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Glaucoma after Lens-Sparing Vitrectomy for Advanced Retinopathy of Prematurity

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Purpose: To report the incidence of, and factors related to, glaucoma after lens-sparing vitrectomy (LSV) surgery in advanced retinopathy of prematurity (ROP).

Design: Retrospective case series at a single tertiary referral pediatric vitreoretinal practice.

Participants: Four hundred and one eyes from 270 patients were included.

Methods: The medical records of patients who underwent LSV for stage 4A, 4B, and 5 ROP were retrospectively reviewed. Data were collected from patient charts including gender, gestational age at birth, birthweight, stage of ROP at presentation, prior treatment (laser or cryotherapy), subsequent retinal surgeries, presence of glaucoma, time to glaucoma (interval between LSV and the onset of glaucoma), date of lensectomy (if performed), and retinal attachment status at last visit. Lensectomy was considered as a time-dependent covariate in the analysis.

Main Outcome Measures: Incidence of glaucoma and potential risk factors for time to glaucoma.

Results: Among 401 eyes with advanced ROP, 40 eyes (10.0%) had glaucoma during a mean of 3.06±4.11 years of follow-up. The incidence of glaucoma was 6.9% (17/247) in stage 4A, 12.0% (16/133) in stage 4B, and 33.3% (7/21) in stage 5 ROP. Twenty-one percent of eyes (87/401) required lensectomy at a mean of 1.23±2.19 years after LSV. In univariate analysis, having stage 5 ROP (vs. stage 4 ROP) and presence of lensectomy were found to be significantly associated with time to glaucoma (hazard ratio = 6.76, 95% confidence interval = 2.19−20.88, $P = 0.001$; hazard ratio = 3.06, 95% confidence interval = 1.56−6.0, $P = 0.001$, respectively). In multivariate analysis, lensectomy was the only significant independent factor associated with time to glaucoma (hazard ratio = 2.76, 95% confidence interval = 1.371−5.581, $P = 0.004$).

Conclusions: Patients with more severe ROP had a higher incidence of glaucoma after lens-sparing vitrectomy. If a patient required lensectomy owing to progression of ROP and/or presence of lens opacity, then the hazard of having glaucoma significantly increased compared with those without lensectomy. *Ophthalmology 2017;■:1−5 © 2017 by the American Academy of Ophthalmology*

Retinopathy of prematurity (ROP) is 1 of the leading causes of childhood blindness worldwide, accounting for 6% to 18% of all cases.[1] Although laser photocoagulation significantly reduces the severity of vision loss in patients with threshold ROP,[2,3] among the cases of eyes undergoing laser treatment, approximately 10% of children require vitrectomy for the treatment of ROP-associated retinal detachment (Ciaccia S, Ibarra M, Capone A, Trese M. Five-year incidence of blindness from retinopathy of prematurity. Presented at: ARVO Annual Meeting, 2004: Fort Lauderdale, FL). Lens-sparing vitrectomy (LSV) has been shown to be an effective surgical approach with a relatively high success rate, ranging from 42.6% to 82.1% depending on the severity.[4−6] Despite successful retina reattachment, approximately 2100 infants in the United States are affected annually by long-term complications of ROP, such as corneal opacity, glaucoma, and amblyopia, which limits the visual recovery.[7−10]

Childhood glaucoma is a severe condition resulting from various pathologies including congenital defects, trauma, inflammation, or secondary to ocular diseases, with an incidence of 1/10 000 to 1/30 000 live births in the western countries.[11] Although there have been several reports suggesting that the risk of glaucoma increases after vitrectomy in adults,[12,13] there is limited data on the risk of glaucoma after LSV. Here we report the incidence of, and risk factors for, glaucoma in a large series of eyes that underwent LSV for advanced ROP.

Methods

The charts of 279 patients who underwent vitrectomy for stage 4A, 4B, and 5 ROP between 1992 and 2013 at a single tertiary referral pediatric retina clinic were retrospectively reviewed. Institutional review board approval for the data collection and the study was granted by the Western Institutional Review Board.

Baseline characteristics of the patients, including gender, gestational age at birth, birthweight, stage of ROP at presentation, and prior ablative treatment (laser photocoagulation or cryotherapy), were collected from the charts. Date of vitrectomy, subsequent retinal surgeries (if performed), status of the retina at last follow-up, history of lensectomy, date of lensectomy

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Table 1. Baseline Demographics of the Patients who Underwent Lens-Sparing Vitrectomy for Advanced Retinopathy of Prematurity

	Stage 4A	Stage 4B	Stage 5	Total
Eyes, n	247	133	21	401
Patients, n	172	80	18	270
Gender, male, %	58.1	51.2	55.5	55.9
Mean gestational age ± SD, weeks (range)	25.3±1.8 (21.7–32.0)	25.4±2.2 (22.7–33)	25.2±2.0 (22.71–30.0)	25.4±1.9 (21.71–33.0)
Mean birth weight ± SD, grams (range)	768±239 (420–1758)	764±258.9 (400–1700)	761.7±288.2 (350–1516)	776±249.72 (400–1758)
Median follow-up duration, years (interquartile range)	0.4 (0.1–3.7)	2.2 (0.3–7.7)	4.11 (2.8–7.1)	0.9 (0.1–5.2)
Mean follow-up duration ± SD, years (range)	2.3±3.5 (0.0–16.7)	4.2±4.7 (0.0–20.1)	5.0±4.0 (0.1–14.0)	3.1±4.1 (0.0–20.1)

SD = standard deviation.

(if performed), and presence of glaucoma were recorded. Patients with a history of retinal surgery at an outside institution before presentation and eyes with scleral buckles (prior, or at time of vitrectomy) were excluded. Glaucoma was defined as an intraocular pressure (IOP) measurement during at least 2 consecutive examinations under anesthesia of ≥23 mmHg. This number was chosen as a cutoff because it is at least twice the average IOP of normal children aged 0 to 1 year.[14–16] LSV was performed as previously described.[17,18] The mean follow-up duration was considered as the interval between the date of LSV and the last follow-up visit that included IOP measurement.

Statistical Analysis

Descriptive continuous variables were presented using the mean and standard deviation, whereas categorical variables were reported as proportions (%). Kaplan-Meier survival plots were generated to show time to glaucoma in each stage of ROP and in the overall study population. Survival time before development of glaucoma was considered to be the interval between LSV and onset of glaucoma. Frailty models, which are a multivariate random-effects survival model, were used to model the association between the hazard of developing glaucoma and individual baseline variables including gender, birthweight, gestational age at birth, presence of prior ablative treatment, and stage of ROP. The proportions of categorical variables were compared using a mixed model with a subject random effect to account for the inter-eye correlation of the same subjects. For the predictors of glaucoma, frailty models were preferred to Cox regression modeling so as to account for the fact that subjects contribute 2 eyes to the study, which are more likely to share similar characteristics to each other than to other patient eyes, violating the assumption that each eye is independent. Because some patients had lensectomy at some point after LSV owing to progression of ROP and/or presence of lens opacity, lensectomy was included as a time-dependent covariate in this analysis. Each covariate was initially fitted in a univariate analysis and significant predictors of survival before developing glaucoma ($P < 0.05$) were used and re-evaluated in a multivariate analysis. Statistical analysis was carried out using SPSS version 23.0 (SPSS, Inc, Chicago, IL) and R software (version 3.1-122; R Foundation for Statistical Computing, Vienna, Austria). For all hypothesis tests, 2-sided P value of <0.05 was considered as statistically significant.

Results

Among 419 eyes of 279 patients, 401 eyes of 270 patients met inclusion criteria. The baseline demographics of the patients are summarized in Table 1. Most of the eyes (61.6%) had stage 4A disease, 133 eyes (33%) had stage 4B, and 21 eyes (5.2%) had stage 5 ROP. The median follow-up duration was 0.85 years in the study population (interquartile range: 0.12–5.21 years).

Table 2. Clinical Characteristics of the Eyes That Underwent Lens-Sparing Vitrectomy for Advanced Retinopathy of Prematurity

	Severity of ROP			
	Stage 4A	*Stage 4B*	*Stage 5*	**Total**
Number of eyes	247	133	21	401
Prior ablative treatment, present, n (%)	244 (98.7%)	125 (93.9%)	20 (95.2%)	389 (97.0%)
PC, n (%)	242 (97.9%)	124 (93.2%)	19 (90.5%)	385 (96.0%)
Cryo, n (%)	2 (0.8%)	0	0	2 (0.5%)
PC+Cryo, n (%)	0	1 (0.7%)	1 (4.8%)	2 (0.5%)
Presence of glaucoma, n	17 (6.9%)	16 (12.0%)	7 (33.3%)	40 (10.0%)
Need for lensectomy during follow-up, n (%)	28 (11.3%)	44 (33.0%)	15 (71.4%)	87 (21.7%)
Mean interval between first LSV and lensectomy ± SD, years (range)	1.4±0.3 (0.1–13.5)	1.1±1.9 (0.1–9.0)	1.3±1.7 (0.0–5.9)	1.2±2.2 (0.0–13.5)
Subsequent retinal surgery, n (%)	38 (15.4%)	41 (30.8%)	7 (33.3%)	86 (21.4%)
Attached retina at last follow-up, n (%)	237 (96%)	121 (91%)	17 (81%)	375 (93.5%)

Cryo = cryotherapy; LSV = lens-sparing vitrectomy; PC = laser photocoagulation; ROP = retinopathy of prematurity; SD = standard deviation.