On causes, treatment, and outcome after rhegmatogenous retinal detachment

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LUND
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Abstract:
Rhegmatogenous retinal detachment (RRD) is one the most common surgical emergencies in ophthalmology. In Sweden and many other countries surgical management has changed considerably over the past twenty to thirty years, from an external to an internal approach, with vitrectomy. The first paper presents an evaluation of results from our clinic from 2011 to 2013. During this period, both methods were in use, enabling their comparison. The main finding was that there was no statistically significant difference in outcome between the two methods, even when cataract surgery was performed together with vitrectomy.

Many of the patients were pseudophakic (38%) and had thus previously undergone cataract surgery with phacoemulsification, followed by replacement of the lens, one of the most common forms of ophthalmological surgery in the world. The per-operative and short-term complications are well known and have been extensively studied. 2they are linked to cataract surgery. The second study was an observational cohort study of patients undergoing cataract surgery in Region Skåne, southern Sweden, during 2015-2017, for whom data were retrieved from the Swedish National Cataract Register. These were then cross-referenced to patients presenting at our clinic with RRD up until the end of 2020. A total of 58 624 cataract surgeries were included, and of these 298 cases of RRD were reported. It was found that age, sex, and axial length of the eye were correlated to the risk of developing RRD. In the high-risk group (<60 years of age, male, axial length □25 mm) almost 10% developed RRD within the study period (mean 4.7 years).

The main indication for cataract surgery has previously been the patient's subjective feeling that their sight has deteriorated, confirmed by measurements of visual acuity. Today, as cataract surgery has become safer, it is often performed earlier in patients with better visual acuity than before. However, the results of Study II showed that many patients have a risk of long-term complications including RRD. In the third study, visual acuity before cataract surgery was compared to the risk of RRD. The findings suggested that many of the patients should have postponed cataract surgery, and that it was important not to induce anisometropia when performing the surgery, as this could lead to unnecessary surgery in the other eye.

Very little is known about the relation between the axial length of the eye and the results of surgery for RRD. In the fourth study, the results of vitrectomy in the patients with RRD from the population-based study were analyzed. Unexpectedly, it was found that eyes with greater axial length (□25 mm) showed better results (91% success rate) than those with shorter axial lengths (76% success rate).

In conclusion, the findings of this work confirm that the current management of RRD including vitrectomy (with or without phacoemulsification) has the same success rate as the external approach. The success rate of surgery for pseudophakic retinal detachment was higher among those eyes with a longer axial length. The long-term effects of cataract surgery on the risk of developing RRD can be high in some groups and should be weighed against the potential benefits of improved visual acuity. This should be considered and discussed thoroughly with the patient before undergoing cataract surgery.

Key words: Cataract surgery, myopia, retinal detachment, axial length

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Contents

Abstract

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Many of the patients were pseudophakic (38%) and had thus previously undergone cataract surgery with phacoemulsification, followed by replacement of the lens, one of the most common forms of ophthalmological surgery in the world. The per-operative and short-term complications are well known and have been extensively studied. However, evaluation of the long-term complications, such as RRD, is more difficult, as it is not known whether or not they are linked to cataract surgery. The second study was an observational cohort study of patients undergoing cataract surgery in Region Skåne, southern Sweden, during 2015-2017, for whom data were retrieved from the Swedish National Cataract Register. These were then cross-referenced to patients presenting at our clinic with RRD up until the end of 2020. A total of 58 624 cataract surgeries were included, and of these 298 cases of RRD were reported. It was found that age, sex, and axial length of the eye were correlated to the risk of developing RRD. In the high-risk group (<60 years of age, male, axial length ≥25 mm) almost 10% developed RRD within the study period (mean 4.7 years).

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Key words: Cataract surgery, myopia, retinal detachment, axial length

Populärvetenskaplig sammanfattning

Näthinneavlossning är en av de akuta ögonåkommor som obehandlad kan leda till blindhet. Orsaken till näthinneavlossning är att det uppstår ett hål på näthinnan, vanligtvis till följd av glaskroppsavlossning, och att det via hålet läcker in vätska vilket gör att näthinnan lossnar och faller framåt. Behandlingen innebär alltid kirurgi och ca 40% uppnår aldrig lässyn igen på ögat, 10-40% kräver ytterligare kirurgi och 5% läker inte alls.

Det är nu cirka 100 år sedan första operationen av näthinneavlossning utfördes och från början opererades ögat på utsidan där ett band eller plombbitar syddes fast för att imprimera rupturen på näthinnan. Sedan 1970 började operationerna istället utföras från insidan av ögat, s.k. vitrektomi då glaskroppen avlägsnas, ytan kring hålet laserbehandlas och tamponad med gas eller olja anläggs. Skiftet av behandlingsregim har skett successivt men idag är det väldigt ovanligt med yttre operationer och en stor del av det kunnandet har sannolikt förfallit. Nackdelen med yttre operation är att det tar längre tid, oftast kräver narkos och mer behandling efteråt med inneliggande vård. Därav har vitrektomi tagit över nästan helt och hållet och flertalet behandlingar sker idag i öppenvård.

Resultaten efter näthinneoperationer kan vara svåra att tolka eftersom studier skiljer sig åt avseende vilka patienter som inkluderas, hur lång uppföljningen är samt hur gruppen med patienter med olja i ögat presenteras i materialet. Vår första studie (I) är en uppföljningsstudie av alla patienter som opererades för näthinneavlossning på Skånes universitetssjukhus under 2011-13. Materialet är förhållandevis stort då det omfattade 918 ögon och perioden är också intressant då vi vid tiden fortfarande gjorde ca 20% yttre behandlingar. Valet av tidsintervall gör det möjligt att jämföra behandlingarna, idag skulle det vara svårt att göra liknande studier. Under perioden gjorde vi också en del behandlingar med en kombination av inre och yttre behandling. Dessutom hade vi då introducerat att behandla patienter med egen lins kvar med kataraktoperation och vitrektomi under samma operation. Detta har varit omtvistat då en del hävdar att komplexiteten i ingreppet ger sämre resultat. Vår studie av hela gruppen visade att andelen patienter med lyckat resultat efter en operation var 86,9% vilket är jämförbart med resultat från andra centra. Intressant nog hittade vi inga signifikanta skillnader mellan de olika behandlingsmetoderna, det vill säga yttre och inre behandling hade samma resultat vilket även gällde för gruppen med vitrektomi och samtidig kataraktoperation.

Det är sedan länge känt att kataraktoperation där patientens egen lins ersätts av en konstgjord lins ökar risken för näthinneavlossningar i efterförloppet. Framförallt ses riskökningen under de första åren men en studie där patienter följts upp under 20 år visade att riskökning bestod under dessa år. Resultaten varierar mellan olika studier men risken för näthinneavlossning efter kataraktkirurgi är ca 0,5% till 1% beroende på patientval och uppföljningstid. Det är känt att yngre ålder, manligt kön och närsynthet (längre öga) ökar risken för näthinneavlossning. För att undersöka detta mer har vi i studie II gjort en populationsstudie i Skåne med hjälp av Svenska Kataraktregistret där vi tittade på alla som genomgått en kataraktoperation under 2015-17 samt korsrefererat mot våra registerdata för operationer av näthinneavlossningar 2015-20. Uppföljningstiden var i genomsnitt 4,7 år och resultaten omfattade 58 624 kataraktoperationer; av dessa utvecklade 298 ögon (0,5% av populationen) näthinneavlossning. När vi delade upp beroende på ålder, kön och hur långt ögat var kunde vi se att risken förändrades radikalt i vissa grupper. Gruppen med störst risk var män under 60 år och som hade ett öga med axiallängd över 25 mm. Denna grupp hade en risk nära 10 % under studiens längd på nästan 5 år. Eftersom vi vet att det finns studier på 20 år som visar fortsatt riskökning vet vi fortfarande inte vad risken är under deras livslängd. Denna riskökning ska man då matcha mot vinsten med att göra en kataraktoperation. För de flesta är vinsten att slippa subjektiva besvär med sämre syn och det finns idag inga egentliga kriterier för när man ska göra en kataraktoperation. Det finns olika graderingssystem, bland annat nationell indikationsmodell för kataraktextraktion (NIKE) men i detta system beaktas inte långtidsrisken för näthinneavlossning. Vi kunde korrelera patienter från studie II med synskärpa före kataraktoperationen. I gruppen under 60 år och axiallängd överstigande 25 mm som enligt studie II hade 6,4% risk för näthinneavlossning under studiens längd kunde vi se att 15% såg 0,8 eller bättre på en Snellen tavla. I vår mening är risken att drabbas av näthinneavlossning för en marginell förbättring av synskärpan alldeles för stor och patienterna borde informeras mer noggrant och eventuellt vänta då resultaten visar att riskökningen minskar med stigande ålder.

Det är känt att närsynthet är en viktig riskfaktor för att få näthinneavlossning men vi vet väldigt lite om längden av ögat och resultaten efter operation av näthinneavlossning. I vår sista studie (IV) tittade vi på axial-längden och korrelerade denna till resultaten efter operation av näthinneavlossning. Studiegruppen bestod av de patienter som i studie II fick näthinneavlossning och genomsnittslängden på uppföljning var 324 dagar. I hela denna grupp lyckades operationen efter en enda operation hos 82,9%. Till vår förvåning hade gruppen med axiallängd över 25 mm ett bättre utfall med en enda operation för 91% av patienterna medan motsvarande siffra för de med axiallängd under 25 mm var 76%. Vi tror att detta delvis hänger ihop med ålder då gruppen med axiallängd ≥25 mm i snitt är 8 år yngre än de med <25 mm i axiallängd när de får sin näthinneavlossning. Yngre patienter har en annan anatomi med infästningen av glaskroppen mot näthinnan i periferin vilket vi tror ger

en enklare operation med större chans för framgång. En annan orsak till bättre resultat för gruppen med ≥25 mm i axiallängd kan vara att de i vår studie i mindre utsträckning drabbades av komplikationer med proliferativ vitreoretinopati, en slags inflammation i näthinnan som ger en skrumpning, vilket oftast leder till fler och mer komplicerade operationer.

Som slutsats har vi lärt oss att förändrade operationsmetoder med vitrektomi och eventuellt tillägg av kataraktoperation av näthinneavlossning resultatmässigt är jämförbart med äldre yttre metoder. Risken för näthinneavlossning efter kataraktoperation varierar stort beroende på ålder, kön och ögats längd. Detta måste vägas emot vinsten man förväntas uppnå och diskuteras ingående före beslut om operation av katarakt. Operation av näthinneavlossning gav förvånansvärt bättre utfall för de med längre ögon jämfört med de med kortare ögon.

List of Papers

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals. The papers are appended at the end of the thesis.

I Anatomical outcome of retinal detachment surgery comparing different surgical approach.
Thylefors J, Zetterberg M and Jakobsson G.
Acta Ophthalmol. 2021 Sep;99(6):e908-e911 doi:10.1111/aos.14678.

II Retinal detachment after cataract surgery: a population-based study.
Thylefors J, Jakobsson G, Zetterberg M and Sheikh R.
Acta Ophthalmol. 2022 Dec;100(8):e1595-e1599. doi:10.1111/aos.15142

III Visual acuity prior to cataract surgery and risk of retinal detachment – A population-based study.
Thylefors J, Jakobsson G, Zetterberg M and Sheikh R.
Clin Ophthalmol. 2023 Jul 12;17:1975-1980. doi: 10.2147/OPTH.S410585

IV The effect of axial length on pseudophakic retinal detachment.
Thylefors J, Sheikh R and Jakobsson G.
Acta Ophthalmol. 2024 Apr 8. doi: 10.1111/aos.16691.

Abbreviations

AL	Axial length
IOL	Intra-ocular lens
PPV	Pars plana vitrectomy
PRD	Pseudophakic retinal detachment
PVD	Posterior vitreous detachment
PVR	Proliferative vitreoretinopathy
RRD	Rhegmatogenous retinal detachment
SB	Scleral buckling

Preface

I still remember the first time I saw vitreoretinal surgery which, by chance, was my co- supervisor Gunnar Jakobsson in Sahlgrenska University Hospital in 1996 doing surgery on a vitreous hemorrhage which fascinated me immensely. When entering the Ophthalmic Department in Malmö in the beginning of the millennia I early on had a chance to assist a vitreoretinal surgery, and looking into the microscope I had the sensation of flying in the eye. After several earlier research work in infectious diseases, pharmacology and dark vision I wanted to integrate my research in my work of vitreoretinal surgery. The vitreoretinal field was at the time developing fast with new techniques and way of working and has proceeded so in the last decade with smaller instruments, omitting some elements while adding some new elements. Simultaneously, the field of refractive lens exchange is growing rapidly. These were the fields were I wanted to do critical scientific research.

Context of this thesis

The thesis was a joint elaboration with the Department of Ophthalmology at the Skåne University Hospital, Lund University, and Department of Ophthalmology at the Sahlgrenska University Hospital.

My starting point was an interest to see whether different methods of attaching the retina in retinal detachment had different results as the field was changing rapidly at the time. In those days we had a quality registry for retinal detachment in Skånes University Hospital where all surgery was entered and this was the base for the first article. The next three articles were based on the Swedish National Cataract Register which has been in use since 1992. The material were all cataract surgeries in the Region Skåne from 2015 to 2017. The first article on the long-term risk for retinal detachment after cataract surgery, the second on the visual acuity before doing cataract surgery and finally the last on the axial length of the eye and the outcome of surgery on retinal detachment.

1. Introduction

Rhegmatogenous retinal detachment (RRD) is a condition that leads to blindness in the affected eye if not treated quickly and is often associated with a significant loss of vision even when treatment is successful. About 40% have a visual function of less than 20/50 and do not achieve reading ability in the affected eye, 10-40% need further surgical intervention and about 5% do not achieve functional or anatomic healing[1-4].

1.1 Pathophysiology of rhegmatogenous retinal detachment

There are several factors leading to rhegmatogenous retinal detachment (RRD) but the key element is that there is a tear in the retina. Under normal condition the osmotic and oncotic pressure with the active transport of the pigment epithelium keeps the retina attached[5]. The tear in the retina makes it possible for the liquid in the vitreous body to migrate to behind the retina and the active transport by the pigment epithelium is thus impaired (fig 1). All treatments of RRD attempts to close the tear and thereby making the active transport valid which cause the retina to reattach again.

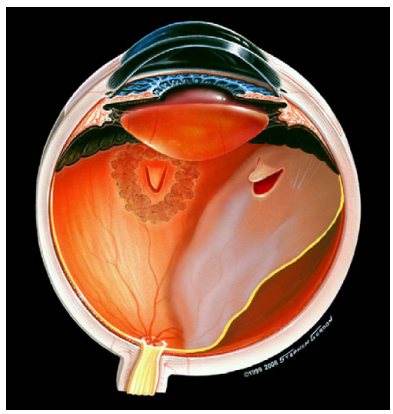


Figure 1. Retinal detachment with a horse-shoe tear and to the left one horse-shoe tear treated with laser. [6] CC BY 3.0

The tear in the retina is most often caused by a posterior vitreous detachment (PVD)[7]. The vitreous humour is from early childhood mainly consistent with a gel state due to the presence of a network of fine collagen fibrils[8]. As we age the collagen fibrils progressively aggregate due to a loss of type IX collagen from their surface which leads to a liquefication of the vitreous humour. With time this liquefication combined with a weakening of the post basal vitreoretinal adhesion leads to a PVD (fig 2). The PVD means that the vitreoretinal adhesion is separated but still it may be too adhesive and which may cause a retinal tear.

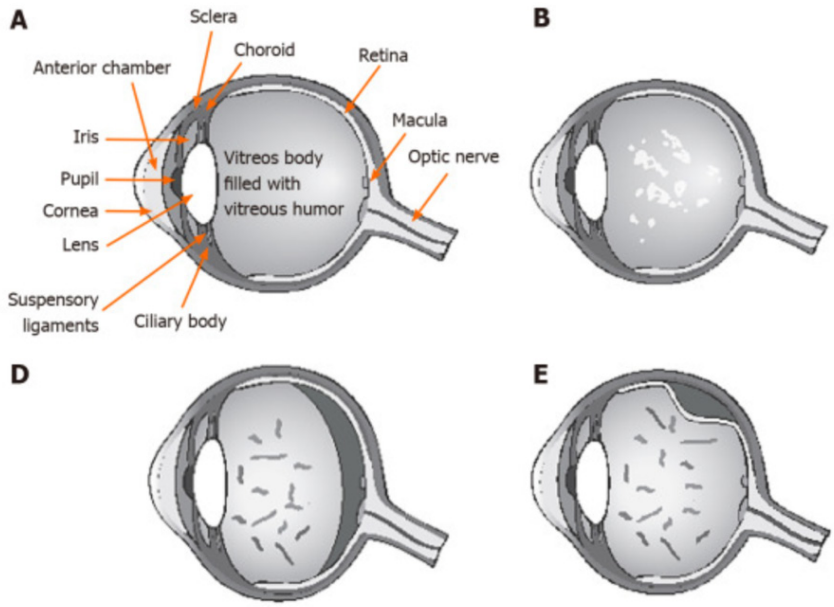


Figure 2. Age-related vitreous liquefaction.[9] CC BY 4.0

The neuroretina is a functional unit from the central nervous system with six neuronal cells (rods, cones, horizontal, bipolar, amacrine and ganglion cells) and three types of glial cells (Müller glial cells, astrocytes and microglial cells) (fig 3). The retina has internal and external blood flow which is finely regulated depending on the need[10]. The internal blood flow is from the retinal vasculature and the external from the choroid circulation beneath the pigment epithelium which means that the different layers of the retina are dependent on the circulation from two directions.

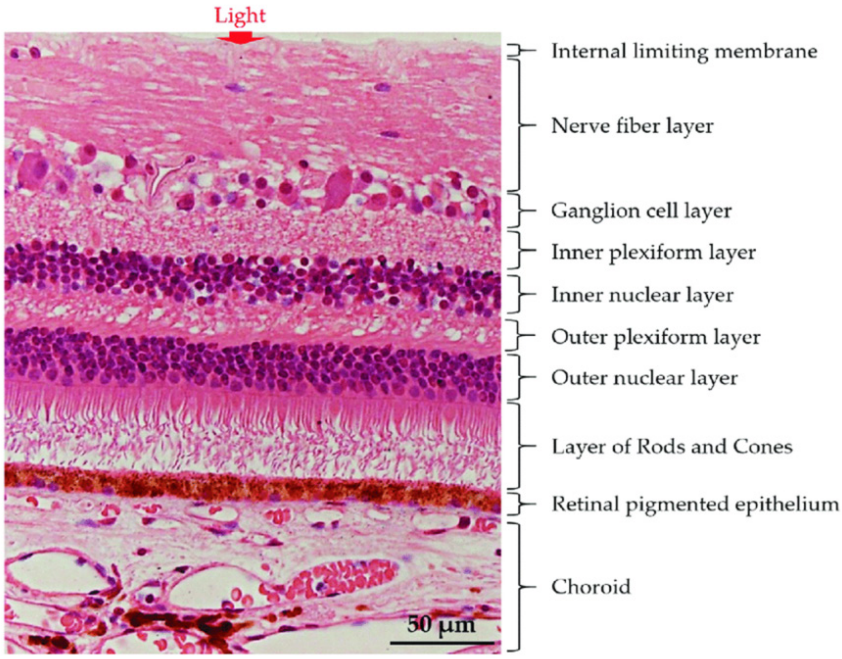


Figure 3. The basic retinal structure. Histological appearance of choroid and retinal layers. Published under CC BY 3.0 license from Trivino A. http://dx.doi.org/10.5772/48359

When the retina is detached the oxygen supply from the choroid disappears which affects the outer layers of the retina, mainly the photoreceptors, cones and rods. The retina loses its vital oxygen supply and then uses anaerobic pathway to degrade glucose. However, the retina loses its function fairly rapidly meaning that the treatment of RRD is urgent. What usually determines the outcome in terms of visual acuity is whether the macula (fovea) is detached or not and this determines the priority of the RRD in the surgical ward. But, as mentioned, the retina becomes permanently damaged and so there has been a change to treat all cases even those with macula-off more rapidly than before[11]. Normally when the macula is on the priority is within 24 hours and when it is off usually within 3 days. This means that a macula on RRD where the detachment is in the periphery may be less prioritized than a macula off RRD which is a completely new idea in vitreoretinal surgery.

1.2 Epidemiology of RRD

There are numerous studies reporting the incidence of RRD, which is typically around 10.5 per 100 000[12] in the population, ranging from 6.1 to 26.2 per 100 000, as reported in the Netherlands in 2016[13]. The incidence of RRD seems to be increasing, as studies from the 1970s reported an incidence of 6.1-9.8 cases per 100

000, whereas in the 1990s it was reported to be 11.8-17.9 cases per 100 000[12, 14-25]. It seems as though the increase is maintained, as the study from the Netherland in 2016 reported 26.2 cases per 100 000. Two main explanations have been suggested for this; the first is the increasing degree of myopia in the population[13], and the second is the higher prevalence of pseudophakia[15, 26, 27]. The pathophysiology leading to RRD involves complicated posterior vitreous detachment[28] (PVD), myopia with a longer eye, and earlier cataract surgery.

1.3 Global variation of incidence

There is a tendency towards global variation in the incidence of RRD. However, as seen in the epidemiology of RRD the standard variation seems very high between the studies so it is difficult to establish any definite conclusion. Normally we are seeing higher incidence in the Asian populations and whether this is due to anatomic differences due to more frequent myopia or whether there are other genetic variations is difficult to differentiate[29]. Much of the genetic work has been focused on the syndromic forms of RRD (e.g. Stickler, Wagner syndrome) but there is genetics for predisposed conditions such as myopia and lattice degenerations. Myopia is more common in Asian populations[30] so it seems reasonable that they have more RRD or at least have them earlier in life. There are a few studies concerning the ethnicity and for example Chandra et al[31] compared European Caucasian with South Asian and found that the South Asian had RRD earlier in life and had a more severe phenotype.

1.4 Treatment of RRD

The treatment is surgical; the first successful surgical intervention being performed by Jules Gonin in Lausanne, Switzerland, about 100 years ago[32]. The treatment at that time was to cauterize the break in the retina from the outside of the sclera. For this to be successful, the height of the retinal detachment had to be low, which was usually achieved by the patient being supine and double patching the eyes.

In the following years scleral buckling (SB) was introduced by Ernst Custodis[33] in 1949, in which the eye is indented from the outside (fig. 4), such that the retinal break is in contact with the choroid and the sclera, which led to an improvement in the success of surgery[34]. However one of the difficulties with the method is to have retina attach to the indentation. Usually it is either done by draining the subretinal fluid with a puncture through sclera and choroidal to the subretinal space or by non-draining using the Bernoulli´s principle[35]. The drawback with the puncture is that there is a risk of bleeding In the subretinal space which could be deleterious for the vision. This is why some prefer the non-draining surgery using the Bernoulli´s principle. In a simplified version it is that the velocity of the liquid decreases the pressure, the same principle is used when flying where the speeds of the air above

the wing and below are different and thus generating a lift. When moving the eye the current of flow within the eye reduces the pressure if there is an indenture beneath the tear and thereby closing it. What is interesting to note is that static posture after surgery implies less movement of the eye which could hinder the reattachment of the retina. Therefore normal physical activity after surgery might imply a faster reattachment of the retina.[36]

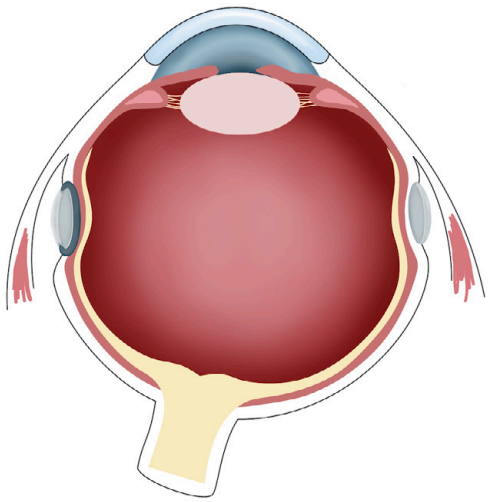


Figure 4. Scleral buckling indenting the eye in the equator. Illustration by Sabina Askelius.

In 1970, Robert Machemer[37] introduced vitrectomy allowing treatment from the inside of the eye through sclerotomy, removing the traction on the break by the vitreous body (fig 5). A third method of repairing RRD is pneumatic retinopexy, in which gas is injected into the eye pushing the retina back onto eye wall, after which the retinal break can be treated by laser or cryo-treatment[38, 39]. It was originally described by Bengt Rosengren who injected air into the vitreous in RRD patients[40, 41]. The use of inert gases (SF6, C2F6, C3F8) were introduced and these remain in the vitreous for a longer period of time compared to air and are standard as tamponade with vitrectomy and in pneumatic retinopexi[42]. Some surgical management are chosen when the circumstances for the patient seem benign, such as few ruptures, limited extent of detachment and no proliferative vitreoretinopathy (PVR). The opposite is probably true when more complicated features are added and certainly when it comes to adding an encircling band to the vitrectomy. This is supported by Storey et al. [43] who reported better results in more complicated cases of RRD with PVR when adding an encircling band to pars plana vitrectomy (PPV).

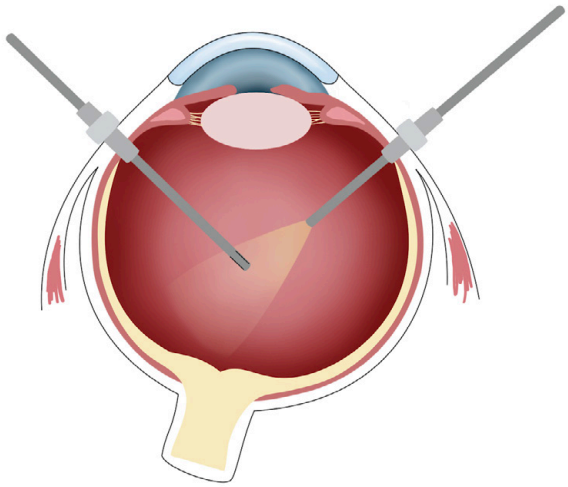


Figure 5. Three-port vitrectomy removing the vitreous from inside the eye. Illustration by Sabina Askelius.

In recent decades, there has been an extensive shift from SB towards vitrectomy[19, 44], but the superiority of the surgical procedure as such does not seem to be driving this change[45]. It can be speculated that other reasons, such as better visualization and control of retinal breaks, the ability to treat complex RRD with PVR, and practical reasons, such as the ease of performing minimally invasive vitrectomy without suturing the wounds and doing surgery under local anesthesia, are partly driving this change. Also, with decreasing number of SB surgeries[16] the threshold for performing SB surgery is higher and it has also become increasingly difficult to teach the practice of SB to vitreoretinal surgeons undergoing training. Vitrectomy is gradually becoming the standard treatment for retinal detachment, but the best method is still the subject of debate.

1.5 Cataract surgery

Cataract, which is the opacification of the lens, is one of the most common causes of loss of useful vision and blindness globally[46]. "Cataracta" is a Latin word meaning waterfall which is probably a metamorphose of the opaque lens. There is no medical method available to halt the progression to cataract so the only therapy is surgery. Historically the earliest evidence of surgery of cataract is couching, where a needle forces the lens back into the vitreous space. It has been seen on illustrations in Egyptian temples and tombs but was first described by an Indian surgeon about 800 BC. As known, the complications were many with the retaining lens in the eye and non-sterile technique soon had deleterious effect on the eye often leading to blindness shortly after the procedure[47]. The technique was replaced by

extracapsular cataract extraction (ECCE) which was first performed in Paris in 1747 by Jacques Daviel. The cornea was incised for about 10 mm, the capsular bag was punctured and the nucleus was expressed and curettage in the bag. It remained as the preferred method for over a hundred years until it was replaced with intracapsular cataract extraction (ICCE). With ICCE the capsular bag with the lens is removed, in the beginning with the thumb but later with cryoextraction. When beginning implanting an intra-ocular lens (IOL) ECCE came back as preferred method in the 1970s. In 1967 Charles Kelman revolutionized cataract surgery with phacoemulsification where the lens is emulsified and aspirated with an ultrasound-driven needle[48]. However it was first in the 1990s that the method replaced ECCE. All patients were aphakic after the surgery needing spectacles of approximately +12. It was first Sir Harold Ridley who realized that injured WWII pilots with plastic windshields materials in their eyes tolerated the material[49]. Initial trials in the 1940s with polymethyl methacrylate (PMMA) as an IOL had many complications and it was not until the 1970s that the procedure gained popularity. In the beginning the IOL was placed in the anterior chamber where many had complications in form of high intra-ocular pressure and corneal oedema. Today the IOL is placed in the capsular bag behind the iris.

An estimated 95 million people are affected by cataract worldwide and the condition still remains the leading source of blindness in middle-income and low-income countries[50]. In high-income countries there is more attention for improving vision with toric IOL and removing the need of reading glasses with refractive lens extraction.

The number of cataract surgeries is increasing globally, and it is being performed on younger patients who will not have had posterior vitreous detachment at the time of surgery, but in whom it may be precipitated by cataract surgery. In Sweden the total number of cataract surgeries has increased from around 70 000 to 80 000 after the millennium shift to in 2022 151 590 eyes[51]. Furthermore, an increase in the number of cataract surgeries will lead to more patients suffering complications, which further increases the risk of RRD[52].

1.6 Incentives for cataract surgery

The indication for cataract surgery differs globally and in a high-income country such as Sweden is highly dependent on the individual subjective experience of poorer vision. There are several grading systems based on images for cataract such as the Beaver Dam eye study[53], LOCS III[54, 55] (Lens Opacities Classification System) and AREDS[56] (Age-Related Eye Disease Study). All are based on images either from the slit lamp or retro illumination for the different types of cataract, nuclear, cortical or posterior subcapsular cataract and graded accordingly. However, in none of these are the grading linked to the cataract linked to the patient outcome, i.e. they do not give the clinicians a clue to which patient will benefit from the

cataract surgery[57]. In a different model the Swedish NIKE[58] (Nationell Indikationsmodell för Katarakt Extraktion) which is based on a questionnaire to the patient and objective criteria such as visual acuity does give the clinician such a guidance, it is linked to the patient outcome after cataract surgery[59].

However, even if there is a link to the patient outcome there are other important markers of the indication mainly the complications and the post operative refraction of the eye. The number of complications have decreased with time and the main ones are rupture of posterior capsule, zonula insufficiency, cystoid macular oedema (Irvine-Gass), endophthalmitis, and RRD. The only one which is not detectable in the immediate post operative period is RRD where it in many times can take months or several years. As the other complications have decreased the surgeons have become more willing to operate patients with less pronounced subjective symptoms.

As the IOL industry have made many advances in the last few decades there are now toric IOL which can remove the astigmatism and also several types of multifocal lenses[60], mainly EDOF (Extended Depth of Focus) and tri-focal IOL, where we can shift focus on several distances without the aid of spectacles. This have made cataract surgery possible in patient without cataract where the focus is removing the spectacles for the patient, i.e. RLE (Refractive Lens Exchange). This surgery is mainly done in private clinics where the patient pays a substantially amount of money for it. This is also reflected on the surgeon who also receives economic gains by it which makes the information to the patient even more important and also to be unbiased as a surgeon.

So the indications has changed from mature cataract with a white opaque lens and almost no vision, to for many years less than 20/40 Snellen which is the limit for driving cars, to today where RLE is common in high income countries where the only gain for the patient is to limit the need for spectacles.

1.7 Risk factors for RRD

The incidence of RRD following cataract surgery has been reported to range from 0.2% to 3.6%[15, 26, 61-67], depending on the follow-up time and patient demographics. It has also been suggested that changes in the method of cataract surgery in the 1990s have led to a decreased risk of RRD[68]. However, in the cataract operated group there are considerable differences in age, sex, axial length (AL) and per-operative complications, including rupture of the posterior capsule and vitreous loss[15, 26, 52, 66, 69]. Myopia is a known risk factor for RRD, as described in several studies[12, 15, 24, 26, 64, 66]. The definition for myopia is that the person is near-sighted i.e. needs concave lenses to see at a far distance. High myopia means that the patient needs spectacles with a correction of 6 diopters.

However these are due to the refractive powers of the cornea, lens and the axial length so it is difficult to give a value in axial length to myopia. Normally these are for the

cornea 43.5D, lens 18.8D and axial length of 23.6 mm[70] (fig 6). High myopia is normally given an axial length of approximately 26.0 – 26.5 mm[71]. As a risk factor for RRD it is reasonable to assume that it is the length of the eye bulb rather than the refractive power of the cornea and the lens. Today we have an easy access to exact axial length using laser measurement giving it in mm with two decimals. Patients who developed RRD had a significantly greater axial length than those who did not develop RRD ,which our studies show similar result to many other studies[66, 72].

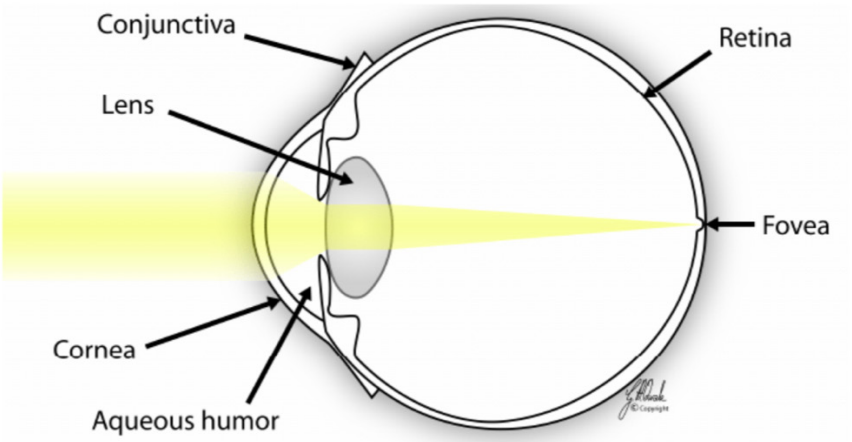


Figure 6. The refractive powers of the eye. In a normal eye cornea 43.5D, lens 18.8D and axial length 23.6 mm. Navaratnam J. DOI:10.3390/jfb6030917 CC BY 4.0

Male sex has also been reported to be a strong predisposing factor for RRD[15, 26, 66]. The reason for this is not known, but anatomical differences have been suggested, as men have greater AL[73] and posterior vitreous detachment seems to occur later[74].

1.8 How do we address the complications

There is always a risk in surgery for complications which is a true and generally cited fact. In many surgical fields there are different grading scores for the risk, most of them are connected to the risk of general anesthesia[75]. Historically, most of the decision to perform an operation or not was based on the surgeons ´gut feeling´ which still plays a large part[76]. In ophthalmology there are several articles reporting from different registers in cataract surgery and also in RRD surgery so there are odds or risk ratios for the complications. However, in what way is the patient able to take a decision based on the numbers? Figure 7 is an outline on how the decision making can be seen.

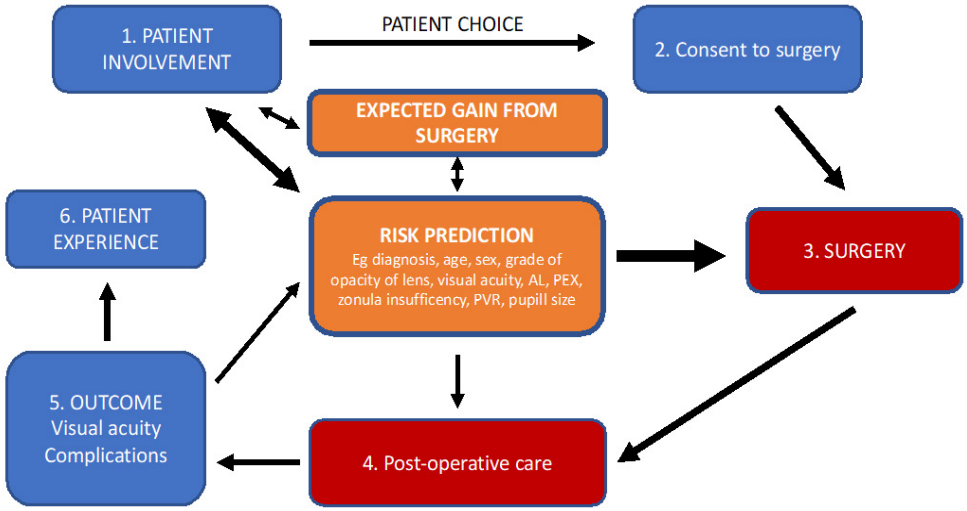


Figure 7. Suggested practical implementation of risk prediction, communication and patient choice in ophthalmological surgery.

To make the decision the conservative approach i.e. outcome of not doing the surgery is also important. In RRD not doing the surgery usually result in blindness of the eye which makes it almost a no-choice situation for the patient to do surgery in almost all conditions. But in cataract surgery where there is a chronic continuing process of deficit in visual acuity the choice is very much up to the patient. Usually the numbers presented for informed consent are 0.5% rupture of posterior capsule, 1 in 5000 risk of endophthalmitis, and 1 in 10 000 the risk of RRD in phakic patients. However, as seen in the chapter above on epidemiology of RRD the numbers have a large variation and also we know they increase after cataract surgery which is highly individual. Therefore the patient needs thorough information before reaching a conclusion on whether or not doing cataract surgery.

1.9 How is RRD perceived by the patients

For most, having an RRD is an emergency where the vision is threatened on the eye. More than half will not have a vision for driving on that eye even after successful surgery. A few percent will not heal despite several surgeries and the eye is left either with oil with almost certain risk of future complications or the eye might degenerate called phthisis. Furthermore about 5-10%[77, 78] will develop a retinal detachment in the fellow eye within a few years. So, the impact on the patient can be very large but fortunately successful surgery is normally the case. There are a few reports on social media from Facebook and Instagram with varying result[79, 80]. About half were emotionally positive to the experience of the surgical ward and

about one third were emotionally negative, typically towards repeated surgery. The surgeons should be aware that the patients seek advice outside the clinic in these social medias and many of these are negative due to misinformation or misunderstanding.

1.10 Precision medicine

There are several definitions of precision medicine but broadly it means using the right diagnostic tools and treatment to an individual based on genetic, biomarker or psychosocial characteristics[81]. Personalized medicine is another term and many times they are treated as equal in their meaning. However, personalized medicine seems to be more oriented to the needs of an individual whereas precision medicine is more public health where the society also gains from it.

I have discussed the incitements for cataract surgery, the complications from it and also the ethical part concerning the patient involvement in decision-making. However, when used right even the society gains from it as it could lower the risk of RRD in younger patients; This means less cost for the healthcare and less sickness absence . In conclusion, precision medicine is crucial for a modern, ethical and cost-effective approach in cataract surgery and can be developed further.

2. Aims

2.1 Study I

To investigate the patient population affected by RRD, the choice of surgical repair method and its effect on the surgical outcome, defined as primary surgical repair with no re-detachment within six months.

2.2 Study II

To investigate the risk of RRD following cataract surgery, and to stratify it according to possible risk factors such as age, sex, AL, and per-operative complications during surgery.

2.3 Study III

To investigate visual acuity before cataract surgery and compare it to the risk of subsequent RRD to determine whether there is a risk-benefit ratio that has not previously been revealed.

2.4 Study IV

To investigate the results of surgery for PRD and a possible correlation with axial length.

3. Methods

3.1 Ethics

All studies included in the thesis adhered to the Declaration of Helsinki of 2013, and were approved by the Swedish Ethical Review Authority (No. 2016/802, No. 2020-07214 & No. 2022-04176-02).

The research material comes from registration of surgery both at the Department of Ophthalmology SUS and from the Swedish National Cataract Register. The material is pseudonymized and it includes only material in retrospective of the treatment. Therefore, it does not have an impact on the treatment chosen or whether the treatment is performed. However, to have a follow-up on the results we needed to enter the patients' medical records and therefore we initially had the social security numbers for all patients which were then pseudonymized. As this is private medical information we retrieved only the necessary information from the ophthalmic medical records before it was pseudonymized. This is one of the ethical dilemmas which we have tried to minimize.

Since the research material comes from a large register the material is very large and it is not possible to have an agreement form from every patient. The material from the Swedish National Cataract Register follows the General Data Protection Regulation (GDPR) and the patients are informed at the center of surgery that they are included. Also, as mentioned above, the material in the studies are retrospective and does not have an impact on the care of the patient and hopefully the findings may have a bearing on the treatment of patients in the future for better results.

3.2 Anatomical outcome depending on surgical approaches

From 1 January 2011 to 31 December 2013, 918 eyes were diagnosed with RRD in 894 consecutive patients, who were treated at the Department of Ophthalmology, Skåne University Hospital, Lund/Malmö, Sweden.

The data collected were age, sex, lens status, type of RRD, and type of surgical treatment (SB, PPV, PPV and encircling band and PPV and phacoemulsification). The inclusion criteria were all cases of primary RRD, also with pre-operative PVR, treated consecutively during the period. Exclusion criteria were previous vitreoretinal surgery and penetrating ocular trauma.

Primary anatomical success was defined as no additional vitreoretinal surgery required during the 6 months following the primary repair procedure. When using silicone oil, it was defined as no additional vitreoretinal surgery required during the 6 months after silicone oil removal.

3.3 Population based study on RRD after phacoemulsification

All cases of cataract surgery performed from 1 January 2015 to 31 December 2017 in Region Skåne, southern Sweden, were retrieved from the Swedish National Cataract Register. Exclusion criteria were cataract surgery in combination with vitrectomy, corneal or glaucoma surgery, or age less than 30 years. The data were then cross-referenced with cases of RRD surgery performed at the Skåne University Hospital between 1 January 2015 and 31 December 2020, and so was RRD following cataract surgery defined.

The data analyzed were age, sex, AL of the eye, date of surgery, and comorbidity (diabetes, glaucoma, macular degeneration, or presence of pseudoexfoliation). Markers of complicated surgery, including staining of the anterior capsule, mechanical dilation of the pupil, iris hooks in the capsulorhexis margin, insertion of a capsular tension ring, or rupture of the posterior capsule, were also noted.

The patients were stratified into groups according to age: <60 years, 60-75 years, and ≥75 years, and AL: <23 mm, 23-25 mm, and ≥25 mm.

3.4 Visual acuity before cataract surgery

The visual acuity in the same population as in Study II was analyzed before cataract surgery. The visual acuity measured using the Snellen chart was converted to LogMAR to allow parametric calculations. The LogMAR in the different groups were then compared to their risk of RRD.

3.5 The axial length and outcome after vitrectomy of PRD

The group analyzed consisted of patients with RRD included in Study II. The outcomes were analyzed in relation to pre-operative characteristics obtained from medical records, such as localization of ruptures, status of the macula, and PVR. The per-operative features of surgical method used, the surgeon, use of perfluorocarbon liquid and use of tamponade were recorded. Post-operative outcomes with number of procedures, silicone-oil removed or not, retina attached, visual function expressed as LogMAR, and the length of the follow-up time.

Primary success was defined as retina attached after one surgery, and when silicone oil was used, after its removal. Data were recorded as long as the medical records were available for the patient.

3.6 Statistics

When analyzing categorical data, Fischer's exact t-test (Study I) or chi-squared test was used (all studies). For continuous data, Welch's t-test was used for parametric data (Studies II, III, and IV), whilst for non-parametric data, the Mann-Whitney U-test was used (Study I). The data in Study I were analyzed using multiple logistic regression to evaluate variables associated with an increased risk of re-detachment. In Study II, multiple logistic regression was used to determine correlations with age, sex, AL, and rupture of the posterior capsule, using primary success as the nominal variable. In Study IV, multiple logistic regression was performed to identify correlations between AL, age at retinal detachment surgery, and sex, using primary success as the nominal variable. A p-value of ≤ 0.05 was considered to indicate a statistically significant difference.

4. Result

4.1 Anatomical outcome depending on surgical approaches

A total of 918 eyes operated on for RRD consecutively were included in the study. Of these, 184 (20.0%) were operated on using SB with or without an encircling band, and 734 (80.0%) were surgically treated with vitrectomy. In those undergoing vitrectomy and the SB procedure, an encircling band was inserted in 116 eyes (16%). Phacoemulsification was combined with vitrectomy in 169 eyes, i.e. 43.6% of all phakic eyes that underwent vitrectomy (n=388) in this study. The retina detached again in 120 eyes during the first six months after surgery. Silicone oil was used as a tamponade in the primary procedure in 46 eyes (6.3% of all vitrectomies). It was left *in situ* in 16 eyes, and five of these were regarded as surgical failures, the other failures were due to multiple illnesses, high age, or the patient declining further surgery. The overall primary success rate was 86.9%, 89.1% for SB, 83.6% for SB+PPV, and 86.7% for PPV only. PPV was performed in combination with cataract surgery in 159 patients, with a primary success rate of 84.9%, PPV was performed alone in 153 eyes, with a success rate of 86.9% (p=0.63).

No significant differences were seen between the different types of surgery (SB+gas, PPV+gas, PPV+SO, SB+PPV+gas or SB+PPV+SO), sclerotomy size, surgeon, or the use of silicone oil.

Multiple logistic regression was used to analyze the effects of the variables age, sex, status of the lens, and external (SB) or internal (vitrectomy) procedures. The only variable found to be significant for re-detachment during the follow-up time was higher age (p=0.042).

4.2 Population based study on RRD after phacoemulsification

A total of 59 044 phacoemulsification cataract surgeries were performed during the period 2015-2017, and the inclusion criteria were met in 58 624 cases (37 059 patients), of which 58.4% were women.

Of these, 298 cases of RRD (0.51%) were reported in the years 2015-2020, and the mean time from cataract surgery to RRD was 667 days. The mean time from cataract surgery until the end of the study, i.e., the mean follow-up time, was 1705 days (4.67 years). Of the 298 cases of RRD, 17 patients (11.4%) developed bilateral RRD

during the study period (mean age 61 years, 76.5% male). The analysis showed a dominance of males with RRD (68.8%).

In the age group <60 years, 2.4% suffered RRD during the follow-up period, compared to 0.65% in the group aged 60-75 years, and 0.17% in those aged ≥75 years. The mean AL in those undergoing cataract surgery was 23.72 mm (SD = 1.25), and in the group with RRD, 25.12 mm (SD = 1.51), *p*-value <0.001. Figure 8 shows the incidence of RRD stratified according to age, sex, and AL. The upper curve shows the results for the whole cataract surgery population, where the risk of RRD was 0.51% during the follow-up period. The lower curves give the results when age < 60 y, AL ≥25 mm, and male sex are successively added. The final curve, including all three variables, comprised data from 465 eyes (0.79% of all eyes), amongst which 44 cases of RRD were identified (14.7% of all RRD cases), i.e. a cumulative incidence of 9.46%. The expected number of RRD if the patient had not been operated is added for the lower two curves (see discussion 5.2).

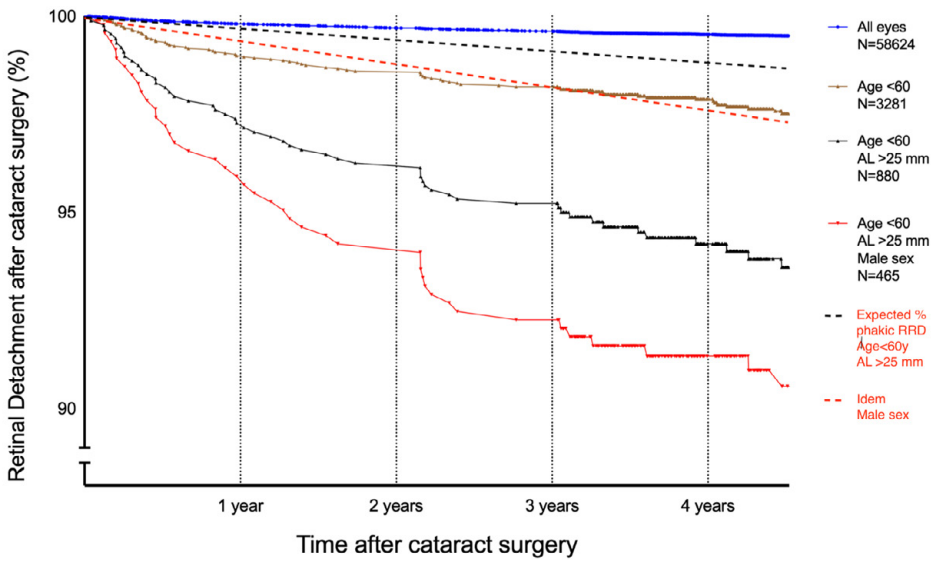


Figure 8. Kaplan–Meier curves showing RRD as a function of time after cataract surgery for different subgroups of patients. Expected number of RRD for patients not operated for cataract.

The variables age at cataract surgery, sex, AL, and rupture of the posterior capsule, were analyzed using multiple logistic regression. Age had an odds ratio (OR) of 0.93 per year (0.92-0.94, 95% confidence interval (CI)). Axial length OR 1.48 per mm (1.39-1.56, 95 CI).

Several per-operative features were analyzed (mechanical pupil dilation, staining of the anterior capsule, iris hooks in the capsulorhexis margin, insertion of a capsular tension ring) but only rupture of the posterior capsule was statistically significant between incidence of no RRD and RRD group (p=0.01). No form of comorbidity, such as glaucoma, pseudoexfoliation, macular degeneration, or diabetic retinopathy had significant impact on the incidence of RRD.

4.3 Visual acuity previous of cataract surgery

The same population as described in Study II was analyzed in this study. No statistically significant difference was found in visual acuity (expressed as LogMAR) in the operated eye between the groups defined in study II. What is noted is the percentage seeing better than 0.5 and 0.8 Snellen. For all eyes it was 57.2% better than 0.5 and 8.3% better than 0.8. For RRD younger than 60 years and an AL more than 25 mm with a risk of RRD of 6.5% in less than 5 years it was 56.1% better than 0.5 and 15.8% better than 0.8. For the fellow eye it was 94.6% better than 0.5 and 76.8% better than 0.8.

4.4 The axial length and outcome after vitrectomy of PRD

The population studied was described in Study II and we used the group with RRD. Postoperative follow-up data on retinal detachment were available for 288 eyes.

PPV was performed in all cases, and no encircling band was used. The use of an additional light source, perfluorocarbon liquid, vitreous staining or the choice of tamponade were left to the surgeon's discretion.

The mean age of the patient with RRD was 67.1 years with a male dominance of two thirds. The axial length was in mean 25.18 mm with minimum 21.55 mm and maximum 30.51 mm. Ruptures inferiorly was observed in 25%. The RRD involved the macula in 48% and was on in 52%. The primary success was 82.9% for the whole population and for males 80.8% and females 87.7%. Concerning PVR there was none in 243 eyes, grade A in 17, grade B in 16, grade C in 10 and finally grade D in 2 with falling number of primary success. In total there was 9 surgeons with on average 32 operations.

The data were divided into groups according to AL to study our hypothesis on the effect of AL on the result. We grouped them in two different ways. First, with a dividing line between the groups at 25 mm regarding more than 25 mm as myopes, presented in table 1. Secondly, we divided them in three groups with less than 25 mm (normal), 25 to 26.5 mm (myopes) and more than 26.5 mm (high myopia). The primary success rate was for AL < 25 mm 75.8% (113/149), AL 25 ≤ 26.5 mm 87.9% (80/91) and AL ≥ 26.5 mm 95.8% (46/48).

The best corrected visual acuity before cataract surgery and after RRD surgery is presented as LogMAR boxplots in Figure 9. The mean number of operations for each patient was 1.38, and in total 96.9% of the patients had an attached retina without tamponade at the last control. The median follow-up was 324 days.

Table 1. Patient data for 288 cases of retinal detachment divided according to axial length (AL), total, AL <25 mm or AL ≥25 mm. Primary success (PS) is defined as retina attached during follow-up time (mean 555 days) after one surgery, or with silicone oil, two surgeries to remove the oil. The *p*-value indicates a significant difference in primary success between the AL groups using the chi-squared test. Parametric values compare the results for the AL groups using the Welch t-test*. The *p*- value for proliferative vitreoretinopathy (PVR) compares grades 0 and A (regarded as normal) with B,C, and D**.

	All patients (PS%)	**AL <25 mm (PS%)**	**AL ≥25 mm (PS%)**	***p*-value**
Primary success	239/288 (82.9%)	113/149(75.8%)	126/139 (90.6%)	<0.001
Female/Male	90 / 198	57 / 92	33 / 106	
Mean age	67.1 years	70.9 years	63 years	<0.001*
Macula-on	148 (91.9%)	66 (92.4%)	82 (91.4%)	0.83
Macula-off	140 (73.6%)	83 (62.7%)	57 (89.5%)	<0.001
Ruptures inferiorly (4-8 o-clock)	73 (75.3%)	40 (65.0%)	33 (87.8%)	<0.05
PVR - 0	243 (87.2)	122 (82.7%)	121 (91.7%)	<0.05**
PVR - A	17 (76.4%)	7 (57.1%)	10 (90.0%)	
PVR - B	16 (62.5%)	11 (54.5%)	5 (80.0%)	
PVR - C	10 (40.0%)	7 (28.6%)	3 (66.7%)	
PVR - D	2 (0%)	2 (0%)	0	
Visual function, LogMAR				
Mean	0.31	0.40	0.21	<0.001*
Macula-on	0.13	0.15	0.12	0.51*
Macula-off	0.49	0.60	0.33	<0.001*

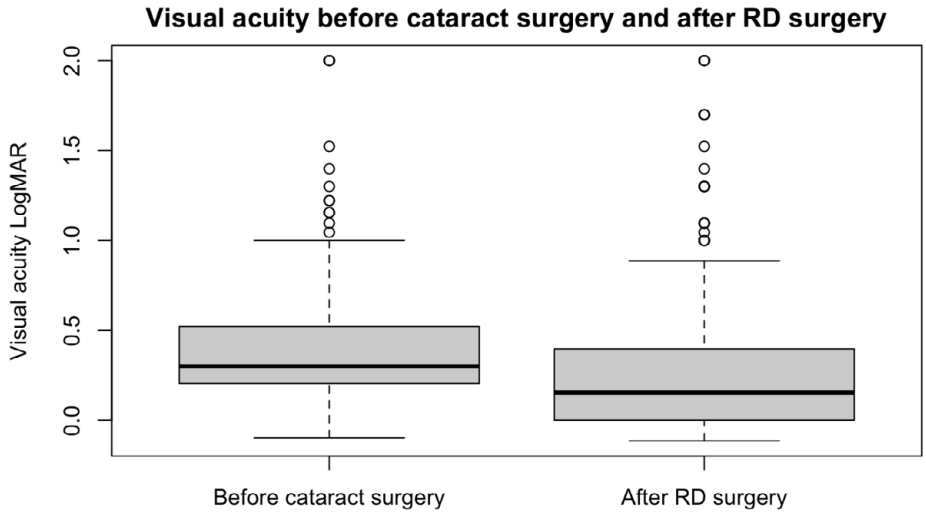


Figure 9. Boxplot with visual acuity in LogMAR before the cataract surgery and at the final visit after surgery of retinal detachment.

Multiple logistic regression was performed between AL, age at retinal detachment surgery, and sex, with primary success as the nominal variable. Increasing the AL had an OR of 1.62 for each mm and for every year older the patient had OR 0.94 primary success.

5. Discussion

5.1 Treatment of rhegmatogenous retinal detachment

The success of the primary procedure in the surgical repair of a detached retina is one of the most important factors in determining how well the patient recovers. Many different surgical approaches can be used, and many studies have focused on comparing these in attempts to identify the method or methods that are best in specific cases[44, 82-91]. This study revealed no significant differences in the rate of primary success with the various kinds of surgery. However, this study was retrospective, and the choice of surgery depended on the surgeon, which introduces the risk of bias. It can therefore not be concluded whether one method was better than any other. However, the results show that SB may still play a role, with or without an encircling band, especially in younger patients who have incomplete posterior vitreous detachment, can still accommodate, and have not yet developed a cataract.

Performing PPV with the lens still in place can be difficult, especially removing the vitreous body or applying laser therapy in the periphery of the retina. Also vitrectomy in phakic patients inevitably leads to cataract[92] within a few years. There has thus been a trend towards performing an increasing number of combined phacoemulsification and vitrectomy procedures[92, 93]. There are conflicting reports in the literature regarding the safety and outcome of this approach, however, there are few reports of complications[87, 92]. Study I revealed no increased risk of surgical failure when PPV was combined with phacoemulsification and intraocular lens implantation. Further advantages of this combination are improved postoperative control of the posterior segment, faster visual recovery, and no need for additional cataract surgery[94].

According to the literature, the use of silicone oil in treating primary RRD varies considerably. For example, in two studies from 2017, the first, from Norway, reports the use of silicone oil in 5.3% of cases[82], while the other, from Cincinatti[86], USA, reports the use of silicone oil in 21% of PPVs, and 23% in PPV with an encircling band. The reason for this wide variation is probably related to the heterogeneity of RRD, some are more difficult cases than others and also there may be different routines that differs between clinics. According to the results of Study I, silicone oil was used in 6.3% of all vitrectomies including all cases regardless of PVR, duration of symptoms, vitreous hemorrhage, or other “high-risk” criteria for PVR and

reoperation[43]. It is important to emphasize the difference between using silicone oil in the primary treatment of RRD as its use means another surgery is required to remove it and complications associated with silicone oil, such as increased intra-ocular pressure and calcific band keratopathy, are well known. Furthermore, it is often unclear whether the silicone oil remains *in situ*, or has been evacuated, and it may thus be difficult to classify these cases as successes or failures. In a national database survey in the UK[19], of the 3403 RRD operations performed from 2002 to 2010, 17.9% were PPV with silicone oil, however, 8.3% of these patients were found to have silicone oil *in situ* at the last follow-up, whereas the value in the present work was 1.5%.

Study IV was performed to investigate how the AL affects the primary success of RRD treatment. The cohort studied included all cases, regardless of the duration of retinal detachment or degree of inflammation with different grades of PVR. When grouping the data into two groups according to AL: <25 mm (normal) and ≥25 mm (myopes). In the group with AL ≥25 mm, the primary success rate was 90.6%, compared to only 75.8% in those with AL <25 mm (p-value <0.001). According to the multiple logistic regression, the probability of primary success increased by an OR of 1.62 for each mm increase in AL, adjusted for age and sex. However apart from a difference in AL, there was a difference in age between the two AL groups; those with AL ≥25 mm being on average 8 years younger, and multiple logistic regression indicated that the primary success rate decreased by an OR of 0.94 for each year older the patient is (adjusted for AL and sex). This age difference could thus partly explain the observed difference, as aging of the vitreous body causes the posterior border of the vitreous base to migrate from the ora serrata to the peripheral retina[8, 95]. This implies that younger patients have a vitreous body straddling a narrower part of the peripheral retina and ora serrata, which may be easier to vitrectomize, and implies less risk of iatrogenic breaks. A difference was also found in the occurrence of PVR in the two groups. There were a total of 28 cases of PVR B to D (9.7%) in the whole study population, which is in agreement with previous studies[96]. Of those with AL ≥25 mm, 5.7% had PVR B – D, while 13.4% of those with AL <25 mm had PVR B – D (p <0.05). Similar observations have been reported in a previous study[97], where more patients were found to have PVR C in eyes with shorter axial length. They had in the whole group 3.6% PVR C; 4.7% in the group with AL <25 mm and 2.2% in the group with AL ≥25 mm. So it seems that eyes with shorter AL may have an increased probability of having more PVR.

Another finding was the higher primary success rate in patients with macula-on PRD. This could be expected, as they are more likely to have PRD of a shorter duration. Looking whether there was a difference between the groups of more or less than 25 mm AL, there was no change within the AL on the primary success macula-on PRD, however, there was a significant difference in the macula-off PRD. The primary success rate for macula-off was for AL <25 mm 62.7% and for AL ≥25 mm 89.5% (p <0.001). The reason for this difference is not known but, a study

carried out at the Jules Gonin Hospital[72] found that those with shorter AL (<25 mm) more frequently had macula-off RRD. The present results are similar, since among those with macula-off RRD, 55.7% had an AL <25 mm, in contrast to cases with AL ≥25 mm, where only 41.1% had macula-off RRD.

Encircling bands were not used in any of the case in Study IV as these are only used at our clinic in cases of more complicated surgery, for example, reoperation and in cases of PVR. The difficulty of attaching the retina when there are tears in the lower part is partly reflected in the present study, as the primary success rate was slightly lower when there were tears in the positions from 4 to 8-o-clock (75.3%)(p <0.01). It could be argued that this finding should lead to the use of encircling bands in this situation in an attempt to increase the probability of primary success. Regarding the AL, there was a statistically significant difference between the two groups regarding inferior tears with a higher primary success in AL ≥25 mm (p<0.05).

5.2 Epidemiology of retinal detachment after cataract surgery

The risk of developing RRD after cataract surgery was addressed in Studies II and III. It is known that the risk is linked to sex, age, and myopia. The incidence of RRD after cataract surgery in males was 68.8% in Study II, which was similar to that found in Study I (66%), despite the fact that the earlier study included all forms of RRD, and not only pseudophakic RRD. Similar results have been presented in a review by Mitry et al.[12], where male to female ratios of 1.3:1 to 2.3:1 were reported. Male sex thus appears to be an independent risk factor for RRD, and not linked to cataract surgery.

When studying the increase in risk due to myopia, the same stratification as Laube et al.[98] was used, in contrast to two studies where a longer AL was used (>26 mm)[99, 100]. AL ≥25 mm as an additional risk factor for RRD in men remains up to the age of 75 years, while for women, it was only visible in the group aged below 60 years. Patients older than 75 years showed no increase in risk regardless of AL. Patients with AL <23 mm showed no increased risk regardless of age.

Age was analyzed as a variable for risk of RRD after cataract surgery, and it is known from previous studies that the incidence of RRD is higher in those of lower ages[15, 26, 66]. The incidence of RRD found in Study II was 2.4% in the group aged < 60 years, 0.64% in those aged 60-75 years, and 0.035% in those aged ≥ 75 years, over the whole follow-up period.

However, it is necessary to combine the parameters to establish which patients are taking a high risk when undergoing cataract surgery and which have a very low risk. In the group with highest risk the incidence was 2012 cases of RRD per 100 000 per year, which is approximately 200 times the normal rate.

It is already known that myopia and male sex are risk factors for RRD, but it is not known how much the risk is increased by cataract surgery. No studies have been performed to estimate this as a very large number of individuals would have to be followed for a long time. A study has been carried out in Denmark by Bjerrum et al.[69], who analyzed patients who underwent cataract surgery on one eye and therefore the other eye could be used as a control. They calculated that the risk increased by a factor of four. In a study by Erie et al.[62], who followed patients up to 20 years after cataract surgery, calculations against a control group gave the same four-fold increase. If this is the case, then according to the lower curve in Figure 7, where almost 10% had RRD, about 2.5% would have developed it without cataract surgery.

It is also useful for the cataract surgeon to know that other markers of complicated cataract surgery were not significantly correlated to RRD, as this indicates that these surgical tools can be used to reduce the risk of capsular rupture. However, capsular rupture is a well-known risk factor[52, 64, 101, 102], and in Study II it was found that 2.01% of the patients with RRD had capsular ruptures, compared to 0.74% in the whole study population.

The risk of developing PRD reported here is based on Study II, where the longest follow-up was six years. However, Erie et al.[62] reported that the risk continued for up to 20 years after cataract surgery and another study reported even an increase in the incidence of PRD after 4 years of follow-up[100]. It can thus be concluded that the high risk found in the present study, and in several other studies, is maintained for several more years.

Bearing in mind the risk associated with cataract surgery, it is necessary to analyze the benefits to be able to correctly inform patients. Study III considered the visual acuity before cataract surgery, and it was possible to compare this to that in Study II. Guidelines on pre-operative visual acuity have previously been used when recommending cataract surgery together with the expected postoperative improvement in visual acuity and the risks associated with surgery. As cataract surgery has become safer, these guidelines are now seldom used. Furthermore, refractive lens exchange has increased in patients without cataracts. The pre-operative visual acuity of those undergoing cataract surgery is therefore now higher than previously, and according to a Finish study in 2012[103] 20% had a Snellen score of 0.8 or better. The authors speculated that these patients could probably have obtained equally good vision by purchasing new spectacles. Thus, cataract surgery can be avoided or delayed in many instances.

Pre-operative visual acuity was compared to the incidence of RRD almost 5 years after cataract surgery in Study III. It is interesting to note that in the groups with the highest risk, i.e. those under 60 years old and those with an AL ≥25 mm, more than 15% had a Snellen score of 0.8 or better. Over 55% in the same groups had a Snellen score over 0.5 (the limit previously used as the indication for cataract surgery in

several regions) This can be contrasted to the results of a study in Spain[104] published in 2010, where only 15% of the patients had a Snellen score of 0.5 or better. Thus, some of these patients should have been advised to delay cataract surgery. Furthermore, it is important not to introduce anisometropia, which would prompt surgery on the other eye. This is underlined by the fact that the mean visual acuity in the fellow eye not undergoing cataract surgery in Study III, was 0.31 ± 0.57 LogMAR (Snellen 20/40), which can be compared to that in the PRD group of 0.20 ± 0.44 (Snellen 20/30) (p<0.001). This means that the patients with a high risk of PRD had similar visual acuity in the operated eye to that in the whole study group, but there was a large difference in the fellow eye, which had better visual function. This indicates that cataract surgery may not be necessary in this group as their binocular vision is still adequate, and that if surgery is performed anisometropia should be avoided.

Visually based grading systems such as the AREDS [56] and LOCS III[55] systems can be used to aid in the indication for cataract surgery, but neither of these can predict the outcome of cataract surgery[57]. In a systematic review and meta-analysis, Kessel et al. found that the Swedish NIKE system was the only system with a documented association between pre-operative grading and the outcome of cataract surgery[59]. However, it is important to note that the NIKE system does not take into account the age of the patient or the AL of the eye, so it does not take the long-term risk of PRD into consideration.

The mean visual acuity after PRD surgery was for the whole group LogMAR 0.31 (Snellen 20/40) compared to the mean visual acuity before cataract surgery of LogMAR 0.42 (Snellen ~20/50). Therefore, even after surgical treatment for retinal detachment the mean visual acuity improved compared to the level before cataract surgery. However, for many patients it deteriorates as the the visual acuity after cataract surgery improves but we have no data for this. Also, as expected, the visual acuity is predetermined by whether the patient has macula-on or macula-off. Those with macula-on having a LogMAR of 0.13 (Snellen ~20/25) and macula-off LogMAR of 0.49 (Snellen ~20/60).

A weakness of Study III is that only visual acuity was analyzed as an indication for cataract surgery. There may be patients with good pre-operative visual acuity with other cataract-associated symptoms, such as increased light sensitivity or reduced night vision.

One of the strengths of Study I is that it includes a relatively large cohort of 918 consecutive patients with RRD. It was decided to include all patients, rather than narrowing down the population by excluding younger patients[86, 88], PVR C and D[44, 85, 88], giant tears, macular holes or cases where silicone oil or SB[85, 89] was used together with vitrectomy. Therefore, it is representative of the overall surgical treatment and results in a tertiary center without any selection bias. In Sweden, almost all vitreoretinal surgery is performed in public hospitals within defined

health regions, and thus very few patients will be lost to follow-up[105]. It is thus reasonable to assume that a lack of surgery in the follow-up period of six months indicates primary success. However, this assumption is also a weakness as a few patients could have had retinal re-detachment, but the patient and/or the surgeon decided against further surgery. Several studies with better results have a shorter follow-up time of three months[43, 86, 88] or one month[90], where the tamponade in many cases will still be in place. Jackson et al. 2014[19] found that the second operation occurred at a median of 1.4 months after the first. The follow-up time of six months in Study I should thus be adequate to determine the success of the primary procedure, and is used in many studies[44, 82, 85, 89]. However, the final control of visual acuity was used in Study IV and the follow-up time was longer (324 days), and perhaps better reflected the final result.

The strength of Studies II and III is the large group of 58 624 eyes, obtained from the Swedish National Cataract Register, for the Region of Skåne. The number of cases of PRD was also quite large, 298, which allowed subgroup analysis to be performed. This register also includes data on visual acuity, AL, patient comorbidity, and other per-operative cataract complications.

Study IV, on PRD, is a large study of 288 patients, with information on the patient before cataract surgery, including visual acuity and AL, per-operative features during the PPV and then post-operative whether retina is attached, if the silicone oil is evacuated and the final visual acuity. The weakness of this study is that it only included pseudophakic patients from the previous population-based study[106], so it cannot be compared to a study on a phakic group. Another weakness is that only PPV was performed, and not any scleral indentations, which could have been interesting to compare, especially regarding tears in the lower part of the retina.

6. Conclusions and Future outlook

6.1 Study I

The choice of type of surgery for RRD did not affect the rate of primary success, even when cataract surgery was performed together with vitrectomy. However, as the choice of surgical technique was left to the discretion of the surgeon, it cannot read as though the surgical method does not affect the outcome.

6.2 Study II

The incidence of RRD following cataract surgery differs considerably depending on age, sex, and axial length. In the whole study group, only 0.51% developed RRD, but in men aged <60 years with AL≥25 mm, almost 10% developed RRD within 5 years. Thus, the risk of a vision-threatening condition such as RRD in some groups means that the benefit of cataract surgery should be carefully considered and the patient thoroughly informed. Ideally, the risk should be calculated for each individual patient and presented on the AL biometry done before surgery to enable a discussion of the risk versus the benefit.

6.3 Study III

In this study, a comparison was made between the patient's pre-operative visual acuity and the risk of developing RRD postoperatively. The visual acuity was often surprisingly good prior to cataract surgery, and the best option for the patient may have been to postpone surgery and perhaps buy new spectacles. Furthermore, it is the responsibility of the surgeon not to induce anisometropia, which could lead to unnecessary cataract surgery on the other eye.

6.4 Study IV

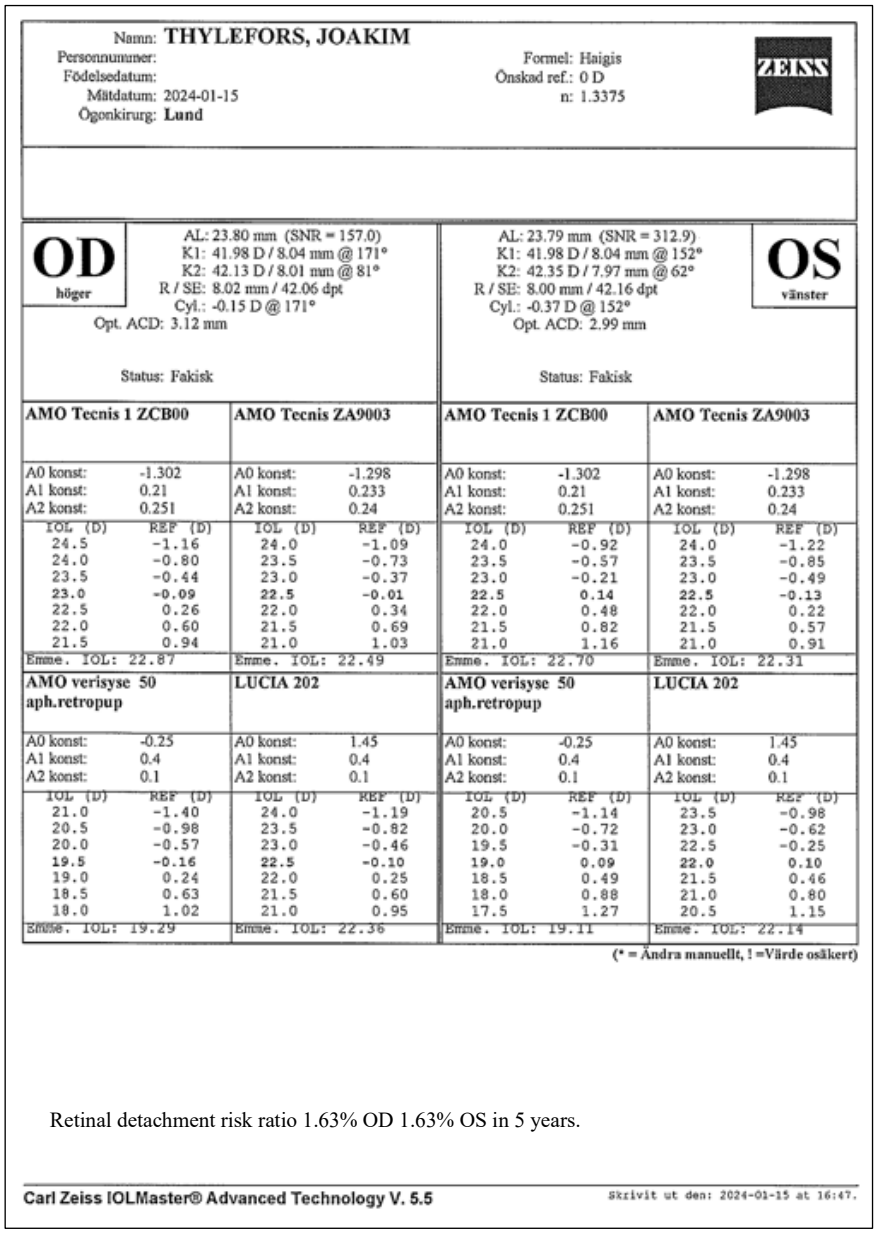
The primary success after PRD surgery for this study population was 82.9%. When grouped according to axial length, myopic eyes (≥25 mm) had a far better primary success rate, of 90.6%, than shorter eyes (75.8%). We have found two possible explanations of this, proportion of PVR and the age when they have their RRD. It appears shorter eyes have a higher proportion of PVR resulting in worse results.

Their age affects how the vitreous body is inserted into the ora serrata and may therefore lead to better results as they are more easily vitrectomized. Finally, the macula-on RRD had a better prognostic factor for primary success, and is therefore not only relevant for the final postoperative visual acuity.

6.5 Future outlook

The risk ratios calculated for high risk individuals in study II are high but these patients are at risk for retinal detachment even without cataract surgery. As mentioned there are other studies who approximate that the risk increase for each individual is fourfold. In the future we would like to study the risk for all phakic patient. In all the phakic RRD we do a combined phacoemulsification and vitrectomy procedure meaning that we have an AL. This could be combined with the population statistics for Region Skåne to get an incidence according to age, sex and AL.

The biometry that all cataract patients perform before a cataract surgery has all the necessary information with age, sex and AL to give an individualized risk ratio. It is an example of precision medicine and the informed consensus to the patient becomes true in the form that it has a true risk increase. Figure 10 serves as example. We hope that it could be a standard in the biometry in the future, perhaps by doing a study on all cataract surgery in Sweden to have more data and narrower groups increasing the precision for each individual.



Namn: THYLEFORS, JOAKIM
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Födelsedatum:
Mätdatum: 2024-01-15
Ögonkirurg: Lund

Formel: Haigis
Önskad ref.: 0 D
n: 1.3375

ZEISS

OD höger

AL: 23.80 mm (SNR = 157.0)
K1: 41.98 D / 8.04 mm @ 171°
K2: 42.13 D / 8.01 mm @ 81°
R / SE: 8.02 mm / 42.06 dpt
Cyl.: -0.15 D @ 171°
Opt. ACD: 3.12 mm

Status: Fakisk

OS vänster

AL: 23.79 mm (SNR = 312.9)
K1: 41.98 D / 8.04 mm @ 152°
K2: 42.35 D / 7.97 mm @ 62°
R / SE: 8.00 mm / 42.16 dpt
Cyl.: -0.37 D @ 152°
Opt. ACD: 2.99 mm

Status: Fakisk

AMO Tecnis 1 ZCB00		**AMO Tecnis ZA9003**		**AMO Tecnis 1 ZCB00**		**AMO Tecnis ZA9003**	
A0 konst:	-1.302	A0 konst:	-1.298	A0 konst:	-1.302	A0 konst:	-1.298
A1 konst:	0.21	A1 konst:	0.233	A1 konst:	0.21	A1 konst:	0.233
A2 konst:	0.251	A2 konst:	0.24	A2 konst:	0.251	A2 konst:	0.24
IOL (D)	REF (D)	IOL (D)	REF (D)	IOL (D)	REF (D)	IOL (D)	REF (D)
24.5	-1.16	24.0	-1.09	24.0	-0.92	24.0	-1.22
24.0	-0.80	23.5	-0.73	23.5	-0.57	23.5	-0.85
23.5	-0.44	23.0	-0.37	23.0	-0.21	23.0	-0.49
23.0	**-0.09**	**22.5**	**-0.01**	**22.5**	**0.14**	**22.5**	**-0.13**
22.5	0.26	22.0	0.34	22.0	0.48	22.0	0.22
22.0	0.60	21.5	0.69	21.5	0.82	21.5	0.57
21.5	0.94	21.0	1.03	21.0	1.16	21.0	0.91
Emme. IOL: 22.87		Emme. IOL: 22.49		Emme. IOL: 22.70		Emme. IOL: 22.31	

AMO verisyse 50 aph.retropup		**LUCIA 202**		**AMO verisyse 50 aph.retropup**		**LUCIA 202**	
A0 konst:	-0.25	A0 konst:	1.45	A0 konst:	-0.25	A0 konst:	1.45
A1 konst:	0.4	A1 konst:	0.4	A1 konst:	0.4	A1 konst:	0.4
A2 konst:	0.1	A2 konst:	0.1	A2 konst:	0.1	A2 konst:	0.1
IOL (D)	REF (D)	IOL (D)	REF (D)	IOL (D)	REF (D)	IOL (D)	REF (D)
21.0	-1.40	24.0	-1.19	20.5	-1.14	23.5	-0.98
20.5	-0.98	23.5	-0.82	20.0	-0.72	23.0	-0.62
20.0	-0.57	23.0	-0.46	19.5	-0.31	22.5	-0.25
19.5	**-0.16**	**22.5**	**-0.10**	**19.0**	**0.09**	**22.0**	**0.10**
19.0	0.24	22.0	0.25	18.5	0.49	21.5	0.46
18.5	0.63	21.5	0.60	18.0	0.88	21.0	0.80
18.0	1.02	21.0	0.95	17.5	1.27	20.5	1.15
Emme. IOL: 19.29		Emme. IOL: 22.36		Emme. IOL: 19.11		Emme. IOL: 22.14	

(* = Ändra manuellt, ! =Värde osäkert)

Retinal detachment risk ratio 1.63% OD 1.63% OS in 5 years.

Carl Zeiss IOLMaster® Advanced Technology V. 5.5

Skrivit ut den: 2024-01-15 at 16:47.

Figure 10. Biometry with Zeiss IOL master 500 with an example of how risk ratio of retinal detachment could be incorporated.

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