On cataract surgery in uveitis –

management and outcome in pediatric and adult patients

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ABSTRACT

Aims: To evaluate surgical procedures and outcomes in cataract surgery in adults and children with uveitis. To compare the results of implantation of two different intraocular lenses (IOLs).

Methods: Retrospective reviews of medical charts of children and adults with cataract and uveitis were performed (papers I and II). A randomized controlled trial to compare a hydrophobic and a hydrophilic IOL was conducted (paper III). Data from the National Cataract Register was analyzed (paper IV).

Results: *Paper I*: In total, 21 pediatric eyes, treated with phacoemulsification, primary IOL implantation and pars plana vitrectomy, were included. Best corrected visual acuity (BCVA) improved in all except one eye. Glaucoma was the most common postoperative complication. *Paper II*: Altogether 58 uveitic eyes were included. Mechanical pupil dilation was more commonly needed in eyes with uveitis. Poor improvement in visual acuity was related to posterior segment abnormalities. *Paper III*: The study included 52 eyes with and 38 eyes without uveitis. Mechanical pupil dilation was more frequently used in eyes with uveitis. Flare measurements were higher in patients with uveitis, but no significant difference in flare or cystoid macular edema (CME) postoperatively related to IOL type was seen. *Paper IV*: Core registrations included 719 eyes with uveitis; 52 uveitic eyes were included in registrations of surgical outcome. Difficulties, e.g., with mechanical pupil dilation, capsular staining, and hooks at the rhexis margin, were more common in eyes with uveitis as well as posterior capsule rupture/zonulolysis. Oral steroids as well as subconjunctival steroids were more frequently used in uveitis. Improvement in BCVA was slightly better in uveitic eyes.

Conclusion: This thesis demonstrates that challenges remain in cataract surgery in uveitis. Despite more challenging surgery and intraoperative difficulties, patients with uveitis showed satisfactory improvement in visual acuity. We did not find support for either hydrophilic or hydrophobic IOLs being advantageous over the other. Children with uveitis constitute a group with particular difficulties.

Keywords: Cataract, uveitis, intraocular lens, register

SAMMANFATTNING PÅ SVENSKA

Grå starr (katarakt) det vill säga en grumling av ögats lins, är en av de vanligaste ögonsjukdomarna i världen. Vanligen är grå starr kopplat till hög ålder men det finns riskfaktorer som kan leda till att man får grå starr i yngre år. Behandlingen består av en operation där man tar bort den grumliga linsen som vanligen ersätts med en konstgjord lins i plast. Grå starroperation är den vanligaste operationen i världen och betraktas som ett rutiningrepp även om det som vid all kirurgi föreligger vissa risker. Några av de vanligast förekommande komplikationerna efter operation är att man får efterstarr, en svullnad i gula fläcken eller högt ögontryck.

Uvea är ett samlingsbegrepp för ögats regnbågshinna (iris), strålkropp (ciliarkropp) och åderhinna (choroidea). Uveit är en inflammation i någon av dessa delar. Uveit kan vara rent inflammatorisk, vilket är vanligast i västvärlden. Den kan också orsakas av en infektion, vilket är vanligare i utvecklingsländer. I vissa fall är uveiter kopplade till en bakomliggande reumatisk sjukdom. Behandlingen består oftast av ögondroppar som innehåller kortison. Vid otillräcklig effekt eller vid biverkningar av lokalbehandlingen kan systemisk behandling med kortison eller immunmodulerande och biologiska läkemedel bli aktuella. Både på grund av inflammationen i sig och behandlingen med kortison har personer med uveit en hög risk för att få problem med synen i form av exempelvis svullnad i gula fläcken, grön starr och grå starr.

I avhandlingen undersöker vi vad som är utmärkande för patienter med uveit och grå starr och hur det går för dem vid en grå starroperation. De två första delarbetena är retrospektiva studier där vi har undersökt resultaten hos vuxna och barn på vår klinik. Det tredje delarbetet är en prospektiv studie där vi jämfört resultaten för två olika plastlinser som slumpmässigt fördelats till studiedeltagarna. Det fjärde arbetet är en registerbaserad studie.

Resultaten visade att grå starroperation hos patienter med uveit innebär större svårigheter än operation vid åldersrelaterad grå starr. Vi kunde också se att komplikationer som högt ögontryck, svullnad i gula fläcken och efterstarr var relativt vanligt efter operation hos dem med uveit. Resultaten på vår klinik liknar de vi kunde se på nationell nivå. Barn med grå starr och uveit var den grupp som uppvisade störst risk för kirurgiska svårigheter och komplikationer. Trots större svårigheter vid operation och ökad risk för komplikationer uppvisade de flesta en bra synskärpa efter operationen.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. **Pålsson S,** Nyström A, Sjödell L, Jakobsson G, Byhr E, Andersson Grönlund M, Zetterberg M. Combined phacoemulsification, primary intraocular lens implantation, and pars plana vitrectomy in children with uveitis. *Ocul Immunol Inflamm. 2015 Apr;23(2): 144–151.*

II. **Pålsson S,** Andersson Grönlund M, Skiljic D, Zetterberg M. Phacoemulsification with primary implantation of an intraocular lens in patients with uveitis. *Clin Ophthalmol. 2017 Aug 22;11:1549–1555.*

III. **Pålsson S**, Schuborg C, Sterner B, Andersson Grönlund M, Zetterberg M. Hydrophobic and hydrophilic IOLs in patients with uveitis – a randomised controlled trial. *Submitted manuscript.*

IV. **Pålsson S**, Pivodic A, Andersson Grönlund M, Lundström M, Viberg A, Behndig A, Zetterberg M. Cataract surgery in patients with uveitis: Data from the Swedish National Cataract Register. *Submitted manuscript.*

Permissions for publication were obtained for pictures of patients, other photos/illustrations and publications where applicable.

CONTENT

ABBREVIATIONS

ACO	anterior capsule opacification
aOR	adjusted odds ratio
AU	anterior uveitis
BAB	blood–aqueous barrier
BCVA	best corrected visual acuity
BIL	bag-in-the-lens
BRB	blood–retinal barrier
CFT	central foveal thickness
CI	confidence interval
CME	cystoid macular edema
dec	decimal
ECCE	extracapsular cataract extraction
EDTA	ethylenediamine tetra-acetic acid
FHU	Fuchs heterochromic uveitis
GC	glucocorticoid
GEE	generalized estimating equation
GSH	glutathione
HLA	human leukocyte antigen
ICCE	intracapsular cataract extraction
IFN	interferon

IL	interleukin
IMT	immunomodulatory therapy
IOL	intraocular lens
IOP	intraocular pressure
IQR	interquartile range
JIA	juvenile idiopathic arthritis
LEC	lens epithelial cell
LOCS	Lens Opacities Classification System
logMAR	logarithm of the minimal angle of resolution
MTX	methotrexate
NCR	National Cataract Register
Nd:YAG	neodymium:yttrium–aluminum–garnet
NSAID	non-steroidal anti-inflammatory drug
OCT	optical coherence tomography
OH	ocular hypertension
PCO	posterior capsule opacification
PMMA	polymethyl methacrylate
PPV	pars plana vitrectomy
PSC	posterior subcapsular cataract
ROS	reactive oxygen species
SD	standard deviation

SLE	systemic lupus erythematosus
SUN	Standardization of Uveitis Nomenclature
Th1	T helper cell type 1
TINU	Tubulointerstitial nephritis and uveitis
TNF	tumor necrosis factor
VA	visual acuity
VAO	visual axis opacification

DEFINITIONS IN SHORT

Amblyopia	Reduced visual acuity due to impaired development of visual acuity.
BCVA	Best achievable visual acuity, which is tested with glasses or contact lenses.
Couching	Procedure used in the past to treat cataract, where the crystalline lens was pushed into the vitreous cavity with a sharp object.
Flare meter	Instrument that measures aqueous flare in the anterior chamber using laser light.
IOL	Artificial lens that is placed in the capsular bag to replace the natural crystalline lens and provide accommodative function.
LOCS	Scheme to systematically grade the degree of cataract.

1 INTRODUCTION

1.1 BASIC ANATOMY

The human lens contributes to the eye's refractive power and helps to focus light on the retina. It is composed of a nucleus and cortex, which are surrounded by a capsule suspended by zonular fibers attaching the lens to the ciliary body. The lens tissue consists of collagen fibers and proteins that are organized in a regular pattern to maintain lens clarity. Growth of the lens continues throughout life though its diameter reaches its maximum, around 9 mm, in adolescence.

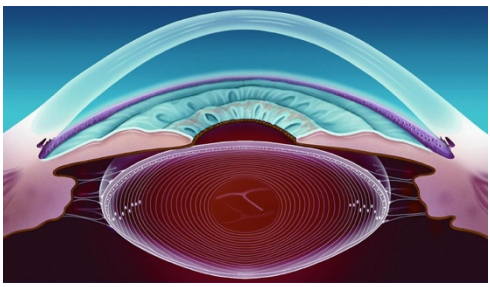

Figure 1. The anterior chamber. Used with permission under Creative Commons license.

The iris, the ciliary body, and the choroid make up the uveal tract and consist of pigmented, vascularized tissue. The iris gives the eye its color and regulates the inlet of light through variation of the pupil size. It is connected to the ciliary body which produces aqueous humor. The choroid is a highly vascularized tissue situated between the retina and the sclera. It supplies the outer retina with blood, helps to regulate the temperature of the eye, and plays a part in the uveoscleral drainage of aqueous humor (Nickla & Wallman 2010).

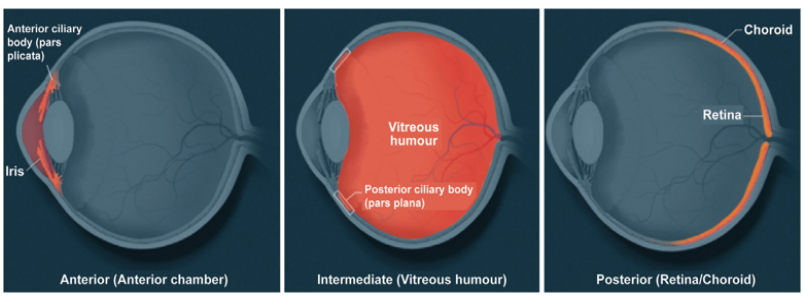

Figure 2. The parts constituting the uvea.

1.2 CATARACT

The word “cataract” originates from the Latin word for waterfall and means clouding of the crystalline lens in the eye. With over 15 million individuals affected globally, cataract is the leading cause of blindness worldwide (Global Burden of Disease Study 2021). The pathophysiology of cataract is not fully understood. However, growing lens fibers that gradually get compressed, in combination with age-related changes in lens proteins, at least in part due to oxidative actions, are believed to play a role in the disruption of the regular organization of the lens, thereby leading to a loss of lens clarity, i.e., cataract formation (Truscott 2005; Wolf et al. 2005; Liu et al. 2017).

Depending on the localization, cataracts are divided into three main types: cortical, nuclear, and posterior subcapsular cataract (PSC). Often, more than one type of cataract is present, a so-called “mixed type cataract.” Posterior subcapsular cataract is more commonly seen in younger individuals developing cataract. It often has a more rapid progress than the other types of cataracts and is associated with steroid use and uveitis.

With the loss of lens clarity, visual acuity gradually deteriorates, and in its end stage, cataract causes blindness. Aging is the most common cause of cataract. However, there are several risk factors that may induce cataract at younger age, such as the use of steroids, as previously mentioned, trauma, and heredity. In its early stages, symptoms may be mild, with increased myopia and glare (Asbell et al. 2005). As the cataract becomes denser, visual acuity (VA) decreases and treatment is through surgical removal of the clouded lens. Today, the lens is usually replaced with an artificial one.

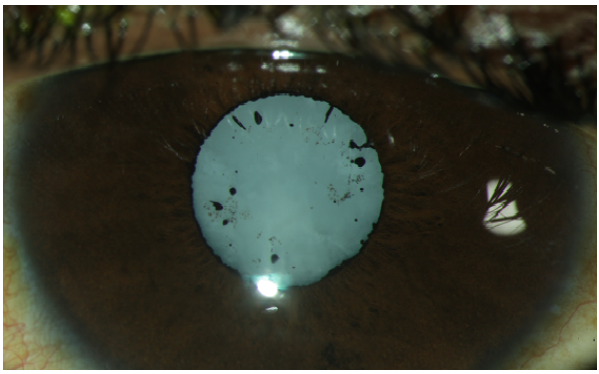

Figure 3. Cataract.

1.3 CATARACT SURGERY

The following quote describes cataract surgery as performed in the past, and illustrates the progress we have made in the treatment of the disease.

> *At the 1924 Academy meeting, A. Greenwood recommended that the term cataract should be avoided as much as possible with patients: "It strikes terror into the soul of some of the timid ones." Cataract often implied impending blindness and a dreadful surgery with uncertain end results, so it is not surprising that many ophthalmologists recommended nonsurgical treatment to suppress the advancement of cataracts.* (Jaffe 1996).

The first procedure to remove cataract was described as early as 800 BC and was known as "couching" (Ashwin et al. 2009). Couching involved a sharp needle that was used to push the crystalline lens to the posterior part of the eye. The procedure was probably mainly performed in dense, blinding cataracts. Hence, the immediate visual improvement was sometimes considerable. However, the procedure was associated with severe complications such as infections and hemorrhages and in the majority of cases, only a brief transitory improvement was achieved.

Figure 4. Couching for cataract was first performed in India. Used with permission under Creative Commons license.

In 1747, extracapsular cataract extraction (ECCE) was performed for the first time, a procedure sometimes referred to as the predecessor of modern cataract surgery (Davis 2016). The surgeon, French ophthalmologist Jacques Daviel, performed incisions over 10 mm long, whereafter the lens capsule was punctured and the lens extracted. Even though this procedure was more successful than couching, it was still associated with a high level of risk. Intracapsular cataract extraction (ICCE) was developed during the same time period. It was initially considered more difficult and riskier than ECCE and its use was limited. However, during the early twentieth century, it regained popularity for a period of time (Jaffe 1996). One clear advantage with ICCE

was the absence of development of secondary cataract, i.e., posterior capsule opacification (PCO).

In 1967, the technique of phacoemulsification was introduced by Charles David Kelman (Pandey et al. 2004). It is said that he was inspired to develop the ultrasonic device by a dentist using an ultrasound probe to remove plaque from his teeth. With the help of this ultrasonic device, the lens could be emulsified and aspirated instead of being removed in one piece as in ECCE. This allowed for considerably smaller incisions while maintaining a stable anterior chamber (Linebarger et al. 1999). Together with the introduction of intraocular lenses (IOLs), phacoemulsification paved the way for modern small incision cataract surgery with implantation of IOLs.

Today, cataract surgery is the most common surgical procedure in the world. In Sweden, 115 746 surgeries were performed in 2020 alone (Behndig et al. 2021). In the Western world, cataract surgery is, in most cases, considered a routine procedure with high safety and good results. But in many parts of the world, cataract is one of the most common causes of blindness (Lee & Afshari 2017) and older methods such as couching are still used in some countries (Isawumi et al. 2013).

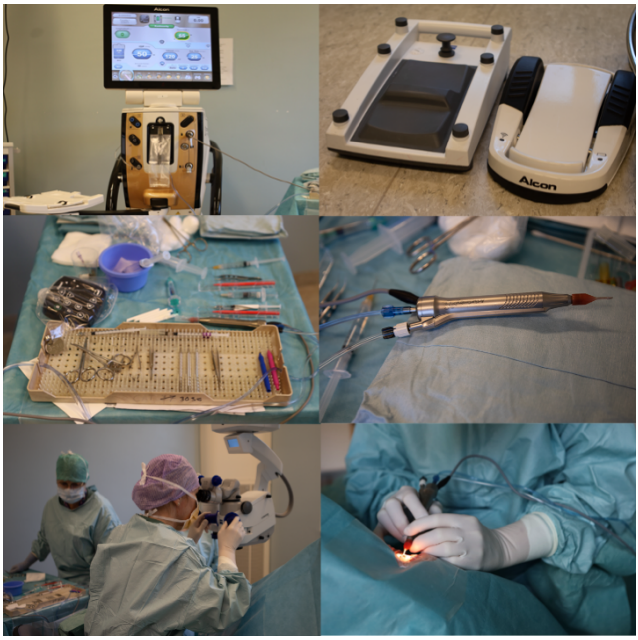

Figure 5. The procedures in modern cataract surgery at the Department of Ophthalmology, Sahlgrenska University Hospital, Mölndal, Sweden, 2022.

1.4 INTRAOCULAR LENSES

Until 1949, patients undergoing cataract surgery were left aphakic, i.e., without a replacement for the removed crystalline lens (Davis 2016). They needed high powered glasses to achieve clear visual acuity; without them, visual acuity was poor. In 1949, Sir Harold Ridley introduced artificial IOLs, initially using polymethyl methacrylate (PMMA, plexiglass) compounds (Ridley 2003). Surgery was performed without a microscope, with light provided by a nurse holding a flashlight (Kohnen 2009). Materials have since then undergone extensive improvements and development is still ongoing.

Today, acrylic hydrophobic or hydrophilic plastics are commonly used. Compared to the initial plexiglass IOLs, they are more flexible and foldable, which enables implantation through small incisions using injectors. Preloaded injectors are now available, reducing surgical time. In addition to the mechanical properties of the IOL material, the tissue response, i.e., the biocompatibility, has been investigated. Biocompatibility can be assessed in terms of uveal and capsular biocompatibility. "Uveal biocompatibility" refers to the inflammatory response and "capsular biocompatibility" concerns the response of lens epithelial cell (LEC) outgrowth and PCO formation. Some previous studies have shown superior uveal biocompatibility with hydrophilic IOLs while hydrophobic IOLs have shown better capsular biocompatibility (Abela-Formanek et al. 2002). In addition to the properties of the IOL materials, attention has also been focused on the IOL design. For example, sharp IOL edges have been shown to reduce the incidence of PCO (Findl et al. 2010).

Since the introduction of IOLs, the lens optics have been monofocal. That is, a single point of focus is obtained, yielding best visual acuity at a specific distance. The need for spectacles for either reading or distance remains. As the surgical results have improved with decreasing intraoperative and postoperative complications, cataract surgery is today considered a routine procedure. With these improvements, increasing interest is directed to methods of improving the refractive capacity of IOLs and reducing the need for glasses postoperatively. Premium IOLs correcting for astigmatism (toric IOLs), as well as IOLs with several points of focus (multifocal IOLs) and accommodating and extended depth of focus IOLs are now available. However, these special IOLs often have the disadvantage of reduced contrast sensitivity and disturbing symptoms such as halos, glare, and photopsia (Breyer et al. 2017).

a. *b.*

Figure 6. The two different types of intraocular lenses (IOLs) used in paper III. a. hydrophilic b. hydrophobic.

1.5 CATARACT SURGERY COMPLICATIONS

Even though great advances have been achieved in cataract surgery since the first surgery by couching, cataract surgery is not without complications. Posterior capsule opacification, one of the most common complications after surgery, is caused by remaining lens epithelial cells that grow on the posterior capsule. As these cells continue to grow, a membrane develops. Once the membrane covers the center of the optic zone, visual acuity deteriorates. Today, PCO can quite easily be treated with neodymium:yttrium–aluminum–garnet (Nd:YAG) laser. An opening in the posterior capsule is created with the laser, allowing for light to pass. The procedure is considered a minor intervention but is not without risks. Cystoid macular edema (CME), IOL cracks, intraocular pressure (IOP) spikes, inflammatory reactions, and retinal detachment have been described as complications of Nd:YAG laser treatment (Karahan et al. 2014).

Pseudophakic CME, also called "Irvine–Gass syndrome," is another postoperative complication not uncommonly seen. Even with uneventful surgery, the intraocular tissue is compromised and an inflammatory reaction is initiated. Released inflammatory mediators, such as prostaglandins and cytokines, are believed to play a major part in causing breakdown of the blood–retinal barrier (BRB), with subsequent leakage through the retinal vessels. Accumulation of fluids in the macula then causes intra- or subretinal edema, which may lead to a decrease in visual acuity depending on localization and degree of edema. The incidence of CME varies widely depending on

diagnostic criteria and risk factors. In a report by (Chu et al. 2016), CME was seen in 1.17–4.04% of cases depending on risk factors, with the highest incidence seen in patients with diabetes. Once CME is confirmed it is often successfully treated with topical non-steroidal anti-inflammatory drugs (NSAIDs) in the form of eye drops. However, in some cases, the edema is refractive to treatment and becomes chronic.

Furthermore, the viscoelastic device, used at surgery to maintain the anterior chamber, may, if incompletely removed, lead to an early rise in intraocular pressure (IOP) postoperatively. In addition, postoperative treatment with topical steroids can induce raised IOP in steroid responsive patients (Chan et al. 2010). Other causes of a postoperative rise in IOP include pigment dispersion, retained lens material, and postoperative inflammation.

Improperly treated postoperative inflammation increases the risk of postoperative pain and photophobia as well as risk of complications such as raised IOP, PCO, CME, and corneal edema (Aptel et al. 2017). Prophylactic anti-inflammatory treatment is commonly given to reduce inflammation and prevent complications after surgery. Topical steroids and/or NSAID drops are most frequently used. Sometimes, when a more pronounced inflammatory reaction is expected, oral or subconjunctival steroids are administered in addition to topical treatment. Subconjunctival steroids can also be used for those with difficulties managing the eyedrops on their own.

The inflammatory reaction after cataract surgery is usually quite discrete and difficult to assess by slit lamp examination. However, (De Maria et al. 2020) has shown an increase in the anterior chamber flare, measured with a laser flare meter, more than 1 month postoperatively. The increase was associated with increased central macular thickness and CME. Postoperative inflammation is attributed to damage of the blood–aqueous barrier (BAB). The inflammation peaks within the first days after surgery and then decreases over the following 2–3 weeks (Taravati et al. 2012). An increased risk for an extended inflammatory reaction is seen in some cases, such as in diabetic eyes, complicated surgery, or young age at surgery. Uveitis also exacerbates the risk of developing an increased and prolonged inflammation. This can be attributed to preexisting BAB damage. Additionally, this group of patients frequently presents with cataract at a younger age and surgery is often more difficult with increased surgical trauma. In this setting, preoperative inflammatory control as well as increased perioperative anti-inflammatory treatment are considered to lower the risk of pronounced inflammation and its associated risks.

1.6 NATIONAL CATARACT REGISTER

One of the oldest known health registers is the leprosy register in Norway, which dates back 200 years. The first Swedish register was an orthopedic register focused on knee surgery, introduced in 1975. Since the 1970s, a number of registers have been started and today there are over 100 national quality registers in Sweden. The purposes of quality registers are to evaluate health care interventions, improve knowledge, aid research, and ultimately achieve improvements and a more equitable health care.

Every person in the Swedish Population Register has a unique personal identification number enabling linkage of information from different registers. These identification numbers, enable the establishment of registers and, therefore, register-based research.

There are four national ophthalmological registers in Sweden: the National Quality Registry for Corneal Transplant, the National Quality Registry for Macula, the National Quality Registry for Rehabilitation for Visual Impairment, and the National Cataract Register (NCR). Furtherly there are registers for pediatric cataract, retinopathy of prematurity and juvenile idiopathic arthritis. In 2005, a national health care guarantee was introduced, in terms of which an appointment in specialized health care was to be offered to a patient within 3 months of referral. The NCR was started in 1992 and initially, its main focus was to explore the consequences of the introduced waiting time guarantee. Later the register has expanded with a wider area of interest.

Today, the NCR consists of a core register with variables covering patient characteristics, waiting time to surgery, ocular comorbidity, visual acuity, and surgical details such as IOL used, difficulties and complications at surgery, and postoperative anti-inflammatory treatment. Outcome registrations were later added (NCR outcome register) with follow-up of visual and refractive outcome as well as registrations of endophthalmitis, i.e., infection of the inner part of the eye. Uveitis was added to the core registrations in 2018 as a specific comorbidity.

The aims and goals of the NCR are to ensure surgical quality. The registrations make it possible to compare results in relation to age, gender, region, and surgical procedures, thereby promoting quality improvement. Cataract surgery is the most common surgical procedure in Sweden. In 2020, 95% of all surgeries performed in Sweden, were registered in the NCR. The large volumes

of data collected facilitate research of rare conditions for which prospective studies are often difficult and time-consuming.

1.7 UVEITIS

Uveitis is a sight-threatening, heterogenic group of inflammatory conditions affecting the uveal tissue of the eye, i.e., the iris, the ciliary body, and the choroid. With a prevalence of 58.0–114.5 per 100 000 persons and an incidence of 17.4–52.4 cases per 100 000 person-years (Tomkins-Netzer et al. 2014) it is rather rare. Although uncommon, it has been shown to account for 2.8–10% of all cases of blindness (Read 2006).

There are infectious as well as non-infectious variants and several types of uveitis are associated with systemic inflammatory diseases such as ankylosing spondylitis, juvenile idiopathic arthritis (JIA), and multiple sclerosis. However, despite thorough diagnosis, idiopathic uveitis, where the etiology remains unknown, constitutes the majority of cases. This is particularly true for anterior and intermediate uveitis (Chang & Wakefield 2002; Tsirouki et al. 2018; Abd El Latif et al. 2020).

Etiology also differs significantly between developed and developing countries, with infectious causes of uveitis accounting for 30–50% of cases in developing countries (Tsirouki et al. 2018) compared to 13.3% reported in an Australian cohort (Hart et al. 2019) and 9.0% in the US (Thorne et al. 2016). Toxoplasmosis and herpes simplex or varicella zoster are the main infectious causes of uveitis in developed countries, whereas the picture is more varied in developing countries. Here, infectious causes include toxoplasmosis, tuberculosis, onchocerciasis, cysticercosis, leprosy, herpes simplex/varicella zoster, leptospirosis, and other parasitic diseases with geographical and age-related variations in prevalence (Tsirouki et al. 2018).

To facilitate the comparison of research findings in uveitis research, the Standardization of Uveitis Nomenclature (SUN) group presented standardized criteria for uveitis classification in 2005 (Trusko et al. 2013). The classification is based on primary site of inflammation, i.e., anterior, intermediate, posterior, or panuveitis, with specifications for onset (sudden or insidious), duration (limited or persistent), and course (acute, recurrent, or chronic). Scales for grading anterior chamber cells and flare, as well as definition of activity (inactive, worsening activity, improved activity, and remission) are also included.

The complications associated with uveitis depend on the type of uveitic entity and the course of the inflammation. For example, Fuchs heterochromic uveitis (FHU) is one of the most common etiologies associated with cataract, ocular hypertension (OH), and glaucoma. Intermediate uveitis, on the other hand, is the most common diagnosis leading to CME. Cataract, CME, and glaucoma are the most common complications generally seen with uveitis. However, subretinal fibrosis, retinal detachment, band keratopathy, retinal neovascularization, and corneal decompensation have also been described following uveitis (Jones 2015). In addition, steroid therapy and other immunomodulatory therapy are associated with ocular as well as systemic drug-related complications such as cataract, glaucoma, diabetes, and a compromised immune system.

Treatment is mainly focused on reducing inflammation, but, depending on etiology, antibiotics or antivirals may be needed.

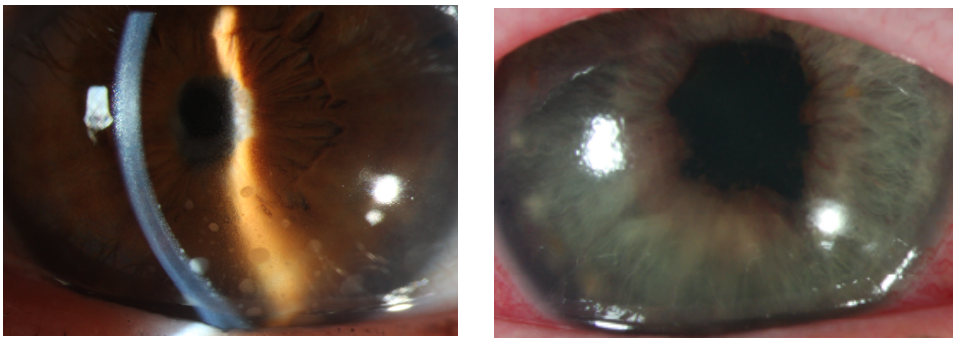

Figure 7. Eyes with uveitis showing synechiae and precipitation.

1.8 UVEITIS IN CHILDREN

When it comes to children with uveitis there are certain features that need to be particularly considered. For instance, pediatric uveitis exhibits a different spectrum of underlying diagnoses compared to adult uveitis, with JIA being one of the most common specific causes of pediatric uveitis. Also, uveitis is the most commonly seen extra-articular manifestation of JIA. Often children present with discrete symptoms, which may delay the diagnosis. Moreover, slit lamp examinations may be inadequate due to lack of cooperation and the risk of inhibited visual development (amblyopia) must be taken into account (Levy-Clarke et al. 2005).

Although symptoms may be discrete at presentation the inflammatory reaction is often more forceful with younger age and presentation at low age is consequently associated with many years of disease and treatment. In addition, uveitis is often bilateral and chronic and childhood uveitis is often associated with a considerable risk of developing sight-threatening complications such as cataract, band keratopathy, glaucoma, and macular edema (Dana et al. 1997; Papadopoulou et al. 2017; Chan et al. 2018). Chan et al. report 83% of cases showing at least one ocular complication at 3 years after presentation.

The advances in IMT have improved our ability to achieve inflammatory control. Ensuring sufficient treatment with inflammatory control can prevent severe complications and visual deterioration (Angeles-Han et al. 2015; Wennink et al. 2022). In spite of advances, severe visual loss has been reported in 25–33% of cases (Cunningham 2000; Levy-Clarke et al. 2005), with cataract being one of the most common causes (Thorne et al. 2007; Cann et al. 2018), occurring in 46% of children with uveitis in a recent report by (Kumar et al. 2021). In addition to eye–related morbidity, arthritic disease needs assessment and the involvement of a multidisciplinary team is considered crucial to achieve optimal results.

1.9 COMPLICATIONS OF UVEITIS

Intraocular hypertension and glaucoma are commonly seen in patients with uveitis and constitute one of the major causes of visual loss. There are several reasons why uveitis patients are at higher risk of developing open angle as well as closed angle glaucoma. Adhesion between the iris and the lens or the trabecular meshwork may occur in uveitis due to the inflammation. Posterior synechiae, i.e., adhesions between the iris and the anterior lens, can lead to acute angle closure and pupillary block, causing an immediate rise in IOP also known as “iris bombée.” Anterior synechiae, i.e., adhesions between the iris

and the trabecular meshwork, on the other hand, obstruct the trabecular meshwork and may thereby cause a chronic form of angle closure glaucoma. Open angle glaucoma represents a more complex pathogenesis which is still incompletely understood. Inflammatory material penetrating and obstructing the trabecular meshwork, as well as inflammatory actions on the trabecular meshwork, causing trabeculitis and a swelling of the trabecular pores, reducing the diameter and thereby reducing outflow of aqueous humor, are mechanisms described (Baneke et al. 2016; Kesav et al. 2020).

Cataract is one of the most common visually disabling complications of uveitis and has been reported to occur in up to 40% of adult patients (Chu et al. 2017) and in up to 64% of children with JIA related uveitis (Kump et al. 2006). Cataract develops as a consequence of the inflammation itself and the treatment with steroids. The association between steroids and cataracts has been known since the early 1960s (Black et al. 1960). Though several papers have investigated the relationship between steroids and cataracts, the pathophysiological mechanisms by which steroids cause cataracts are incompletely understood and most likely multifactorial. The existence and role of glucocorticoid receptor pathways, as well as receptor–independent pathways, have been discussed (Petersen et al. 2008), as has the role of ocular growth factor imbalance, proposed as one factor involved in cataractogenesis (Jobling & Augusteyn 2002). Abnormal proliferation and differentiation of LECs, possibly influenced by indirect effects of steroids on the metabolic environment, have been described in PSC. Effects of steroids on growth factors, and on glucocorticoid receptors in other cells, are known to change cell actions, which is why these mechanisms seem likely to occur in the eye as well. However, it is unknown whether these effects are transferable to the ocular environment (James 2007).

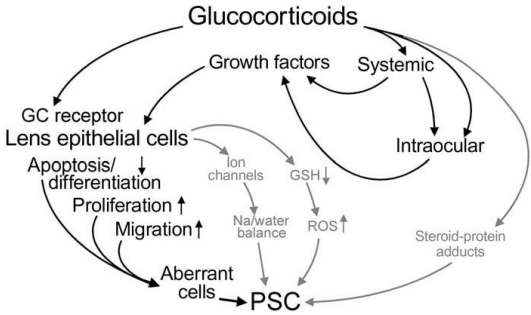

Figure 8. Pathophysiological mechanisms in cataract caused by steroids.
GC = glucocorticoid; GSH = glutathione; PCS = posterior subcapsular cataract; ROS = reactive oxygen species.

Another common cause of visual loss in uveitis is CME. T cell–derived cytokines such as interferon-γ (IFN-γ), interleukin (IL) 2, IL 10, and tumor necrosis factor (TNF)-α are elevated and considered to function as major inflammatory mediators in uveitis. With T cells entering the eye, compromised BRB has been shown, indicating that T cell-derived cytokines are involved in the process. As long as the BRB remains compromised a leakage of fluid into the retina is possible, causing intraretinal edema (Okhravi & Lightman 2003) and, consequently, visual deterioration. Diagnosis is usually easily confirmed with optical coherence tomography (OCT), in eyes with clear media.

1.10 INFLAMMATORY TREATMENT

Topical steroids are generally the first choice of treatment in uveitis. When topical treatment is insufficient, oral steroids are commonly added in adults. However, oral steroids, when used in higher doses and over longer periods, are associated with several serious adverse advents, systemic as well as ocular. For example, there are risks of developing diabetes, osteoporosis, and hypertension. Development of cataract and glaucoma is also well known in patients on long-term treatment with steroids. During the last decades, linked to increased knowledge of the immune system, progress has been made in IMT and development of biological agents, which offer a way of treating inflammation and reducing the use of steroids (Rosenbaum et al. 2019). Antimetabolites, e.g., methotrexate (MTX), mycophenolate mofetil, and azathioprine, as well as calcineurin inhibitors, cyclosporine, and, less commonly, alkylating agents such as cyclophosphamide are considered as conventional IMT and are usually used as a first line of choice (Thomas 2019). So far, in most cases, biological agents come into consideration primarily when the effect of conventional IMT is insufficient. There are several biological agents targeting different inflammatory mediators primarily. Treatment with biological agents in the setting of uveitis is not as well explored as, e.g., in rheumatology. Although knowledge of inflammatory mediators in uveitis is incomplete, the cytokines IL 2 and TNF-α and T helper cell type 1 (Th1) mediators IFN-γ and IL 12 are believed to be major culprits, with increased levels found in eyes with active uveitis. This was described by Levy-Clarke et al. whose review found support for using anti-TNF therapies in uveitis of certain etiology (Levy-Clarke et al. 2014).

1.11 CATARACT SURGERY IN UVEITIS

While surgery in age-related cataract generally exhibits relatively few complications there are conditions that increase the risk of adverse advents during and after surgery. Uveitis represents such a condition, with increased risks of postoperative complications related to inflammation as well as structural changes, rendering surgery more difficult. Synechiae causing small pupils, abnormal vascularization with increased risk of hemorrhage, and band keratopathy decreasing visual acuity are illustrative examples as to why surgery in uveitis poses difficulties that need to be managed (Moshirfar et al. 2020). Difficult surgery additionally increases the risk of severe inflammatory reaction postoperatively and its related consequences, such as CME, increased IOP, and hypotony.

For a long time, cataract surgery in uveitis was considered as associated with poor results and in most cases, surgery was delayed or refrained from. During the times of ECCE, severe inflammatory reactions were commonly seen postoperatively, due to retained lens material and/or vitreous loss. As a result of the inflammation, many patients suffered from complications such as hypotony, pupillary membrane formation, and macular edema, rendering poor results. In 1978, Diamond and Kaplan presented encouraging results with an approach combining lensectomy and vitrectomy (Diamond & Kaplan 1978). The first report of posterior lens implantation following ECCE was presented by Jones, who compared results with and without IOL implantation in patients with FHU (Jones 1990). He concluded that good results were achievable with IOL implantation. However, complications such as severe uveitis, glaucoma, and vitreous opacification were more common in patients with IOL and careful selection of cases was advised.

Along with improvements in surgical technique, IOL materials, and means to control inflammation, results for uveitic patients undergoing cataract surgery have improved. Today, satisfactory results are obtained in most adult cases undergoing phacoemulsification and primary IOL implantation after meticulous inflammatory control (Mehta et al. 2014). Although IOL implantation in children has remained a controversial issue, a recent review has shown encouraging results achieved with IOL implantation in children with uveitis (Schmidt et al. 2021).

Even though great successes have been achieved in cataract surgery, surgery in uveitic eyes needs more careful planning to achieve inflammatory control before as well as after surgery to prevent complications. However, evidence of optimal surgical techniques and anti-inflammatory treatment is still lacking

and routines vary between centers. Also, children with cataract and uveitis represent a group where complications are still commonly seen and further improvements are desirable.

2 AIM

2.1 GENERAL AIMS

The overall aim of this thesis was to evaluate cataract surgery outcomes in adults and children with uveitis.

2.2 SPECIFIC AIMS

To evaluate cataract surgery with primary IOL implantation combined with pars plana vitrectomy (PPV) in children with uveitis.

To evaluate cataract surgery in adults with uveitis at Sahlgrenska University Hospital, Gothenburg, Sweden, as well as in a national cohort.

To compare the results of implantation of a hydrophobic versus a hydrophilic IOL in adult patients with and without uveitis.

3 PATIENTS AND METHODS

3.1 PAPER I - II

In papers I and II, retrospective reviews of medical charts were performed.

In paper I, patients with uveitis aged ≤16 years who underwent combined phacoemulsification, primary IOL implantation, and PPV in 2002–2011 were included. Nineteen children who underwent the combined procedure were identified. Written or oral consent was obtained. In two cases, the patients could not be reached and were therefore excluded. A further two cases with uveitis and cataract were identified during the study period. However, in one of these children presenting with very severe uveitis, IOL implantation was considered contraindicated; the second of these two children presented with a mild idiopathic anterior uveitis and PPV was considered unjustified. Neither of these two children were eligible for the study. In total, 17 children (21 eyes) were included.

Three months of minimal inflammation was confirmed before surgery. Phacoemulsification and IOL implantation were performed by the same surgeon (A.N.) and PPV was performed by either one of two surgeons (E.B. or G.J.).

In paper II, patients with all etiologies of uveitis and cataract between January 2005 and December 2009 were included. Patients aged ≤16 years and patients undergoing a combined procedure were excluded. If both eyes had surgery during the named period, only the right eye was selected. Eyes without uveitis undergoing surgery on the same day by the same surgeon were selected as controls. Standard clear cornea cataract surgery with IOL implantation was performed.

In both paper I and II, a retrospective review of the medical charts was performed. Demographics, sex, age at surgery, uveitic etiology, presence of coexisting rheumatic disease, laboratory evaluation, ocular comorbidity, best corrected visual acuity (BCVA), surgical difficulties, and complications, as well as perioperative anti-inflammatory treatment, were analyzed and classification according to SUN criteria was performed retrospectively. Snellen charts were used to test BCVA. In paper I, ocular status at 4 and 6 months, as well as postoperative complications until last follow-up, was noted. In paper II, charts were analyzed from uveitic debut until last follow-up. Where

postoperative controls were performed in other clinics, the medical charts were obtained from the home clinic.

3.2 PAPER III

The study reported in paper III was a prospective randomized controlled trial evaluating a hydrophobic versus a hydrophilic IOL in patients with and without uveitis. Patients with uveitis who were eligible for cataract surgery between January 2017 and December 2019 were asked to participate after oral and written information. Patients without uveitis during the same period were recruited as controls. The study was registered on ClinicalTrials.gov (NCT02975895). Patients were randomized to an intraocular lens type in a blockwise manner, using a web-based online software. Uveitic and non-uveitic patients were randomized separately and if the other eye was in need of surgery, the IOL not used in the first eye was implanted. In total, 34 patients (52 eyes) with uveitis and 22 patients (38 eyes) without uveitis were included.

Before surgery, at least 3 months of non-existing or stable inflammation was confirmed. Standard clear corneal phacoemulsification was performed by either of two experienced surgeons and difficulties were addressed as needed. Standard anti-inflammatory treatment perioperatively was with dexamethasone (Isopto Maxidex®) 1 mg/mL, three times daily, and nepafenac (Nevanac®) 3 mg/mL, once daily. In routine surgery for eyes without uveitis, treatment was started immediately after surgery and continued for 3 weeks postoperatively. Uveitis cases were asked to start treatment 1 week before surgery and continued 6 weeks postoperatively, with adjustments as needed according to inflammatory response. Adjunctive oral prednisolone was administered to uveitic patients except for those with FHU and cases with a single episode of uveitis without systemic association.

Participants were examined preoperatively by an ophthalmologist (S.P). In addition to routine slit lamp examination, and a review of the medical history, degree of cataract was graded according to the Lens Opacities Classification System (LOCS) III. Grading of inflammation was done according to SUN criteria. Flare meter measurements and OCT were performed in all patients.

Follow-up visits were planned at 2 weeks, 2 months, and 6 months for all patients. Additionally, uveitic patients were seen on days 1 and 5. At follow-up, BCVA, IOP, slit lamp examination, flare meter measurements, and OCT

were performed. Follow-up examinations were performed by either an experienced optician or an ophthalmologist.

3.3 PAPER IV

Paper IV reports a retrospective register-based study. For baseline analysis, data on all patients registered in the NCR between January 2018 and December 2019 was collected. Uveitic cases were identified and non-uveitic patients were included as controls. Follow-up registrations were analyzed regarding visual outcome. Patients under the age of 18 years at surgery and patients undergoing other surgical procedures at the same time as cataract surgery were excluded.

Core registrations included information on demographics, time to surgery, BCVA, ocular comorbidity, surgical procedures, IOL characteristics, surgical difficulties/complications, and anti-inflammatory treatment. Outcome registrations related to visual and refractive outcome.

3.4 STATISTICS

Descriptive statistics included mean ± standard deviation (SD) or median with range or interquartile range (IQR) as appropriate. Continuous variables were analyzed with *t*-test whereas categorical parameters were analyzed using Fisher's exact test. Best corrected visual acuity (BCVA) was converted into logarithm of the minimum angle of resolution (logMAR) prior to analysis.

In paper III, binary logistic regression was performed using a backward stepwise procedure with flare as dependent variable, and age at surgery, gender, uveitis, IOL type, mechanical pupil dilation, pseudoexfoliations, and staining of the anterior lens capsule as covariates. The parameter flare was dichotomized for this purpose, using a cutoff at 9.4 ph/ms, which was the mean flare at 6 months for the entire cohort.

In paper IV, to adjust for intraindividual correlation (both eyes included), testing between groups was performed using generalized estimating equations (GEEs). Univariable models were used for descriptive data and multivariable models were selected using backward selection, with postoperative BCVA ≤0.3 logMAR, BCVA <0.0 logMAR, no change, or deterioration of BCVA, and posterior capsule rupture as dependent variables and each characteristic as

an independent variable. Results were presented as adjusted odds ratios (aORs) and 95% confidence intervals (CIs).

In papers I–III, IBM SPSS statistics for Mac, version 20.0 (paper II) and 27 (paper III) (IBM Corp., Armonk, N.Y., USA), was used.
In paper IV, SAS software, version 9.4 (SAS Institute, Inc., Cary, NC, USA), was used for statistical analysis. A p-value <0.05 was considered statistically significant.

4 RESULTS

4.1 PAPER I

Study population

In total, 17 children with uveitis (21 eyes) underwent combined cataract surgery and PPV between 2002 and 2011. The median age at surgery was 6.5 years (range 3.4–14.8). The majority of the children were female (10; 59%). The most common etiology was JIA, seen in 13 eyes (76%); eleven eyes (52%) were classified as anterior uveitis. During the study period, four of the patients underwent surgery in both eyes.

Surgical difficulties

In one eye, an ora serrata defect was suspected, and in another eye, an iatrogenic retinal break was observed; both were treated with endolaser. In a third eye, the IOL was luxated into the vitreous body intraoperatively with a subsequent posterior capsule defect. The IOL was therefore placed in the sulcus.

Postoperative complications

Postoperatively, CME developed in three eyes (14%). In seven eyes (33%), OH or glaucoma developed, and in four of these (19%), filtering surgery was required. Hypotony developed in two eyes after surgery. Five eyes (24%) were treated with Nd:YAG laser capsulotomy or surgical discission because of visual axis opacification (VAO). Finally, pupillary block developed in three eyes.

Visual outcome

Visual acuity improved in all except one eye, with a median preoperative VA of 1.70 logMAR (0.02 Snellen decimal [dec], range light perception to 0.52 logMAR) compared to 0.17 logMAR (0.67 dec, range 1.05-0.00 logMAR) at 12 months postoperatively. Poor visual acuity was detected in three eyes. In the first of these, pupillary block developed, with anterior chamber hemorrhage after iridectomy and subsequent blood staining of the cornea. In the second eye, visual acuity was recorded soon after surgical discission of VAO resulting in hypotony and choroidal swelling. Finally, the third eye exhibited severe band keratopathy requiring repeated treatment with ethylenediamine tetra-

acetic acid (EDTA) chelation. Furthermore, this eye showed retinal engagement with vascular sheathing and ghost vessels and Behçet's disease was suspected.

4.2 PAPER II

Study population

The study cohort comprised 58 eyes with and 225 eyes without uveitis. A similar gender distribution, with a majority of female patients (60.3% of those with uveitis and 60.0% of those without uveitis), was seen. Patients with uveitis, however, were significantly younger at surgery, with a median age of 60.5 years (range 30–90) compared to those without uveitis (70 years range 27-93) ($p = 0.001$). Additionally, PSC was significantly more common in the uveitis group where it was seen in 18 eyes (31.0%) compared to 14 eyes in the non-uveitic group (6.5%; $p<0.001$). Idiopathic anterior uveitis and FHU were the most common uveitic etiologies. Preoperatively, one of the eyes with uveitis had CME and seven eyes were treated with eye pressure-lowering drops.

Surgical difficulties

Mechanical pupil dilation was needed more frequently in eyes with uveitis, where it was used in nine eyes (15.5%) compared to twelve eyes (5.4%) in the control group ($p = 0.02$). No significant difference was seen in the use of capsular dye or hooks in rhexis margin, and intraoperative complications with posterior capsular tear were seen in none of the uveitic patients.

Postoperative complications

Postoperative CME was seen in one eye with uveitis and two without uveitis. In the uveitic group, an increase in IOP was seen in two eyes at 4 weeks, but this normalized later without the need of treatment and no new cases of glaucoma were seen at 6 months follow-up. Rate of PCO requiring Nd:YAG laser capsulotomy did not differ significantly between groups, with eleven eyes (19%) in the uveitic group and 28 eyes (12.4%) in the control group ($p = 0.204$). Neither could any difference related to type of IOL (hydrophobic or hydrophilic) be shown.

Visual outcome

Mean BCVA preoperatively in patients with uveitis was 0.63 ± 0.52 logMAR (geometrical mean 0.3 dec) compared to 0.21 ± 0.29 logMAR (geometrical mean 0.6 dec) at 6 months. Corresponding values in the control group were 0.61 ± 0.53 logMAR (0.40 dec) compared to 0.30 ± 0.54 logMAR (0.70 dec), giving a median change in visual acuity preoperatively compared to 6 months postoperatively of 0.33 logMAR (range -2.90–0.25) in uveitis eyes and -0.21 logMAR (range -2.00–1.30) in those without uveitis. In patients with uveitis, poor visual results could be explained by previous radiation of choroidal melanoma, posterior segment abnormalities due to vasculitis, diabetic macular pathology, scarring after toxoplasmosis, and previous surgery for retinal detachment. In the control group, coexisting diabetic retinopathy, maculopathy, intraocular hypertension/glaucoma, amblyopia, or prior surgery of retinal detachment, PCO, CME/epiretinal membrane, and corneal erosion were causes of poor visual acuity.

4.3 PAPER III

Study population

A total of 34 patients with uveitis (52 eyes) and 22 patients (38 eyes) without uveitis were included. Uveitic patients were younger at surgery, with a mean age of 66 years (SD ± 10) compared to 74 years (SD ± 8; $p<0.001$) in non-uveitic patients. Posterior subcapsular cataract was more pronounced in patients with uveitis, presenting with a median PSC LOCS III score of 2.5 (IQR 1.5–3.5) compared to 1.5 (IQR 1.0–2.5) in those without uveitis. A large majority were classified as anterior uveitis with idiopathic uveitis (20 eyes; 22%), the most common diagnosis, and ankylosing spondylitis (nine eyes; 10%), the most common systemic association with uveitis. In eight patients (24%), IMT was administered systemically to control uveitis.

Surgical difficulties

Fifteen uveitic eyes (28.8%) underwent mechanical pupil dilation. None of the non-uveitic eyes did ($p<0.001$). Although staining of the anterior capsule and iris hooks at the capsulorhexis margin were also more commonly needed in eyes with uveitis, no significant difference compared to non-uveitic eyes was seen.

Intraocular lenses

The different IOL types were equally distributed between groups. A hydrophobic IOL was used in 25 eyes (48.1%) with uveitis and 20 eyes (52.6%) without uveitis and a hydrophilic IOL was implanted in 27 eyes (51.9%) with uveitis and 18 eyes (47.4%) without uveitis.

Flare

As expected, flare measurements in uveitic patients compared to non-uveitis patients were higher preoperatively as well as postoperatively. No significant difference in flare was seen at 6 months postoperatively, regardless of whether a hydrophilic or a hydrophobic IOL was implanted, with a median flare of 10.6 (IQR 8.5–19.3) for hydrophilic IOLs and 12.8 (IQR 8.0–17.1) for hydrophobic IOLs. Neither was any difference seen between the eyes of patients undergoing bilateral surgery at 6 months postoperatively receiving a hydrophobic IOL in one eye and a hydrophilic IOL in the other. The mean difference between eyes of the same individual undergoing bilateral surgery in the uveitic group was 4.0 ± 20.3 ph/ms. Flare >9.4 ph/ms at 6 months was correlated with gender, age at surgery, mechanical pupil dilatation, and pseudoexfoliations but not with uveitis diagnosis or type of IOL.

Central foveal thickness

Eyes with a hydrophilic IOL (n = 6; 22.2%) developed CME more frequently than did those with a hydrophobic IOL (n = 2; 8.0%). They also developed CME earlier in the postoperative period (63.5 ± 54.4 days as compared to 78.5 ± 89.8 days); still, no significant difference was seen (p = 0.25). All groups showed a slight increase in central foveal thickness (CFT), as measured by OCT at 6 months. In figure 9 change of flare and CFT over time is shown.

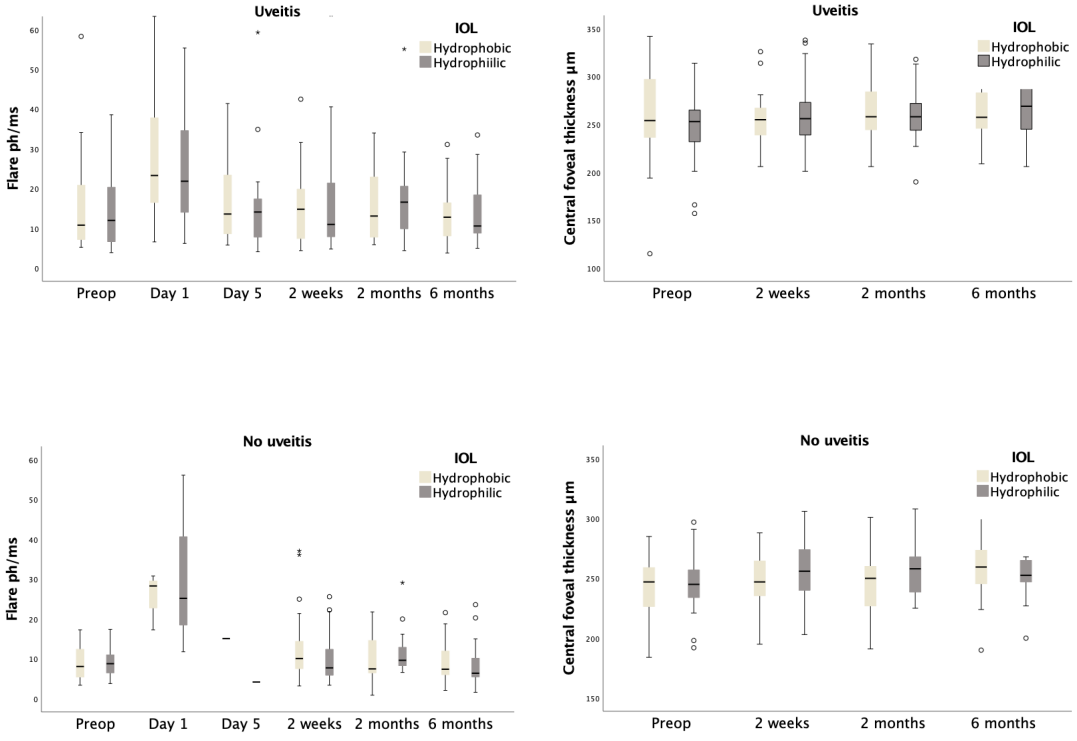

Figure 9. Flare and central foveal thickness (CFT) with hydrophobic and hydrophilic intraocular lenses (IOLs) in patients with and without uveitis.

4.4 PAPER IV

Study population

In total, the core register comprised 719 eyes with uveitis and 256 360 eyes without uveitis. The outcome register included 52 eyes with uveitis and 14 489 without. Mean age at surgery was 66.0 ± 13.5 years in the uveitic group compared to 74.3 ± 8.7 years in controls (p<0.001). Pseudoexfoliations and macular degeneration were more commonly seen in controls. Glaucoma, however, was more frequently seen in uveitic eyes (94 eyes; 13.1%) compared to non-uveitic eyes (18 723 eyes; 7.3%; p<0.001).

Surgical details

Difficulties at surgery were more frequently encountered in eyes with uveitis (27%) compared to eyes without uveitis (7.1%). Posterior capsule rupture or zonulolysis was also more common in eyes with uveitis (1.3%) compared to control eyes (0.6%; p = 0.02). However, no association between uveitis and posterior capsule rupture/zonulolysis was seen in the adjusted model. Furthermore, an association between posterior capsule rupture or zonulolysis and mechanical pupil dilation, capsular staining, and rhexis hooks was seen (aOR 3.53; CI 3.05–4.09; p<0.0001).

Perioperative anti-inflammatory treatment

Used in 666 eyes with uveitis (92.6%) and 207 797 controls (81.8%), topical steroids were the most common treatment (p<0.001). Subconjunctival steroids (n = 125; 17.4%), as well as other anti-inflammatory treatment including oral steroids (n = 60; 8.3%), were more commonly used in eyes with uveitis. However, topical NSAIDs were more often used in eyes without uveitis (69.9% compared to 57%; p<0.001).

Visual outcome

Eyes with uveitis had worse BCVA preoperatively (mean BCVA = 0.61 ± 0.49 logMAR) compared to controls (mean BCVA 0.41 ± 0.34 logMAR; p = <0.001). Although uveitis was associated with no improvement or deterioration of BCVA (aOR 2.38; CI 1.05–5.38; p = 0.04), the change in BCVA, postoperatively compared to preoperatively, was slightly better (mean change -0.38 ± 0.38) for uveitic eyes than for non-uveitic eyes (-0.30 ± 0.30; p= 0.04).

5 DISCUSSION

5.1 THE UVEITIC COHORT

Coexisting uveitis and cataract constitute only 0.3% of the eyes in the NCR core registrations for 2018–2019 (paper IV). Although they receive a small proportion of all cataract surgeries, patients with uveitis account for a disproportionately high number of difficulties and complications. Uveitic patients are a heterogenic group of patients and the risks of complications and visual loss differ and are related to type and severity of uveitis as well as age at diagnosis. Consequently, knowledge of etiology and type of uveitis improves treatment decisions and aids prognostication.

Looking at uveitis from a global perspective, the etiologies of uveitis have been shown to differ between countries, with a larger part of infectious causes in developing countries compared to developed countries, where non-infectious causes are more common as a rule. Furthermore, age-related differences are seen, which is consistent with our findings. In our studies, the majority of children were diagnosed with JIA (paper I). More heterogeneity was seen among adults, with the most common associated diagnosis being idiopathic anterior uveitis, FHU, and ankylosing spondylitis (papers II–III). None of the children had any infectious causes in contrast to adults in whom herpes, toxoplasmosis, and lues were seen (Table 1). As in most developed countries, anterior uveitis (AU) (Chang & Wakefield 2002) was the most common localization of uveitis in our studies and the associated diseases were also similarly distributed as in the review by Chang & Wakefield (2002). However, at a referral center such as ours, a larger percentage of intermediate and posterior uveitis might have been expected.

Diagnosis also depends on the method and local workup routines. With prolonged follow-up, those initially diagnosed with idiopathic uveitis might, if necessary, diagnostic facilities (i.e. radiology, labs and consultant rheumatologists) are available, later receive a specific diagnosis. This contributes to uncertain data on prevalence of different types of uveitis.

To improve comparability between different research studies, the SUN group introduced a system in 2005 to standardize classification of uveitic localization, based on descriptors of uveitis, i.e., onset, duration, and course, a grading scheme for anterior chamber cells and flare, as well as a description of uveitic activity (Jabs et al. 2005). Although contributing to an improvement,

the classifications are dependent on subjective assessment, which explains why a measure of uncertainty remains.

Since 1988, laser flare–cell photometry has been available (Sawa et al. 1988) to quantify aqueous humor cells and protein in a non-invasive way. Reports comparing flare meter measurements and clinical assessment of flare have shown that each clinical grade of flare corresponds to a wide range of flare readings (Tugal-Tutkun & Herbort 2010; Konstantopoulou et al. 2015). In paper III, we performed flare meter measurements as well as clinical grading, illustrating that the flare meter measurements add precision. As proposed by (Agrawal et al. 2016), flare meter measurements classified into groups may improve assessment of flare, giving a more precise quantification of the degree of flare, and represent a useful adjunctive tool in a clinical as well as research setting.

Table 1. Etiology of uveitis in adults and children, papers I–III.

Parameter	**Paper I** Patients, n (%)	**Paper II** Patients, n (%)	**Paper III** Patients, n (%)
Bechet's disease	1 (10)	1 (1.7)	
Enthesitis			1 (2.9)
FHU		12 (20.7)	2 (5.9)
Herpes-related uveitis		3 (5.2)	1 (2.9)
HLA–B27-related uveitis		2 (3.4)	3 (8.8)
Idiopathic uveitis	3 (23)	16 (27.6)	12 (35.3)
Idiopathic vasculitis		1 (1.7)	
JIA	13 (76)		
Lues			1 (2.9)
Ankylosing spondylitis		6 (10.3)	7 (20.6)
Crohn´s disease			1 (2.9)
Polymyalgia/temporalis arteritis		1 (1.7)	
Posner-Schlossman syndrome		1 (1.7)	
Psoriasis arthritis		2 (3.4)	1 (2.9)
Sarcoidosis		7 (12.1)	3 (8.8)
SLE		1 (1.7)	
TINU			1 (2.9)
Toxoplasmosis		2 (3.4)	
Ulcerative colitis		1 (1.7)	
Wegener's granulomatosis		2 (3.4)	

5.2 NATIONAL QUALITY REGISTERS

National quality registers have a long-standing history in Sweden. Individual identification numbers enable linkage of data between the register and specific individuals, as well as between different registers. The Swedish NCR includes information on a high proportion of cataract surgeries, making analysis of large populations possible. This is most useful for rare diseases where clinical trials can be very costly and time-consuming. However, analysis is restricted to the variables included in the registration form. In the case of uveitis, uveitis-specific information is not included. Also, the time point when the patient had confirmed uveitis is not defined. Therefore, subgroup analyses become more difficult to perform. Also, it is difficult to relate outcome to specific diagnoses, and prevalence estimates are uncertain. In addition, even though the variables in the register are clearly defined, these definitions are not stated in the registration form. There is a risk of differences in interpretation during registration and consequently analysis results are uncertain.

Looking at the question on postoperative anti-inflammatory treatment in the NCR, one of the answer options is “other anti-inflammatory treatment not specified.” This opens up for subjective interpretation. Traditionally, oral steroids are used in cases where additional treatment is required. Therefore, in most cases, “other postoperative anti-inflammatory treatment” equals oral steroids. However, steroid implants are sometimes inserted at surgery instead of being administered as an oral formulation not specified in the registrations. Furthermore, all questions in the NCR form are not mandatory, adding uncertainty to prevalence estimates.

The NCR includes information on surgical difficulties, including capsular staining, mechanical pupil dilation, hooks at the rhexis border, and capsular tension rings. These are so-called “surrogate markers,” i.e., they are used as indicators of dense cataract, small pupils, and zonular instability. The purpose of surrogate markers is to simplify and standardize assessment of these conditions. Even though measurement using these markers is a more objective method than individual judgment it is not certain that the markers accurately measure the underlying condition. When using surrogate markers, careful consideration must be taken if there are several markers for the same condition. For example, dense cataract is captured by both low visual acuity and capsular staining, where either might indicate advanced cataract. However, in this case, capsular staining is probably a more accurate marker because visual acuity is influenced by other factors, such as corneal and posterior segment abnormalities.

In our register-based report (paper IV), it would have been useful to include variables of uveitic entity as well as registrations of postoperative complications. However, it has been shown that an increase in variables in the register increases the risk of reduced coverage, and therefore, adding more variables has to be weighed against this risk.

Finally, often with register-based research containing large amounts of data, high levels of significance are obtained, which puts high demands on interpreting the clinical relevance.

5.3 SURGICAL DIFFICULTIES

Surgery in the setting of uveitis is associated with increased risks of difficulties compared to standard surgery in age-related cataract. These difficulties need to be properly assessed and handled to achieve optimal results. The surgeon performs surgery in the face of the consequences of uveitis, such as band keratopathy or corneal scarring, small pupils with synechiae, and decreased visibility, as well as fragile vessels increasing the risk of intraoperative hemorrhage. Greater difficulties in surgery of patients with uveitis were confirmed by our reports, with mechanical pupil dilatation shown to be the most common difficulty (papers II–IV). In a larger context such as our registry-based study (paper IV), capsular dye was significantly more common in patients with uveitis, as were iris hooks at the rhexis margin, indicating denser cataract as well as zonular instability. This was further reflected in a large proportion of patients with capsular tear/zonulolysis (Table 2).

Even though uveitic patients as a group show increased risks at surgery, the condition is heterogenic and risks vary depending on uveitic etiology and course of inflammation. Those with a more severe disease, chronic inflammation, and young age are at greater risk of experiencing more difficulties intra- and postoperatively (Secchi 2008). Linking the risks to a specific etiology to identify those with particular difficulties would be useful in uveitis. However, this kind of analysis would be difficult as uveitic patients are a relatively small group of patients and subgroups of uveitis are even smaller entities. Analysis of subgroups would then be underpowered or, alternatively, time-consuming, or would require a multicenter design for collection of sufficient data.

As shown in paper III, mechanical pupil dilatation was associated with higher levels of flare postoperatively. Regardless of prognostic and complicating

factors related to the uveitic etiology, performing surgery as atraumatically as possible is of great importance and even though synechiolysis and mechanical pupil dilation may be needed, minimizing iris manipulation is probably advisable.

Table 2. Intraoperative difficulties and complications at surgery in uveitic eyes.

Parameter	**Paper II** n = 58 eyes n (%)	**Paper III** n = 52 eyes n (%)	**Paper IV** n = 719 eyes n (%)
Mechanical pupil dilation	9 (15.5)	15 (28.8)	121 (16.8)
Capsular dye	1 (1.7)	10 (19.2)	91 (12.7)
Iris hook at rhexis margin	0	1 (1.9)	19 (2.6)
Capsular tension ring	2 (3.3)	0	23 (3.2)
Posterior capsular tear, zonulolysis	0	0	9 (1.3)

5.4 INTRAOCULAR LENSES

In modern cataract surgery, an artificial lens is as a rule implanted into the capsule to replace the refractive power of the removed, own lens. However, in a uveitic setting, IOL implantation is considered to induce more severe postoperative inflammation leading to complications such as synechiae, ciliary membrane formation, and hypotony, and has therefore been considered contraindicated. Gradually, with encouraging results of IOL implantation in uveitis, a more positive attitude has developed, and today, IOL implantation is encouraged in most adults with uveitis. In JIA, IOL implantation remained controversial until 1996 when Probst and Holland presented positive results of IOL implantation in adults with JIA (Probst & Holland 1996). Children with JIA remain a topic of further investigation. (Lam et al. 2003) have shown that favorable results can be achieved with an IOL in children given optimal pre- and postoperative anti-inflammatory treatment. In all of our reports (papers I–IV), the majority of the patients received an IOL, with satisfactory visual results in most cases. None of the eyes in our studies required an IOL-explantation during the periods studied.

To further optimize surgical results, different IOL materials and designs were investigated. Since the first IOLs made of PMMA, silicone and hydrophobic or hydrophilic acrylics have been used. In the development of IOLs, the aim was to minimize wound size, improve postoperative refraction, and avoid postoperative complications such as prolonged inflammation, PCO, and CME. The IOL's biocompatibility, by which is meant how well the tissue of the eye tolerates the artificial lens, is a serious criterion. To define and assess the IOL's biocompatibility in the eye, biocompatibility can be classified into uveal and capsular biocompatibility. Uveal biocompatibility is assessed by flare and degree of foreign-body reaction on the IOL surface whereas capsular biocompatibility is determined by degree of anterior capsule opacification (ACO) and PCO. Although it has been proposed that hydrophilic IOLs show better uveal biocompatibility while hydrophobic IOLs demonstrate better capsular biocompatibility, the clinical effects remain unclear. With preexisting BAB damage as in the uveitic eye, optimal uveal biocompatibility would be desirable. Therefore, in paper III, we compared a hydrophilic and a hydrophobic acrylic IOL in eyes with and without uveitis, the hypothesis being that a hydrophilic IOL might be preferable in a uveitic context. However, no significant difference was seen in flare between the different IOL types. Performing logistic regression with flare >9.4 ph/ms at 6 months postoperatively as dependent factor was correlated with gender, age at surgery, pseudoexfoliations, and mechanical pupil dilation but did not correlate with IOL type, indicating minor differences between the IOLs tested.

In papers I and II, VAO or PCO was more commonly seen in patients receiving hydrophobic or PMMA IOLs. However, hydrophilic IOLs were rarely implanted in the included adult patients and in the pediatric group the hydrophilic IOL was a bag in the lens (BIL) type, rendering assessment of capsular biocompatibility uncertain. None of the children receiving a BIL IOL developed VAO, showing the importance of the optic design. Square optic edges are generally considered to obstruct ingrowth of LECs, thereby reducing the incidence of PCO. With BIL, a posterior in addition to an anterior capsulorhexis is performed and both edges are inserted into a groove in the IOL encapsulating LECs, preventing anterior and posterior ingrowth of the IOL (Werner et al. 2010).

5.5 POSTOPERATIVE COMPLICATIONS

Despite improvements in surgical technique and advancements in IOL materials, eyes with uveitis still have increased risk of postoperative complications. In addition to surgery often being complicated and, as a consequence, more time-consuming, uveitic eyes with preexisting BAB damage that are prone to inflammation are predisposed to postoperative complications (Eakins et al. 1972; Nguyen et al. 2005).

One of the most common complications after cataract surgery is CME, with a wide range of reported incidence of 2–56% (Krishna et al. 1998; Estafanous et al. 2001; Kawaguchi et al. 2007; Yoeruek et al. 2010; Chu et al. 2017; Ozates et al. 2020). Our reports show similar results, with postoperative CME in 24% (paper I), 1.8% (paper II), and 22.2% of cases for hydrophilic IOLs and 8.0% for hydrophobic IOLs (paper III) (Table 3). The highest incidence of CME was seen in the pediatric group, which is in accordance with previous reports showing increased risks and challenges with children (Chan et al. 2018; Yangzes et al. 2019). The exact mechanisms of postoperative macular edema are incompletely understood. However, inflammatory actions are believed to play a major part through prostaglandins diffusing posteriorly to the vitreous, causing disruption of the BRB, with a subsequent leakage of fluids through the compromised capillaries (Grzybowski et al. 2016). Moreover, (Ursell et al. 1999) showed higher values of flare and cells in patients developing CME. Although knowledge of cataract surgery and postoperative complications in children with uveitis is limited and mainly based on retrospective studies, these findings offer an explanation for results in children with a more active inflammatory system, exhibiting a higher risk of developing CME. However, in our studies, even though there were slightly more cases of CME in adult patients receiving a hydrophilic IOL no significant difference was seen between the IOLs (paper III).

Posterior capsule opacification, another complication of cataract surgery, has been reported in up to 46% of patients (Schartmüller et al. 2020). Although PCO can easily be treated with Nd:Yag laser today, the treatment is not without risks and has been associated with increased inflammation, CME, a rise in IOP, and retinal detachment (Kohnen 2011; Apple et al. 2020). Additionally, there are considerable costs linked to the treatment; and in children and adults who are unable to cooperate, surgical removal of PCO sometimes has to be performed under general anesthesia. In children, the risk of amblyopia also needs to be considered and therefore PCO sometimes has to be treated more urgently to prevent permanent visual loss. As previously described by others, we could show that PCO was more common in patients with uveitis (Shoughy

et al. 2020) compared to patients without uveitis (paper II) as was also VAO in children (Knight-Nanan et al. 1996; BenEzra & Cohen 1997) (paper I). However, even though our pediatric patient material was small, BIL IOLs seemed advantageous, with none of the children developing VAO, and may be a preferable choice of IOL in groups with high risk of PCO (Tassignon et al. 2002; Nyström et al. 2018) (Table 3). Inflammation is considered a possible risk factor for developing PCO; however, Dana et al. report that younger age is primarily associated with PCO and less so with uveitis. Disregarding the more forceful inflammatory reaction seen with younger age at surgery, these authors report that an age-related decrease in viable LECs may be a possible mechanism for more frequent development of PCO in younger patients (Dana et al. 1997).

In general, cataract surgery results in a decrease in IOP. However, in some cases, for instance in those with coexisting glaucoma, an initial increase in IOP is seen (Young et al. 2020). (Slabaugh et al. 2014) describe patients with long axial length, deep anterior chamber, numerous eyedrops, and previous laser trabeculoplasty in need of additional observation and treatment. Uveitic eyes are at risk of developing glaucoma due to inflammatory actions and prolonged treatment with steroids (Baneke et al. 2016). The risk varies widely depending on background etiology and course of inflammation. In a pediatric cohort with JIA, 50% of patients developed glaucoma postoperatively and of these, 39% later required filtering surgery (Kotaniemi & Penttila 2006). Active inflammation was considered a major risk factor. Cataract surgery is associated with a disruption of the BAB (Sanders et al. 1982) and in patients with uveitis with preexisting BAB damage, the risk of a more severe inflammatory course and, consequently, of inflammatory-related complications such as glaucoma is increased. In our patient material, glaucoma was numerically more common in adults with uveitis than in non-uveitic adults preoperatively as well as postoperatively (paper II). In paper III, no difference in glaucoma was seen preoperatively. One possible explanation for the higher incidence of glaucoma in paper II might be that FHU was a more common etiology. In our pediatric cohort (paper I), 67% had OH or glaucoma postoperatively, 33% of which the condition had developed after surgery (Table 3). The high incidence of uveitic glaucoma as well as postoperative glaucoma demonstrates the increased risks in children.

Even though we could show a more severe inflammatory reaction with a higher flare at all time points postoperatively in patients with uveitis compared to patients without uveitis (paper III), we were unable to show either IOL, hydrophobic or hydrophilic, as being advantageous over the other regarding postoperative flare.

Table 3. Postoperative complications in eyes with uveitis (papers I–III).

Parameter	**Paper I** n = 21 eyes n (%)	**Paper II** n = 58 eyes n (%)	**Paper III** n = 42 eyes n (%)	
			Hydrophilic	**Hydrophobic**
CME	3 (14)	1 (1.8)	6 (22)	2 (8)
PCO/VAO	5 (24)	11 (19)	-	-
Glaucoma/ glaucoma treatment	7 (33)*	7 (18)**	-	-

* Excluding eyes with glaucoma treatment preoperatively.

** At 6 months postoperatively.

a.

b.

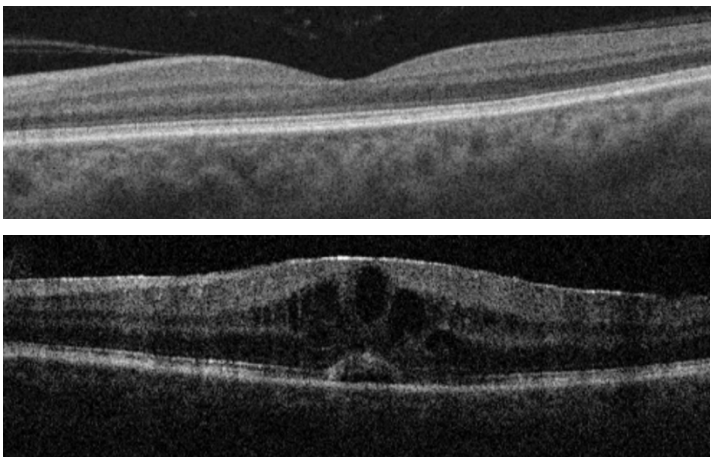

Figure 10. Macular optical coherence tomography (OCT) showing a. Normal foveal configuration. b. Postoperative cystoid macular edema (CME).

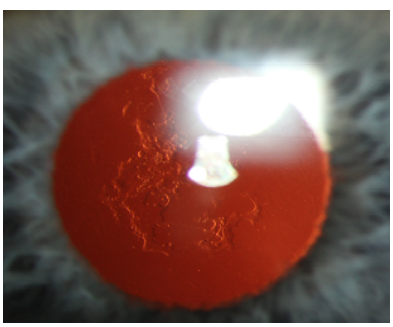

Figure 11. Posterior capsular opacification (PCO).

5.6 ANTI-INFLAMMATORY TREATMENT

Active inflammation has been observed to indicate worse postoperative outcome, as reported in a recent review (Mehta et al. 2014). Consequently, optimal treatment of inflammation has been shown to be preventive of complications in uveitis preoperatively as well as postoperatively.

Today, topical and oral steroids as well as immunomodulatory and biologic agents are available treatment options. Topical steroids are generally the first line of choice though with more severe and chronic inflammatory disease, oral steroids are commonly needed at least in adults. However, topical and systemic steroids are associated with several serious side effects. To minimize these, immunomodulatory and biological agents can be considered as an alternative.

Conventional immunosuppressive treatment has been used since 1951 when nitrogen mustard was used in treating a case of steroid-resistant uveitis. Since then, several reports have shown effectiveness in controlling inflammation in uveitis with antimetabolites such as MTX (Heiligenhaus et al. 2007), azathioprine (Pasadhika et al. 2009), and cyclophosphamide (Buckley & Gills 1969).

With increased understanding of the cells and cytokines responsible in uveitis, more biological agents have evolved, targeting specific inflammatory mediators. In general, these are used as third line of choice. However, with the advances in development of, and positive results with, biological drugs, an increasingly positive attitude towards the early introduction of biological agents either as monotherapy or used in combination with conventional immunosuppressant is seen (Schwartzman & Schwartzman 2015).

Parallel to progress in the development of substances with different target actions, a variety of alternative drug release types such as pharmaceutical implants and nano drugs are being developed. The rationale for using these is that they have prolonged action, that the release is concentrated to the main site of inflammation, and that they are associated with few complications and increased compliance. Using them hopefully increases the effect where needed and reduces unwanted side effects, as discussed by (Johnson et al. 2021). Although topical administration of drugs is preferable to reduce side effects, the structure of the eye is complex, with several barriers to penetrate and, consequently, poor permeability and low bioavailability of traditional eye drops. To overcome these obstacles and achieve efficient drug delivery to all parts of the eye, nano drugs have been developed as an alternative, and have shown promising results (Kang-Mieler et al. 2020; Zhang et al. 2021). In a

review by (Himawan et al. 2019), a combination of nanoparticles including dexamethasone, prednisolone sodium phosphate, and methylprednisolone hemisuccinate showed increased bioavailability, increased time on the surface, and protection from experimental autoimmune uveitis, as well as fewer patients with IOP elevation.

In our pediatric cohort (paper I), 82% of the children were treated with systemic IMT including traditional as well as biological agents, compared to 23% of adults (paper III).

5.7 UVEITIS AND CATARACT IN CHILDREN

As discussed previously, children with uveitis and cataract constitute a group where particular precautions are needed. Increased risks of developing complications are due to more severe and often chronic inflammation in this patient group. Additionally, young age at presentation leads to many years of disease.

Developments of immunosuppressive treatment have led to improved inflammatory control and, combined with improved surgical technique, possibility of good results in children even with IOL implantation. Combining a biological agent with a conventional immunosuppressive drug in children with JIA has been shown to achieve better control of inflammation (Ramanan et al. 2017). With early initiation of immunosuppression, the risk of developing complications related to inflammation may be reduced. Cataract surgery has sometimes been combined with PPV. In addition to treat structural changes such as vitreal opacities and epiretinal membranes the rationale has been that the vitreous acts as a reservoir of inflammatory mediators and removal of the vitreous would then subsequently lead to a reduction of the inflammatory response (Heiligenhaus et al. 1994; Henry et al. 2018). However, with better inflammatory control, complications of surgery can be prevented or postponed and more extensive surgery such as PPV might become unnecessary.

After our report was published (paper I), routines were changed. Today, PPV is no longer performed routinely but is reserved for those with extensive vitreal opacities present and those with a more severe inflammatory course.

5.8 VISUAL ACUITY

Overall, an improvement in visual acuity was seen in patients with and without uveitis after cataract surgery (papers I–IV). Compared to our reports in adults, children with uveitis presented with worse BCVA both preoperatively and postoperatively. However, the youngest child in paper I was 3.4 years, and the difference in BCVA might, rather than actual inferior visual acuity, reflect normal visual development in addition to less reliable measurements due to lacking cooperation in children. The change in visual acuity at 6 months postoperatively compared to preoperatively was slightly more substantial in uveitic patients, as shown in papers II–IV.

In the pediatric cohort (paper I), poor visual acuity postoperatively was related to postoperative complications in two eyes. In these eyes, treatment of pupillary block and VAO was needed leading to further complications i.e. blood staining of the cornea and hypotony and choroidal swelling. In a third eye coexisting pathology, band keratopathy as well as retinal pathology explained poor visual outcome.

As opposed to children, in adult patients with uveitis (paper II), little of no improvement in BCVA after surgery was related to coexisting retinal pathology and no immediate connection to surgical complications was seen. Further evidence of coexisting pathologies being the main reason for poor visual acuity was seen in paper IV. Here, BCVA ≤0.3 logMAR (0.5 dec) was seen to be significantly correlated with other vision-threatening comorbidity, macular degeneration, diabetic retinopathy, glaucoma, and any comorbidity.

5.9 METHODOLOGICAL CONSIDERATIONS

Uveitis is a relatively rare condition, making prospective studies time-consuming and difficult to perform. Additionally, uveitis constitutes a heterogenic group of infectious as well as non-infectious etiologies of different severity where each subtype might be represented by only a few cases. Given these circumstances, even though subgroup analysis would be useful for pointing out those with particular difficulties, subgroup analysis would be irrelevant because of small amounts of data. With a prospective design, blinding can avoid bias due to knowledge of the treatment. However, blinding is not always possible, for instance when comparing different IOLs where IOL type is seen by the surgeon as well as at follow-up (paper III). A further advantage of a prospective design is the possibility to plan examinations in a

more structured manner, improving means to compare the results between test subjects.

A retrospective cohort study is less time-consuming, especially when research is performed in rare conditions. This design is, however, restricted to preexisting parameters and differences in follow-up can impair interpretation of the data. Also, there may be difficulties identifying those eligible for inclusion based on how the diagnosis is registered.

When coverage is high, register-based research has the great advantage of providing large amounts of data. With national quality registers, comparisons between different centers are possible. However, the limitations are similar to those seen with a retrospective cohort design. Analysis is restricted to parameters included in the register. In addition, not all fields in the register form are mandatory, so the data is dependent on each surgeon's accuracy.

With rare diseases, multicenter trials have the advantage of enrolling large numbers of participants in a shorter time. However, meticulous planning is needed to avoid differences in inclusion/exclusion criteria and clinical practices.

6 CONCLUSIONS

Despite requiring more challenging surgery and in spite of increased risks of postoperative complications, patients with uveitis showed satisfactory improvement in visual acuity.

We could not find support for making a combined procedure with PPV, phacoemulsification, and IOL implantation a standard procedure in children.

Children often present with more severe and chronic uveitis. Therefore, particularly careful measures may be needed in a pediatric cohort.

In adults, improvement in visual acuity was more pronounced in patients with uveitis than in patients without uveitis.

We did not find support for either the hydrophilic or the hydrophobic IOL being advantageous over the other, with similar levels of postoperative flare and CME.

Multicenter trials could provide the information needed to optimize routines and outcomes for patients with uveitis undergoing cataract surgery.

7 FUTURE PERSPECTIVES

The goal in patients with uveitis and cataract is to achieve a low degree of inflammation and for the surgery to induce as little inflammation and as few complications as possible.

In many uveitic cases, the cause is unknown. Future research might increase our knowledge in these cases, leading to a specific diagnosis. With improved diagnostic possibilities, new ways of treatment might be available.

Although advances continue to be made with new and improved immunosuppressive drugs, treatment resistance can occur and some drugs cause severe adverse events. Identifying genetic markers could open up possibilities for targeted treatment with improved drug effect and a reduction of adverse events. With better inflammatory control, complications of the inflammation might be reduced; also, when surgery is performed, there might be a less complicated course postoperatively.

Questions regarding optimal perioperative treatment and timing of surgery remain. Uveitis patients constitute a heterogenic group of patients with different severity. In most studies, each etiology is represented by only a few cases. Additional multicenter trials could add knowledge which will allow us to differentiate difficulties between etiologies, providing conditions to further customize treatments.

Surgical trauma has been reduced with improved technique, but surgery is still associated with an inflammatory reaction, and BAB damage and its consequences. Additional improvements in surgical techniques and IOL materials may result in enhanced refractive outcome as well as contribute to a smoother postoperative course. Multifocal IOLs are available, giving more than one focus point, thus simulating the eye's own accommodative ability. Although the multifocal IOLs available today can reduce the need for spectacles they are often associated with reduced contrast sensitivity as well as visual phenomena such as haloes and glare. In cases of coexisting eye pathology that might influence visual acuity, multifocal IOLs are commonly advised against. Further developments are, however, ongoing and, with improved technique, this kind of IOL might be considered even with coexisting pathology such as uveitis, with increased patient satisfaction. Though IOL materials have improved since the first IOLs, further improvements in biocompatibility might contribute to reduced inflammation postoperatively as well as to decreased incidence of PCO.

With increased knowledge of the mechanisms causing cataract, different ways of delaying or treating cataract without surgery are being investigated. Increasing interest in the potential of stem cells has shown regenerative potential of LECs with regeneration of transparent lens structures. With continued progress, minimally invasive surgery obtaining an own regenerated accommodative lens might be achieved.

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APPENDIX

Formulär 1

Basregistret för 2022 års kataraktoperationer

1. Kliniknummer ☐☐☐

2. Personnummer (12 siffror)

☐☐☐☐☐☐☐☐-☐☐☐☐

Temporär? ☐

3. Öga som ska opereras

Höger ☐ **Vänster** ☐

4. Preoperativ synskärpa
med bästa korrektion (ej stp hål)

		Blind
Höger öga	☐,☐☐	☐
Vänster öga	☐,☐☐	☐

5. Indikationsgrupp (1-4)
(ej grupperad enl. NIKE:0) ☐

6. Uppsättning på väntelistan

☐☐	☐☐	☐☐
år	**månad**	**dag**

7. Operationsdatum

☐☐	☐☐	☐☐
år	**månad**	**dag**

8. Föreligger något av följande tillstånd i operationsögat?
Om Ja – markera ett/flera

- ☐ Glaukom
- ☐ Makulasjukdom
- ☐ Diabetesretinopati
- ☐ Cornea Guttata
- ☐ Pseudoexfoliationer
- ☐ Uveit
- ☐ Tidigare vitrektomi
- ☐ Tidigare refraktiv kirurgi
- ☐ Annat synhotande

9. Annan operationsindikation än synnedsättning
Om Ja – markera ett/flera

- ☐ Anisometropi
- ☐ Förhöjt ögontryck
- ☐ Andra subjektiva synbesvär
- ☐ Annan medicinsk indikation

10. Operationstyp

- ☐ Fako+BKL
- ☐ Fako+BKL+annan samtida operation
- ☐ Annan

11. Linsmaterial markera bara en typ

- ☐ Acryl hydrofob
- ☐ Acryl hydrofil
- ☐ Annan
- ☐ Ingen lins

12. Särskilda linsegenskaper
markera ett/flera

- ☐ Gulfärgad lins
- ☐ Multifokal lins
- ☐ Torisk lins
- ☐ EDOF lins

13. Peroperativa åtgärder
Om Ja – markera ett/flera

- ☐ Mekaniskt vidgad pupill
- ☐ Kapselfärgning
- ☐ Hakar i Rexiskanten
- ☐ Kapselring inlagd
- ☐ Generell anestesi

14. Antibiotika intrakameralt?
markera ett/flera

- ☐ Cefuroxim
- ☐ Doktacillin
- ☐ Vigamox
- ☐ Annat
- ☐ Nej

15. Peroperativ skada på bakre kapsel eller zonulae

- ☐ Nej
- ☐ Ja

16. Postoperativt inflammationsprofylax
Om Ja – markera ett/flera

- ☐ Topikala NSAID
- ☐ Topikala steroider
- ☐ Subkonjunktivala steroider
- ☐ Annat
- ☐ Ingen

17. Sign av kirurg_____

Formulär 2A

2022 års kataraktregistrering
Uppföljningsformulär
Nationella Kataraktregistret

Namn:
Adress:
Postadress:

1. Kliniknummer ☐☐☐ **2. Öga** Höger ☐ Vänster ☐

3. Personnummer ☐☐☐☐☐☐☐☐☐☐☐☐

4. Preoperativa K-värden

K1 ☐☐,☐☐ i ☐☐☐°

K2 ☐☐,☐☐ i ☐☐☐°

5. Planerad refraktion +/- ☐☐,☐☐

6. Axellängd (mm) ☐☐,☐☐

9. Linsformel markera en/flera

SRK/T ☐
Haigis ☐
Hoffer Q ☐
Holladay ☐
Barrett ☐
Annat ☐

7. Refraktion höger preoperativt

Sfär+/- ☐☐☐,☐☐ Cyl ☐☐,☐☐ Grader ☐☐☐

8. Refraktion vänster preoperativt

Sfär+/- ☐☐☐,☐☐ Cyl ☐☐,☐☐ Grader ☐☐☐

Formulär 2B

Efterkontroller pågår ☐ Patientmedverkan otillräcklig ☐ Patienten avliden ☐

Slutkontroll: Datum då medicinsk kontroll ej längre behövs och glasögon kan föreskrivas

1. Datum för slutkontroll **2022 -** ☐☐ ☐☐

2. Visus Höger öga ☐,☐☐

Med refraktion Sfär+/- ☐☐☐,☐☐ Cyl ☐☐,☐☐ Grader ☐☐☐

3. Visus Vänster öga ☐,☐☐

Med refraktion Sfär+/- ☐☐☐,☐☐ Cyl ☐☐,☐☐ Grad ☐☐☐

Ansvarig läkare för slutkontroll