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Clinical characteristics and management of retinitis pigmentosa

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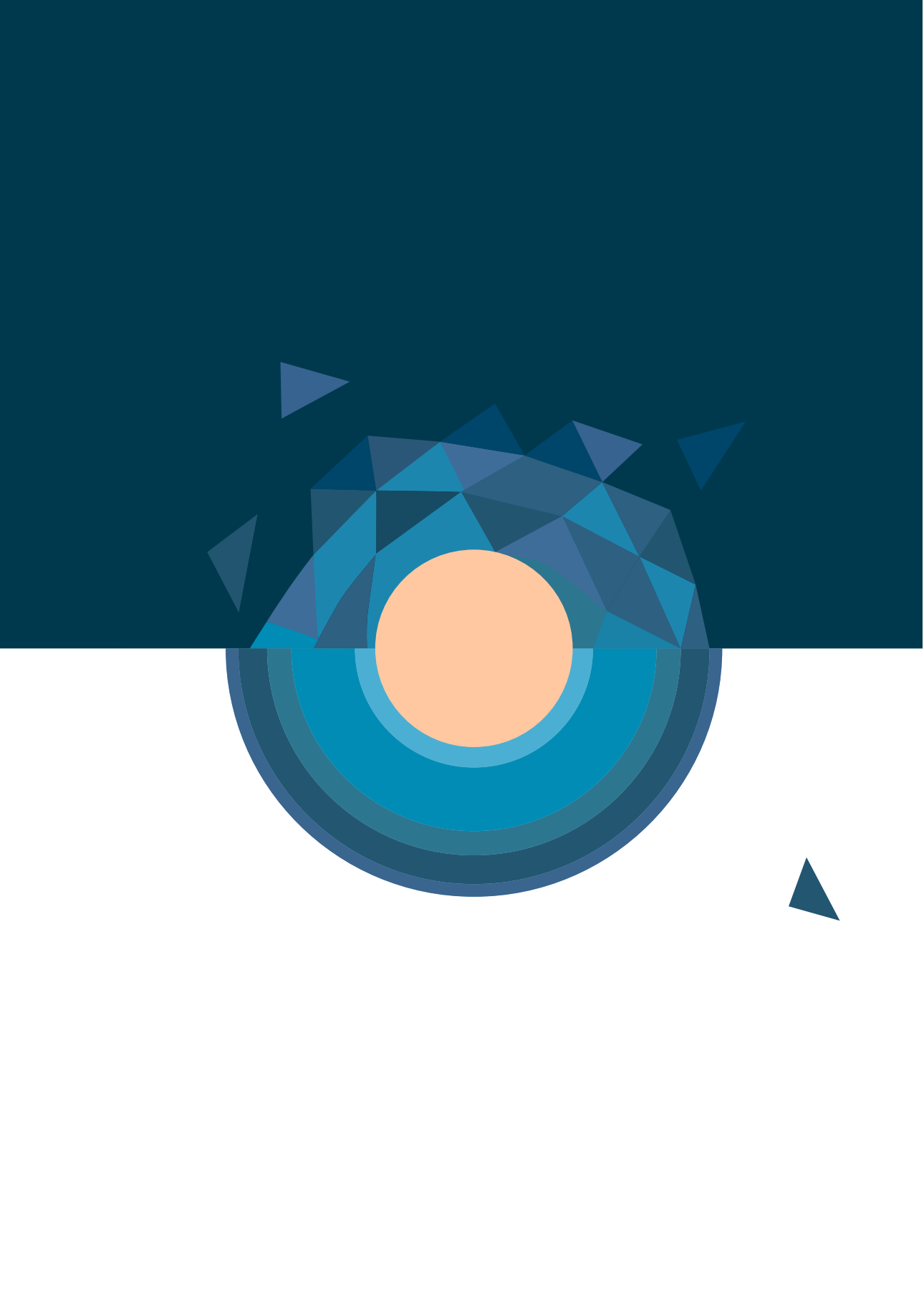
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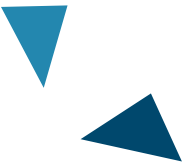
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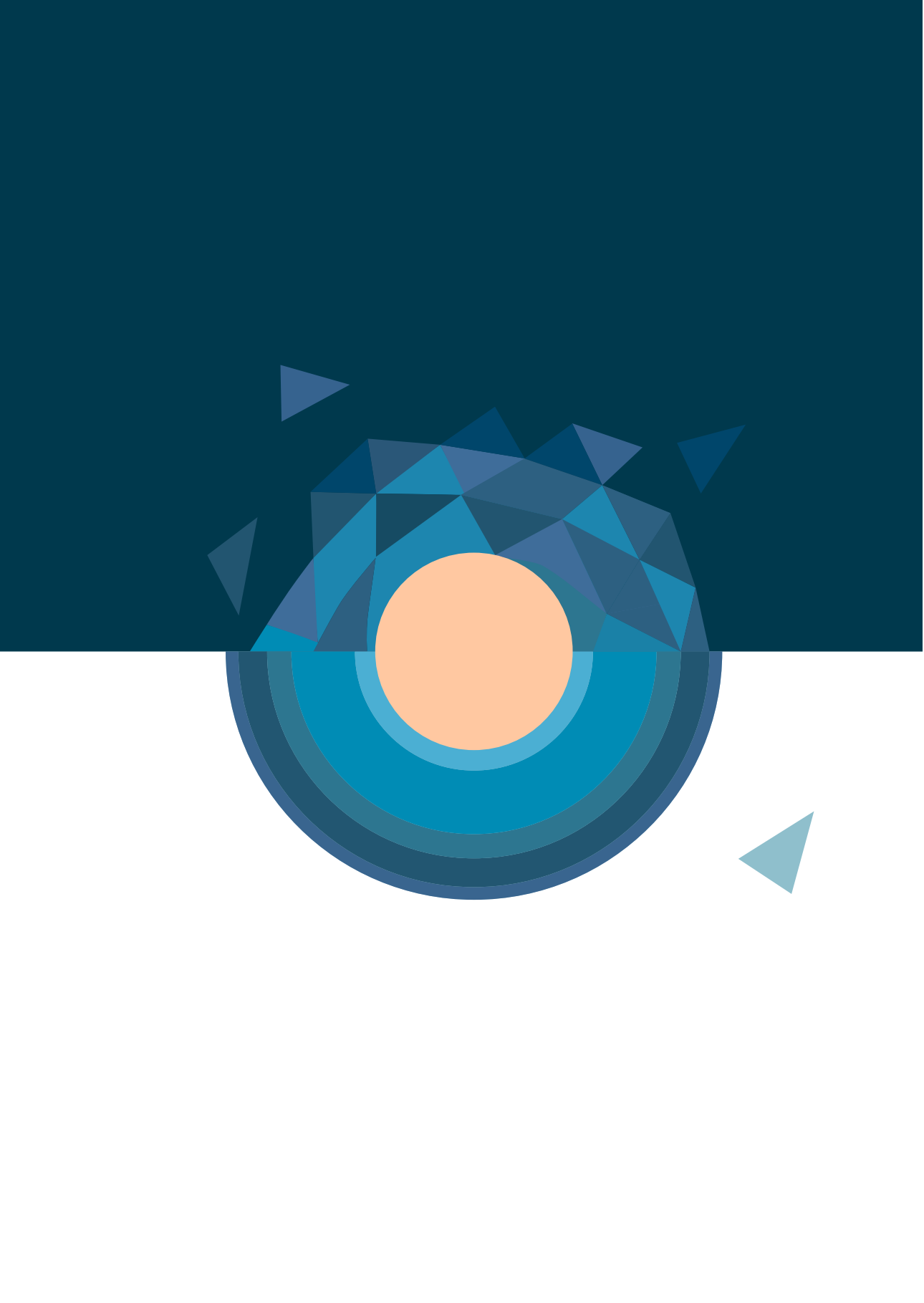
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PART II

CLINICAL MANAGEMENT OF RETINITIS PIGMENTOSA





CHAPTER 3.1

OUTCOME OF CATARACT SURGERY IN PATIENTS WITH RETINITIS PIGMENTOSA

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ABSTRACT

Purpose

To assess the visual outcome of cataract surgery in patients with retinitis pigmentosa (RP).

Design

Retrospective, non-comparative clinical study.

Methods

Preoperative, intraoperative and postoperative data of patients with RP undergoing cataract surgery were collected from several expertise centers across Europe.

Result

In total, 295 eyes of 225 patients were included in the study. The mean age at surgery of the first eye was 56.1 ± 17.9 years. Following surgery, best-corrected visual acuity (BCVA) improved significantly from 1.03 to 0.81 logMAR (i.e. 20/214 to 20/129 Snellen) in the first treated eye (-0.22 logMAR; 95% CI: -0.31 to -0.13 ; $p < 0.001$), and from 0.80 to 0.56 logMAR (i.e. 20/126 to 20/73 Snellen) in the second treated eye (-0.24 logMAR; 95% CI: -0.32 to -0.15 ; $p < 0.001$). Marked BCVA improvements (postoperative change in BCVA of ≥ 0.3 logMAR) were observed in 87 out of 226 patients (39%). Greater odds for marked visual improvements were observed in patients with moderate visual impairment or worse. The most common complications were zonular dialysis ($n = 15$; 5%), and (exacerbation of) cystoid macular edema ($n = 14$; 5%), respectively. Postoperative posterior capsular opacifications were present in 111 out of 295 (38%) eyes.

Conclusion

Significant improvements in BCVA are observed in most patients with RP following cataract surgery. Baseline BCVA is a predictor for visual outcome. Preoperative evaluation should include the assessment of potential zonular insufficiency and the presence of CME, as they are relatively common, and may increase the risk for complications.

INTRODUCTION

Retinitis pigmentosa (RP) is a collective term for inherited retinal dystrophies that are characterized by degeneration of primarily rod photoreceptors, followed by loss of cone photoreceptors.^{1,2} As result of photoreceptor degeneration, patients may experience symptoms of night blindness, concentric loss of peripheral visual fields, and ultimately, central vision loss.² There is great variability in patients with RP with regards to their disease onset, severity, progression and their potential complications. The most common anterior segment complication described in RP is cataract, with the most common type being posterior subcapsular cataract (PSC).³⁻⁵ Cataract develops at a relatively younger age in patients with RP compared to patients with age-related cataract, which is presumably caused by an early inflammation response invoked by RP.^{3,4,6-8} Depending on the severity and morphology of cataract, loss of visual function is accompanied or preceded by visual disturbances, including symptoms of glare, photophobia and decreased contrast sensitivity, among others.⁹⁻¹¹ In patients with RP, cataracts may cause disproportionate functional symptoms due to the presence of both lenticular and retinal pathology.⁷

Surgical removal of cataract, followed by the implantation of an intraocular lens (IOL), is the primary treatment to improve visual function and/or to alleviate perceived visual disturbances.^{7,12} In absence of ocular comorbidities and surgical complications, cataract surgery leads to significant improvements in objective and subjective visual function.^{13,14} However, in patients with RP, the visual prognosis following cataract surgery is uncertain, as gradual loss of visual function can be attributed either to the development of lens opacities or to the ongoing retinal degeneration process by RP.^{3,15,16} Furthermore, patients with RP are predisposed to intraoperative phototoxic retinal damage, cystoid macular edema (CME), and weakened lens zonules, which may negatively influence the visual prognosis and increase the risk of surgical complications.^{7,15,17-19} Postoperatively, higher incidences of posterior capsular opacifications (PCO) and anterior capsular contraction have also been reported in RP, which may also impact the visual outcome if left untreated.^{3,4,6,7,12,15}

Despite the uncertain visual prognosis and surgical risks, cataract surgery should still be considered in patients with RP.^{6,7,9,12,15} However, there is limited information to date on the outcome of cataract surgery in RP.^{3,7,12,17,20} Evaluating factors that are predictive of visual outcome in patients with RP undergoing cataract surgery could prove beneficial in selecting those who are most likely to benefit from surgery. Also, this information will provide some insights into the necessary precautions that can be taken in order to minimize intra-operative and/or postoperative complications. For this purpose, this study aimed to evaluate the outcome of cataract surgery using retrospective data from multiple expertise centers across Europe. We report the objective and subjective visual benefit of cataract surgery, the impact of risk factors on the visual outcome, and the

incidence of intraoperative and postoperative complications. Using this knowledge, recommendations and considerations will be provided that may aid the counselling and clinical management of cataract in patients with RP.

METHODS

Data collection

This international, multicenter, retrospective study was performed in collaboration with several academic centers across Europe, which included Leiden University Medical Center (Leiden, The Netherlands), Amsterdam University Medical Centers (Amsterdam, The Netherlands), Erasmus University Medical Center (Rotterdam, The Netherlands), Radboud University Medical Center (Nijmegen, The Netherlands), University Medical Center Groningen (Groningen, The Netherlands), Leeds Teaching Hospital (Leeds, United Kingdom), Ghent University Hospital (Ghent, Belgium), Charles University and General University Hospital (Prague, Czech Republic), and the Hospital of Lithuanian University of Health Sciences (Kaunas, Lithuania). This study adhered to the tenets of the Declaration of Helsinki, and the protocol was approved the Medical Ethics Committee of the Leiden University Medical Center. Informed consent was not required due to the anonymized nature of this study.

Clinical data on cataract surgery in patients with RP were extracted from electronic patient medical records. Inclusion criteria were: clinical diagnosis of RP; medical history of cataract extraction surgery; and available pre-operative and postoperative visual acuity data. Patients were excluded if cataract surgery did not include the implementation of an IOL, or if patients underwent a combined anterior and posterior segment surgery (e.g. phacovitrectomy). Genetic confirmation of RP was not a requirement for this study.

When available, preoperative data closest to surgery were collected and included: patient demographics, ocular comorbidities, best-corrected visual acuity data (BCVA) and refraction, lens morphology, ocular biometry, and target refraction. Intraoperative clinical data obtained were: anesthetic procedure, IOL type and material, the use of a capsular tension ring during surgery, and intraoperative complications (e.g. posterior capsule tears, vitreous prolapse, dropped nucleus). Postoperative data included: BCVA and refraction, subjective visual improvement, multimodal imaging, and postoperative complications (e.g. corneal edema, CME, and PCO).

Statistical analysis

Data analysis was performed using the R statistical program (version 3.6.2). The normality of data was visually inspected and tested by using the normality tests. In case of violation of the normality assumption, continuous data were presented as

median, interquartile ranges (IQR) and range; otherwise data were reported as mean $\pm$ standard deviation (SD). Categorical data were shown as frequencies (n =) and percentages (%). Preoperative BCVA of patients were classified into different categories of visual impairment based on the guidelines of the World Health Organization: no visual impairment ($BCVA \geq 20/40$), mild visual impairment ($20/67 \leq BCVA < 20/40$), low vision ($20/200 \leq BCVA < 20/67$), severe visual impairment ($20/400 \leq BCVA < 20/200$) or blindness ($BCVA < 20/400$).²¹ For statistical analysis, BCVA data were converted to Logarithm of the Minimum Angle of Resolution (logMAR) values. Vision classifications of counting fingers, hand motion, light perception and no light perception were given the logMAR values 2.1, 2.4, 2.7 and 3.0, respectively.^{22, 23} Logistic regression models were estimated to investigate the association between risk factors and visual outcome. The level of significance was set at 0.05.

RESULTS

Patient characteristics

A summary of the clinical characteristics of this cohort is provided in Table 1. A total of 295 eyes from 226 patients with RP were included in the study. The mean age at time of first surgery was 56.1 ± 17.9 years. In patients that also underwent surgery in the fellow eye (n = 69; 31%), the median waiting time between surgeries was 0.8 years (IQR 0.9, range 0.0 – 10.0 years). The mode of inheritance was reported in 89 out of 226 patients (39%), which included autosomal recessive (n = 47, 53%), autosomal dominant (n = 32, 36%) and X-linked (n = 10, 11%) inheritance forms (Supplemental Table 1). In addition to RP, 38 out of 226 patients (17%) had other ocular comorbidities that could compromise visual outcome (Table 1). Cataract morphology was described in 180 out of 295 eyes (61%), with PSC (n = 109; 61%) being the most common, followed by mixed (n = 38, 21%), nuclear (n = 23, 13%), mature (n = 6, 3%) and cortical (n = 4, 2%) cataract, respectively. The mean preoperative BCVA of the first treated eye was 1.03 ± 0.79 logMAR (approximately 20/214 Snellen), and the mean preoperative BCVA of the second treated eye was 0.80 ± 0.71 logMAR (approximately 20/129 Snellen). SD-OCT imaging data was available at pre-operative intake in 36 out of 226 patients (16%), revealing CME in 27 out of 72 eyes (38%).

Table 1. Baseline characteristics of patients with retinitis pigmentosa planned for cataract surgery.

Characteristic	
Total no. of patients	226
Total no. of operated eyes	295
Follow-up time in years	
Mean $\pm$ SD	0.8 $\pm$ 1.6 years
Median (IQR, range)	0.2 years (IQR 1.0, range 0.1 – 15.6 years)
Sex	
Male	112 (49%)
Female	113 (50%)
Not recorded	1 (1%)
Visual impairment at baseline	
No VI (BCVA $\geq$ 20/40)	39 (17%)
Mild VI (20/67 $\leq$ BCVA < 20/40)	37 (16%)
Moderate VI (20/200 $\leq$ BCVA < 20/67)	77 (34%)
Severe VI (20/400 $\leq$ BCVA < 20/200)	7 (3%)
Blindness (BCVA $\leq$ 20/400)	66 (30%)
SER at baseline in diopters (D)	
Mean $\pm$ SD	-1.2 $\pm$ 4.3 D
Median (IQR, range)	-0.5 D (IQR 2.3, range -28.3 to 25.5 D)
Ocular comorbidities	
None (n, %)	187 (83%)
Glaucoma (n, %)	12 (5%)
Epiretinal membrane (n, %)	1 (<1%)
Diabetic retinopathy (n, %)	2 (1%)
Fuchs endothelial dystrophy (n, %)	2 (1%)
Age-related macular degeneration (n, %)	2 (1%)
Retinal vascular occlusion (n, %)	2 (1%)
High myopia (n, %)	1 (<1%)
Corneal pathology (n, %)	2 (1%)
Retinal detachment (n, %)	2 (1%)
Amblyopia (n, %)	1 (<1%)
Laser refractive surgery (n, %)	2 (1%)
Optic nerve disease (n, %)	1 (<1%)
Unspecified macular pathology (n, %)	4 (2%)
Other (n, %)	4 (2%)

BCVA = best-corrected visual acuity; IQR = interquartile range; SD = standard deviation; SER = spherical equivalent of the refractive error; VI = visual impairment.

Intraoperative assessment

Cataract surgery was performed under general anesthesia (n = 91; 31%), or via local anesthesia using subtenon (n = 84; 29%), topical (n = 71; 24%), retrobulbar (n = 32; 11%) or unspecified (n = 17; 6%) techniques. All cataract extractions were performed using phacoemulsification techniques. The types of implanted IOLs, available for 287 cases, included monofocal IOLs (n = 279; 97%), and toric IOLs (n = 8; 3%). The

biomaterial of the implemented IOL lenses was hydrophobic acrylic ($n = 271$; 92%), hydrophilic acrylic ($n = 13$; 4%), silicon ($n = 2$; 1%), or unspecified ($n = 9$; 3%). Nineteen surgeries (6%) reported the use of blue-light filtering IOLs. The prophylactic use of a capsular tension ring was recorded in 17 out of 295 surgeries (6%). In total, 19 (6%) intraoperative complications were recorded, of which 15 (79%) were incidences of zonular dialysis; 2 were posterior capsular ruptures without vitreous loss; 1 case of intraoperative miosis; and 1 case reported a broken haptic IOL during surgery.

Postoperative assessment

Figure 1 shows a comparison between preoperative and postoperative BCVA after surgery. Following surgery, BCVA improved from 1.03 to 0.81 logMAR (-0.22 ; 95% CI: -0.31 to -0.13 ; $p < 0.001$) in the first eye, or approximately from 20/214 to 20/129 Snellen. In patients that also underwent surgery in the fellow eye, BCVA improved from 0.80 to 0.56 logMAR (-0.24 ; 95% CI: -0.32 to -0.15 ; $p < 0.001$), or approximately from 20/126 to 20/73 Snellen. Visual improvements, defined as a postoperative improvement in logMAR BCVA ≥ 0.1 , were seen in 166 eyes (56%). In the remaining eyes, 36 eyes (12%) showed worse BCVA (reduction of logMAR BCVA ≥ 0.1), and remained unchanged in 93 eyes (32%, BCVA changes in logMAR < 0.1). These patients showed a postoperative change in BCVA of $+0.19$ logMAR (95% CI -0.28 to -0.11 ; $p < 0.001$). The clinical characteristics and the complications of patients having worse postoperative BCVA are summarized in Supplemental Table 2. Marked BCVA improvements, defined as a BCVA change equal or greater than 0.3 logMAR (i.e., 15 ETDRS letter change), were observed in 87 out of 226 cases after first surgery (39%), and in 22 out of 69 eyes (32%) in patients with surgery in the contralateral eye. Odds of achieving marked BCVA improvements, adjusted for age and gender, were seen in patients with moderate visual impairment (odds ratio: 3.60; 95% CI: 1.74 – 7.46) and in patients with severe visual impairment to blindness (odds ratio: 4.36; 95% CI: 2.0 – 9.46) compared to patients with mild to no visual impairment (Table 2). Ocular comorbidities, intraoperative, or postoperative complications did not influence the presence of marked BCVA improvements. Patient-reported outcome data were available for 101 out of 226 patients (45%). Seventy-four out of 101 patients (73%) reported a subjective improvement in visual function following their first surgery, of whom 5 patients had showed no objective postoperative change in BCVA. The remaining patients with patient-reported outcome data reported no change ($n = 20$; 20%) or worse subjective visual function ($n = 7$; 7%) after surgery. In these patients with stable or worse subjective visual function, there was no marked BCVA improvement in 24 patients (89%). The remaining 3 patients with no subjective changes who did demonstrate marked BCVA changes postoperatively included 2 severely visually impaired or blind patients with minimal improvements in BCVA, and 1 patient who developed marked anterior capsular phimosis after surgery. Postoperative complications, excluding PCO, were reported in 32 out of 295 cases (11%). The most common postoperative complication was the exacerbation of pre-existing CME ($n = 8$; 25%), followed by the development of new CME ($n = 6$; 19%),

corneal edema (n = 5; 16%), capsular phimosis (n = 5; 16%), increase of intraocular pressure (n = 4; 13%), IOL subluxation (n = 3; 9%) and endophthalmitis (n = 1; 3%). In total, 111 out of 295 eyes (38%) developed significant PCO that required laser posterior capsulotomy during follow-up. Figure 2 shows that the median time for patients to undergo laser posterior capsulotomy was 15.0 months (95% CI: 12.8 – 17.2) after cataract surgery.

Table 2. Unadjusted and adjusted odds ratios of patients with retinitis pigmentosa following cataract surgery using marked BCVA improvement (postoperative improvement of > 0.3 logMAR) as dependent variable .

Characteristic	Unadjusted OR (95% CI:)	Adjusted OR (95% CI:)
Sex		
Male	1.00 [reference]	1.00 [reference]
Female	1.09 (95% CI: 0.64 – 1.87)	1.15 (95% CI: 0.66 – 1.99)
Age at surgery		
< 20 years	1.00 [reference]	1.00 [reference]
20 to 39 years	0.20 (95% CI: 0.02 – 2.02)	0.23 (95% CI: 0.02 – 2.27)
40 to 59 years	0.64 (95% CI: 0.20 – 2.00)	0.70 (95% CI: 0.22 – 2.67)
60 to 79 years	0.90 (95% CI: 0.34 – 2.39)	1.02 (95% CI: 0.37 – 2.77)
≥ 80 years	0.34 (95% CI: 0.23 – 1.75)	0.72 (95% CI: 0.255 – 2.03)
Preoperative BCVA		
Mild VI or better (BCVA ≥ 20/67)	1.00 [reference]	1.00 [reference]
Moderate VI (20/200 ≤ BCVA < 20/67)	3.36 (95% CI: 1.65 – 6.83)	3.60 (95% CI: 1.74 – 7.46)
Severe VI or worse (BCVA < 20/200)	4.32 (95% CI: 2.05 – 9.08)	4.36 (95% CI: 2.0 – 9.46)
Ocular comorbidities		
Not present	1.00 [reference]	1.00 [reference]
Present	1.55 (95% CI: 0.77 – 3.13)	1.51 (95% CI: 0.73 – 3.13)
Intraoperative complications		
Absent	1.00 [reference]	1.00 [reference]
Present	0.91 (95% CI: 0.26 – 3.2)	0.94 (95% CI: 0.26 – 3.32)
Postoperative complications		
Absent	1.00 [reference]	1.00 [reference]
Present	0.53 (95% CI: 0.20 – 1.4)	0.78 (95% CI: 0.22 – 1.54)
Posterior capsular opacifications		
Absent	1.00 [reference]	1.00 [reference]
Present	0.78 (95% CI: 0.47 – 1.27)	0.84 (95% CI: 0.50 – 1.40)

BCVA = best-corrected visual acuity; CI = confidence interval; OR = odds ratio; VI = visual impairment. Adjusted for age and gender. Analysis was performed using the first eye of each patient undergoing surgery. Intraoperative complications included zonulolysis, capsule rupture, dropped nucleus. Postoperative complications included cystoid macular edema, corneal edema, capsular phimosis, increased intraocular pressure, lens (sub)luxation, and endophthalmitis. Significant findings are shown in bold.

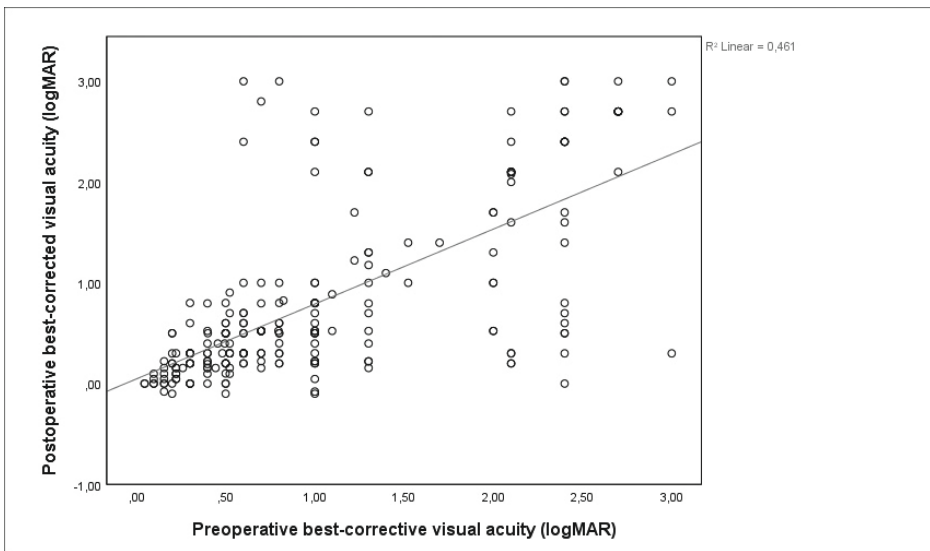


Figure 1. Scatterplot of preoperative best-corrected visual acuity using logarithm of the minimum angle of resolution (logMAR) values and postoperative best-corrected visual acuity in patients with retinitis pigmentosa that underwent cataract surgery. Analysis was performed using the first eye of each patient undergoing surgery.

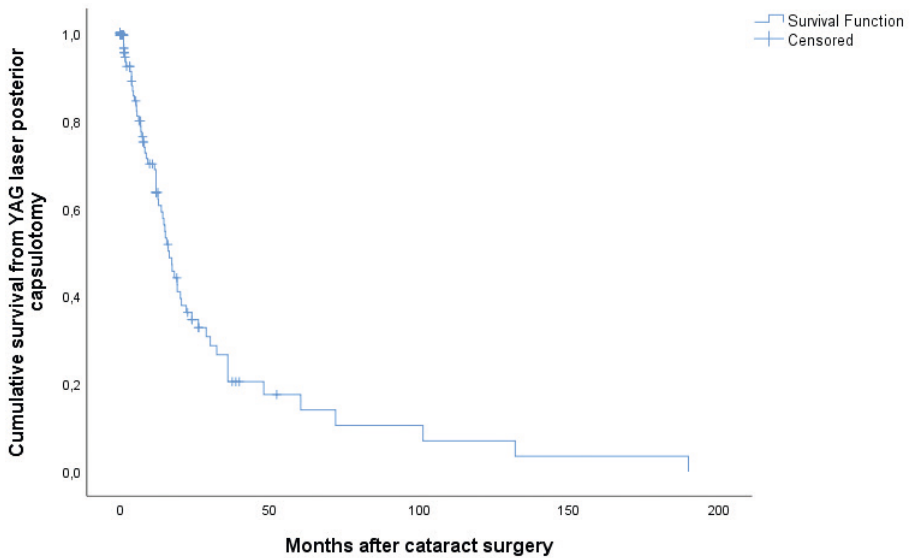


Figure 2. Kaplan-Meier survival curve showing the association between neodymium-doped yttrium-aluminum-garnet (YAG) laser posterior capsulotomy and the time after cataract surgery in patients with retinitis pigmentosa.

DISCUSSION

Our study demonstrates that cataract surgery in patients with RP leads to significant improvements in visual acuity, with more than half of the eyes included having better BCVA postoperatively than preoperatively. On average, BCVA improvements of 0.22-0.24 logMAR were observed, which is comparable to a 2- to 3-line BCVA increase measured on Snellen charts. These observations are consistent with BCVA outcomes in from previous smaller studies, who have reported postoperative BCVA improvements between 0.09-0.47 logMAR.^{3, 6, 7, 12, 17, 24} Despite the impact of RP on visual acuity, we found that marked BCVA improvements (greater than 0.3 logMAR) were also possible in this cohort following cataract surgery. We found that preoperative BCVA was a predictor for marked BCVA improvements, as groups with a BCVA of 20/200-20/67 Snellen (i.e. moderate visual impairment) and 20/200 or worse (i.e. severe impairment/blindness) had better odds of achieving marked BCVA improvements than patients with a BCVA of 20/67 or better (i.e. mild/no visual impairment). This would be expected, as patients preserved visual acuities are limited in their BCVA improvements due to a ceiling effect.⁷ Another possible and additional explanation is that patients with poor preoperative BCVA have more severe vision-impairing cataracts, which, in turn, yields higher gains in BCVA following surgery.

The severity of cataracts was not possible to ascertain in the current study, as cataract grading systems such as the Lens Opacities Classification System III are not routinely used in the clinical setting of the involved centers.^{11, 25} Still, in the remaining 44% of operated eyes, we found no BCVA improvements following surgery. We postulate that patients with no BCVA improvements may have extensive macular involvement causing irreversible vision loss, which precludes any BCVA improvement following cataract surgery.²⁶ Despite yielding no BCVA improvements, removal of significant cataract can be useful to rule out the contribution of cataract in disease progression. Additionally, removal of optically significant cataracts may allow for better visualization of retinal structures on fundoscopy and multimodal imaging. While the majority of patients underwent cataract surgery under local anesthesia, a relatively large group of patients (31%) in this study underwent surgery under general anesthesia. From our own clinical experience, the vast majority of cataract surgeries can be performed under local anesthesia. However, local anaesthesia may not be desirable in relatively younger patients and patients with significant associated extra-ocular abnormalities e.g. cognitive or hearing impairments, in whom general anesthesia is a viable alternative.²⁷⁻
²⁹Although our study did not investigate the degree of photoreceptor integrity on SD-OCT, it is well-known that preserved photoreceptor layers are associated with better visual acuity in patients of RP.^{26, 30-32} In addition, a previous study by Yoshida and colleagues demonstrated that postoperative BCVA was significantly better in patients with intact photoreceptor layers on OCT imaging following cataract surgery.³ Further investigation is needed into the potential predictive value of OCT imaging on visual

outcome following cataract surgery in patients with RP, as it was limited performed in this study.

In patients with available subjective data, subjective visual improvements were reported by most patients (73%), despite some having no objective change in BCVA following surgery. This suggests that objective BCVA improvement is not the sole indicator for successful cataract surgery. Due to the presence of both cataract and RP, it is possible that patients may perceive visual disturbances, such as glare, halo's and decreased contrast sensitivity, potentially at greater levels than those with age-related cataract.³ Alleviation of these visual disturbances through cataract surgery may prove more important than potential improvements in BCVA. Therefore, patients should be assessed for any perceived visual disturbances at preoperative and postoperative assessment.

The most common intraoperative complication was zonular dialysis, occurring in 15 (5%) of all cases. The occurrence of zonular dialysis is rare in surgeries for age-related cataract, as a previous large cohort study reported an incidence rate for zonular dialysis of 0.5%.²⁰ While the underlying mechanism remains unclear, it is believed that an inflammatory process may be the main cause for weakened zonular attachments.⁷ It has been postulated that increased levels of cytokines and chemokines are released into the aqueous humor and vitreous fluid as response to the diffusion of toxins derived from the degenerating retina by RP.³³ In turn, these may cause damage to zonular attachments, weakening their stability.^{7,19} When zonular weakness is present, this may result in complications including zonular dialysis, capsule tears, intraoperative miosis, and IOL (sub)luxation, which were all reported to some degree in the current study.¹⁷ Therefore, preoperative assessment in patients with RP should include the identification of possible signs of zonular weakness, such as phacodonesis and lens subluxation, which are indicative of severe zonular weakness.³⁴ Ultrasound biomicroscopy has also been used for zonular evaluation in previous studies, and allows for the assessment of the extent of zonular damage pre-operatively.^{35,36} Intraoperative signs include prominent anterior capsule stria during capsulorrhexis and difficulties with nucleus rotation after hydrodissection.³⁷ Necessary precautions can then be taken during surgery, such as extra attention to avoidance of unnecessary manipulation and strain on the lens zonules, for instance by optimal hydrodissection, and bimanual rotation of the nucleus; or by using nuclear fragmentation techniques that require minimal rotation such as the 'cross chop' technique.^{17,38} In this regard, creating a larger-than average capsulorrhexis can also be helpful for better mobilization of lens fragments, and may also help to reduce the risk of postoperative capsular phimosis. Some studies advocate the use of a capsular tension ring to provide stability to the lens equator, although this remains to be a subject of controversy.^{19,39} The use of a capsular tension ring may decrease the risk for IOL (sub)luxation, anterior capsule phimosis, and

PCO.^{17,40} The use of a capsular tension ring was reported in 6% of our cases, although the use of this ring may be underreported in our current retrospective study.

Postoperatively, the most common complications were the development of new CME, or the exacerbation of pre-existing CME, which collectively were found in 14 out of 295 eyes (5%). CME is a well-known complication associated with RP, and has been reported in 10-50% of all patients with RP.⁴¹ We reported the presence of CME in 16% of the patients at pre-operative intake, although its prevalence is likely underreported in this study as this information may not be automatically extracted from electronic health records. A recent study by Antonio-Aguirre and colleagues suggested that patients with RP were 4 times more likely to develop CME following cataract surgery.⁴² The mechanism of CME in RP remains unclear, but is presumably due to a dysfunction of the retinal pigment epithelium pumping mechanism and/or breakdown of the blood-retina-barrier.^{2, 43} Persistent CME may result in photoreceptor damage, and subsequently in loss of visual function if left untreated.⁴¹ Identifying the presence of CME at preoperative assessment on funduscopy or SD-OCT imaging can aid in pre-emptive management (e.g. administering topical non-steroidal anti-inflammatory drops postoperatively) and recognition of this complication. While limited evidence is available on the treatment of CME in patients with RP, several studies suggest the use of topical or oral carbon anhydrase inhibitors as a first-line approach.^{41, 44} Our study revealed that 38% of cases developed PCO that required Nd:YAG posterior capsulotomy, which reiterates that PCO is a common complication in patients with RP after cataract surgery.^{3, 4, 7, 12} The occurrence of PCO in this study is lower than reported rates of 43-52% by previous studies, although not all patients were available for follow-up, and thus the exact rate of PCO is probably underreported.^{6,7} We reported a median time of 15 months for patients to require Nd:YAG posterior capsulotomy, which is comparable to the period of 12 months described by Dikopf and co-workers.⁷ It has also been previously shown that the IOL biomaterial is one of the main risk factors for the development of PCO, with hydrophobic IOLs showing lower PCO rates than hydrophilic IOLs after cataract surgery.⁴⁵ We were not able to investigate the phenomenon in this study, as the majority of patients received hydrophobic IOLs. Nevertheless, patients with RP should be informed of the relatively high occurrence of PCO and its possible symptoms, in order to facilitate early intervention.

The results of this study should be interpreted with caution in light of its study design. An inherent flaw of a retrospective study design is the lack of complete and standardized data, and several parameters of interest (e.g. OCT imaging, patient-reported outcome data, or genetic data) were unavailable for a sizeable proportion of patients, as they were not routinely performed per standard care.⁷ Additionally, several comorbidities that may compromise visual acuity or pre-operative planning (e.g. presence of epiretinal membranes, CME or laser refractive surgery) showed unexpected low incidences and were most likely underreported, as these parameters

are not automatically recorded and extracted from electronic patient records. Nevertheless, this large study highlights some important features and outcomes in patients with RP, which may aid patient counselling and perioperative management.

In conclusion, this study suggests that cataract surgery leads to significant improvements in BCVA in the majority of patients with RP, with baseline BCVA being a potential predictive factor. Patients may experience subjective visual improvement, irrespective of their visual outcome. Surgeons should be aware of the high prevalence of zonular weakness and CME, which may warrant additional preparation. A high rate of PCO is also present, which requires early treatment with laser posterior capsulotomy. Further studies should include SD-OCT imaging, and the use of patient-reported outcome measures, as they are potentially important parameters for the evaluation of visual outcome.

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SUPPLEMENTAL CONTENT

Supplemental Table S1. Mode of inheritance and molecular diagnosis of this cohort.

Characteristic	Frequency (n)
Total patients	226
Mode of inheritance available	89
Mode of inheritance unavailable	137
Autosomal recessive	47
USH2A	16
EYS	5
PDE6A	2
PDE6B	2
MERTK	1
IFT140	1
Unknown/not recorded	20
Autosomal dominant	32
RHO	3
PRPF31	3
RP1	2
SRNP200	2
CA4	1
IMPHD1	1
KLHL7	1
PRPF8	1
Unknown/not recorded	18
X-linked	10
RPGR	6
Unknown/not recorded	4

The mode of inheritance and molecular diagnosis were extracted anonymously from electronic patient records and were available for a limited amount of patients.

Supplemental Table S2. Clinical characteristics of patients with RP that had worse visual acuity following cataract surgery.

Characteristic	
Total no. of cases	36
Visual impairment at baseline	
No VI (BCVA $\geq$ 20/40)	6 (17%)
Mild VI (20/67 $\leq$ BCVA < 20/40)	4 (11)
Moderate VI (20/200 $\leq$ BCVA < 20/67)	15 (42%)
Severe VI (20/400 $\leq$ BCVA < 20/200)	3 (8%)
Blindness (BCVA $\leq$ 20/400)	8 (22%)
Preoperative BCVA in logMAR	
Mean $\pm$ SD	1.00 $\pm$ 0.75 logMAR
Postoperative BCVA in logMAR	
Mean $\pm$ SD	1.71 $\pm$ 0.97 logMAR
Ocular comorbidities	
None (n, %)	27 (75%)
Glaucoma (n, %)	4 (10%)
Fuchs endothelial dystrophy (n, %)	1 (3%)
Retinal detachment (n, %)	1 (3%)
Optic nerve disease (n, %)	1 (3%)
Unspecified macular pathology (n, %)	1 (3%)
Other unspecified disease (n, %)	1 (3%)
Surgical complications	
None (n, %)	35 (97%)
Zonulysis (n, %)	1 (3%)
Postoperative complications	
None (n, %)	28 (78%)
Increase of CME (n, %)	2 (6%)
New CME (n, %)	2 (6%)
Increase of intraocular pressure (n, %)	3 (8%)
Corneal edema (n, %)	1 (2%)
Posterior capsular opacifications	
None (n, %)	27 (75%)
Present (n, %)	9 (25%)

Worse visual acuity was defined as a postoperative worsening of best-corrected visual acuity (BCVA) greater than 0.1 logarithm of the minimum angle of resolution (logMAR). CME = cystoid macular edema, IQR = interquartile range; SD = standard deviation; SER = spherical equivalent of the refractive error; VI = visual impairment.

