with the possibility of receiving the treatment being far smaller in the developing world. Factors such as these make research such as this paper essential for minimizing PCO and improving the life quality of patients, as well as make the health care more effective in using its resources.

Populärvetenskaplig sammanfattning

En undersökning om efterstarr, en vanlig komplikation efter operation av grå starr

Det vanligaste kirurgiska ingreppet i Sverige är operation av grå starr - en grumling av ögats lins som kan leda till synnedsättning. Vid operation av grå starr tas patientens grumliga lins bort och ersätts av en plastlins, vilket leder till återställd syn. Det vanligaste besväret efter operation av gråstarr är efterstarr, en komplikation som ger synnedsättning på samma sätt som vid grå starr. Man har sett att efterstarr är vanligare hos patienter med uveit, en inflammation i ögat. De olika plastlinserna man opererar in vid operation av grå starr har olika design och består av olika material, vilket kan påverka utvecklingen av efterstarr. Man har inte kunnat avgöra vilken typ av plastlins som är bäst för att undvika utveckling av efterstarr hos olika patienter och det är därför viktigt att fortsätta utreda detta. Syftet med vår studie var att undersöka vilken av två plastlinser av olika material som ger minst efterstarr hos patienter med och utan inflammation i ögat.

I studien undersöktes 20 patienter som opererades för grå starr, varav 9 patienter hade det inflammatoriska tillståndet uveit. Patienterna fick en plastlins i vartdera ögat; en plastlins med högt vatteninnehåll i ena ögat och en plastlins med lågt vatteninnehåll i andra ögat. Ett år efter operationen togs bilder av patienternas ögon där man bedömde om patienten utvecklat efterstarr och i så fall hur mycket efterstarr som hade utvecklats.

Resultatet blev att de flesta ögon inte hade utvecklat efterstarr 1 år efter operation. Patienterna med inflammation i ögat hade i högre utsträckning utvecklat efterstarr. Ytterligare ett resultat från studien var att det var vanligare med efterstarr i ögon med plastlinsen som hade högt vatteninnehåll.

Resultaten från studien kan tala för att patienter med inflammation i ögat i större utsträckning utvecklar efterstarr. Dessutom kan resultaten tala för att plastlinser med lägre vatteninnehåll kan vara mer lämpliga att använda för att undvika efterstarr. Dock var studien liten och därför behövs större framtida studier för att dra bättre slutsatser kring vilken plastlins som är mest lämplig för att undvika efterstarr.

Acknowledgements

There are many people I would like to thank for making this thesis possible. First and foremost, I am so very grateful for my supervisor Professor Madeleine Zetterberg, MD, PhD. I cannot thank you enough for acknowledging my interest in ophthalmology and giving me the chance to enter the world of the Ophthalmology department at Mölndals sjukhus. As someone who is just beginning her journey in medicine, it is not always easy to get a chance working in the field you are interested in, and I am immensely thankful for this chance. Thank you for being my supervisor, guiding and encouraging me greatly through the work of this thesis, as well as increasing my knowledge and interest for research in the ophthalmologic field. Your door has always been open, and I am thankful for all your help!

Furthermore, I would like to thank Sara Pålsson, for introducing me to her research project and her help with writing this thesis. I sincerely thank Karin Svedberg for taking the time to help grading in this study and share her invaluable knowledge in the field of posterior capsule opacification. Our discussions as well as the knowledge I have received from reading your previous work has been important for this thesis as well as for developing my knowledge in the field of ophthalmology.

I extend my sincerest thanks to the amazing doctors and other staff at the department of Ophthalmology, for creating a warm, welcoming environment and always being helpful. A special thanks to Emad Abu Iskheidem, for your never-ending enthusiasm and amazing ability to teach. You have made ophthalmology even more interesting, and you are a role model for how a mentor should be. Thank you for all your valuable lessons!

My sincere gratitude to Anne Petersen, for teaching me ImageJ. A sincere thanks is also due to Nils-Gunnar Pehrsson and Hussein Hamoodi at Statistiska Konsultgruppen for their help with statistical analyses for the study.

I would like to thank all the patients in the study for participating, making this thesis possible.

Lastly, I thank my family and my partner, without all of you there would be no me and I owe you everything.

References

1. Behndig, A., *Svensk kataraktkirurgi : årsrapport 2019 baserad på data från Nationella kataraktregistret (Swedish National Cataract Register Annual Report 2019)*. 2020, Karlskrona: Nationella kataraktregistret.
2. Lang, G.K., *Ophthalmology*. 3rd ed. Augenheilkunde, ed. G.G. Champe. 2016: Stuttgart u.a. : Thieme.
3. Riordan-Eva, P. and J.J. Augsburger, *Vaughan & Asburys general ophthalmology*. A Lange medical book. 528 s. :.
4. Kugelberg, M., *Ögonboken*. 1. uppl. ed, ed. J. Ygge and J. Robertsson. 2010: Stockholm : Liber.
5. Borooah, S., M. Wright, and B. Dhillon, *Ophthalmology*. Pocket tutor. 2012, London :: JP Medical ltd. 298 s. :.
6. Hugosson, M. and C. Ekström, *Prevalence and risk factors for age-related cataract in Sweden.* Ups J Med Sci, 2020. **125**(4): p. 311-315.
7. Olson, R.J., et al., *Cataract treatment in the beginning of the 21st century.* Am J Ophthalmol, 2003. **136**(1): p. 146-54.
8. Bowling, B., *Kanski's clinical ophthalmology : a systematic approach*. 2016, Edinburgh :: Elsevier. 917 s. :.
9. Taban, M., et al., *Acute endophthalmitis following cataract surgery: a systematic review of the literature.* Arch Ophthalmol, 2005. **123**(5): p. 613-20.
10. Raj, S.M., et al., *Post-operative capsular opacification: a review.* Int J Biomed Sci, 2007. **3**(4): p. 237-50.
11. Saika, S., et al., *Immunolocalization of prolyl 4-hydroxylase subunits, alpha-smooth muscle actin, and extracellular matrix components in human lens capsules with lens implants.* Exp Eye Res, 1998. **66**(3): p. 283-94.
12. Apple, D.J., et al., *Posterior capsule opacification.* Surv Ophthalmol, 1992. **37**(2): p. 73-116.
13. Tetz, M.R., et al., *Photographic image analysis system of posterior capsule opacification.* J Cataract Refract Surg, 1997. **23**(10): p. 1515-20.
14. Barman, S.A., et al., *Quantification of posterior capsular opacification in digital images after cataract surgery.* Invest Ophthalmol Vis Sci, 2000. **41**(12): p. 3882-92.
15. Buehl, W., et al., *Reproducibility of standardized retroillumination photography for quantification of posterior capsule opacification.* J Cataract Refract Surg, 2002. **28**(2): p. 265-70.
16. Allen, D. and A. Vasavada, *Cataract and surgery for cataract.* Bmj, 2006. **333**(7559): p. 128-32.
17. Maedel, S., et al., *Intraocular lens optic edge design for the prevention of posterior capsule opacification after cataract surgery.* Cochrane Database Syst Rev, 2021. **8**(8): p. Cd012516.
18. Hayashi, H., et al., *Quantitative comparison of posterior capsule opacification after polymethylmethacrylate, silicone, and soft acrylic intraocular lens implantation.* Arch Ophthalmol, 1998. **116**(12): p. 1579-82.
19. Nagata, T. and I. Watanabe, *Optic sharp edge or convexity: comparison of effects on posterior capsular opacification.* Jpn J Ophthalmol, 1996. **40**(3): p. 397-403.
20. Buehl, W., et al., *Effect of an acrylic intraocular lens with a sharp posterior optic edge on posterior capsule opacification.* J Cataract Refract Surg, 2002. **28**(7): p. 1105-11.

21. Tetz, M. and A. Wildeck, *Evaluating and defining the sharpness of intraocular lenses: part 1: Influence of optic design on the growth of the lens epithelial cells in vitro.* J Cataract Refract Surg, 2005. **31**(11): p. 2172-9.
22. Wejde, G., M. Kugelberg, and C. Zetterström, *Posterior capsule opacification: comparison of 3 intraocular lenses of different materials and design.* J Cataract Refract Surg, 2003. **29**(8): p. 1556-9.
23. Kruger, A.J., et al., *Two year results: sharp versus rounded optic edges on silicone lenses.* J Cataract Refract Surg, 2000. **26**(4): p. 566-70.
24. Bellucci, R., *An introduction to intraocular lenses: material, optics, haptics, design and aberration*, in *Cataract*. 2013, Karger Publishers. p. 38-55.
25. Li, Y., et al., *Effect of hydrophobic acrylic versus hydrophilic acrylic intraocular lens on posterior capsule opacification: meta-analysis.* PLoS One, 2013. **8**(11): p. e77864.
26. Vasavada, A.R., et al., *Comparison of posterior capsule opacification with hydrophobic acrylic and hydrophilic acrylic intraocular lenses.* J Cataract Refract Surg, 2011. **37**(6): p. 1050-9.
27. Findl, O., et al., *Interventions for preventing posterior capsule opacification.* Cochrane Database Syst Rev, 2010(2): p. Cd003738.
28. Koshy, J., et al., *Comparing capsular bag performance of a hydrophilic and a hydrophobic intraocular lens: A randomised two-centre study.* Eur J Ophthalmol, 2018. **28**(6): p. 639-644.
29. González, M.M., et al., *Epidemiology of uveitis in a US population-based study.* J Ophthalmic Inflamm Infect, 2018. **8**(1): p. 6.
30. Trusko, B., et al., *The Standardization of Uveitis Nomenclature (SUN) Project. Development of a clinical evidence base utilizing informatics tools and techniques.* Methods Inf Med, 2013. **52**(3): p. 259-65, s1-6.
31. Abela-Formanek, C., et al., *Uveal and capsular biocompatibility of hydrophilic acrylic, hydrophobic acrylic, and silicone intraocular lenses.* J Cataract Refract Surg, 2002. **28**(1): p. 50-61.
32. Abela-Formanek, C., et al., *Results of hydrophilic acrylic, hydrophobic acrylic, and silicone intraocular lenses in uveitic eyes with cataract: comparison to a control group.* J Cataract Refract Surg, 2002. **28**(7): p. 1141-52.
33. Richter-Mueksch, S., et al., *Uveal and capsular biocompatibility after implantation of sharp-edged hydrophilic acrylic, hydrophobic acrylic, and silicone intraocular lenses in eyes with pseudoexfoliation syndrome.* J Cataract Refract Surg, 2007. **33**(8): p. 1414-8.
34. Roesel, M., et al., *Uveal and capsular biocompatibility of two foldable acrylic intraocular lenses in patients with endogenous uveitis--a prospective randomized study.* Graefes Arch Clin Exp Ophthalmol, 2008. **246**(11): p. 1609-15.
35. Rauz, S., P. Stavrou, and P.I. Murray, *Evaluation of foldable intraocular lenses in patients with uveitis.* Ophthalmology, 2000. **107**(5): p. 909-19.
36. Öhnell, H., et al., *Structural and Functional Progression in the Early Manifest Glaucoma Trial.* Ophthalmology, 2016. **123**(6): p. 1173-80.
37. Landis, J.R. and G.G. Koch, *The Measurement of Observer Agreement for Categorical Data.* Biometrics, 1977. **33**(1): p. 159-174.
38. Ram, J., et al., *Phacoemulsification with intraocular lens implantation in patients with uveitis.* J Cataract Refract Surg, 2010. **36**(8): p. 1283-8.
39. Abela-Formanek, C., et al., *Uveal and capsular biocompatibility of 2 foldable acrylic intraocular lenses in patients with uveitis or pseudoexfoliation syndrome: comparison to a control group.* J Cataract Refract Surg, 2002. **28**(7): p. 1160-72.

40. Cimino, L., et al., *The causes of uveitis in a referral centre of Northern Italy.* Int Ophthalmol, 2010. **30**(5): p. 521-9.
41. Mercanti, A., et al., *Epidemiology of endogenous uveitis in north-eastern Italy. Analysis of 655 new cases.* Acta Ophthalmol Scand, 2001. **79**(1): p. 64-8.
42. Suhler, E.B., et al., *Incidence and prevalence of uveitis in Veterans Affairs Medical Centers of the Pacific Northwest.* Am J Ophthalmol, 2008. **146**(6): p. 890-6.e8.
43. Kugelberg, M., et al., *Posterior capsule opacification after implantation of a hydrophilic or a hydrophobic acrylic intraocular lens: one-year follow-up.* J Cataract Refract Surg, 2006. **32**(10): p. 1627-31.
44. Iwase, T., et al., *Hydrophobic versus double-square-edged hydrophilic foldable acrylic intraocular lens: effect on posterior capsule opacification.* J Cataract Refract Surg, 2011. **37**(6): p. 1060-8.
45. Heatley, C.J., et al., *Comparison of posterior capsule opacification rates between hydrophilic and hydrophobic single-piece acrylic intraocular lenses.* J Cataract Refract Surg, 2005. **31**(4): p. 718-24.
46. Hayashi, K. and H. Hayashi, *Posterior capsule opacification after implantation of a hydrogel intraocular lens.* Br J Ophthalmol, 2004. **88**(2): p. 182-5.
47. Zhao, Y., et al., *Comparison of hydrophobic and hydrophilic intraocular lens in preventing posterior capsule opacification after cataract surgery: An updated meta-analysis.* Medicine (Baltimore), 2017. **96**(44): p. e8301.
48. Linnola, R.J., *Sandwich theory: bioactivity-based explanation for posterior capsule opacification.* J Cataract Refract Surg, 1997. **23**(10): p. 1539-42.
49. Linnola, R.J., et al., *Adhesion of soluble fibronectin, laminin, and collagen type IV to intraocular lens materials.* J Cataract Refract Surg, 1999. **25**(11): p. 1486-91.
50. Buehl, W., et al., *Long-term effect of optic edge design in an acrylic intraocular lens on posterior capsule opacification.* J Cataract Refract Surg, 2005. **31**(5): p. 954-61.
51. Buehl, W., et al., *Effect of a silicone intraocular lens with a sharp posterior optic edge on posterior capsule opacification.* J Cataract Refract Surg, 2004. **30**(8): p. 1661-7.
52. Nishi, O. and K. Nishi, *Preventing posterior capsule opacification by creating a discontinuous sharp bend in the capsule.* J Cataract Refract Surg, 1999. **25**(4): p. 521-6.
53. Nanavaty, M.A., I. Zukaite, and J. Salvage, *Edge profile of commercially available square-edged intraocular lenses: Part 2.* J Cataract Refract Surg, 2019. **45**(6): p. 847-853.
54. Leydolt, C., et al., *Posterior Capsule Opacification With Two Hydrophobic Acrylic Intraocular Lenses: 3-Year Results of a Randomized Trial.* Am J Ophthalmol, 2020. **217**: p. 224-231.
55. Lubiński, W., M. Kirkiewicz, and K. Podborączyńska-Jodko, *Clinical results after microincision biaxial cataract surgery and implantation of an Incise intraocular lens.* Int Ophthalmol, 2018. **38**(5): p. 1977-1983.
56. Toygar, B., et al., *Early clinical outcome with a new monofocal microincision intraocular lens.* Int Ophthalmol, 2016. **36**(5): p. 657-64.
57. Prajna, N.V., et al., *The madurai intraocular lens study IV: posterior capsule opacification.* Am J Ophthalmol, 2000. **130**(3): p. 304-9.
58. Wu, S., et al., *Retrospective Analyses of Potential Risk Factors for Posterior Capsule Opacification after Cataract Surgery.* J Ophthalmol, 2018. **2018**: p. 9089285.
59. Moisseiev, J., et al., *Long-term study of the prevalence of capsular opacification following extracapsular cataract extraction.* J Cataract Refract Surg, 1989. **15**(5): p. 531-3.

60. Bélair, M.L., et al., *Incidence of cystoid macular edema after cataract surgery in patients with and without uveitis using optical coherence tomography.* Am J Ophthalmol, 2009. **148**(1): p. 128-35.e2.
61. Almenara, C., et al., *Comparison of posterior capsule opacification between Clareon CNA0T0 and Tecnis ZCB00 intraocular lenses.* Eur J Ophthalmol, 2021: p. 1120672121991718.
62. Dowler, J.G., P.G. Hykin, and A.M. Hamilton, *Phacoemulsification versus extracapsular cataract extraction in patients with diabetes.* Ophthalmology, 2000. **107**(3): p. 457-62.
63. Ram, J., et al., *Effect of in-the-bag intraocular lens fixation on the prevention of posterior capsule opacification.* J Cataract Refract Surg, 2001. **27**(7): p. 1039-46.
64. Oshika, T., et al., *Two year clinical study of a soft acrylic intraocular lens.* J Cataract Refract Surg, 1996. **22**(1): p. 104-9.
65. Sundelin, K., et al., *Posterior capsule opacification with AcrySof and poly(methyl methacrylate) intraocular lenses. Comparative study with a 3-year follow-up.* J Cataract Refract Surg, 2001. **27**(10): p. 1586-90.
66. Bender, L.E., et al., *Predicting posterior capsule opacification: value of early retroillumination imaging.* J Cataract Refract Surg, 2003. **29**(3): p. 526-31.
67. Shah, A.R., M.R. Praveen, and A.R. Vasavada, *Posterior capsule opacification after extra capsular cataract extraction in Indian rural population: foldable acrylic vs poly (methyl-methacrylate) intraocular lenses a randomized clinical trial.* Eye (Lond), 2008. **22**(7): p. 889-94.
68. Hancox, J., et al., *Fellow-eye comparison of posterior capsule opacification rates after implantation of 1CU accommodating and AcrySof MA30 monofocal intraocular lenses.* J Cataract Refract Surg, 2007. **33**(3): p. 413-7.
69. Nanavaty, M.A., et al., *Fellow-eye comparison of posterior capsule opacification between 2 aspheric microincision intraocular lenses.* J Cataract Refract Surg, 2013. **39**(5): p. 705-11.
70. Hillenmayer, A., et al., *Evaluation of posterior capsule opacification of the Alcon Clareon IOL vs the Alcon Acrysof IOL using a human capsular bag model.* BMC Ophthalmol, 2020. **20**(1): p. 77.
71. Sharma, P. and M. Panwar, *Trypan blue injection into the capsular bag during phacoemulsification: initial postoperative posterior capsule opacification results.* J Cataract Refract Surg, 2013. **39**(5): p. 699-704.