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Immediate Sequential vs. Delayed Sequential Bilateral Cataract Surgery

Retrospective Comparison of Postoperative Visual Outcomes

Lisa J. Herrinton, PhD,[1] Liyan Liu, MD, MSc,[1] Stacey Alexeeff, PhD,[1] James Carolan, MD,[2] Neal H. Shorstein, MD[3]

Objective: We conducted a retrospective comparative-effectiveness study of best-corrected visual acuity (BCVA) and refractive error (RE) after immediate sequential (ISBCS) and delayed sequential (DSBCS) bilateral cataract surgery. We tested 2 hypotheses: (1) among DSBCS patients, second-eye outcomes were no different than first-eye outcomes; (2) averaged between each patient's 2 eyes, outcomes did not differ between ISBCS and DSBCS patients.

Design: Retrospective comparative-effectiveness study.

Participants: Kaiser Permanente Northern California members who underwent noncomplex bilateral cataract surgery from January 1, 2013, through June 30, 2015.

Methods: We performed an intention-to-treat analysis comparing ISBCS to DSBCS using conditional logistic regression analysis, accounting for surgeon and patient-level factors.

Main Outcome Measures: BCVA, RE.

Results: The analysis of visual outcomes included both eyes of 13 711 DSBCS and 3561 ISBCS patients. Because of the large sample size, some statistical differences lacked clinical significance. Ocular comorbidities were slightly more prevalent in DSBCS patients. Postoperative BCVA was 20/20 or better in 48% of DSBCS first eyes, 49% of DSBCS second eyes, 53% of ISBCS right eyes, and 51% of ISBCS left eyes. The within-person difference in postoperative BCVA averaged zero (0.00) between the first and second DSBCS eyes, and between the ISBCS right and left eyes. After adjustment, average postoperative BCVA was better in ISBCS patients, although the difference was not statistically significant (compared with 20/20 or better: odds ratio for worse than 20/20 was 0.91, 95% confidence interval 0.83–1.01). Emmetropia (spherical equivalent -0.5 to 0 diopter) was achieved in 61% of first DSBCS eyes, 61% of second DSBCS eyes, 63% of ISBCS right eyes, and 63% of ISBCS left eyes. After adjustment, average postoperative RE was no different in ISBCS compared with DSBCS patients (compared with emmetropia: odds ratio for ametropia was 1.02, confidence interval 0.92–1.12). We confirmed 1 case of postoperative endophthalmitis in 10 494 ISBCS eyes (1.0 per 10 000 eyes) and 2 cases in 38 736 DSBCS eyes (0.5 per 10 000 eyes) ($P = 0.6$), and no patient had bilateral endophthalmitis.

Conclusions: Compared with DSBCS, we found no evidence that ISBCS was associated with worse postoperative BCVA or RE, or with an increased complication risk. *Ophthalmology 2017;124:1126-1135 © 2017 by the American Academy of Ophthalmology*

Supplemental material available at www.aaojournal.org.

We conducted a retrospective comparative-effectiveness study to assess whether immediate sequential bilateral cataract surgery (ISBCS) offers visual outcomes similar to delayed sequential bilateral cataract surgery (DSBCS). We used the community-based population and electronic health record data of Kaiser Permanente Northern California to examine postoperative best-corrected visual acuity (BCVA), refractive error (RE), and surgical complications. We hypothesized that in DSBCS patients, the outcome of the second eye would be no different than in the first eye. This hypothesis was motivated by the assertion that DSBCS offers the opportunity to improve refractive outcomes by allowing the surgeon to use the refractive outcome of the first eye to guide selection of the intraocular lens (IOL) for the second eye.[1,2] In addition, we hypothesized that visual outcomes averaged between each patient's 2 eyes did not differ between ISBCS and DSBCS patients. We also compared surgical complication rates between the 2 approaches.

Methods

The study was approved by the Kaiser Foundation Research Institute's institutional review board.

Setting

Kaiser Permanente Northern California is a community-based health care system that owns its hospitals and medical offices.

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For most patients, care is capitated (prepaid), and members receive comprehensive services. During 2013−2015, clear cornea phacoemulsification using standardized phacoemulsification machines (Alcon, Irvine, CA) and IOLs (Alcon) was performed by 152 cataract surgeons at 22 surgical centers. In 2014, medical offices switched biometry equipment from IOLMaster to Lenstar, at which time biometry information became available for research. The only systemic practice modifications during the study period were the adoption of intracameral injection of antibiotic in 2013 and the increasing adoption of ISBCS. Otherwise, surgeons practiced according to the guidelines in their own department or according to their training and continuing education.

Study Population

The study included health plan members who underwent their first noncomplex phacoemulsification for cataract (Current Procedural Terminology [CPT] code 66984; International Classification of Diseases, Ninth Revision [ICD-9] codes 13.41, 13.71) from January 1, 2013, through June 30, 2015. As with past studies,[3,4] we excluded complex phacoemulsification cases and cases performed by glaucoma, oculoplastic, or retinal specialists, as well as procedures by any surgeon combined with corneal transplant (ICD-9 code 11.6; CPT4 codes 65710−65715) or glaucoma surgery (ICD-9 codes 12.54, 12.64, 12.66, 12.69, 12.7; CPT4 codes 65850, 66170, 66172, 66180, 66185).

For the present analyses, we also excluded cases with previous endophthalmitis (ICD-9 codes 360.00, 360.01, 360.03, 360.13, 360.19, 098.42), and we required information from manifest refractions for postoperative BCVA analysis.

The study focused on 2 cohorts of patients undergoing bilateral cataract surgery: ISBCS, with surgery in the right and left eyes performed back-to-back on the same day, and DSBCS, with the 2 eyes operated on separate days, the second eye within 1 year of the first. ISBCS were identified from a procedure code used by the health plan (bilateral surgery, code 1215493) and from a laterality variable recorded into structured operative data. Second surgeries that were performed >1 year after the first were not included because most did not represent planned bilateral surgeries. To characterize each patient's history, we required at least 1 year of enrollment before cataract surgery on the first eye. We restricted the look-back to the 1 year before cataract surgery in the first eye to eliminate information bias that would have resulted had we given the DSBCS patients separate 1-year look-backs for each eye. A longer period of look-back in the DSBCS patients would have resulted in more diagnostic codes being written into the electronic medical record for mild visual complaints, including postoperative complaints recorded after the first surgery.

Data Collection

Visual Acuity and Refractive Error. Postoperative RE was calculated as the spherical equivalent (sphere + cylinder/2), measured in diopters (D), as recorded from manifest refractions performed by licensed optometrists. Best-corrected visual acuity was obtained using Snellen charts projected by standardized equipment (Nikon, Tokyo, Japan) and was converted to logarithm of the minimum angle of resolution (logMAR) equivalents. We did not include BCVA measurements from automated refractions, cycloplegic refractions, refractions obtained over contact lenses or glasses, retinoscopy, or "unaided acuity" because these represented <2% of the measurements and would have complicated the analysis.

We obtained preoperative BCVA from measurements recorded nearest the surgery date, up to 1 year before surgery. For postoperative BCVA and RE, we obtained the measurement recorded nearest the date of surgery during the interval 3 weeks to 1 year after surgery. The interval 3 weeks to 1 year was selected to optimize the completeness of postoperative data while providing time for vision to stabilize after surgery. We included refractions recorded as late as 1 year after surgery because patients with good postoperative visual acuity may not schedule an appointment for refraction for some time. We used the earliest measurement to minimize the late postoperative effects of ocular comorbidities and posterior capsular opacification.

Surgical Complications. We captured intraoperative posterior capsular rupture (PCR) and vitrectomy using natural language processing.[3,5] We identified cases with incident endophthalmitis recorded during the 120 days after the cataract surgery using ICD-9 codes (Supplemental Material, available at www.aaojournal.org) that were then confirmed by a study ophthalmologist (N.H.S.). We also captured postoperative macular edema cases during the 120 days after the first cataract surgery using ICD codes. In most patients, the second surgery was performed within 120 days of the first. We counted only 1 case of macular edema per patient because it was not possible based on coding alone to determine the laterality of the macular edema or whether the condition was unilateral or bilateral. To improve specificity,[4] we required macular edema patients to have undergone optical coherence tomography and to have filled a prescription for ophthalmic prednisolone during the 120 days after surgery.

Demographic Factors and Systemic Comorbidity. Patient age, sex, and race/ethnicity were obtained from self-reported membership information. Charlson comorbidities were calculated from diagnostic and procedure codes recorded during the year before surgery.

Ocular Comorbidity. Preexisting ocular diseases were obtained from inpatient and outpatient data using the codes detailed in the Supplemental Material (available at www.aaojournal.org).

Medications. We obtained records for dispensed glaucoma medications including prostaglandin analogues, α agonists, and carbonic anhydrase inhibitors. Because exposure of oral α-1 agonists has been associated with floppy iris syndrome, we obtained medication records for up to 10 years before surgery.[6]

Biometry. Lenstar data were available for the final 12 months of the 30-month study period. For these patients, we obtained axial length, anterior chamber depth, and lens thickness (all in millimeters).

Data Analysis

We performed intention-to-treat analyses, in which patients scheduled for ISBCS who were converted to DSBCS were nonetheless retained in the ISBCS group.

Hypothesis 1 compared visual outcome between the second and first eyes of DSBCS patients to test whether the RE after implantation of the second IOL was closer to emmetropia than the first. We examined the ISBCS cohort (left eye compared with right eye) as a negative control group. For this hypothesis, we tested whether there was a difference in the distributions of outcomes between DSBCS and ISBCS patients using a chi-square test. For these analyses, it was not appropriate to adjust for surgeon-level or patient-level factors because they did not vary within the patient.

Hypothesis 2 compared within-patient average visual outcome between the ISBCS and DSBCS cohorts. For this hypothesis, we dichotomized average postoperative BCVA as 20/20 or better compared with worse than 20/20, because half of the patients achieved BCVA of 20/20 or better. Analysis of postoperative RE excluded patients with RE −2.1 or greater myopia because most were intended for near working distance. Emmetropia was defined as spherical error of −0.5 to 0 D, whereas eyes that were more myopic or hyperopic were defined as ametropic. We estimated the adjusted odds ratio (OR) and 95% confidence interval (CI) for the association of ISBCS compared with DSBCS for each dichotomous outcome by fitting a conditional logistic regression model that stratified by surgeon. This approach ensured adjustment for a variety of practice variations across surgeons, including choice of formula for IOL power calculations. To control for potential confounding by patient factors, the regression model also adjusted for patient-level variables, including time to postoperative refraction.

In subgroup analyses, we examined biometric variables and patients without ocular comorbidities. We coded biometric variables into quartiles to obtain statistical efficiency. We also considered examining extreme values of axial length and anterior chamber depth, but the numbers of patients with extreme values were limited.

For surgical complications, we calculated 95% CIs for the incidence rates using the Fisher exact method. All analyses were performed in SAS 9.3 (SAS Institute, Inc., Cary, NC).

Results

Eligibility

Before exclusions, the number of ISBCS and DSBCS patients was 28 116. Among these, we excluded 2521 (9%) who underwent 1 or both surgeries by a glaucoma, oculoplastics, or retinal specialist; 51 who had a concurrent cornea transplant or glaucoma surgery in 1 or both eyes; 26 with a prior diagnosis of endophthalmitis; and 903 (3%) who lacked ≥1 year enrollment preceding their surgery. After these exclusions, the study included 24 615 patients (5247 ISBCS patients and 19 368 DSBCS patients). In this cohort, continuity of membership was 95% in the year following surgery. We estimated rates of postoperative endophthalmitis and macular edema in these 24 615 patients.

Among these 24 615 patients, 1686 of 5247 ISBCS patients (32%) and 5657 of 19 368 DSBCS patients (29%) were missing information on postoperative BCVA for 1 or both eyes. Thus, the number available for the analysis of BCVA was 3561 ISBCS patients (7122 eyes) and 13 711 DSBCS patients (27 422 eyes). Among those with BCVA information, the number of ISBCS and DSBCS patients with bilateral information on RE was 3342 (94%) and 13 072 (95%), respectively. Of these, 122 (4%) ISBCS and 442 (3%) DSBCS patients had RE −2.1 or more myopia and were excluded from the analysis of RE, although they were retained in the analysis of BCVA. Thus, the RE analysis included 3220 ISBCS and 12 630 DSBCS patients. Among patients with information on postoperative BCVA, we obtained biometry data for subgroup analysis of 1451 ISBCS (41%) and 2596 DSBCS (19%) patients.

Characteristics of Patients

ISBCS and DSBCS patients with and without information on BCVA were nearly identical (Table 1), although ISBCS patients with short axial length were more likely to have BCVA recorded. ISBCS and DSBCS patients differed somewhat from each other. Compared with DSBCS patients, the ISBCS patients underwent their surgery during later years of the study, reflecting increasing adoption of ISBCS. They were less likely to receive a multifocal or toric lens. In addition, ISBCS patients had slightly lower prevalence of a preexisting ocular comorbidity (Table 1). The groups were similar with respect to systemic comorbidities, use of α-1 agonists, ocular biometry, and prevalence of diabetic retinopathy.

Among DSBCS patients, the 2 surgeries were separated by a median of 37 days (lower and upper quartiles: 23 and 66 days). The average time to refraction was 51 days for ISBCS, 65 days for the first DSBCS eye, and 48 days for the second DSBCS eye. Preoperative BCVA averaged 20/53 (0.42 logMAR) among ISBCS patients and 20/55 (0.44 logMAR) among DSBCS patients. For DSBCS patients, and consistent with the practice of performing surgery on the worse-seeing eye first, preoperative BCVA averaged 20/63 (0.50 logMAR) in the first eye and 20/48 (0.38 logMAR) in the second eye.

Hypothesis 1: Among Delayed Sequential Bilateral Cataract Surgery Patients, Outcomes in the Second Eye Were No Different Than in the First Eye

Postoperative BCVA was 20/20 or better in 48% of DSBCS first eyes, 49% of DSBCS second eyes, 53% of ISBCS right eyes, and 51% of ISBCS left eyes (Fig 1A). Within patients, the difference in postoperative BCVA (logMAR) between the second and first eyes was 0 (0.00) for 60% of DSBCS patients (Fig 1B). The difference between the left and right eyes was 0 (0.00) for 68% of ISBCS patients. Among DSBCS patients, BCVA in the second eye was better than the first for 20% and worse than the first for 19% of patients. Among ISBCS patients, the left eye had better acuity than the right for 15% and worse than the right for 17% of patients. These distributions differed between DSBCS and ISBCS patients in this large study ($P < 0.001$). Because of the large sample size, some statistical differences lacked clinical significance.

RE averaged −0.38 D in the DSBCS first eye, −0.40 D in the DSBCS second eye, −0.36 D in the ISBCS right eye, and −0.35 in the ISBCS left eye (Fig 2A). Emmetropia was achieved in 61% of both DSBCS first eyes and second eyes, and in 63% of both ISBCS right and left eyes. Within-person differences in emmetropia and ametropia between the second and first eyes in DSBCS patients and between the left and right eyes in ISBCS patients are shown in Figure 2B. These distributions among DSBCS and ISBCS patients differed in this large study ($P < 0.001$). Subgroup analysis focused on patients who received toric lenses in both eyes (ISBCS, n = 170; DSBCS, n = 415). Among these patients, the distributions of refractive results were similar in the 2 groups ($P = 0.31$). In patients who received all types of lenses, postoperative anisometropia >2 D occurred in 1.4% (n = 44) of ISBCS and 1.7% (n = 212) of DSBCS patients ($P = 0.21$); in patients who received toric lenses in both eyes, anisometropia >2 D occurred in 4.1% (n = 7) of ISBCS and 2.4% (n = 10) of DSBCS patients ($P = 0.26$).

Hypothesis 2: Averaged Between the 2 Eyes, Outcomes Do Not Differ Between Delayed Sequential and Immediate Sequential Bilateral Cataract Surgery Patients

Average postoperative BCVA (average of within-patient averages) was 20/20 or better in 49% of DSBCS patients and 52% of ISBCS patients. Average postoperative RE was −0.39 D in DSBCS and −0.36 D in ISBCS patients. Emmetropia was achieved in 61% of DSBCS eyes and 63% of ISBCS eyes. Logistic regression analyses for hypothesis 2 are shown in Table 2. Model 1 examines BCVA and is shown in the center of the table. Model 2 examines RE and is shown on the right side of Table 2. The odds of having average postoperative BCVA worse than 20/20 (compared with 20/20 or better) was higher in older patients, women, African Americans, and patients with specific systemic and ocular comorbidities. Comparing outcomes from the ISBCS and the DSBCS group, we found no evidence for differences in postoperative BCVA worse than 20/20 (OR, 0.91; 95% CI 0.83−1.01) or with ametropia (OR, 1.02; 95% CI 0.92−1.12).

Lenstar data were available for 1451 ISBCS patients and 2596 DSBCS patients. In this subgroup of patients, before adjustment for biometry, the OR for the association of ISBCS versus DSBCS for

Table 1. Characteristics of Immediate and Delayed Sequential Bilateral Cataract Surgery Patients With and Without Postoperative Best-Corrected Visual Acuity, Kaiser Permanente Northern California, January 1, 2013, Through June 30, 2015

	ISBCS Patients		DSBCS Patients		DSBCS vs. ISBCS (With BCVA Data) P Value
	With BCVA Data (n = 3561)	*Missing BCVA Data (n = 1686)*	*With BCVA Data (n = 13 711)*	*Missing BCVA Data (n = 5657)*	
Duration of enrollment, years					
<5	6	6	6	7	Ref
5–10	8	9	8	8	0.16
>10	86	85	86	85	0.51
Year of first surgery					
2013	16	19	46	47	Ref
2014	48	48	40	40	<0.0001
2015	36	33	13	13	<0.0001
Sex					
Female	61	62	62	61	Ref
Male	39	38	38	39	0.48
Age, years					
≤74	54	55	51	53	Ref
75–79	22	21	23	22	0.76
80–84	15	15	17	16	0.09
≥85	9	8	9	9	0.99
Race/ethnicity					
African American	5	5	5	5	0.43
Asian American	13	12	15	15	<0.01
Latino/Hispanic	12	12	10	10	0.02
White	64	65	63	63	Ref
Multiracial	5	5	6	5	0.24
Other	1	1	1	1	0.81
Diabetes	28	28	27	27	0.17
Charlson-Deyo comorbidity index					
0	41	41	41	41	Ref
1	18	19	19	19	0.31
≥2	41	40	40	40	0.26
Preoperative medications					
Tamsulosin	9	8	8	8	0.38
Other α-1 agonist	8	8	9	9	0.06
Warfarin	2	2	2	2	0.32
Lens type					
Monofocal	94.6	94.1	92.7	90.6	Ref
Multifocal, 1 or both eyes	0.7	0.8	1.5	2.5	<0.001
Toric, 1 or both eyes	4.7	5.1	5.8	6.9	0.02
Axial length,* mm					
≤22.9	25	18	25	23	Ref
23.0–23.9	37	40	37	37	0.74
24.0–24.9	21	28	21	21	0.90
≥25.0	18	14	18	19	0.86
Cataract thickness, mm*					
≤4.3	33	30	31	35	Ref
4.4–4.6	27	28	26	23	0.21
4.7–4.8	16	15	18	17	0.20
≥4.9	23	27	26	25	0.18
Anterior chamber depth,* mm					
≤2.8	26	29	28	25	Ref
2.9–3.1	29	26	29	32	0.72
3.2–3.4	26	30	25	24	0.75
≥3.5	19	15	18	19	0.29
Preoperative ocular conditions					
Vitrectomy	0.3	0.02	0.4	0	0.29
Other retinovitreal procedures	0.1	0.2	0.4	0.5	0.02
Other ophthalmic procedures	0.7	0.6	0.9	0.6	0.36
Glaucoma without medication	13	13	16	15	<0.001
Glaucoma with medication	3	3	4	3	<0.01
Pseudoexfoliation glaucoma	0.1	0.1	0.3	0.3	0.06
Diabetic retinopathy, NOS	2	2	3	3	0.02
Proliferative diabetic retinopathy	1	1	1	1	0.28

(*Continued*)

Table 1. (Continued.)

	ISBCS Patients		DSBCS Patients		DSBCS vs. ISBCS (With BCVA Data) P Value
	With BCVA Data (n = 3561)	*Missing BCVA Data (n = 1686)*	*With BCVA Data (n = 13 711)*	*Missing BCVA Data (n = 5657)*	
Nonproliferative diabetic retinopathy	5	5	5	5	0.44
Macular edema with diabetes	0.7	0.7	1	1.3	0.03
Macular edema without diabetes	0.1	0.2	0.3	0.3	0.08
Age-related macular degeneration	9	9	11	11	<0.001
Posterior vitreous detachment	4	4	5	5	0.002
Epiretinal membrane	3	3	5	5	<0.001
Retinal vein occlusion	0.8	0.9	1.2	1.2	0.08
Iritis or uveitis	0.2	0.2	0.5	0.6	0.05
Fuchs' dystrophy	0.6	0.5	1.3	1.2	0.001
Other corneal disorder	2	2	3	3	<0.01
Blepharitis	3	4	5	5	<0.001
Dry eye syndrome	8	8	10	10	0.08

BCVA = best-corrected visual acuity; DSBCS = delayed sequential bilateral cataract surgery; ISBCS = immediate sequential bilateral cataract surgery; NOS = not otherwise specified; Ref = reference category.
Data are percentages unless otherwise indicated.
*Biometry data were obtained from Lenstar and were available during the last 12 months of the study, which included 1664 ISBCS patients and 2347 DSBCS patients. Best-corrected visual acuity was obtained from manifest refraction using Snellen charts projected by standardized equipment (Nikon, Tokyo, Japan). Postoperative BCVA was obtained from the earliest measurement recorded nearest the date of surgery during the interval 3 weeks to 1 year after surgery. Preoperative medications were obtained from automated pharmacy data. Preoperative medical conditions were obtained from diagnosis codes recorded into the electronic medical record.

postoperative BCVA worse than 20/20 was 0.99 (95% CI, 0.82−1.18) and for ametropia was 1.14 (95% CI, 0.95−1.37). After adjustment for biometry (axial length, cataract thickness, anterior chamber depth) the ORs changed only negligibly for both BCVA worse than 20/20 (OR, 1.00; 95% CI, 0.84−1.21) and ametropia (OR, 1.15; 95% CI, 0.96−1.38) (see Supplemental Material, available at www.aaojournal.org).

Subgroup Analysis Restricted to Patients Without an Ocular Comorbidity

In subgroup analysis restricted to patients without an ocular comorbidity (2412 ISBCS and 8343 DSBCS patients with postoperative BCVA), the OR for the association of ISBCS with BCVA worse than 20/20 was 0.95 (95% CI, 0.84−1.07). The OR for the association of ISBCS with ametropia was 0.98 (95% CI, 0.86−1.10) (see Supplemental Material, available at www.aaojournal.org).

Surgical Complications

Twenty-five cases (0.7%) were converted from ISBCS to DSBCS because surgery in the first eye did not proceed as planned and the second-eye surgery was aborted that day. Review of the operative report showed that 6 were cases with PCR/vitrectomy; 4 with patient agitation or blood pressure elevation; 3 with a delay in surgery because of an equipment problem, for example; 3 iris-related problems; 2 in which the IOL had to be removed; 2 concerns about intraoperative corneal edema; 2 instances of zonular dehiscence; 1 "floppy capsular bag"; 1 anterior capsular tear; and 1 case with intraoperative bleeding. We found 6 other cases (0.2%) of ISBCS in which the first eye had a small posterior capsular rent or

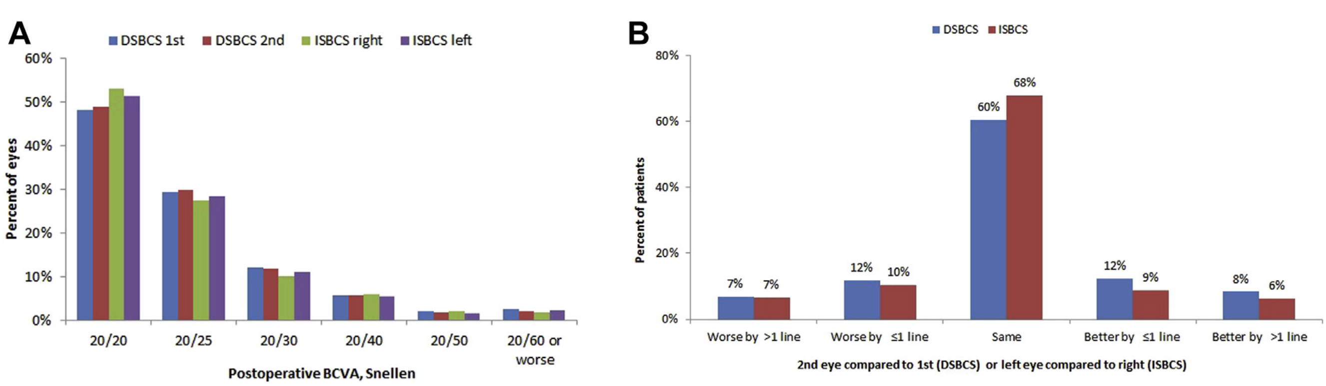

Figure 1. Postoperative best-corrected visual acuity (BCVA) in 13 711 delayed sequential bilateral cataract surgery (DSBCS) patients and 3561 immediate sequential bilateral cataract surgery (ISBCS) patients, Kaiser Permanente Northern California, January 1, 2013, through June 30, 2015. **A**, Best-corrected visual acuity in each eye. **B**, Within-patient difference in BCVA (logarithm of the minimum angle of resolution) between the 2 eyes ($P < 0.001$, chi-square test). For DSBCS, we report the first eye followed by the second eye. For ISBCS, we report the right eye followed by the left eye, although the order of surgery was not obtained for the study.

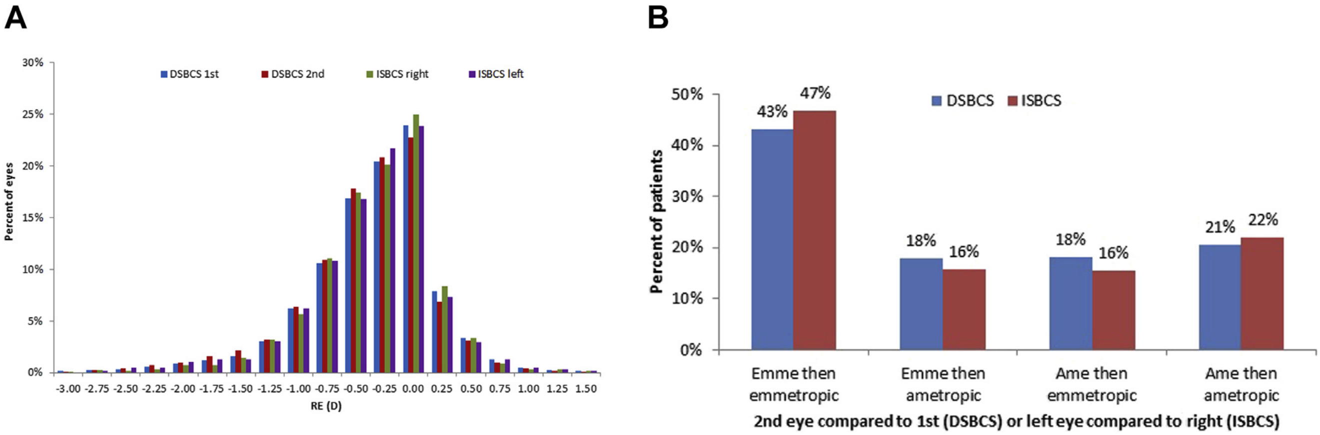

Figure 2. Postoperative refractive error (RE) in 12 630 delayed sequential bilateral cataract surgery (DSBCS) patients and 3220 immediate sequential bilateral cataract surgery (ISBCS) patients, Kaiser Permanente Northern California, January 1, 2013, through June 30, 2015. **A**, Refractive error in each eye. **B**, Within-patient difference in RE (diopters [D]) between the 2 eyes ($P < 0.001$, chi-square test). For DSBCS, we report the first eye followed by the second eye. For ISBCS, we report the right eye followed by the left eye, although the actual order of surgery was not obtained for the study. Emmetropia (Emme) was defined as −0.5 to 0 D. Ame = ametropia.

underwent a planned vitrectomy, and the surgeon nonetheless completed the second eye as an ISBCS.

The incidence rates of PCR and vitrectomy did not differ between ISBCS and DSBCS, or between the DSBCS first and second eyes (Table 3). In 10 494 ISBCS eyes (5247 patients), we confirmed 1 postoperative endophthalmitis case (rate, 1 per 10 000 eyes), whereas in 38 736 DSBCS eyes (19 368 patients) we confirmed 2 endophthalmitis cases (rate, 0.5 per 10 000 eyes; $P = 0.32$). No patient had bilateral endophthalmitis (95% CI upper limit, 17 bilateral cases per 10 000 patients). In the ISBCS cohort we observed 29 patients with macular edema (rate, 0.55%), whereas in the DSBCS cohort we observed 165 macular edema patients (rate, 0.85%; $P = 0.03$).

Unintended IOL implantation occurred in 1 ISBCS eye and in 3 DSBCS eyes. In the ISBCS patient, a 22.0-D IOL intended for the second eye was implanted into the first eye, in which a 22.5-D (same model) lens was intended.

Discussion

Kaiser Permanente surgeons began offering ISBCS in 2010. To assess whether outcomes obtained from ISBCS were similar to those from DSBCS, we compared postoperative visual outcomes and the risk of complications between the 2 procedures.

Effectiveness of Immediate Sequential Bilateral Cataract Surgery

Averaging between the 2 eyes, we found no evidence for an important or convincing difference in BCVA or RE between ISBCS and DSBCS patients after accounting for surgeon differences and patient baseline characteristics, most importantly ocular comorbidities. Some have argued that one potential disadvantage of ISBCS is the loss of the opportunity to adjust the IOL power of the second eye when the postoperative refraction from the first eye differs from the intended target.[7] This is based on studies showing improved target accuracy when adjusting the second IOL power by half of the difference between the expected and actual refraction of the first eye.[2,8] Recent formulae improve estimates of effective lens position by incorporating parameters such as anterior chamber depth and lens thickness that increase accuracy and reduce the need for adjustments to the target for the second eye.[1] The clinically relevant benefits of adjustments are felt to be less significant with the advent of newer, more accurate formulae. Furthermore, contemporary IOLs are available in minimum 0.5-D increments, making smaller adjustments in power infeasible.[9] We compared RE between the first and second DSBCS eyes, and found no evidence for a difference.

Nearly one-third of patients in our study did not have a BCVA or RE measurement during the period 21 days to 1 year after their surgery, and this is a potential study limitation. To assess the potential magnitude of this limitation, we compared patients with and without these data, finding their baseline characteristics to be nearly identical (Table 1). Based on this comparison of patients with complete and missing data, we believe the missing data were missing at random and did not bias the study.

The surgeon's intended refractive targets are recorded on the consent form, which is accessible at the clinician-facing front end of the electronic medical record, but not the back end where the research team extracts data using batch processing. For analysis of postoperative RE, we were unable to efficiently and reliably ascertain the surgeons' intended refractive targets owing to this limitation. We therefore uniformly assigned target refraction between 0 and −0.5 D, and we excluded patients with a postoperative RE <−2.1 D, which are more likely to have been targeted for near or arm's-length working distances. Nor could we exclude intentional mini-monovision, in which the second eye was targeted from −0.75 to −1.50 D. Although systematic differences may exist between the ISBCS and DSBCS groups in the proportion of eyes targeted for working distances other than emmetropia, Figure 2A gives no evidence for this. Moreover, we could not reliably ascertain whether

Table 2. Hypothesis 2: Adjusted Odds Ratio (95% Confidence Interval) for the Association of Immediate vs. Delayed Sequential Bilateral Cataract Surgery With Postoperative Visual Outcomes (Within-Patient Average Between the 2 Eyes), Kaiser Permanente Northern California, January 1, 2013, Through June 30, 2015

	Model 1			Model 2		
	BCVA Worse Than 20/20 vs. 20/20 or Better (Includes 3561 ISBCS and 13 711 DSBCS Patients)			*RE Ametropia vs. Emmetropia (Includes 3220 ISBCS and 12 630 DSBCS Patients)*		
Characteristics	*OR*	*95% CI*	*P Value*	*OR*	*95% CI*	*P Value*
Surgery						
ISBCS	0.91	0.83–1.01	0.07	1.02	0.92–1.12	0.75
DSBCS	1.00	Ref.		1.00	Ref.	
Year of surgery						
2013	1.00	Ref.		1.00	Ref.	
2014	1.03	0.96–1.11	0.43	1.02	0.95–1.10	0.60
2015	1.08	0.98–1.20	0.12	1.05	0.96–1.16	0.34
Patient age, years						
≤74	1.00	Ref.		1.00	Ref.	
75–79	1.91	1.76–2.07	<0.0001	0.93	0.86–1.01	0.09
80–84	2.80	2.54–3.09	<0.0001	1.04	0.94–1.14	0.46
≥85	5.18	4.46–6.00	<0.0001	1.22	1.09–1.38	0.0008
Patient sex						
Male	1.00	Ref.		1.00	Ref.	
Female	1.12	1.04–1.20	0.003	1.07	1.00–1.15	0.05
Patient race/ethnicity						
White	1.00	Ref.		1.00	Ref.	
African American	1.30	1.11–1.53	0.001	1.20	1.02–1.40	0.02
Asian American	1.82	1.64–2.02	<0.0001	1.06	0.96–1.17	0.25
Hispanic	1.23	1.10–1.38	0.003	0.98	0.88–1.09	0.69
Other	1.32	1.15–1.51	<0.001	0.90	0.79–1.02	0.09
Charlson comorbidity						
0	1.00	Ref.		1.00	Ref.	
1	1.08	0.98–1.18	0.13	0.93	0.85–1.02	0.14
≥2	1.28	1.17–1.40	<0.0001	1.00	0.92–1.09	0.96
Clinical history (yes/no)						
Diabetes	1.08	0.98–1.18	0.12	0.92	0.84–1.00	0.05
Flomax	1.03	0.91–1.17	0.65	0.93	0.83–1.06	0.27
Warfarin	1.13	0.88–1.44	0.34	0.93	0.74–1.16	0.53
AMD	2.15	1.90–2.43	<0.0001	1.01	0.91–1.13	0.79
Corneal disease	2.71	2.16–3.40	<0.0001	1.37	1.13–1.66	0.001
DMR	1.80	1.55–2.01	<0.0001	1.11	1.00–1.28	0.13
ERM	1.95	1.64–2.32	<0.0001	1.01	0.87–1.18	0.88
Glaucoma	1.22	1.12–1.33	<0.0001	1.03	0.96–1.12	0.45
Retinovitreal procedure	3.88	1.78–8.46	0.0007	1.04	0.60–1.81	0.90
PCR	1.60	1.20–2.13	0.001	1.26	1.00–1.63	0.09
Average time to refraction, weeks						
3–4	1.00	Ref.		1.00	Ref.	
5–7	0.91	0.83–1.01	0.07	1.03	0.93–1.14	0.60
≥8	0.92	0.82–1.03	0.15	1.08	0.96–1.21	0.23

AMD = age-related macular degeneration; CI = confidence interval; DMR = diabetic macular retinopathy; DSBCS = delayed sequential bilateral cataract surgery; ERM = epiretinal membrane; ISBCS = immediate sequential bilateral cataract surgery; OR = odds ratio; PCR = postcapsular rupture; Ref. = reference group.

The logistic regression analyses were stratified on the identity of the surgeon and included every variable shown in the table, as coded in the table. Refractive error (RE) and best-correct visual acuity (BCVA) were obtained from manifest refraction using Snellen charts projected by standardized equipment (Nikon, Tokyo, Japan). Analysis of postoperative RE excluded patients with RE −2.1 or greater myopia. Emmetropia was defined as spherical error of −0.5 to 0 diopters, whereas eyes that were more myopic or hyperopic were defined as ametropic. Postoperative BCVA was obtained from the earliest measurement recorded nearest the date of surgery during the interval 3 weeks to 1 year after surgery. Tamsulosin dispensings were obtained from automated pharmacy data recorded up to 10 years before the first cataract surgery date. Preoperative medical conditions were obtained from diagnosis codes recorded into the electronic medical record.

eyes had received a corneal refractive procedure before cataract surgery.

Comparative effectiveness studies are subject to confounding by indication. This would occur, for example, if patients selected for ISBCS compared with DSBCS had fewer ocular comorbidities and we could not account for this difference using statistical adjustment, either because we did not have the information or because we lacked adequate sample size to perform the adjustment. The results in Table 1 indicate that, indeed, patients selected for ISBCS were slightly less likely to have an ocular comorbidity recorded in the year before their surgery. This is

Table 3. Incidence of Intraoperative Complications (%), Kaiser Permanente Northern California, January 1, 2013, Through June 30, 2015

Complication	ISBCS and DSBCS: Average Between the 2 Eyes			DSBCS: First Eye vs. Second Eye		
	ISBCS (n = 5247)	*DSBCS (n = 19 368)*	P *Value*	*First Eye (n = 19 368)*	*Second Eye (n = 19 368)*	P *Value*
Posterior capsular rupture	0.84	0.67	0.23	0.66	0.67	0.94
Vitrectomy	0.42	0.45	0.82	0.48	0.42	0.42
Either of the above	0.93	0.88	0.79	0.91	0.85	0.61

DSBCS = delayed sequential bilateral cataract surgery; ISBCS = immediate sequential bilateral cataract surgery.
Posterior capsular rupture and vitrectomy were obtained from natural language processing of operative reports.

consistent with some surgeon practices to exclude from ISBCS those patients with ocular comorbidities potentially predisposing to complications or adverse events. Fortunately, because the sample size was large and detailed information was available from the electronic medical record, we could carefully adjust for the occurrence of these diagnoses. We then extended the data analysis to assess whether differences in the *severity* of ocular comorbidities were important. In this subgroup analysis, we restricted the cohort to patients without any baseline ocular comorbidity. The results of this subgroup analysis were very similar to the main results (BCVA of entire population: OR, 0.91; BCVA of subgroup without ocular comorbidity: OR, 0.95) and argue in favor of study validity.

In 2015, Malvankar-Mehta et al[10] published a systematic review contrasting postoperative BCVA after ISBCS and DSBCS. The review, which included 10 randomized and observational studies of 3657 subjects, reported that improvement in BCVA after ISBCS and DSBCS was similar.[10] The results of our study are consistent with this conclusion. The populations studied in the reports reviewed by Malvankar-Mehta et al differed somewhat from one another and from our own cohort. However, 2 of the reviewed studies seemed to be based in populations that were similar to ours with respect to the severity of cataract, as indicated by preoperative BCVA. Average preoperative BCVA in our study population (mean, 0.42 logMAR) was similar to a 2011 Finnish study population (mean, 0.42 logMAR)[11] and a 2009 multicenter study population located in New Zealand, Australia, and Japan (mean, 0.48 logMAR).[12] We note that average postoperative BCVA was somewhat better in our cohort than these 2 past studies (0.08 logMAR compared with 0.13 and 0.20 logMAR, respectively), most likely because of recent advances in surgical techniques.

Our study is also consistent with other reports[1,2] in refuting the assertion that DSBCS leads to improved outcomes in the second eye. If surgeons did indeed make adjustments to the refractive target for the second eye based on the results from the first eye, these adjustments did not translate into improved outcomes for the second eye. One reason for this may be the excellent outcomes achieved with contemporary biometry equipment and later-generation formulae for the IOL power calculation.

Key strengths of our findings for the effectiveness of ISBCS include the diversity of the population; the size of the population, which enabled detailed adjustment and subgroup analysis; and the ability to account for differences in outcomes across surgeons. Our population was community-based and generalizable. The study was innovative in reporting not only postoperative BCVA but also RE, including anisometropia.

Safety of Immediate Sequential Bilateral Cataract Surgery

We found no evidence for differences in the rates of PCR or vitrectomy between ISBCS and DSBCS. This is consistent with past reports.[11–13] Many surgeons who perform ISBCS abort surgery for the second eye when PCR occurs in the first in order to give the eye and the patient time to heal. For this reason, we recommend obtaining the patient's agreement on which eye is to be operated on first (generally the worse-seeing eye) and recording the agreement on the consent form that is signed by the patient. In addition, to prevent unintended IOL errors, *each* eye's IOL type (multifocal, toric, monofocal) and working distance should be clearly designated on the consent form. We also recommend that the consent form, indicating IOL type and working distance, and biometry printout be present in the operating room for only 1 eye at a time.

The rate of endophthalmitis in our study was very low (1 in 10 000 patients) and did not differ between the ISBCS and DSBCS cohorts. We observed no case of bilateral endophthalmitis following ISBCS among 5247 patients (95% CI upper limit, 17 per 10 000 patients). An editorial by Li et al[14] described 4 cases of bilateral endophthalmitis after ISBCS, all stemming from inadequate sterilization and lack of separating instrument trays between the 2 eyes. The use of intracameral antibiotic together with clinical workflow changes to reduce infection and toxic anterior segment syndrome, such as inspecting the surgical venue and cleaning and sterilization processes, are important aspects of risk reduction.[15] Practice recommendations for ISBCS[16] merit further consideration, given the publication of new studies and evidence.[15]

DSBCS patients had about twice the rate of ophthalmology and optometry utilization in the weeks after their surgery compared with ISBCS patients. The higher rate of macular edema in DSBCS compared with ISBCS patients (0.85% vs. 0.55%; $P = 0.03$) may have resulted from the DSBCS patients' greater opportunity, consequent to their higher utilization, to receive a diagnosis in response to reporting a minor postoperative visual complaint. Because they are rare, serious complications are difficult to study.

Differences in complication rates will remain a salient research topic until larger sample sizes can be obtained in settings such as ours and in meta-analyses.[17]

Implications

ISBCS has been shown to save health care resources in other parts of the world[18,19] and to halve the cost of bilateral cataract surgery.[20] Lower costs could increase access to care. Despite the potential economic benefit to payers, patients, and society,[21,22] the current Medicare reimbursement model is a barrier to widespread adoption of ISBCS in the United States[23] owing to a reduction in total reimbursement compared with DSBCS.[24] Future research to investigate the impact on the patient's experience and access to cataract surgery may demonstrate that, combined with high-quality clinical processes, ISBCS is a valuable modality to improve the effectiveness, safety, and experience of care.

References

1. Olsen T. Use of fellow eye data in the calculation of intraocular lens power for the second eye. *Ophthalmology*. 2011;118: 1710-1715.
2. Jivrajka RV, Shammas MC, Shammas HJ. Improving the second-eye refractive error in patients undergoing bilateral sequential cataract surgery. *Ophthalmology*. 2012;119:1097-1101.
3. Herrinton LJ, Shorstein NH, Paschal JF, et al. Comparative effectiveness of antibiotic prophylaxis in cataract surgery. *Ophthalmology*. 2016;123:287-294.
4. Shorstein NH, Liu L, Waxman MD, Herrinton LJ. Comparative effectiveness of three prophylactic strategies to prevent clinical macular edema after phacoemulsification surgery. *Ophthalmology*. 2015;122:2450-2456.
5. Liu L, Shorstein NH, Amsden LB, Herrinton LJ. Natural language processing to ascertain two key variables from operative reports in ophthalmology. *Pharmacoepidemiol Drug Saf*. 2017;26:378-385.
6. Chang DF, Braga-Mele R, Mamalis N, et al, ASCRS Cataract Clinical Committee. ASCRS White Paper: clinical review of intraoperative floppy-iris syndrome. *J Cataract Refract Surg*. 2008;34:2153-2162.
7. Henderson BA, Schneider J. Same-day cataract surgery should not be the standard of care for patients with bilateral visually significant cataract. *Surv Ophthalmol*. 2012;57:580-583.
8. Covert DJ, Henry CR, Koenig SB. Intraocular lens power selection in the second eye of patients undergoing bilateral, sequential cataract extraction. *Ophthalmology*. 2010;117:49-54.
9. Arshinoff SA. IOL power prediction. *Ophthalmology*. 2012;119:2646.
10. Malvankar-Mehta MS, Chen YN, Patel S, et al. Immediate versus delayed sequential bilateral cataract surgery: a systematic review and meta-analysis. *PLoS One*. 2015;10: e0131857.
11. Sarikkola AU, Uusitalo RJ, Hellstedt T, et al. Simultaneous bilateral versus sequential bilateral cataract surgery: Helsinki Simultaneous Bilateral Cataract Surgery Study Report 1. *J Cataract Refract Surg*. 2011;37:992-1002.
12. Chung J, Park SH, Lee WJ, Lee SJ. Bilateral cataract surgery: a controlled clinical trial. *Jpn J Ophthalmol*. 2009;53:107-113.
13. Serrano-Aguilar P, Ramallo-Farina Y, Cabrera-Hernandez JM, et al. Immediately sequential versus delayed sequential bilateral cataract surgery: safety and effectiveness. *J Cataract Refractive Surg*. 2012;38:1734-1742.
14. Li O, Kapetanakis V, Claoue C. Simultaneous bilateral endophthalmitis after immediate sequential bilateral cataract surgery: what's the risk of functional blindness? *Am J Ophthalmol*. 2014;157:749-751.
15. Shorstein NH, Lucido C, Carolan J, et al. Failure modes and effects analysis for bilateral same-day cataract surgery. *J Cataract Refractive Surg*. 2017;43:318-323.
16. Arshinoff S, Claoue C, Johansson B. iSBCS General Principles for Excellence in ISBCS 2009; 2009. Available at: http://www.isbcs.org/wp-content/uploads/2011/03/2010-07-20-FINAL-ISBCS-SBCS-suggestions-from-ESCRS-Barcelona.pdf. Accessed December 6, 2016.
17. Kessel L, Andresen J, Erngaard D, et al. Immediate sequential bilateral cataract surgery: a systematic review and meta-analysis. *J Ophthalmol*. 2015;2015:912481.
18. Lansingh VC, Eckert KA, Strauss G. Benefits and risks of immediately sequential bilateral cataract surgery: a literature review. *Clin Exp Ophthalmol*. 2015;43:666-672.
19. Arshinoff SA, Chen SH. Simultaneous bilateral cataract surgery: financial differences among nations and jurisdictions. *J Cataract Refract Surg*. 2006;32:1355-1360.
20. Malvankar-Mehta MS, Filek R, Iqbal M, et al. Immediately sequential bilateral cataract surgery: a cost-effective procedure. *Can J Ophthalmol*. 2013;48:482-488.
21. Rush SW, Gerald AE, Smith JC, et al. Prospective analysis of outcomes and economic factors of same-day bilateral cataract surgery in the United States. *J Cataract Refract Surg*. 2015;41: 732-739.
22. Neel ST. A cost-minimization analysis comparing immediate sequential cataract surgery and delayed sequential cataract surgery from the payer, patient, and societal perspectives in the United States. *JAMA Ophthalmol*. 2014;132:1282-1288.
23. Singh R, Dohlman TH, Sun G. Immediately sequential bilateral cataract surgery: advantages and disadvantages. *Curr Opin Ophthalmol*. 2017;28:81-86.
24. Neel ST. A cost and policy analysis comparing immediate sequential cataract surgery and delayed sequential cataract surgery from the physician perspective in the United States. *JAMA Ophthalmol*. 2014;132:1359-1362.

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[1] Division of Research, Kaiser Permanente Northern California, Oakland, California.

[2] Department of Ophthalmology, Kaiser Permanente San Rafael, San Rafael, California.

[3] Departments of Ophthalmology and Quality, Kaiser Permanente, Walnut Creek, California.

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Author Contributions:

Conception and design: Herrinton, Carolan, Shorstein

Analysis and interpretation: Herrinton, Liu, Alexeeff, Carolan, Shorstein

Data collection: Herrinton, Liu, Alexeeff

Obtained funding: Herrinton, Shorstein

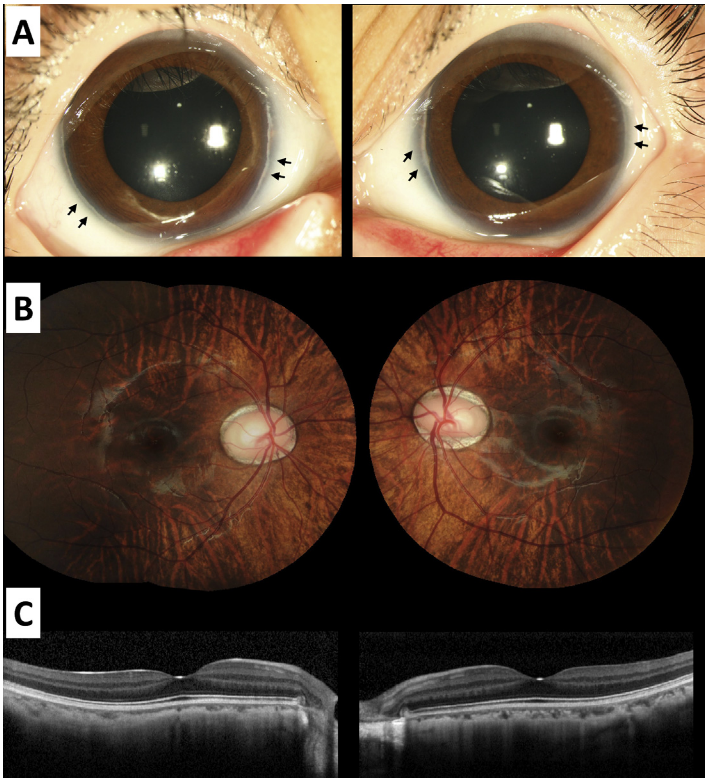
Overall responsibility: Herrinton, Liu, Alexeeff, Carolan, Shorstein

Abbreviations and Acronyms:

BCVA = best-corrected visual acuity; **CI** = confidence interval; **CPT** = Current Procedural Terminology; **D** = diopters; **DSBCS** = delayed sequential bilateral cataract surgery; **ICD-9** = International Classification of Diseases, Ninth Revision; **IOL** = intraocular lens; **ISBCS** = immediate sequential bilateral cataract surgery; **logMAR** = logarithm of the minimum angle of resolution; **OR** = odds ratio; **PCR** = postcapsular rupture; **RE** = refractive error.

Correspondence:
Neal H. Shorstein, MD, Department of Ophthalmology, Kaiser Permanente, 320 Lennon Lane, Walnut Creek, CA 94598. E-mail: nshorstein@eyeonsight.org.

Pictures & Perspectives



Leptochoroid in a Case of Alagille Syndrome (Arterio-hepatic Dysplasia)

A 9-year-old emmetropic boy was referred for diffuse fundus hypopigmentation. His visual acuity was 20/20 with axial length of 23.8 mm in both eyes. Slit-lamp examination revealed bilateral posterior embryotoxon (Fig 1**A**). The fundus showed diffuse choroidal hypopigmentation and paucity of underlying vessels (Fig 1**B**). Optical coherence tomography revealed decreased choroidal thickness ("lepto-" choroid) bilaterally (Fig 1**C**). Hypercholesterolemia, aortic and tricuspid regurgitation, scoliosis of T-L spine, irregularity of the L5 body, and S1 spinal bifida were found. Direct sequencing of the *JAG1* gene confirmed the diagnosis of Alagille syndrome. The leptochoroid might be related to impaired *JAG1* transcription during embryogenesis.

Jen-Hsiang Shen, MD[1]
Kuan-Jen Chen, MD[1,2]
Nan-Kai Wang, MD, PhD[1,2]

[1]*Department of Ophthalmology, Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan;* [2]*College of Medicine, Chang Gung University, Taoyuan, Taiwan*

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