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Postoperative Endophthalmitis in Immediate Sequential Bilateral Cataract Surgery

A Nationwide Registry Study

Emma Friling, MD,[1,2] Björn Johansson, MD, PhD,[3] Mats Lundström, MD, PhD,[4] Per Montan, MD, PhD[1,5]

Purpose: To report the incidence of postoperative endophthalmitis (PE) after immediate sequential bilateral cataract surgery (ISBCS) in Sweden.

Design: Retrospective cohort registry study.

Participants: Patient data from 1 457 172 cataract extractions, including 1 364 934 unilateral surgeries and 92 238 ISBCSs.

Methods: Endophthalmitis cases reported to the Swedish National Cataract Register (NCR) during a 16-year period (2002–2017) were analyzed in comparison to all control cases with regard to patient characteristics, surgical technique, and capsule complication.

Main Outcome Measure: Incidence and determinants for PE in ISBCS compared with unilateral surgeries.

Results: A total of 422 cases of PE were identified in 1 457 172 cataract extractions, yielding an overall incidence of 0.029% (95% confidence interval [CI], 0.0262–0.0317). For unilateral procedures, the rate was 0.0299% (95% CI, 0.0270–0.0328) or 408 cases in 1 364 934 operations, whereas that for ISBCS was 0.0152% (95% CI, 0.0072–0.0231) or 14 incidents in 92 238 operations ($P = 0.01$). In a logistic regression model including all cataract procedures, nonuse of intracameral (IC) antibiotics (ABs), capsule complication, age 85 years or more, male gender, and ocular comorbidity were found to be independent risk factors for PE. All these parameters were less frequent in ISBCS. Notwithstanding, in the same multivariate analysis, ISBCS in itself was associated with a significantly lower risk for PE. At follow-up, 5 of the 14 PE cases in the ISBCS cohort had a visual acuity (VA) of 20/200 or worse. Of these, one 93-year-old ISBCS patient developed bilateral infection.

Conclusions: After ISBCS in Sweden, PE occurred once in 6600 surgeries. The risk of sustaining a final VA of 20/200 or less was 1 incident in 18 000 operated eyes. When counseling potential ISBCS patients about the risk of PE, it seems reasonable to state that the reported risk in the literature is lower than that with unilateral surgery but not negligible. Precautions remain necessary. *Ophthalmology 2022;129:26-34 © 2021 by the American Academy of Ophthalmology. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).*

With the evident safety and efficacy of phacoemulsification,[1] managing bilateral cataract with immediate sequential bilateral cataract surgery (ISBCS) has become a viable option in many parts of the world. Increased patient convenience, faster overall vision recovery, and logistic advantages translating into cost savings are among the strongest arguments for this practice.[2-9] However, there is a general consensus among cataract surgeons in Europe and North America that this approach should be reserved for patients without ophthalmic risk factors such as visually significant ocular comorbidities, biometry outliers,[10] dense cataracts, or loose zonules, which can all jeopardize the outcome, be it in 1 or both eyes.[5,8,11-14] Nonetheless, the fear of largely unforeseen sight-threatening complications such as postoperative endophthalmitis (PE), which in the worst scenario can occur bilaterally,[15-17] has been a major obstacle for many surgeons to implement ISBCS even on a small scale.[14,18] The literature on endophthalmitis after cataract surgery is vast. Recent studies relying on large databases show incidence figures ranging from 0.01% to 0.05%,[19-23] but there are few publications that specifically address the PE rates in the context of ISBCS.[9,11] This retrospective study investigates the rates of PE after ISBCS and unilateral procedures, based on data reported to the Swedish National Cataract Register (NCR) over a 16-year period. In this timeframe, there has been a gradual adoption of ISBCS in the country, although no officially endorsed guidelines for patient selection exist on a national level.

Methods

Data from the NCR from January 1, 2002, to December 31, 2017, were reviewed. Since 1998, cases of PE after cataract operations have been reported to the NCR. All ophthalmic surgical units are taking part by a commitment that is renewed on a yearly basis. The validity of the reporting of the previous year is checked via e-mail queries during the month of April. Diagnosis of endophthalmitis is based on clinical suspicion, that is, an inflammatory reaction out of

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proportion with the surgical trauma warranting intraocular sampling for bacterial culture or polymerase chain reaction testing. Both culture-proven cases and negatively tested cases are reported. For the latter category, the diagnosis of PE is deemed definite if there is a poor visual outcome or the visual recovery is slow, as reported in previous publications.[19,20] No specific time span for the diagnosis is set. The endophthalmitis report holds information on case identification, prophylactic regimen, identified species from the intraocular samples, and visual acuity (VA) attained approximately 3 months after the diagnosis. Treatment of presumed endophthalmitis in Sweden is carried out in line with the recommendations of the Endophthalmitis Vitrectomy study.[24]

The PE cases can be traced in the large core registry of the NCR by the clinic, date, and consecutive number of the cataract surgery, but since 2010 the matching is simplified since identification by use of the unique personal Social Security Number has been implemented. The NCR contains data on 96% of all cataract extractions performed in Sweden. The entire registry was exploited to calculate the incidence and identify independent predictive factors for the development of PE. The following information relevant to this study was retrieved: ISBCS or not; age 85 years and above; sex; preoperative VA 20/200 and worse; presence of glaucoma, age-related macular degeneration (AMD), diabetic retinopathy (DRP) or "other" comorbidity (including, e.g., corneal disease, retinal disorder other than AMD or DRP, previous intraocular interventions), all amalgamated and designated ocular comorbidity; type of cataract extraction (phacoemulsification with implantation of posterior chamber intraocular lens [IOL] or any "other procedure" such as phacoemulsification with anterior chamber IOL implantation or no IOL implant, other kinds of cataract extraction or cataract extraction combined with another procedure); IOL material (acrylic hydrophobic or other materials including acrylic hydrophilic or no IOL implant); intraoperative capsule rupture or zonular dehiscence designated as capsule complication and use of intracameral (IC) antibiotic (AB).

To investigate how ISBCS was organized in a representative sample of more proficient units, we searched the database for centers that any year during the period 2002 to 2013 performed ISBCS in 10% or more of their total surgical volume. The centers in question (n = 17) received in 2015 an inquiry about principles for selection of candidate patients, degree of separation of the procedures, measures to achieve and maintain sterility, and use of infection prophylaxis.

Approval for this project was received from the Swedish Ethical Review Authority, Number 2019-02899. The research adhered to the tenets of the Declaration of Helsinki. Because this was a register-based retrospective study, written patient consent was not required. All statistical calculations were performed with version 27 of IBM SPSS (SPSS Inc.). P values < 0.05 were considered statistically significant. Pearson's chi-square test was used for categorical data, and the SPSS explore function was used to calculate the 95% confidence intervals (CIs) of rates. Poisson analysis for single factor comparisons was used computing odds ratios (ORs) for PE among unilateral and ISBCS cases and then applied in a multiple regression model identifying independent risk factors for PE in the entire material. Possible interactions between these factors were investigated by exploring multicollinearity in a logistic regression analysis. No variance inflation factor exceeded 1.1.

Results

Figures 1 and 2 display cataract surgery volumes and the evolvement of the frequency of ISBCS and the incidence of endophthalmitis, respectively, in this 16-year time span in Sweden. A total of 422 cases of PE were identified in 1 457 172 cataract extractions, corresponding to an incidence of 0.029% (95% CI, 0.0262−0.0317) in the study period. For unilateral procedures, the rate was 0.0299% (95% CI, 0.0270−0.0328) or 408 cases in 1 364 934 operations and for ISBCS, the rate was 0.0152% (95% CI, 0.0072−0.0231) or 14 incidents in 92 238 operations ($P = 0.01$). Mean age was 74.7 ± 9.6 years for cases undergoing unilateral procedures and 73.8 ± 9.8 years for ISBCS ($P < 0.001$). Table 1 demonstrates univariate analyses of the relation between preoperative and peroperative variables and PE in the unilateral and ISBCS groups, respectively. In a subsequent multivariate logistic regression model based on the entire material, nonuse of IC AB, capsule complication, age 85 years or more, male gender, and ocular comorbidity were all found to be independent risk factors for PE, whereas ISBCS per se was associated with a lower risk for PE (Table 2). The distribution of putative or proven risk factors for PE differed significantly between unilateral operations and ISBCS procedures, suggesting a risk-limiting approach in the performance of the latter kind of surgery (Table 3).

The incidence of PE after ISBCS did not differ between the early (2002−2010; 5 cases in 27 572 operations = 0.0181%) (95% CI, 0.0022−0.0340) and the late (2011−2017; 9 cases in 64 657 operations = 0.0139%) (95% CI, 0.0048−0.0230) ($P = 0.85$) phases of the study or between high-volume units (≥3000 surgeries/unit; 9 cases in 41 908 surgeries = 0.022%) (95% CI, 0.0074−0.036) and low-volume units (<3000 surgeries/unit; 5 cases in 50 330 surgeries = 0.01%) (95% CI, 0.0012−0.019) ($P = 0.16$). The ISBCS sites that were surveyed in 2015 for practice principles gave the following responses. Six of 17 sites had written guidelines for the selection of candidate patients, and the remaining clinics left the decision to the surgeon's discretion. Informed consent was always obtained and documented in the patient record. All centers organized the surgeries as separated procedures with change of instruments, drapings and sterile gowns, and gloves for the surgeon and assistant. Intraocular solutions and devices were without exception taken from different units for the right and left eyes, but product batch separation was not practiced as a rule. Instrument cleaning and sterilization were systematically quality assured, adequately monitored by process recordings, and as for the autoclave process verified by chemical indicators. Segregated sterilization cycles of the surgical instruments for the 2 eyes were generally not used. Use of IC AB was practically mandatory with 1 mg of cefuroxime as a standard in the beginning of the study period. With time, it was supplemented with 100 μg IC ampicillin in the majority of centers. The aim was to target enterococci, which are feared causative organisms of PE not covered by cefuroxime. More rarely, 0.2 mg of moxifloxacin was instilled as a single AB, which is less than the globally more common 0.5 mg dose.[22]

Details of the endophthalmitis incidents after ISBCS are shown in Table 4. Causative isolates and final VA were on par with PE cases after unilateral surgery.

One patient developed bilateral endophthalmitis: a 93-year-old woman, living in a care home for the elderly, who presented with visually affecting cataract in both eyes. Her VA was 20/80 in the right eye and 20/60 in the left eye. Referring to poor general health, mainly cardiovascular disease, she wanted to undergo bilateral surgery to minimize hospital visits. The operations, performed under local anesthesia, were uneventful, and she received IC cefuroxime 1 mg and ampicillin 100 μg as prophylaxis. The staff were experienced in ISBCS, and the routines for a complete separation between eyes were followed. The planned postoperative visit at 1 week revealed quiet eyes with no signs of inflammation. Six days later, the patient experienced decreased vision bilaterally and some pain in the right eye. At the examination the following day in a tertiary referral center, vision of hand movements in both

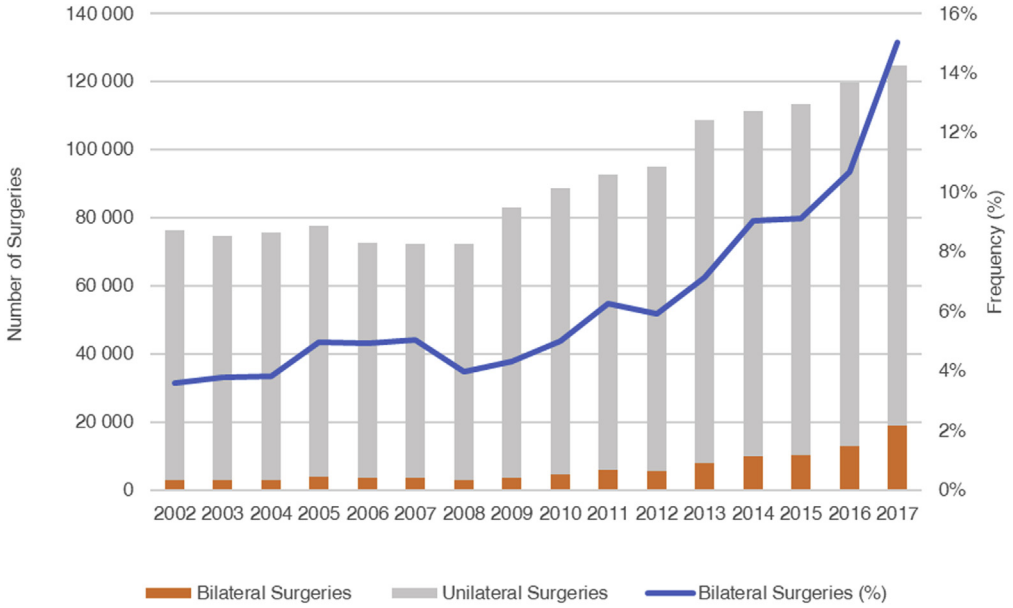

Figure 1. Evolvement of cataract surgery volumes demonstrating numbers of unilateral and immediate sequential bilateral surgery (ISBCS) and the percentage of ISBCS in Sweden according to the Swedish National Cataract Register (NCR) 2002–2017.

eyes, dense flare, and a hypopyon of 0.5 mm were recorded. Intraocular taps with injection of intravitreal gentamicin and vancomycin were performed, and in addition, oral steroids were administered. Cultures from both eyes showed coagulase-negative staphylococci resistant to methicillin, signifying resistance to both IC prophylactic agents given perioperatively, but sensitivity to vancomycin. At 1.5 months after surgery, VA had improved to 20/125 in the right eye and counting fingers at 1 m in the left eye. No further clinical follow-up was possible because she died of worsening general health 1 month later.

Discussion

High-volume registry data are extremely valuable in terms of providing sufficient statistical power for studying rare events such as PE after cataract surgery and even more so after ISBCS, which is less commonly practiced in many parts of the world. The NCR with a 96% coverage of all cataract operations in the country includes PE as a reported item since 1998. A number of investigations of PE covering different time periods have been published from the NCR. For this project, the database of 2002–2010, already analyzed in 2 articles,[19,20] was added to data from 2011–2017 to reach a more solid number of ISBCS procedures. Surgical volume data were fairly equal between periods with the exception of ISBCS, of which 66% were carried out in the latter period.

Our national incidence of PE in ISBCS over a 16-year time span, 0.0152%, was significantly lower than that of unilateral surgery, 0.0299%, but is somewhat higher than the rates from

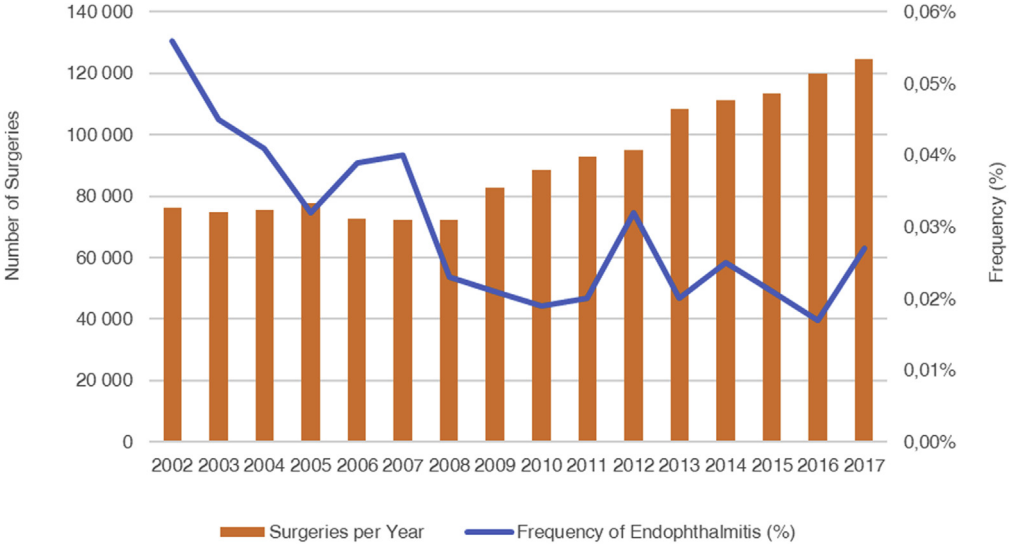

Figure 2. The rate of postoperative endophthalmitis (PE) according to registry data in the Swedish NCR 2002–2017.

Table 1. Single Risk Factors with Poisson Analysis in 1 457 172 Surgeries with 408 Cases of PE in 1 364 934 Unilateral Operations and 14 Incidents of PE in 92 238 ISBCS Operations

Patient Factor or Surgical Factor	Unilateral					ISBCS				
	PE Cases/Total Number	*% [95% CI]*	*OR*	*95% CI*	*P Value*	*PE Cases/Total Number*	*% [95% CI]*	*OR*	*95% CI*	*P Value*
Age										
8–84 yrs	314/1 177 169	0.0267 [0.0237–0.0296]	1.0			8/81 551	0.0098 [0.00300–0.00166]	1.0		
≥85 yrs	94/187 765	0.0501 [0.0399–0.0602]	1.887	1.483–2.353	< 0.001	6/10 687	0.0561 [0.0112–0.1011]	5.724	1.885–16.457	< 0.001
Gender										
Female	230/832 741	0.0276 [0.0240–0.0312]	1.0			8/57 549	0.0139 [0.0043–0.0235]	1.0		
Male	178/532 193	0.0334 [0.0285–0.0384]	1.211	0.995–1.472	0.055	6/34 689	0.0173 [0.0035–0.0311]	1.244	0.432–3.586	0.686
VA										
>20/200	317/1 132 235	0.0280 [0.0249–0.0311]	1.0			13/82 988	0.0157 [0.0072–0.0242]	1.0		
≤20/200	91/232 699	0.0391 [0.0311–0.0471]	1.397	1.106–1.755	0.005	1/9250	0.0108 [0.0104–0.0320]	0.690	0.0380–3.465	0.721
Comorbidity										
No	229/866 231	0.0264 [0.0230–0.0299]	1.0			8/69 518	0.0115 [0.0035–0.0195]	1.0		
Yes	179/498 703	0.0359 [0.0306–0.0411]	1.358	1.116–1.650	0.002	6/22 720	0.0264 [0.0053–0.0475]	2.295	0.795–6.598	0.124
Procedure type										
Phaco + PC IOL	393/1 348 589	0.0291 [0.0263–0.0320]	1.0			14/91 913	0.0152 [0.0073–0.0232]			
Other	15/16 345	0.0918 [0.0453–0.1382]	3.149	1.798–5.079	< 0.001	0/325	0			1.000
IOL type										
Hydrophobic acrylic	377/1 285 270	0.0293 [0.0264–0.0323]	1.0			13/84 002	0.0155 [0.0071–0.0239]			
Other	22/75 616	0.0291 [0.0169–0.0413]*	1.0			1/8206*	0.0122 [0.0117–0.0361]			
No IOL	9/4048	0.2223 [0.0772–0.3675]	7.598	3.917–14.682	< 0.001	0/30	0			1.000
IC AB										
Yes	384/1 357 283	0.0283 [0.0255–0.0311]	1.0			12/91 912	0.0131 [0.0057–0.0204]	1.0		
No	24/7651	0.3137 [0.1884–0.4390]	11.088	7.314–16.748	< 0.001	2/326	0.6135 [0.2386–1.4656]	46.990	10.517–209.952	< 0.001
Capsule complication										
No	372/1 343 950	0.0277 [0.0249–0.0305]	1.0			13/91 596	0.0142 [0.0065–0.0219]	1.0		
Yes	36/20 976	0.1716 [0.1156–0.2276]	6.201	4.404–8.730	< 0.001	1/642	0.1558 [0.1501–0.4616]	10.975	1.436–83.894	0.021

AB = antibiotic; CI = confidence interval; IC = intracameral; IOL = intraocular lens; ISBCS = immediate sequential bilateral cataract surgery; OR = odds ratio; PC = posterior chamber; PE = postoperative endophthalmitis; VA = visual acuity.
*Comparison between all IOLs and no IOL.

Table 2. Poisson Regression Model of Independent Factors Signifying Increased or Reduced Risk for the Dependent Variable Postoperative Endophthalmitis

Parameter	B Coefficient	Standard Error	P Value	Exp of B	95% CI for Exp B
Age ≥ 85 yrs	0.621	0.1159	0.001	1.861	1.483–2.336
Male sex	0.212	0.0983	0.031	1.236	1.019–1.498
Comorbidity	0.212	0.0994	0.033	1.236	1.018–1.502
ISBCS	−0.571	0.2723	0.036	0.565	0.331–0.963
Capsule complication	1.590	0.1763	< 0.001	4.903	3.470–6.926
No IC AB	2.274	0.2071	< 0.001	9.714	6.474–14.577

AB = antibiotic; Exp = exponentiation; IC = intracameral; ISBCS = immediate sequential bilateral cataract surgery.

a retrospective study including 10 500 ISBC surgeries performed at Kaiser Permanente, a hospital group in the United States, and from a retrospective survey based on 95 606 ISBCS eyes reported by members of the International Society of Bilateral Cataract Surgeons.[9,11] These overall results point to a low incidence of PE in ISBCS, but it is of note that they are all generated in a population offered IC prophylactic AB, which in the majority of studies on PE has outperformed topically given prophylaxis.[9,11,20-22,25] Still, ISBCS candidates should be informed that the planned surgery is not entirely without risk of infection, which our bilateral PE case certainly attests to.

Reports in the literature on bilateral endophthalmitis after ISBCS are scarce.[15-17] In 2 cases, there was a sharing of infusion bottle and surgical instruments, respectively, implying a breaching of the separation protocol.[15,16] A third case history penned by Puvanachandra and Humphry[17] presents an otherwise healthy 81-year-old woman who developed PE 4 days after the operations that were done as segregated procedures and concluded with prophylactic IC cefuroxime. The same strain of *Staphylococcus epidermidis* sensitive to vancomycin was cultured in intraocular samples from both eyes. The patient eventually recovered to 6/9 vision bilaterally. In a correspondence about this case, a point was made that using operating instruments taken from the same sterilization cycle, without using chemical indicator verification, was actually a violation of the separation protocol proposed by the International Society of Bilateral Cataract Surgeons.[26] The authors retorted that the decontamination technique conformed to accepted standards, which made it a highly unlikely source of the infection. They assumed that the bacterium rather came from the patient's own ocular flora. Our bilateral incident presented herein shows obvious similarities to that of Puvanachandra and Humphry.[17] The autoclave cycle was shared for the instrument trays for both eyes, but unlike in the British case, chemical indicator confirmation was used in accordance with Swedish regulations. Prophylaxis with IC cefuroxime was given, but in our case, it was combined with ampicillin. The isolate, a methicillin-resistant and thus cefuroxime-resistant (and for that matter ampicillin-resistant) coagulase-negative staphylococcus (CoNS), also seems to have been a common feature between the cases. This strain is not infrequent in the conjunctival flora,[27,28] and not surprisingly, it has been shown to cause PE previously in Sweden with IC cefuroxime use, although rarely.[29] The late onset of the infection of our bilateral case, 13 days after the surgery, may seem odd but is typical for endophthalmitis due to CoNS. When reviewing 80 infections caused by CoNS registered in the NCR database of the study period, the median and average intervals between the surgery and presentation were 8 and 14.2 ± 17.6 days, respectively. In the notes of the bilateral PE case, there was no proof of incompetent incisions, patient noncompliance, or any other irregularity. We do not

Table 3. Variable Distribution among Unilateral and ISBCS Cases

Preoperative Variable	Unilateral (%) N = 1 364 934	95% CI	ISBCS (%) N = 92 238	95% CI	P Value
Age > 85 yrs	13.76	13.70–13.81	11.59	11.38–11.79	< 0.001
Male	38.99	38.91–39.07	37.61	37.30–37.92	< 0.001
VA ≤ 20/200	17.05	16.99–17.11	10.03	9.83–10.22	< 0.001
Comorbidity	36.54	36.62–36.45	24.63	24.35–24.91	< 0.001
Operation Variable					
Other procedure than phaco + PC IOL	1.20	1.18–1.22	0.35	0.31–0.39	< 0.001
No IOL	0.297	0.287–0.306	0.033	0.021–0.044	< 0.001
Capsule complication	1.54	1.52–1.56	0.70	0.64–0.75	< 0.001
No IC AB	0.561	0.548–0.573	0.353	0.315–0.392	< 0.001

AB = antibiotic; CI = confidence interval; IC = intracameral; ISBCS = immediate sequential bilateral cataract surgery; IOL = intraocular lens; PC IOL = posterior chamber intraocular lens; VA = visual acuity.

Table 4. Postoperative Endophthalmitis Cases after ISBCS

Year of Operation	Age, yrs	Gender	IC Prophylaxis	Bacterium	Resistance to IC Prophylaxis	Final VA
2002	63	Female	None	CoNS	†	20/25
2002	86	Male	Cefuroxime + Ampicillin	CoNS	†	20/60
2003	82	Male	Cefuroxime	Enterococci	Yes	NLP
2009	83	Female	Cefuroxime	Enterococci	Yes	20/60
2010	74	Female	Cefuroxime	Enterococci	Yes	20/30
2011	82	Female	Cefuroxime	Enterococci	Yes	HM
2011	90	Male	Cefuroxime	No Growth	-	20/200
2012	93	Female*	Cefuroxime + Ampicillin	CoNS	Yes	CF
2012	93	Female*	Cefuroxime + Ampicillin	CoNS	Yes	20/160
2012	75	Male	Cefuroxime	Enterococci	Yes	LP
2013	87	Female	Cefuroxime	CoNS	No	20/20
2014	87	Male	Cefuroxime	*Proteus vulgaris*	†	20/50
2014	66	Female	None	CoNS	‡	20/25
2017	67	Male	Cefuroxime + Ampicillin	No Growth	-	20/20

CF = counting fingers; CoNS = coagulase negative staphylococci; HM = hand motion; IC = intracameral; ISBCS = immediate sequential bilateral cataract surgery; LP = light perception; NLP = no light perception; VA = visual acuity.
*The bilateral PE case.
†No sensitivity data available.
‡Sensitive to cefuroxime but no IC AB was given.

suspect the bacterium to have been a contaminant from a failed sterilization of the instruments or emanating from the operating room environment. If this would have been the explanation, a gram-negative bacterium rather than CoNS would have been the causative organism, and moreover, an epidemic with additional affected patients would have been expected.[30,31] In all, we are convinced that this highly unusual and unfortunate case was due to the presence of 2 risk factors for developing PE: (1) the high patient age (Tables 1 and 2) and (2) the apparent bilateral conjunctival colonization with a resistant strain overcoming the disinfectant and the IC ABs used.

Regarding general determinants for PE, nonuse of IC AB, capsule complication, and age 85 years or more were identified as the most important ones in the logistic regression analysis (Table 2). This is not surprising because our prior endophthalmitis studies encompassing the period 2002−2010 demonstrated the same.[19,20] A subanalysis, data not shown, confirmed the overwhelming weight of these factors in the most recent period 2011 to 2017.

As has been pointed out, IC ABs decrease the risk of intraocular infection by approximately 5 times,[11,19-22,25] and we agree with conclusions in previous epidemiologic reports that their use in ISBCS is paramount.[9,11] Still, 326 patients in our ISBCS cohort were not offered IC AB, the majority of whom were operated in the early phase of the study period when IC prophylaxis was not universally accepted. It is of note that in this small group, 2 incidents of PE occurred.

Capsule complication is a rightfully feared adverse event because it increases the rate of a number of vision-threatening complications, such as cystoid macular edema, retinal detachment,[32] and above all PE.[19,20,22,33] The low rate of capsule complication observed in ISBCS may be the result of a judicious selection of cases with a low risk for sustaining this adverse event[34] (Table 3). Another factor contributing to the low frequency may have been abandoning the planned ISBCS if a capsule problem happened in the first eye surgery, but from the registry it is not evident to what extent the complication occurred in the first or second eye in cases completed as ISBCS.

Elderly patients, in the present investigation defined as those aged 85 years or older, were found to be more susceptible to PE. The rate, regardless whether unilateral surgery or ISBCS was performed, was approximately 0.05%, whereas in younger subjects the corresponding rate was 0.027% in unilateral surgery but as low as 0.0098% in ISBCS (Table 1). We consider this finding important, and it is in line with most other large-scale studies,[33,35] although not with all.[21,23] The logistic advantages of ISBCS are obvious in the frail, that is, usually the oldest, patient population. The approach appears even more appealing when health care is put under heavy strain, for instance, by a pandemic such as that of Coronavirus Disease 2019 in 2020 and 2021.[36] Still, the overall benefits of ISBCS in the very elderly have to be weighed against a rate of PE that is approximately equal to 1 in 2000 eyes or substantially higher than among younger patients.

Male gender was also found to be an independent overall determinant for PE, confirming evidence from other large-scale studies (Table 2).[21,23,33,35] This may be explained by the fact that men seem to be colonized with more bacteria in the conjunctiva than women.[37] In our investigation, the impact of male sex on the PE incidence was modest and driven by the result in the unilateral group (Table 1), and thus its implications when opting for ISBCS are unclear. Ocular comorbidity was another modestly predictive factor for PE (Tables 1 and 2), which, in contrast, should not be overlooked in allocation for ISBCS. Ocular comorbidity in this study was a composite variable consisting of the presence of at least 1 of registered conditions AMD, glaucoma, DRP, or "any other disorder affecting VA." These parameters were tested individually in the logistic

regression model (data not shown), but none of them alone proved to be a statistically significant risk factor. It is imaginable that those who have undergone intraocular surgery to treat glaucoma, retinal, or corneal diseases may be at increased risk for PE, but the registry does not include detailed information in this respect.

The lower incidence of endophthalmitis in ISBCS in our investigation may be driven by patient selection demonstrated in Table 3. However, performing ISBCS per se turned out to be a protective factor against PE in the logistic regression model (Table 2), which then must have been due to practice strategies not evaluated in our model. High-volume surgeons are more likely to perform ISBCS, and their skills in performing nontraumatic surgery[38] and constructing well-sealed incisions may have played a role. One Medicare study from the United States demonstrated an inverse relationship between surgical volumes and endophthalmitis, but capsule complication was not entered as a covariate.[35] Another more common routine in ISBCS has been the addition of ampicillin to IC cefuroxime, which extends the antibacterial spectrum and appears to have reduced the incidence of enterococcal endophthalmitis. Although the different kinds of given IC ABs are presently registered in the NCR, they were not reported in the early phase of the study period and could not be analyzed in the entire dataset for this investigation. Future endophthalmitis research based on the NCR registrations for 2011−2017 is planned to focus on the bacteriology and resistance patterns with reference to the administered IC AB regimens and a wide range of factors with possible impact on the development of PE.

Study Limitations

There are weaknesses in our study. The sample size of our ISBCS cohort was not large enough to generate solid statistics in certain subgroups. The dilemma in analyzing PE within ISBCS cases that sustained a capsule complication or among those who did not receive IC ABs is evident from the extreme 95% CI limits of the odds ratios (Table 1). Still, the results for the major risk factors agree between the ISBCS group and controls. On the other hand, the comparisons of parameters in overall large samples involve the problem that even modest differences in proportions may reach a high level of statistical significance. This is well illustrated by the similar but statistically significantly different distribution of male gender and age 85 years or more in the study and control groups (Table 3). Yet, the consistently lower frequency in ISBCS procedures of all independent predictors is considered to have affected the PE incidence. Another limitation is the retrospective design, which made it difficult to assess the standard operation protocols for ISBCS apart from those of the most active units in the mid-phase of the study. Nevertheless, our analysis showed that PE incidents were fairly evenly spread over the study period (Table 4) and among clinics regardless of their level of experience.

In conclusion, the results in this study show a low rate for PE in ISBCS and low risk for significant vision disability after infection (1 in 18 000 operated eyes). Notwithstanding, 1 case of bilateral PE occurred, corresponding to a rate of 1 incident in 46 000 ISBCS patients. Nonuse of IC AB, capsule complication, and age 85 years or more were found to be major risk factors for PE, regardless if the surgery was performed unilaterally or as ISBCS. From our findings, it can be hypothesized that if surgeons performing ISBCS consistently would have used IC AB prophylaxis and refrained from offering this surgical option to patients aged 85 years or more, the incidence of PE could have been as low as 0.0073%, or 6 in 81 226 eyes (and no case of bilateral PE), which is comparable to the results of the few published reports in this field.[9,11] We consider the data presented in this research of great value for a proper balancing of benefits and risks when surgeons and patients contemplate ISBCS.

Footnotes and Disclosures

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[1] Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden.

[2] Stockholms Ögonklinik, Stockholm, Sweden.

[3] Department of Ophthalmology in Linköping and Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden.

[4] Department of Clinical Sciences, Ophthalmology, Faculty of Medicine, Lund University, Lund, Sweden.

[5] Department of Anterior Segment Surgery, St. Erik Eye Hospital, Stockholm, Sweden.

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HUMAN SUBJECTS: Human subjects were included in this study. Approval for this project was received from the Swedish Ethical Review Authority, no. 2019-02899. The research adhered to the tenets of the Declaration of Helsinki. Since this was a register-based retrospective study, written patient consent was not required.

No animal subjects were used in this study.

Author Contributions:

Conception and design: Friling, Johansson, Lundström, Montan

Data collection: Friling, Johansson, Lundström, Montan

Analysis and interpretation: Friling, Johansson, Lundström, Montan

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Overall responsibility: Friling, Johansson, Lundström, Montan

Abbreviations and Acronyms:
AB = antibiotic; **AMD** = age-related macular degeneration; **CI** = confidence interval; **CoNS** = coagulase-negative staphylococcus; **DRP** = diabetic retinopathy; **IC** = intracameral; **IOL** = intraocular lens; **ISBCS** = immediate sequential bilateral cataract surgery; **NCR** = National Cataract Register; **PE** = postoperative endophthalmitis; **VA** = visual acuity.

Keywords:
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Correspondence:
Emma Friling, MD, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden. E-mail: emma.friling@ki.se.

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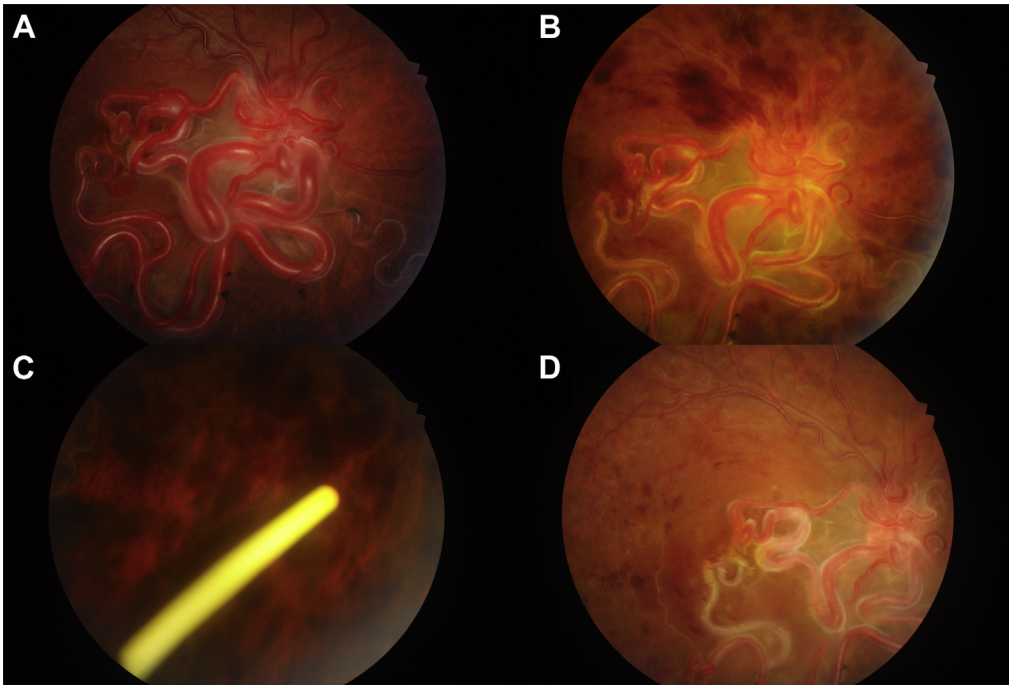
Pictures & Perspectives



Central Retinal Vein Occlusion Secondary to Bonnet-Dechaume-Blanc Syndrome

A 23-year-old woman with Bonnet-Dechaume-Blanc syndrome recognized by arteriovenous malformations in the retina (Fig **A**) and the right suprasellar region reported an acute onset of blurred vision with visual acuity deteriorating from 20/60 to counting finger at 20 cm. Dilated examination revealed central retinal vein occlusion related to the arteriovenous abnormality (Fig **B**). Intravitreal implantation of slow-release dexamethasone was performed (Fig **C**). The diffuse retinal flame-shaped hemorrhages and the vascular tortuosity were reduced (Fig **D**). The patient recovered her visual acuity to 20/60 without other ocular symptoms at the 3-year follow-up visit (Magnified version of Fig **A**-**D** is available online at www.aaojournal.org).

Shao-Lun Hsu, MD, MS[1]
Tsung-Jen Wang, MD, PhD[2,3]

[1]Medical Education Department, Taipei Medical University Hospital, Taipei, Taiwan; [2]Department of Ophthalmology, Taipei Medical University Hospital, Taipei, Taiwan; [3]Department of Ophthalmology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan