Long-term visual and anatomic outcomes following early surgery for persistent fetal vasculature: a single-center, 20-year review

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BACKGROUND Persistent fetal vasculature (PFV) is a spectrum of congenital anomalies caused by complete or partial failure of the ocular fetal vasculature to regress. We report the visual and anatomic outcomes in a large cohort of patients who underwent early surgery for PFV.

METHODS We retrospectively reviewed the medical records of patients who underwent lensectomy and anterior or core vitrectomy for unilateral PFV without primary intraocular lens implantation through limbal or pars plana/plicata approach. Inclusion criteria were surgery prior to 7 months of age, with at least 12 months of follow-up. Eyes with severe posterior segment involvement and retinal detachment deemed beyond repair were excluded.

RESULTS A total of 58 patients met inclusion criteria. Mean age at surgery was 2.1 ± 1.5 months. Mean follow-up was 6.7 ± 4.2 years. At final follow-up, 19 eyes (33%) had visual acuity better than 1.0 logMAR. Thirty-three eyes (57%) developed 1 or more postoperative adverse events: glaucoma in 21 (36%) and retinal detachment in 11 (19%), 8 of which occurred in eyes that had pars plana or pars plicata incisions ($P = 0.002$). In patients with limbal incisions, 17 of 40 (43%) achieved a visual acuity better than 1.0 logMAR, compared with 2 of 18 patients (11%) with a pars plana/pars plicata incision ($P = 0.03$).

CONCLUSIONS In our study cohort, early surgery for PFV achieved functional visual acuity in about one-third of patients. Limbal approach to surgery may result in better visual acuity and anatomic results. (J AAPOS 2019;23:327.e1-5)

Persistent fetal vasculature (PFV) was first described by Reese as the postnatal persistence of intraocular blood vessels in the retrolental space that ordinarily regress before birth.[1,2] The disease is typically unilateral, but about 10% of cases are bilateral and often occur in association with other ocular and systemic abnormalities.[3] Characteristic features include a white vascularized retrolental tissue, with or without a lenticular opacity, a persistent patent hyaloid artery, centrally dragged ciliary processes, retinal detachment (RD), macular hypoplasia or dysplasia, optic disk hypoplasia or dysplasia, and microphthalmos.[4]

Surgical treatment of PFV aims to clear the pupillary area to prevent the development of amblyopia. Several studies have shown that useful vision can be obtained, particularly in eyes with anterior PFV.[5-7] However, eyes with PFV have a poorer visual prognosis and a higher complication rate than eyes with a non-PFV cataract.[6,8-11] The purpose of this study was to assess the visual and anatomic outcomes of surgery in a large, homogenous cohort of eyes with PFV and compare our results to the contact lens group of the Infant Aphakia Treatment Study (IATS) with and without PFV.[12]

Subjects and Methods

The study was approved by the Research Ethics Board at the Hospital for Sick Children. The medical records of patients who had undergone surgery for PFV over a 20-year period, between September 1995 and December 2015, at the Hospital for Sick Children, Toronto, a tertiary-care pediatric hospital, were reviewed retrospectively. Inclusion criteria were presence of unilateral PFV, lensectomy before 7 months of age without primary intraocular lens (IOL) implantation, and at least 12 months of follow-up. Eyes with RD or retinal dysplasia at presentation were excluded. Eyes with features suggestive of other ocular disorders, such as familial exudative vitreoretinopathy or retinopathy of prematurity, or a definite or suspected diagnosis of a systemic disorder known to cause similar ocular abnormalities (eg, Norrie

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disease) were also excluded. Lensectomy was performed through either limbal or pars plana/pars plicata incisions. All eyes had a posterior capsulotomy and anterior or core vitrectomy.

The primary outcome was visual acuity (converted to logMAR) measured using age-appropriate tests at the final follow-up examination. In patients in whom recognition visual acuity could not be performed, visual acuity was extrapolated from fixation pattern using a technique modified from Zipf[13] by Karr and Scott,[14] where central-steady-unmaintained visual acuity was equivalent to 20/30 to 20/100 (0.2–0.7 logMAR); uncentral-steady-unmaintained visual acuity, to ≤20/300 (1.2 logMAR); and uncentral-unsteady-unmaintained visual acuity, to ≤5/200 (1.6 logMAR). For the purpose of analysis, visual acuity was classified as worse or equal to 1.0 logMAR and better than 1.0 logMAR. Secondary outcomes included the rate and type of adverse events at final available follow-up and the number of subsequent intraocular procedures. Microphthalmia was diagnosed clinically by the operating surgeon as an abnormally small eye. A diagnosis of postoperative glaucoma was made based on the presence of an intraocular pressure (IOP) of ≥21, in addition to one or more of the following: corneal findings, such as Haab striae; edema or enlarged corneal diameter; ocular enlargement evidenced by progressive increase in axial length; optic disk cupping; and a reproducible visual field defect.[15]

For comparison with the IATS patient cohort, visual acuity, the rate of adverse events, and the number of subsequent intraocular procedures were also analyzed at the 4.5-year postoperative examination where available. For the 4.5-year visit, a 2-year window (3.5-5.5 years) was allowed. If there was more than one appointment within this period, the closest in time to 4.5 years was chosen.

A two-sided Fisher exact test was used to examine the significance of associations between clinical features of PFV and visual outcome. All statistical analyses were performed using IBM SPSS Statistics for Windows (version 25.0; IBM Corp, Armonk, NY).

Results

A total of 130 eyes of 125 patients with PFV during the study period were identified. Of these, 58 (32 females [55%]) with unilateral PFV met inclusion criteria. None of the included patients had any associated systemic disease. Mean age at presentation was 1.5 ± 1.3 months (range, 0.1-6.0). The clinical features at presentation are provided in Table 1. The most common features were lenticular or retrolenticular opacity in 57 eyes (98%), fibrovascular stalk in 44 (76%), and microphthalmia in 21 (36%). Of the 3 eyes with an optic disk anomaly, 2 had tilted optic disks and 1 had an optic disk pit (none had optic disk hypoplasia). In 7 individuals, strabismus was the presenting feature (esodeviation, 3; exodeviation, 4). None of the eyes had glaucoma preoperatively.

All 58 eyes underwent lensectomy and anterior/core vitrectomy without primary IOL implantation at a mean age of 2.1 ± 1.5 months (range, 0.2-6.3). Limbal incisions were used in 40 eyes (69%); pars plana or pars plicata incisions, in 18 eyes (31%). Table 2 shows intraoperative adverse events. Six eyes (10%) had 1 or more intraoperative adverse events. All 3 eyes with an iatrogenic RD had pars plana/pars plicata incisions ($P = 0.03$) and had the retina reattached by the end of surgery.

Table 1. Clinical features on presentation in 58 infants who underwent surgery for unilateral anterior persistent fetal vasculature

Clinical feature	No. (%)
Lenticular or retrolenticular opacity	57 (98.3)
Fibrovascular stalk	44 (75.9)
Microphthalmia	21 (36.2)
Central dragging of ciliary processes	9 (15.5)
Strabismus	7 (12.1)
Optic nerve head anomaly	3 (5.2)
Corneal opacity	2 (3.4)
Nystagmus	1 (1.7)

Table 2. Intraoperative adverse events in 58 infants who underwent surgery for unilateral anterior persistent fetal vasculature

Adverse event	No. (%)
Any intraoperative adverse event	6 (10.3)
Retinal tears	3 (5.2)
Iatrogenic retinal detachment	3 (5.2)
Vitreous hemorrhage	1 (1.7)

Postoperative visual rehabilitation was contact lens in 52 eyes and spectacles in 2; all patients received amblyopia management as appropriate. The 4 remaining eyes did not receive optical correction or amblyopia management, because they had poor visual potential (1 with phthisis bulbi, 2 with early postoperative RD, and 1 with severe microphthalmia); hence, no treatment was deemed appropriate after discussion with parents. Mean follow-up time was 6.7 ± 4.2 years (median, 5.6; range, 1.2-17.5). For the 4.5-year follow-up subgroup, the mean follow-up time was 4.8 ± 0.6 years (median, 4.7; range, 3.6-5.4).

Visual Outcomes

Visual outcomes are shown in Figure 1. Visual acuity of better than 1.0 logMAR was achieved in 19 of 58 patients (33%) at final follow-up and 13 of 40 (33%) of those who had a 4.5-year follow-up visit, compared to 29 of 57 (51%) in the IATS contact lens group (Table 3).[16] At final follow-up, 17 of 40 (43%) with limbal incisions achieved a visual acuity of better than 1.0 logMAR compared to only 2 of 18 eyes (11%) with pars plana or pars plicata incisions, which was statistically significant ($P = 0.03$). There was no difference in the mean age at surgery for eyes that achieved visual acuity better than 1.0 logMAR compared to those that did not (2.0 vs 2.1 months [$P = 0.75$]).

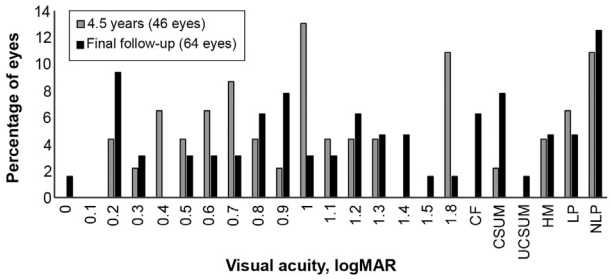

FIG 1. Visual outcomes (logMAR) in eyes that underwent surgery for persistent fetal vasculature. *CF*, counting fingers; *CSUM*, central, steady, unmaintained; *HM*, hand movement; *LP*, light perception; *NLP*, no light perception; *UCSUM*, noncentral, steady, unmaintained.

Table 3. Visual outcome in eyes after surgery for persistent fetal vasculature

	Follow-up, no. (%)	
Visual acuity, logMAR	4.5 years (n = 40)	Final (n = 58)
1.0 and worse	27 (67.5)	39 (67.2)
0.6 to better than 1.0	7 (17.5)	10 (17.2)
0.3 to better than 0.6	4 (10.0)	4 (6.9)
Better than 0.3	2 (5.0)	5 (8.6)

Adverse Events

At final follow-up, a total of 33 of 58 patients (57%) developed at least 1 postoperative adverse event, the most common of which was glaucoma (36%). See Table 4. Glaucoma was controlled in 16 of the 21 eyes (76%) with medications, surgical procedures, or a combination of both. Five patients had IOP >21 mm Hg despite medical and surgical management. Postoperative glaucoma occurred in 8 of 15 patients (53%) who had surgery within the first month of life, which reduced to 13 of 43 (30%) for those operated on between months 4 and 7 ($P = 0.13$). Postoperative glaucoma occurred in 16 of 40 patients (40%) had limbal incisions compared to 5 of 18 (28%) who had pars plana or pars plicata incisions, which was not statistically significant ($P = 0.17$).

The second most common adverse event was postoperative RD, which occurred in 11 eyes (19%), including 8 eyes that had pars plana or pars plicata incisions ($P = 0.002$). Six eyes underwent successful RD repair. Five eyes developed phthisis bulbi following unsuccessful surgery (n = 2) or inoperable, longstanding RD (n = 3).

Similar to the overall cohort, in the 4.5-year visit subgroup, 22 eyes (55%) developed 1 or more adverse events, the most common of which was also glaucoma (35%), followed by RD (20%). In the IATS contact lens group, glaucoma was diagnosed in 16%, with an additional 19% that were glaucoma suspects by 5 years of age (ie 35% risk of a glaucoma-related adverse event).[17]

Subsequent Procedures

Thirty-one eyes (53%) underwent 1 or more subsequent intraocular procedures following lensectomy and vitrectomy for PFV. The mean number of subsequent intraocular procedures in those eyes was 1.8 (median, 1; range, 1-7). Subsequent surgery was most commonly performed for glaucoma (11 eyes [19%]), followed by RD repair (8 eyes [14%]). See Table 5. Seven eyes (12%) had secondary IOL at a mean age of 35.0 ± 13.8 months (median, 41; range, 9-50), one of which needed IOL repositioning. Secondary IOL implantation did not have a statistically significant effect on whether or not the visual acuity at last follow-up was better than 1.0 logMAR nor on the rate of postoperative adverse events including glaucoma. In the subgroup of eyes at the 4.5-year follow-up examination, 20 eyes (50%) had 1 or more subsequent intraocular procedures.

Table 4. Adverse events in eyes with persistent fetal vasculature (may have more than one)

	Follow-up, no. (%)	
Adverse event	4.5 years (n = 40)	Final (n = 58)
Any adverse event	22 (55.0)	33 (56.9)
Glaucoma	14 (35.0)	21 (36.2)
Retinal detachment	8 (20.0)	11 (19.0)
Phthisis bulbi	5 (12.5)	7 (12.1)
Posterior synechiae	4 (10.0)	6 (10.3)
Band keratopathy	2 (5.0)	4 (6.9)
Persistent corneal edema	1 (2.5)	2 (3.4)

Discussion

It is well established that outcomes of surgery in eyes with PFV are not as good as in non-PFV unilateral cataracts; however, good and functional visual acuity can be obtained in some cases. To date, studies on PFV surgical outcomes have been heterogeneous in their inclusion criteria and outcomes reporting; hence, the literature on PFV is difficult to interpret and compare. Sisk and colleagues[11] included 70 eyes that underwent surgery; 70% achieved visual acuity of counting fingers or better with a mean follow-up of 4 years. Their study reported the whole spectrum of PFV, including severe posterior segment involvement, and eyes that underwent surgery at an older age, with a follow-up time as short as 6 months. Hunt and colleagues[7] found that 18% of cases achieved visual acuity of 20/200 or better. A number of eyes with severe posterior segment involvement and patients who had other systemic and neurologic disorders were included with a follow-up of 28 months. Anteby and colleagues[10] reported a visual outcome of 20/200 or better in 24.1% of cases. The mean age in their study was over a year, and almost half the cohort received IOL implant. A subgroup analysis in the IoLunder2 study reported visual acuity that was normal for age for 24% of unilateral and 20% of bilateral PFV cases. Normal vision was based on normative age-related values for each test modality used.[18-20] The median age at surgery was 9 weeks but ranged from 4 to 100 weeks, and one-third of eyes received primary IOL implantation. Follow-up was only 1 year.[21] The IATS had the most

Table 5. Additional intraocular surgical procedures following surgery for persistent fetal vasculature

Procedure	Follow-up, no. (%)	
	4.5 years (n = 40)	Final (n = 58)
Any one or more procedures	20 (50.0)	27 (46.6)
Any glaucoma surgery	7 (17.5)	11 (19.0)
Cyclodestructive procedure	4 (10.0)	5 (8.6)
Glaucoma drainage device	3 (7.5)	4 (6.9)
Angle surgery	1 (2.5)	5 (8.6)
Retinal detachment repair	7 (17.5)	8 (13.8)
Secondary IOL implantation	6 (15.0)	7 (12.1)
Membranectomy	3 (7.5)	4 (6.9)
Pupilloplasty	2 (5.0)	3 (5.2)
Penetrating keratoplasty	1 (2.5)	1 (1.7)

IOL, intraocular lens.

homogeneous group of patients with mild PFV (n = 18) that were incidentally found at the time of cataract surgery.[22] The median logMAR visual acuity achieved in the PFV subgroup was 0.88 logMAR at 1 year, which did not differ significantly from that achieved in the non-PFV subgroup.

In this study, we included patients with surgery <7 months of age and a subgroup of patients with a 4.5 year follow-up in order to facilitate comparison to the IATS contact lens group. Patients in this cohort were less likely to achieve visual acuity better than 1.0 logMAR (33%) compared to patients in IATS contact lens group (51%).[16] A difference was also noted comparing eyes achieving a visual acuity better than 0.3 logMAR (5% vs 23% in the IATS). Nevertheless, it is still encouraging that a significant proportion of patients in our cohort with unilateral PFV cataracts achieved good functional vision after early surgery.

We excluded severe posterior segment involvement, as good visual outcomes following surgery is often unattainable.[23] Patients with optic nerve hypoplasia were not specifically excluded from our study, but this is a rare finding with PFV and was not present in our patient cohort. A significant finding was that patients who had a pars plana or pars plicata incision were less likely to achieve a visual acuity of better than 1.0 logMAR and more likely to have RD compared with patients who had limbal incisions. Pars plana/pars plicata incisions for PFV were formerly performed by vitreoretinal surgeons at our institution; however, as it has become clear that there is an increased risk of complications with this approach, limbal incisions are now preferred for cataract extraction in patients with PFV. The increased risk of retinal tears and detachment with pars plana/pars plicata incisions in PFV may be explained by the increased recognition of the presence of a thickened, adherent hyaloid face or anteriorly displaced retina in the region of the pars plana/pars plicata. This can be detected as a double linear echo on high-frequency ultrasound and would lead to traction on the peripheral retina.[24] Despite steps taken to avoid performing surgery on eyes with no visual potential, some patients still had no light perception, and most of those eyes eventually developed phthisis bulbi, consistent with the report by Sisk and colleagues.[11]

Unilateral cataract surgery, even without PFV, is associated with high complication rates. The total rate of glaucoma-related adverse events in this cohort (35%) was almost identical to the IATS contact lens group (35%) after 4.5 years of follow-up. In the IATS, a glaucoma suspect was defined as an eye with an IOP above 21 on 2 consecutive occasions requiring glaucoma medication. Using the same definition, there were no glaucoma suspects in our study, because all patients receiving glaucoma medication had anatomical evidence of glaucoma. The difference in the rate of true glaucoma (35% in this study vs 16% in IATS) is likely explained by the more severe nature of the PFV and associated anterior segment anomalies in our cohort. The rate of glaucoma in PFV studies with shorter follow-up ranges from 11% to 23%.[10,11] Pollard[22] suggested that an aim of surgery in PFV is to prevent complications like glaucoma, which results from the lens-iris diaphragm being pushed forward to cause secondary angle-closure glaucoma. By contrast, Sisk and colleagues[11] found a higher rate of glaucoma in operated eyes than in unoperated eyes. Therefore, operating on PFV eyes with the aim of preventing glaucoma may be justified in selected cases, particularly if the anterior segment is crowded and there is an increased risk of angle closure.

Our study is limited by its retrospective nature and by the lack of standardization in surgical approach. The presence of microphthalmia was determined according to the documentation in the patient's record and based only on the clinical impression of an abnormally small eye. Because no specific diagnostic criteria were used to establish the presence or severity of microphthalmia, the incidence may have been underestimated, particularly for mild cases. The variability in compliance with contact lens wear or occlusion therapy and the number of hours of patching per day may have influenced visual acuity outcomes.

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