



In-depth analysis of risk factors for pseudophakic retinal detachments and retinal breaks

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ABSTRACT.

Purpose: To provide a detailed analysis of risk factors for pseudophakic retinal detachments (PRD) and pseudophakic retinal breaks (PRB).

Materials and methods: We reviewed the medical records of cataract surgeries between 1996 and 2017 at a tertiary care hospital in Austria. A Cox proportional-hazard regression model was used to analyse risk factors for PRD and PRB.

Results: Sixty-five thousand six hundred and sixty-two eyes (45 043 patients) underwent phacoemulsification, and 393 eyes (cumulative incidence 0.6%) were diagnosed with PRD (327 eyes) or PRB (66 eyes) during the follow-up (median 7.1 years, range 0–21). Calculation of adjusted hazard ratios (HR) revealed a hierarchy of risk factors for either event including (from the highest to the lowest risk) posterior capsular rupture (PCR), patient age <65 years (compared with the age group >75 years), male gender and high myopia. Diabetes mellitus was associated with a lower risk. PCR was the strongest risk factor for PRD both in patients with and without perioperative vitrectomy (i.e. vitreous loss), but time to PRD was significantly reduced only following PCR with vitrectomy.

Conclusions: Posterior capsular rupture, young patient age, male gender and high myopia were risk factors for PRD, but diabetes mellitus was associated with a lower risk. PCR had the strongest association with PRD, regardless of the need for perioperative vitrectomy due to vitreous loss. Time to PRD was reduced in patients with PCR and vitrectomy compared with PCR without the need for vitrectomy or uneventful surgery.

Key words: capsular rupture – cataract – myopia – phacoemulsification – pseudophakia – retinal breaks – retinal detachment

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Introduction

Global cataract prevalence has recently been estimated at 17.2% over all age groups with significant variations by region and age group (Hashemi et al. 2020). Cataract surgery is regarded as one of the most cost-effective treatments

and the socioeconomic effects of cataract surgery are substantial (Liu et al. 2017). Pseudophakic retinal detachment (PRD) has received increased attention in recent years because it can significantly antagonize the positive effects achieved by cataract surgery. Previous investigations identified numerous risk

factors for PRD and reported an inferred annual incidence between 0.04 and 0.25% (Clark et al. 2012; Bjerrum et al. 2013; Daien et al. 2015; Day et al. 2015; Day et al. 2016; Petousis et al. 2016; Kim et al. 2019). A French national population study by Daien et al. (2015) included 2.68 million eyes and reported high myopia, young age, vitrectomy for posterior capsular rupture (PCR), history of eye trauma, extracapsular operation, male gender and diabetes mellitus as risk factors for PRD. Similarly, Kim et al. (2019) (2.19 million eyes) found an increased risk for anterior vitrectomy, myopia, male gender, young age, residence in non-metropolitan areas and low household income. Day et al. (2015, 2016) investigated PRD in two studies (180 114 and 61 907 eyes) and identified capsular rupture (with and without vitrectomy) as a major risk factor. Finally, an investigation by Clark et al. (2012) (65 055 eyes) revealed that surgeries performed in the early years of their study period (1989–2001), young patient age, male gender and anterior vitrectomy were risk factors for PRD and a single-centre study by Petousis et al. (2016) specified capsular rupture with vitreous loss, high myopia, male gender and young patient age as risk factors. The impact of PCR has probably been underestimated by previous studies because only three publications (Day et al. 2015; Day et al. 2016; Petousis et al. 2016) explicitly included PCR without vitreous loss and vitrectomy in their definition of capsular rupture. Only three publications (Clark et al. 2012; Bjerrum et al. 2013; Daien et al. 2015)

explicitly included retinal breaks in their definition of PRD, but none revealed the absolute and relative numbers of retinal detachments and retinal breaks.

With this investigation, we want to provide a detailed analysis of risk factors for pseudophakic retinal detachments and retinal breaks. Special attention has been dedicated to posterior capsular rupture (PCR), as this well-known intraoperative complication was identified as the predominant risk factor in the majority of studies, although PCR without the need for anterior vitrectomy was mostly not included.

Materials and Methods

We retrospectively reviewed the medical records of patients operated for cataract using phacoemulsification between July 1996 and July 2017 at the Department of Ophthalmology of the Medical University Graz. This tertiary care hospital is the only facility offering retinal surgery for a geographically discrete population in Austria, where few if any patients travel to seek surgery in neighbouring units. All data were collected from a customized in-house documentation database. The associated software requires the surgeon to choose preassembled text modules in his surgical report. These modules can be selected by clicking a drop-down list and the selected value is then integrated in the report. An infinite number of reports can be exported together, and the values of any list can be arranged in the same column of a spreadsheet. This system enabled us to retrieve specific and reliable information of each case.

Parameters extracted for analysis included patient age, gender, laterality of the operated eye, the presence of high myopia, diabetes mellitus (parsed from text), cataract extraction technique, the failure to implant an intraocular lens, posterior capsular status, zonulysis (parsed from text), perioperative vitrectomy, time to and management of retinal detachment (pars-plana vitrectomy, scleral buckling or argon laser photocoagulation). High myopia was defined as a refractive error of -6 dioptres or more. Posterior capsular rupture (PCR) was defined as any perioperative tear to the posterior lens capsule, regardless of the need for vitrectomy due to vitreous loss. Except for diabetic tractional retinal

detachments, patients with diabetes mellitus were included. Proliferative vitreoretinopathy associated detachments were only excluded if they were redetachments.

Selection process

Patients <18 years, combined phacovitrectomies, intracapsular cataract extractions and extracapsular cataract extractions that did not involve phacoemulsification were excluded. Then, interventions for retinal detachments during the study period (vitrectomies, buckling procedures and argon laser photocoagulation) were evaluated. Diabetic tractional retinal detachments, non-diabetic tractional retinal detachments, serous retinal detachments (caused by uveal melanomas, uveitis, uveal effusion and macular haemorrhages), traumatic retinal detachments and redetachments were excluded, leaving only procedures that were associated with rhegmatogenous retinal detachments. These were then compared with the list of cataract surgeries in order to include only retinal procedures of eyes that were previously operated for cataracts (i.e. pseudophakic retinal detachments).

Approval of the study protocol was obtained from the Ethics Committee of the Medical University Graz (EK-30-235 ex 17/18), and the study adhered to the tenets of the Declaration of Helsinki.

Statistics

Metric parameters are descriptively summarized using either mean and standard deviation (SD) or median and range (minimum–maximum). Categorical parameters are given as absolute and relative frequencies. Follow-up time was defined as date of cataract surgery to either the last follow-up recorded in our database, the date of presentation at the department with a retinal event or the estimated life expectancy at the time of cataract surgery. The latter was calculated with annual national census data provided by the Statistics Austria Federal Institute, taking into account patient age, gender and operation year.

A Cox proportional-hazard regression model was used to analyse risk factors for both PRD and PRB after phacoemulsification. Clustering of the

data due to up to two eyes per person was considered in the models by estimating robust standard errors. Both univariable and multivariable analyses were performed for risk factors, and hazard ratios (HR) and the respective 95% confidence intervals (CI) are presented. Differences in time to event of patients with uneventful surgery were compared with PCR with and without the need for perioperative vitrectomy by generalized estimating equations (van der Geest et al. 2016), again taking into account clustering for each patient. All analyses are regarded exploratory in nature and a p -value of <0.05 was considered significant.

Statistical analysis was performed using R version 4.0.3 (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Seventy-two thousand three hundred and forty-four eyes of 49 403 patients were operated for cataract between July 1996 and July 2017 and were, therefore, reviewed. After exclusion of patients <18 years, combined phacovitrectomies, intracapsular cataract extractions ($n = 381$) and extracapsular cataract extractions ($n = 3620$) that did not involve phacoemulsification, 65 662 eyes of 45 043 patients were included (see Fig. 1 for distribution of cataract surgeries over the years). In total, 13 788 interventions for retinal detachment (vitrectomies, buckling procedures and argon laser photocoagulation) were performed during the study period. 2708 non-rhegmatogenous retinal detachments were excluded, leaving 11 080 procedures that were associated with rhegmatogenous retinal detachments. These were then compared with cataract surgeries in order to include only retinal procedures of eyes that were operated for cataract before (i.e. pseudophakic retinal detachments). Ultimately, 393 of the 65 662 eyes (cumulative incidence 0.6%) were diagnosed with PRD (327 eyes) or PRB (66 eyes) during the follow-up period (median 7.1 years, range 0–21).

Mean patient age at the time of cataract surgery was 73.8 years (SD 10.6, range 18–101), 60.1% of patients were female and 50.7% were right eyes (Table 1). The distribution of retinal interventions for either event (argon laser photocoagulation, pars-plana vitrectomy

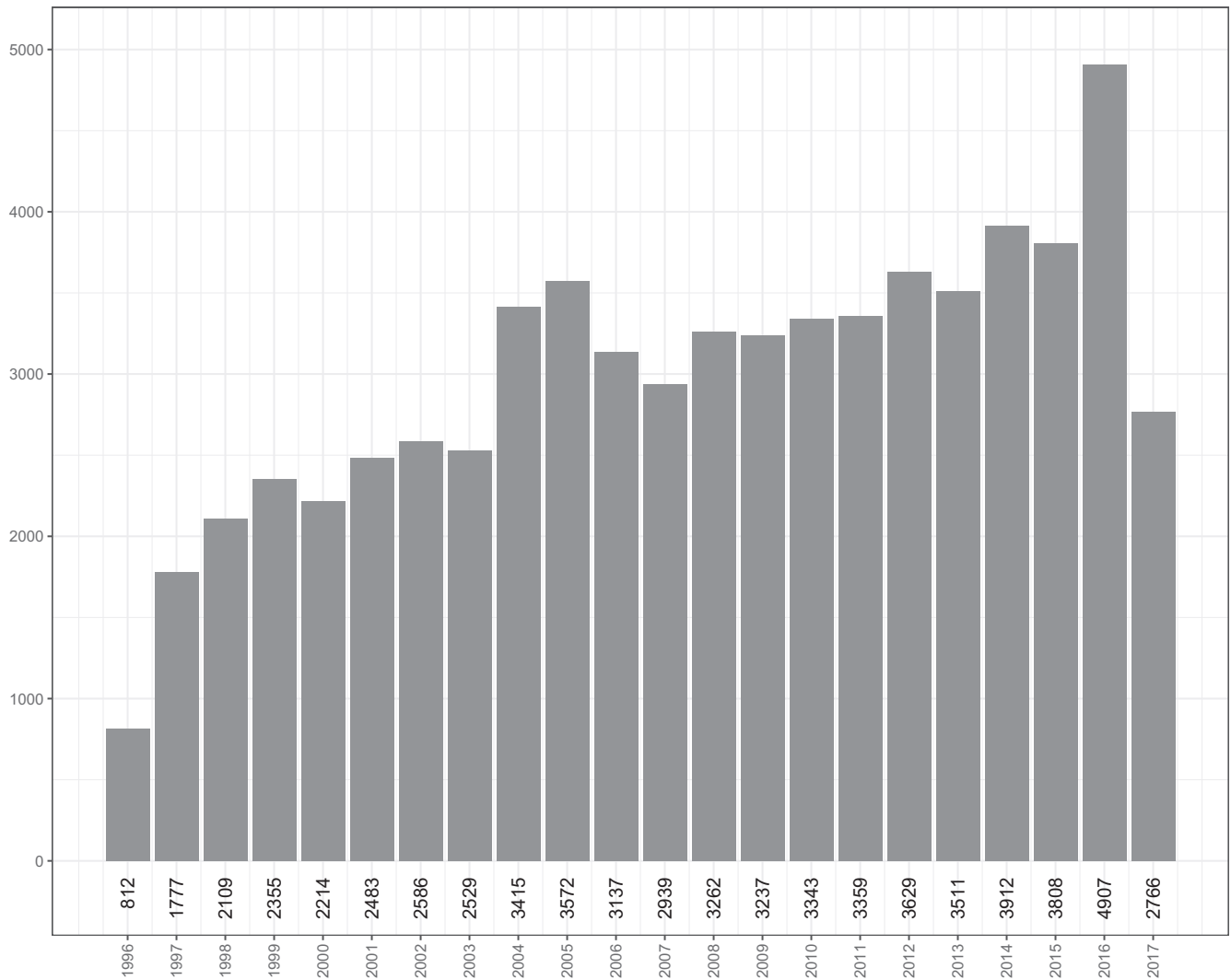


Fig. 1. Distribution of cataract surgeries over the years. The annual count of cataract surgeries is specified by the numbers next to the years.

or scleral buckling) is illustrated in Fig. 2. Patients with and without posterior capsular rupture (PCR) are characterized in Table 2a. Median time to PRD and/or PRB was 1.8 years for all patients (range 0–17.5 years, Table 2b). In patients with uneventful surgery, median time to PRD and/or PRB was 2.0 years (range 0–17.5 years). When PCR occurred and anterior vitrectomy had to be performed for vitreous loss, median time to PRD and/or PRB was 0.2 years (range 0–4.1 years), which was significantly different from patients with uneventful surgery (median 1.9 years, range 0–17.5, $p < 0.001$). When PCR without vitreous loss occurred, median time to PRD and/or PRB was 1.2 years (range 0–12 years), which was not significantly different from uneventful surgery ($p = 0.33$).

In the univariable Cox regression analysis, PCR, the failure to implant an artificial intraocular lens (IOL)

during primary surgery, male gender, high myopia and young patient age were significantly associated with a higher risk of a subsequent retinal event (either PRD or PRB), but diabetes mellitus was associated with a lower risk. In a multivariable model considering PCR, IOL implantation, age, refractive error, diabetes mellitus, zonulysis and gender, PCR had the highest risk of a retinal event, but patient age under 65 years, male gender and high myopia were also significantly associated. Diabetes mellitus was associated with a lower risk for either retinal event. The results of the multivariable analyses are presented in Table 3.

Discussion

We reviewed the medical records of cataract patients over a 21-year period and were able to determine incidence

rates and risk factors for PRD and PRB. The cumulative incidence for PRD and PRB was 0.6% in our study population. Different groups have previously investigated the incidence of PRD with results that were not identical, but revealed the association between cataract surgery and PRD (Clark et al. 2012; Bjerrum et al. 2013; Daien et al. 2015; Day et al. 2015; Day et al. 2016; Petousis et al. 2016; Kim et al. 2019). A recently published review used inferred annual PRD rates, that is cumulative PRD incidence rates divided by the observation period (assuming a linear cumulation of PRD), to compare results from different studies (Qureshi & Steel 2020). These rates were 0.04 (Petousis et al. 2016), 0.05 (Day et al. 2016), 0.068 (Clark et al. 2012), 0.12 (Day et al. 2015), 0.14 (Bjerrum et al. 2013), 0.238 (Kim et al. 2019) and 0.25% (Daien

Table 1. Descriptive statistics of patients with cataract surgery.

	No event (n = 65 269)	PRB (n = 66)	PRD (n = 327)	Total (n = 65 662)
Age (years)	73.9 ± 10.5	66.0 ± 11.1	63.4 ± 12.8	73.8 ± 10.6
(range)	(18–101)	(28–85)	(18–101)	(24–93)
Age < 65	10721 (16.4%)	29 (43.9%)	170 (52.0%)	10920 (16.6%)
Age 65–74	18422 (28.2%)	19 (28.8%)	88 (26.9%)	18529 (28.2%)
Age ≥ 75	36126 (55.3%)	18 (27.3%)	69 (21.1%)	36213 (55.2%)
No high myopia	62926 (96.4%)	61 (92.4%)	296 (90.5%)	63283 (96.4%)
High myopia	2343 (3.6%)	5 (7.6%)	31 (9.5%)	2379 (3.6%)
Female	39354 (60.3%)	27 (40.9%)	105 (32.1%)	39486 (60.1%)
Male	25915 (39.7%)	39 (59.1%)	222 (67.9%)	26176 (39.9%)
Left eyes	32191 (49.3%)	28 (42.4%)	141 (43.1%)	32360 (49.3%)
Right eyes	33078 (50.7%)	38 (57.6%)	186 (56.9%)	33302 (50.7%)
No diabetes mellitus	62112 (95.2%)	63 (95.5%)	321 (98.2%)	62496 (95.2%)
Diabetes mellitus	3157 (4.8%)	3 (4.5%)	6 (1.8%)	3166 (4.8%)
Intact zonules	64719 (99.2%)	65 (98.5%)	323 (98.8%)	65107 (99.2%)
Zonulysis	550 (0.8%)	1 (1.5%)	4 (1.2%)	555 (0.8%)
Posterior capsular status unknown	108	1	1	110
Intact posterior capsule	63936 (98.1%)	64 (98.5%)	285 (87.4%)	64285 (98.1%)
Posterior capsular rupture total	1225 (1.9%)	1 (1.5%)	41 (12.6%)	1267 (1.9%)
Posterior capsular rupture with vitrectomy	605 (0.9%)	–	27 (8.3%)	632 (1.0%)
Posterior capsular rupture without vitrectomy	620 (1.0%)	1 (1.5%)	14 (4.3%)	635 (1.0%)
Scleral buckling surgery	–	–	79 (24.5%)	79 (20.5%)
Argon laser photocoagulation (focal)	–	64 (100.0%)	22 (6.8%)	86 (22.3%)
Vitrectomy	–	–	221 (68.6%)	221 (57.3%)

Data are presented as either mean ± standard deviation (SD) or n (%). Percentages refer to available observations.

PRB = pseudophakic retinal breaks; PRD = pseudophakic retinal detachment.

et al. 2015) in the aforementioned studies. Considering the great number of cataract cases, these differences become relevant in absolute numbers and may be caused by multiple factors including differences in sample size, study design (national population studies vs. single-centre studies), adjustment for retinal detachment in the general population, follow-up and inclusion criteria. National population studies have the advantage of a more reliable follow-up, as patients moving within their country are not lost. Indeed, the largest published national population study has reported the highest incidence of PRD, even though cataract operations until the end of the study period were included, and follow-up time was limited to four years, which could result in an underestimation of the PRD rate (Daien et al. 2015).

Young patient age and male gender were risk factors for PRD in our investigation and in previous studies (Clark et al. 2012; Daien et al. 2015; Petousis et al. 2016; Kim et al. 2019). The association between male gender and retinal detachment remains unclear. Young patient age and male gender are also associated with retinal detachment in the general population

(Qureshi & Steel 2020) and appropriate adjustment prevents overestimating the PRD rate. Bjerrum et al. used non-operated fellow eyes as reference and concluded that age and male gender are not risk factors for retinal detachment specifically after cataract surgery (i.e. PRD), but rather general risk factors for retinal detachment (Bjerrum et al. 2013). While this study was the first to make this adjustment, the median follow-up time was limited (0.23 years), and other risk factors were not investigated.

We further report an increased hazard ratio for high myopia, which is in agreement with three other investigations (Daien et al. 2015; Petousis et al. 2016; Kim et al. 2019). Because rhegmatogenous retinal detachment is caused by posterior vitreous detachment (PVD), there appears to be increasing interest in the influence of PVD on retinal detachment specifically after phacoemulsification in myopic eyes. To provide a reference, Ivastinovic et al. have previously analysed the incidence of PVD in emmetropic patients after uneventful phacoemulsification and report a PVD rate of 71.4% three months after surgery (Ivastinovic et al. 2012). Time to PRD was not significantly different between

myopes and non-myopes in our study (p = 0.317, calculated using generalized estimating equations to account for clustering of eyes within patients), which could imply that development of PVD is not accelerated by high myopia in the context of surgery. However, it is possible that pseudophakic myopes may sustain a more dynamic (but not earlier) detachment of the posterior vitreous, although this is speculative. We believe that replacing a myopic lens with a thin artificial intraocular lens could provoke a displacement of the lens-iris diaphragm, which may in turn cause increased dynamics. Further studies will eventually be required to specifically analyse pseudophakic PVD in myopic patients.

Diabetes mellitus without traction was associated with a lower risk for PRD in our study and in the investigation by Kim et al. (2019), but associated with an increased risk for PRD in the paper by Daien et al. (2015). We can only speculate about the reasons for these inconsistent results and further investigations are needed to assess diabetes mellitus as a risk factor for PRD and PRB.

In total, 1267 eyes had PCR in our study, but only 632 (49.9%) had vitreous loss that required anterior

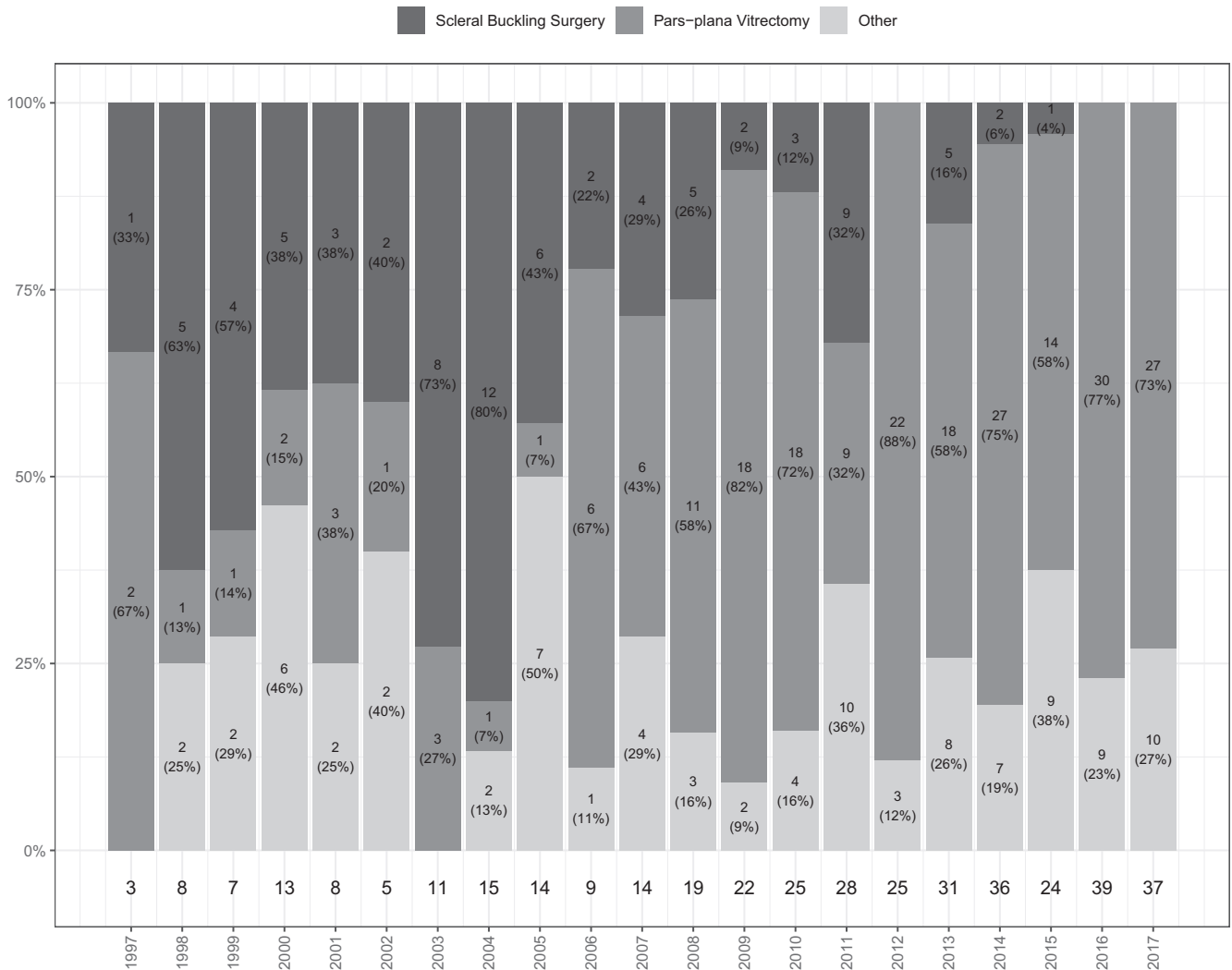


Fig. 2. Distribution of retinal interventions for either event (pars-plana vitrectomy, scleral buckling and other = argon laser photocoagulation and unknown). The annual count of retinal interventions is specified by the numbers next to the years.

vitrectomy and 635 (50.1%) were managed without vitrectomy. Analysed separately, PCR with vitreous loss was more likely to result in PRD in our study, but PCR without vitreous loss was associated with PRD nevertheless. Compared with uneventful surgery (median time to PRD 1.9 years), time to PRD was significantly reduced following PCR and anterior vitrectomy (median time to PRD 0.2 years, $p < 0.001$), but time to PRD following PCR without the need for anterior vitrectomy was not (median time to PRD 1.2 years, $p = 0.33$). We want to point out that PCR without anterior vitrectomy was, therefore, associated with an increased risk for, but not with a reduced time to PRD, which is an interesting observation. PCR can be managed without anterior vitrectomy if vitreous loss is not

observed by the surgeon, typically when the posterior capsule ruptures during later steps of the operation. Even though increased anteroposterior traction seems to be less relevant immediately after these cases because time to PRD is not reduced, we hypothesize that mechanical and/or biochemical modifications of the vitreous could play a role later on because the risk to develop PRD is increased. Accordingly, we believe that the distinction between PCR with and without vitrectomy is essential. Anterior vitrectomy alone is an established risk factor for PRD and hazard ratios have been reported with 2.6 (Kim et al. 2019), 4.4 (Daien et al. 2015), 12.8 (Petousis et al. 2016) and 27.6 (Clark et al. 2012). Day et al. (2015, 2016) previously reported higher PRD rates after PCR with and without anterior

vitrectomy, albeit without specifying hazard ratios. Similar to our data, time to PRD after PCR with vitreous loss was reduced in another investigation, but no cases of PRD were observed after PCR without vitreous loss (Petousis et al. 2016). Other studies potentially missed a significant number of patients with PCR (but without vitreous loss) as they searched for the diagnostic codes associated with anterior vitrectomy and, therefore, potentially underestimated the impact of PCR on PRD. Interestingly, Naderi et al. (2020) recently reported that following anterior vitrectomy for PCR, the risk for PRD might be lower in eyes that require subsequent posterior vitrectomy for dropped nuclear lens fragments, which raises the question of the best management following PCR. Further investigations will

Table 2a. Descriptive statistics of patients with and without posterior capsular rupture (PCR).

	PCR (n = 1267)	No PCR (n = 64 285)
Age (years) (range)	74.6 ± 10.9 (19–97)	73.8 ± 10.6 (18–101)
Age < 65	181 (14.3%)	10 711 (16.7%)
Age 65–74	338 (26.7%)	18 159 (28.2%)
Age ≥ 75	748 (59.0%)	35 415 (55.1%)
No high myopia	1238 (97.7%)	61 938 (96.3%)
High myopia	29 (2.3%)	2347 (3.7%)
Female	710 (56.0%)	38 714 (60.2%)
Male	557 (44.0%)	25 571 (39.8%)
Posterior capsular rupture with vitrectomy	632 (49.9%)	–
Posterior capsular rupture without vitrectomy	635 (50.1%)	–
Intact zonules	1267 (100.0%)	63 733 (99.1%)
Zonulysis	0 (0.0%)	552 (0.9%)
Implantation of IOL	1205 (95.1%)	64 189 (99.9%)
No implantation of IOL	62 (4.9%)	96 (0.1%)

Posterior capsular status was not available for 110 cases. Data are presented as either mean ± standard deviation (SD) or *n* (%). Percentages refer to available observations. IOL = intraocular lens.

Table 2b. Time to PRD.

	No PCR (n = 285)	All PCR (n = 41)	PCR (no VE) (n = 14)	PCR (VE) (n = 27)	Total (n = 327)
Median (Q1–Q3)	2.0 (0.7–4.9)	0.4 (0.1–1.9)	1.5 (0.4–2.7)	0.2 (0.1–0.8)	1.8 (0.5–4.4)

PCR = posterior capsular rupture; Q = quartile; VE = vitrectomy.

Table 3. Multivariable Cox regression analyses investigating risk factors for PRB or PRD.

	PRD or PRB		
	HR	95% CI	p
PCR	5.94	4.21–8.38	<0.001
No IOL	1.88	0.84–4.21	0.126
High myopia	1.87	1.30–2.68	0.001
Male gender	2.40	1.93–2.99	<0.001
Age 65–74*	0.37	0.29–0.47	<0.001
Age ≥ 75*	0.18	0.14–0.24	<0.001
Diabetes	0.41	0.21–0.79	0.008
Zonulysis	1.33	0.55–3.26	0.528
PCR with vitrectomy [†]	8.66	5.53–13.54	<0.001
PCR without vitrectomy [†]	3.92	2.32–6.61	<0.001

The analyses of PCR with and without vitrectomy, respectively, were derived from an analogous model considering the 3-group factor and all parameters otherwise depicted.

CI = confidence interval; HR = hazard ratio; No IOL = failure to implant an intraocular lens; PCR = posterior capsular rupture; PRB = pseudophakic retinal breaks; PRD = pseudophakic retinal detachment.

*Compared to <65.

[†]Compared to no PCR.

eventually be required to evaluate which type of vitrectomy is beneficial in complicated cataract cases involving PCR with and without vitreous loss.

We further report that PCR mostly resulted in PRD (41 cases) compared with PRB (one case) in our series. It is

imaginable that the posterior vitreous not only detaches earlier than usual, but also with increased dynamics in patients with PCR and vitreous loss compared with patients after uneventful cataract surgery. This would consequently accelerate the development of PRD and give

patients less time to self-refer to a medical facility. Although this aspect of our investigation is debatable and speculative, we suggest attentive follow-up in patients with posterior capsular rupture and meticulous patient information about vitreoretinal symptoms, because previous reports have established that macula-ON patients are well-informed and more sensitive to floaters compared with macula-OFF patients (Eijk et al. 2016).

To our knowledge, this is the first investigation that was able to characterize cases with posterior capsular rupture in great detail. The main limitation of our study is its single-centre setting, which could have led to patients self-referring to other hospitals. Also, some extramural physicians in our area have the equipment to perform argon laser photocoagulation, which could mean that patients with PRB self-referred to these physicians, and we missed them in our analysis. This may in part explain the relatively small number of retinal breaks that we observed. However, the vast majority of patients primarily seek treatment in our unit or are referred to our unit by the extramural sector when they present with vitreoretinal symptoms. Another limitation of our study is the non-adjustment for retinal detachment in the general population. The strength of our study is its large sample size and the integrity of its data, which allowed us to evaluate all essential risk factors in a homogeneous study population over a 21-year period with a median follow-up time of 7.1 years. We calculated the third quartile of either retinal event at 4.2 years, which could mean that observation periods of 4 years or less may not be enough to collect all relevant data.

In summary, the cumulative incidence for PRD or PRB was 0.6% in our study setting. PCR, male gender, high myopia and young patient age were risk factors for either retinal event. We separately analysed PCR with and without anterior vitrectomy and found that PCR is the most prominent risk factor for PRD regardless of anterior vitrectomy. However, time to PRD was reduced in patients with vitreous loss, but not in patients without vitreous loss. We suggest careful patient information and postoperative follow-up in these patients.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Fig. S1. Supplement. Cataract surgeries per year and annual incidence of posterior capsular rupture (absolute numbers and percentages inside the bars).