

# Staged lensectomy and vitrectomy in the management of stage 5C retinopathy of prematurity with corneal opacification: long-term follow up

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## Abstract

• **AIM:** To verify the feasibility and safety of staged lensectomy and vitrectomy in stage 5C retinopathy of prematurity (ROP) with corneal opacification.

• **METHODS:** This was a retrospective, interventional, consecutive case series. Twenty-two eyes of 18 stage 5C ROP patients with corneal opacification were included. Regular combined lensectomy and vitrectomy were not prescribed due to the invisible fundus. Staged lensectomy and posterior vitrectomy were performed. The anatomical and visual outcomes were reviewed at the final follow-up visit.

• **RESULTS:** The mean gestational age of ROP patients was  $29.3 \pm 1.6$ wk (range: 27-32wk), comprising 8 males and 10 females. The average birth weight was  $1363.0 \pm 300.0$  g. All the eyes had corneal opacity and flat or disappeared anterior chambers pre-operatively. Two eyes had complicated cataract and 7 eyes had retrolental fibroplasia. Six eyes had posterior pupillary synechiae or membranes. Seven (31.8%) eyes had vascularly active retinas. The average interval between two procedures was  $6.8 \pm 4.6$ mo (2.5-18.5mo). After surgeries, all the patients had normal anterior chambers. Fourteen eyes had clear corneas. The intraocular pressure of 3 eyes with glaucoma was controlled by medication. Two eyes had ocular phthisis. The retina was reattached in 3 eyes and partially attached in 11 eyes. Visual acuity ranged from no light perception to hand motion.

• **CONCLUSION:** Staged lensectomy and vitrectomy

are procedures that can halt progression to further complications and preserve some useful eyesight in stage 5C ROP patients with corneal opacification. The earlier the lensectomy is performed, the better the prognosis is.

• **KEYWORDS:** lensectomy; vitrectomy; staged surgery; retinopathy of prematurity; corneal opacification; retinal detachment

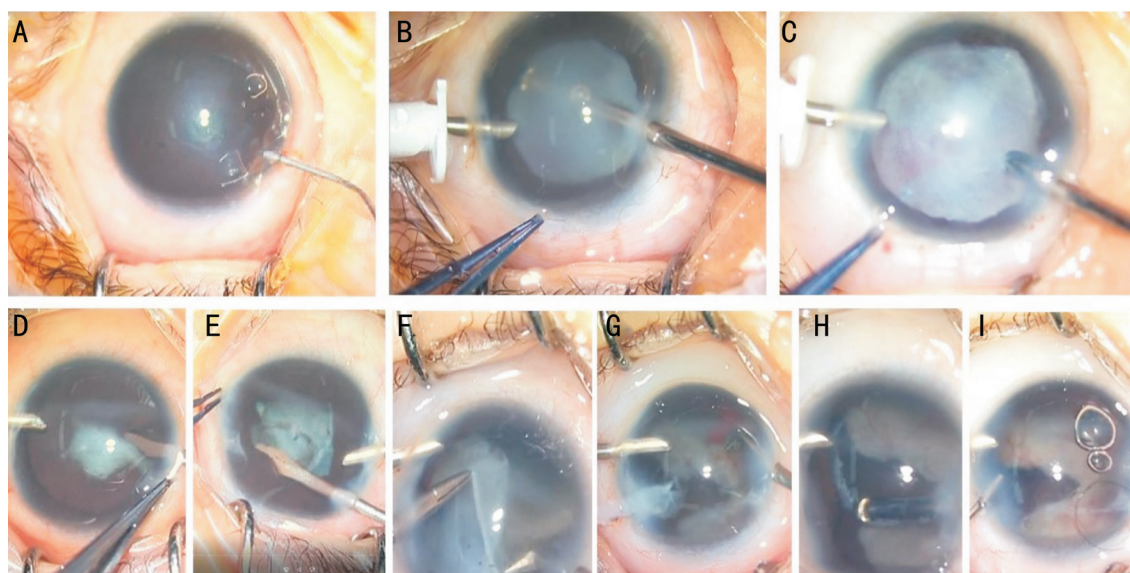
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## INTRODUCTION

Retinopathy of prematurity (ROP) is an avoidable cause of childhood blindness<sup>[1]</sup>. Undergoing screening protocols and meticulous examinations by an experienced ophthalmologist is one of the main approaches that could reduce the burden of this type of blindness<sup>[2]</sup>. However, later presentation is significantly associated with more advanced ROP. In developing countries and even in rural areas, quite a few patients are still not referred to ophthalmologists until leukocoria is noticed mainly due to lack of routine screening for ROP<sup>[3-6]</sup>.

The surgical techniques for stage 5 ROP are demanding<sup>[7]</sup>. Successful anatomical results after surgery are only seen in 9%-45% of cases and, even with a successful anatomical result, the visual outcome may be limited<sup>[8-9]</sup>. Stage 5 ROP was defined as 3 subcategories, according to the International Classification of Retinopathy of Prematurity, 3<sup>rd</sup> edition, in terms of their anterior and posterior configurations. Stage 5C, was defined as total retinal detachment of closed-funnel configuration accompanied by anterior segment changes (e.g., marked anterior chamber shallowing, iridocorneolenticular adhesions, corneal opacification)<sup>[10]</sup>. There are several studies about surgical management of stage 5 ROP<sup>[11-13]</sup>. However, there is few studies about the management of stage 5C ROP with corneal opacification, which called for urgent surgery to



**Figure 1** Surgical procedures of staged lensectomy (A-C) and vitrectomy (D-I) A: Inject viscoelastics into the anterior chamber to separate the anterior and posterior iris synechiae; B: Trim the edge of the iris to enlarge the pupil; C: Perform lensectomy; D: Make limbal ports; E: Separate the iris synechiae and enlarge the pupil; F, G: Remove the pre-retinal tissue completely without retinal break formation; H: Trim the residual fibrous membrane with a vitreous cutter; I: Inject the viscoelastic solution to achieve retinal reattachment and to maintain eyeball pressure.

resolve the complications, but is more challenging to manage due to the invisible fundus<sup>[14-15]</sup>. Whether and how to perform surgeries in these cases remain questionable. Regular combined lensectomy and vitrectomy were not advocated due to the corneal opacity and invisible fundus. Here, we presented a series of cases in which staged lensectomy and vitrectomy were performed. Thereafter, the long-term anatomical and visual outcomes were analyzed.

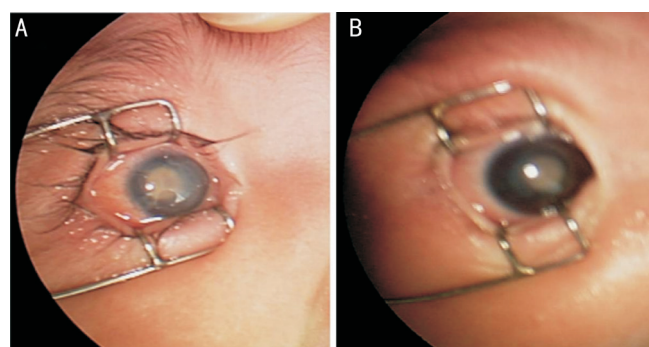
#### SUBJECTS AND METHODS

**Ethical Approval** This study was approved by the Ethics Committee of Xinhua Hospital, Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China. All parents of the patients provided informed consent before the surgeries were undertaken. Written informed consent was also obtained from the parents for the enrollment of their children in the study.

**Study Design** This study was a retrospective, interventional, consecutive case series. Twenty-two eyes of 18 stage 5C ROP patients with corneal opacification who underwent staged lensectomy and vitrectomy at Xinhua Hospital, Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China, from 2008 to 2017 were included in this analysis.

All patients underwent comprehensive examinations. Pre-operative clinical findings, including the patients' gestational age at birth and surgeries, birth weight, gender, manner of delivery, ROP status, pre- and post-operative status, and treatment were recorded.

We performed staged lensectomy and posterior vitrectomy in all 22 eyes. Lensectomy was performed firstly to avoid further deterioration. Topical steroids were applied to reduce the corneal edema after lensectomy. Vitrectomy was advocated if



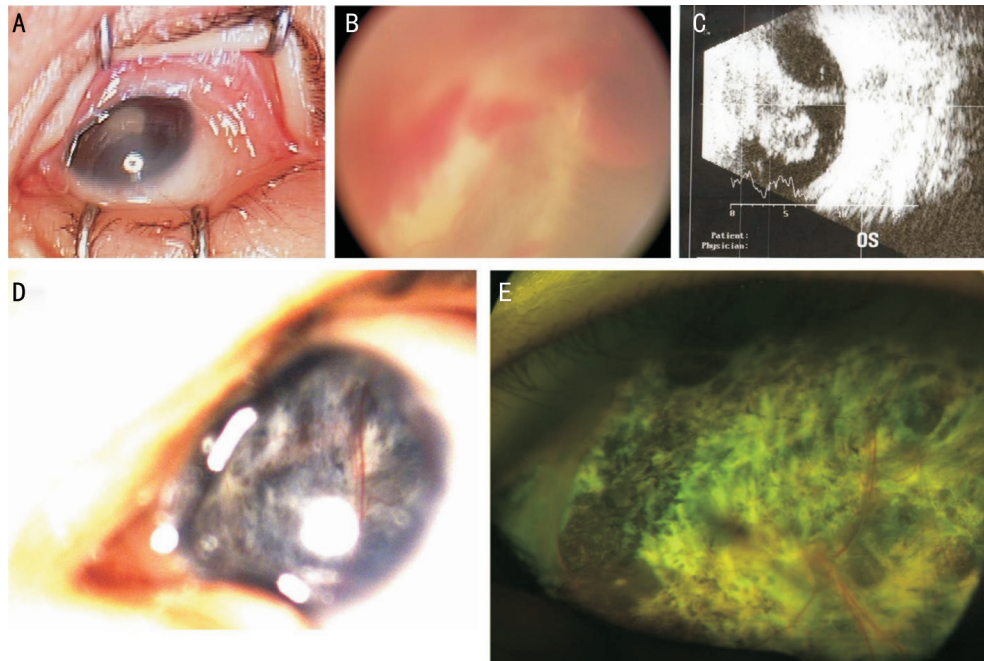
**Figure 2** Corneal status of stage 5C ROP patient before and after surgery A: Before operation, opaque cornea and flat anterior chamber; B: After staged lensectomy and vitrectomy, clear cornea and formed anterior chamber. ROP: Retinopathy of prematurity.

the corneal edema improved and the fundus was visible during the follow up after lensectomy. All the patients were operated on by one surgeon (Zhao PQ). All the eyes were followed for at least three years post-operatively (average  $8.9 \pm 2.6$ y).

**Surgical Procedures** Staged lensectomy and vitrectomy (Figure 1).

Primary procedure: lensectomy (Online supplementary Video 1): 1) Apply the two-port limbal approach; 2) Drain the subretinal fluid to soften the eyeball if necessary. Then, inject viscoelastics into the anterior chamber to separate the anterior and posterior iris synechiae. Trim the edge of the iris to enlarge the pupil. 3) Perform lensectomy; 4) Remove the anterior capsule and aspirate the lens material under low suction using the vitrectomy cutter.

Second procedure: vitrectomy (Figure 2, Online supplementary Video 2).



**Figure 3** Patient of staged 5C ROP before (A-C) and after surgery (D, E) A: Corneal edema and flat anterior chamber; B: Total retinal detachment with vascularly active status; C: Ultrasound showed closed funnel of TRD; D: Clear cornea after surgery; E: Retina partly attached. ROP: Retinopathy of prematurity.

Vitrectomy was performed when the corneal edema alleviated and did not obscure the view of the retina and/or the retina turned vascularly inactive. 1) Apply the three-port limbal approach; 2) Remove the pre-retinal tissue completely without retinal break formation using 23/25G intraocular forceps and scissors through bimanual dissection under coaxial illumination of the microscope; 3) Inject the viscoelastic solution to achieve retinal reattachment and to maintain the eyeball pressure at the end of the surgery. Use silicone oil tamponade in the surgery if retinal break was present during vitrectomy. 4) Suture the sclerotomies.

Follow-up examinations were conducted periodically. The anatomical outcomes were evaluated, including retinal status, cornea, and anterior chambers (Figure 3). Visual acuity was measured accordingly, marked as hand motion (HM), light perception (LP), and no light perception (NLP).

## RESULTS

The demographics of the patients are presented in Table 1. Twenty-two eyes of 18 stage 5C ROP patients with advanced complications were included in this study. Eight patients were males and 10 were females. Their birth weight ranged from 940 to 2000 g (mean  $1363.0 \pm 300.0$  g). Gestational age (GA) at birth ranged from 27 to 32wk (mean  $29.3 \pm 1.6$ wk). The average corrected GA at the time of the first surgery was  $73.6 \pm 18.0$ wk (ranging from 50 to 123wk). The average corrected GA at the secondary vitrectomy was  $102.4 \pm 21.3$ wk (ranging from 69 to 143wk). The mean interval between the two surgeries was  $6.8 \pm 4.6$ mo (2.5-18.5mo).

Before lensectomy, all 22 eyes had corneal opacity and flat or disappeared anterior chambers. Eighteen eyes had corneal edema and the remaining 4 eyes had corneal nebula. Two eyes had complicated cataract and 7 eyes had retrolental fibroplasia. Six eyes had posterior pupillary synechiae or membranes. Seven (40%) eyes had vascularly active retinas.

During long-term follow-up after the two procedures, all the patients formed an anterior chamber. Fourteen eyes had clear corneas after surgery, while 8 eyes retained their corneal opacity. Three eyes had secondary glaucoma, which was controlled by medical treatment. Two eyes had ocular phthisis. The retina was reattached in 3 eyes and partially attached in 11 eyes. The retina of the remaining 8 eyes were detached, including 6 open-open or partially open funnel configurations but expanding and 2 closed configuration detachments. Visual acuities ranged from NLP to HM (Table 2). There were no statistical differences between the mean intervals of the staged surgeries among different groups of post-operative retinal status or the final visual acuity. Table 3 presents the demographics and outcomes of staged lensectomy and vitrectomy in individual patients.

## DISCUSSION

Surgical intervention in ROP has been described as early as 1977 by Treister and Machemer<sup>[16]</sup>. Two common surgery approaches used in stage 5 ROP are open-sky vitrectomy and closed vitrectomy<sup>[17]</sup>. Open-sky vitrectomy has the advantage of allowing two-hand dissection from a larger anterior incision; however, the maintenance of intraocular pressure

**Table 1 Patients' demographic characteristics**

No. of eyes/patients	22/18
Male/female	8/10
OD/OS	12/10
GA (wk)	29.3±1.6 (27-32)
BW (g)	1363.0±300.0 (940-2000)
Singleton/twin	12/6
CGA at first surgery (wk)	73.6±18.0 (50-123)
CGA at second surgery (wk)	102.4±21.3 (69-143)
Interval between two surgeries (mo)	6.8±4.6 (2.5-18.5)
Follow-up (y)	8.9±2.6 (3-13)
Pre-operative status, <i>n</i> (%)	
Diagnosis (ROP stage 5)	22 (100.0)
Corneal edema/opacity	22 (100.0)
Corneal edema	18 (81.8)
Corneal nebula	4 (18.2)
Flat or disappeared AC	22 (100.0)
Flat AC	11 (50.0)
Disappeared AC	11 (50.0)
Cataract	2 (9.1)
Pupillary synechia/membrane	6 (27.3)
Posterior synechia	4 (18.2)
Pupillary membrane	2 (9.1)
Vascularly active retina	7 (31.8)
RLF	7 (31.8)
Surgical procedure, <i>n</i> (%)	
Staged lensectomy+vitrectomy	16 (72.7)
Staged lensectomy+vitrectomy+membrane peeling	5 (22.7)
Staged lensectomy+vitrectomy+silicone oil tamponade	1 (4.5)

OD: The right eye; OS: The left eye; GA: Gestational age; BW: Birth weight; CGA: Corrected gestational age; ROP: Retinopathy of prematurity; AC: Anterior chamber; RLF: Retrolental fibroplasia.

**Table 2 Visual outcomes and prevalence of complications in eyes with reattached and detached retinas**

Outcomes	<i>n</i> (%)
Final retinal status	
Attached	3 (13.6)
Partly attached	11 (50.0)
Open-open or partially open funnel configurations	6 (27.3)
Closed configuration detachments	2 (9.1)
Complications	
Secondary glaucoma	3 (13.6)
Phthisis	2 (9.1)
Corneal opacity (pre/post-operative)	22 (100.0)/8 (36.4)
Retinal break	1 (4.5)
Visual acuities	
HM	8 (36.4)
LP	5 (22.7)
NLP	3 (13.6)

HM: Hand motion; LP: Light perception; NLP: No light perception.

(IOP) during surgery may be difficult, and there is a risk of corneal rejection post-operatively after re-suturing the cornea. Due to this, the focus has gradually shifted to closed vitrectomy with or without lensectomy<sup>[18]</sup>.

Closed vitrectomy combined with lensectomy were performed in stage 5 ROP with retrolental fibroplasia or other complications, such as a flat anterior chamber or cataract. Whether surgical intervention is necessary in these cases remains questionable<sup>[19]</sup>. When making a surgical decision, controversies still exist regarding when the surgery should be performed and which surgical techniques are the most beneficial for the treatment of stage 5 ROP with advanced complications. Combined vitrectomy and lensectomy are not advocated for stage 5C ROP eyes with invisible fundus due to corneal opacity.

In this study, we recommended staged lensectomy and vitrectomy as an alternative choice. Lensectomy was performed first. Then, vitrectomy was recommended if the corneal opacity was alleviated and the fundus was visible during the follow-up period after lensectomy.

In our case series, all the stage 5C ROP cases had flat or disappeared anterior chambers, which indicated an urgent need for lensectomy to avoid permanent corneal damage. However, all the eyes had corneal opacity due to corneal edema or dense corneal nebula, which made it difficult to view the fundus clearly to perform vitrectomy. Additionally, in our case series, 7 eyes had vascularly active retinas. If vitrectomy is performed when the retina is vascularly, severe complications such as vitreous hemorrhage may occur<sup>[20]</sup>. Gopal *et al*<sup>[11]</sup> and Fuchino *et al*<sup>[21]</sup> suggested that since the disease was more vascularly active in babies less than 6 months of age, operating within 6mo has a marked risk of post-operative hemorrhages. Machemer and DeJuan<sup>[22]</sup> and Cusick *et al*<sup>[8]</sup> reported a higher success rate when babies were operated after six months of age. Anti-angiogenic treatment can possibly be an adjunctive therapy for vascularly active retina<sup>[23-24]</sup>, however, eyes must be monitored closely since intense fibrous contraction with complex retinal detachments can occur<sup>[25]</sup>. Staged lensectomy can rescue the cornea in stage 5C ROP and also avoid the risk of post-operative hemorrhages when the retina is vascularly active. The mean interval between the two staged surgeries in our study was 6.8±4.6mo, ranging from 2.5 to 18.5mo, which depended on the status of the corneal opacity and the vascular activity of the retina. Treatment with topical anti-inflammatory drops may be considered after lensectomy to reduce the corneal edema.

In our case series, all the patients had normal anterior chambers after surgery. Fourteen out of 22 eyes had clear corneas post-operatively. Secondary glaucoma has been reported to be another complication of ROP<sup>[26-27]</sup>, in our study, 3 cases had complicated glaucoma and were under medical control. Fourteen (63.6%) eyes obtained at least partial retinal reattachment after the second procedure, the successful anatomical result was higher than the result (57%) reported in the previous study with 87 eyes by Choi and Yu<sup>[28]</sup>.

**Table 3 The demographics and outcomes of staged lensectomy and vitrectomy in individual patients**

Eye Patient No.	Gender	GA at birth (wk)	BW (g)	Single fetation/ multifetation	Way of delivery	Eye operation-1 (wk)	CGA at operation-2 (wk)	Interval between 2 operations (mo)	Follow-up stage (y)	Diagnosis	Pre-operative complications			Surgical procedures	Post-operative status		Complications
											Corneal opacity	Flat/disappeared AC	Cataract		Pupillary membrane/synechia	Vascularly active retina	
1	M	29	1400	Single	V	OD	69	3	8	5	+	++	+	Staged lensectomy + vitrectomy	Partly attached	HM	
2	M	28	1300	Twin	V	OD	74	5	9	5	+	++	+	Staged lensectomy + vitrectomy	Open funnel	LP	
3	M	30	1400	Twin	C	OD	74	9	10	5	++	++	+	Staged lensectomy + vitrectomy	Open funnel	LP	Corneal opacity
4	F	31	2000	Single	V	OS	62	7	10	5	++	++	+	Staged lensectomy + vitrectomy + membrane peeling	Partly attached	HM	Corneal opacity
5	F	29	1200	Single	V	OD	82	2.5	9	5	+	+	+	Staged lensectomy + vitrectomy + membrane peeling	Open funnel	LP	
6	F	30	940	Single	C	OS	101	2.5	9	5	++	++	+	Staged lensectomy + vitrectomy	Open funnel	NLP	Corneal opacity
7	F	29	1500	Single	V	OS	59	2	6	5	+	++	+	Staged lensectomy + vitrectomy	Closed funnel	LP	Corneal opacity
8	F	32	1500	Swim	C	OS	69	5	9	5	++	++	+	Staged lensectomy + vitrectomy	Open funnel	NLP	
9	M	28	1000	Single	V	OD	83	4	12	5	+	+	+	Staged lensectomy + vitrectomy	Attached	HM	
10						OS	83	5	12	5	+	+	+	Staged lensectomy + vitrectomy	Partly attached	HM	Phthisis
11	M	28	1400	Single	V	OD	85	4	9	5	+	++	+	Staged lensectomy + vitrectomy + membrane peeling	Closed funnel	NLP	
12						OS	85	5.5	9	5	+	++	+	Staged lensectomy + vitrectomy + membrane peeling	Partly attached	HM	Glaucoma
13	F	28	1900	Single	V	OD	123	4	10	5	+	+	+	Staged lensectomy + vitrectomy	Partly attached	NLP	Phthisis Corneal opacity
14	F	32	1150	Twin	C	OD	92	8	11	5	+	++	++	Staged lensectomy + vitrectomy	Partly attached	HM	
15	F	32	1400	Single	V	OD	84	4.5	9	5	+	+	+	Staged lensectomy + vitrectomy	Attached	LP	Glaucoma Corneal opacity
16						OS	71	5.5	9	5	+	++	+	Staged lensectomy + vitrectomy	Partly attached	HM	
17	M	29	1000	Twin	C	OS	67	15	13	5	+	+	+	Staged lensectomy + vitrectomy	Attached	HM	Glaucoma Corneal opacity
18	F	30	1750	Twin	C	OD	72	3	9	5	+	+	+	Staged lensectomy + vitrectomy + membrane peeling	Partly attached	NLP	
19	M	29	1450	Single	V	OS	63	14.3	12	5	+	+	+	Staged lensectomy + vitrectomy + silicone oil tamponade	Partly attached	LP	Retinal break
20	M	27	1150	Single	V	OD	57	14	4	5	+	+	+	Staged lensectomy + vitrectomy	Open funnel	LP	Corneal opacity
21						OS	57	14	4	5	+	+	+	Staged lensectomy + vitrectomy	Partly attached	LP	
22	F	27	1100	Single	V	OD	52	8	3	5	+	+	+	Staged lensectomy + vitrectomy	Partly attached	HM	

M: Male; F: Female; GA: Gestational age; BW: Birth weight; V: Vaginal birth; C: C-section; CGA: Corrected gestational age; AC: Anterior chamber; HM: Hand motion; LP: Light perception; NLP: No light perception; Corneal opacity: + corneal edema, ++ corneal nebulia; flat/disappeared AC: + flat AC, ++ disappeared AC; Pupillary membrane/synechia: + pupillary synechia, ++ pupillary membrane.

The authors also demonstrated that staged lensectomy and vitrectomy for stage 5C ROP with opaque cornea might be beneficial in helping preserve vision. The purpose of the surgeries is to rescue the cornea and even partly attach the retina with less complications<sup>[29]</sup>. Surgical intervention may prevent further ocular atrophy, improve the appearance of the eye, and somehow restore visual function (e.g., perception of light)<sup>[30]</sup>, which is very important to the patients with low-vision.

Our study has several limitations. First, it was a retrospective and non-comparative consecutive case series study. Second, the study was based on one surgeon's experience.

In conclusion, the management of the condition of stage 5C ROP patients with flat anterior chamber and central corneal opacity is challenging. Staged lensectomy and posterior vitrectomy are procedures that can prevent further complications, such as corneal endothelium decompensation, leukoma, and secondary glaucoma. Surgical intervention can achieve a favorable retinal status to some extent and preserve some useful eyesight in advanced ROP cases.

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