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Surgical Management of Severe Retinopathy of Prematurity

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Abstract

Retinopathy of prematurity (ROP) is a leading cause of childhood blindness in the world. Appropriate eye screening and interventions, such as laser ablation and/or anti-vascular endothelial growth factor therapy, are useful to prevent blindness by ROP. However, some eyes are refractory to these treatments and develop tractional retinal detachment, which requires surgical intervention, such as vitrectomy and/or the scleral buckling procedure. When vitrectomy was introduced for ROP, it was initially performed at stage 5 (total retinal detachment). Vitrectomy for stage 5 ROP is beneficial to prevent total blindness in some eyes; however, its anatomical and functional results are disappointing. It is now well-established that vitrectomy, if possible lens-sparing vitrectomy, should be performed at stage 4A ROP (partial tractional retinal detachment not involving the macula) before the macula is affected. The anatomical and functional surgical results of vitrectomy for stage 4A ROP are better than those for stage 5 ROP.

Key words：retinopathy of prematurity, vitrectomy, lensectomy, lens-sparing vitrectomy, retinal detachment, scleral buckling procedure

Introduction

Retinopathy of prematurity (ROP) was first described by an American ophthalmologist, Terry, in 1943.[1] Knowledge has accumulated on the pathogenesis of ROP, and its treatment modalities have been evolving. However, ROP is still a leading cause of childhood blindness in the world, both in industrialized and developing countries.[2] The Early Treatment for Retinopathy of Prematurity (ET-ROP) Cooperative Group [3] showed that, by performing retinal laser ablation at prethreshold retinopathy rather than threshold retinopathy, the rates of unfavorable functional and structural outcomes decreased from 19.5 to 14.5% and from 15.6 to 9.1%, respectively. Therefore, by treating ROP earlier, treatment results can be improved. However, approximately 10% of patients still have severe vision loss because of the development of retinal folds, retinal detachment, or retrolental fibroplasia.[3]

One marked advance in our understanding of the ROP mechanism came from the discovery of vascular endothelial growth factor (VEGF) involvement in the pathogenesis of ROP, [4-6] like other neovascular diseases such as diabetic retinopathy (DR) [7] or age-related macular degeneration (AMD).[8] After the introduction of monoclonal antibody of VEGF (bevacizumab) as an off-label use for the treatment of DR or AMD, it was also used for ROP.[9-11] It has been shown that anti-VEGF therapy is effective for reducing disease activity, leading better treatment outcomes for ROP, especially severe ROP, such as zone 1 plus [11]. However, there are some limitations to the use of anti-VEGF therapy for ROP treatment. First, it is currently an off-label treatment and requires an institutional review board approval. Secondly, there are systemic safety concerns as systemic VEGF levels are suppressed after anti-VEGF therapy.[12,13] With the introduction of anti-VEGF therapy, the number of eyes with ROP that progress to tractional retinal detachment (TRD) has decreased; however, there are still some cases that require vitrectomy, even after laser ablation and/or anti-VEGF therapy. In this

article, the current understanding of ROP and surgical treatment, such as vitrectomy or scleral buckling for ROP will be discussed.

Vitrectomy for Stage 4 ROP

If the disease activity is not sufficiently reduced by laser ablation and/or anti-VEGF therapy, focal retinal detachment may develop by vitreous traction to the fibrovascular tissue (Figures 1, 2). This usually takes several weeks from the appearance of ROP (appearance of demarcation line), except for aggressive-posterior ROP, in which tractional retinal detachment may develop within one or two weeks. Usually, TRD develops from approximately 36 to 39 post-conceptional weeks of age. To obtain a good postoperative visual function, vitrectomy should be performed at stage 4A, before the macula is affected (Figure 3), since, as described later, both anatomical and functional results for stage 5 ROP are usually poor.

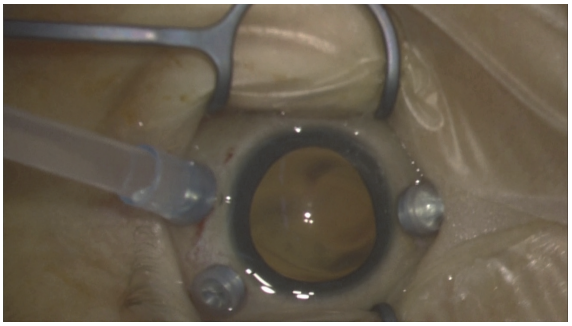

Figure 1 Intraoperative image of lens-sparing vitrectomy for stage 4A retinopathy of prematurity (ROP) using a 27-gauge system. Cannulas are placed 1 mm posterior to the limbus.

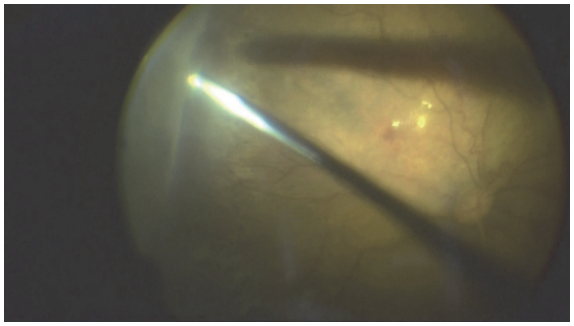

Figure 2 Intraoperative view of lens-sparing vitrectomy for stage 4A ROP using a 27-gauge system. Under observation using a wide-angle viewing system, dissection between the fibrovascular membranes and lens is performed using a 27-gauge vitrectomy cutter.

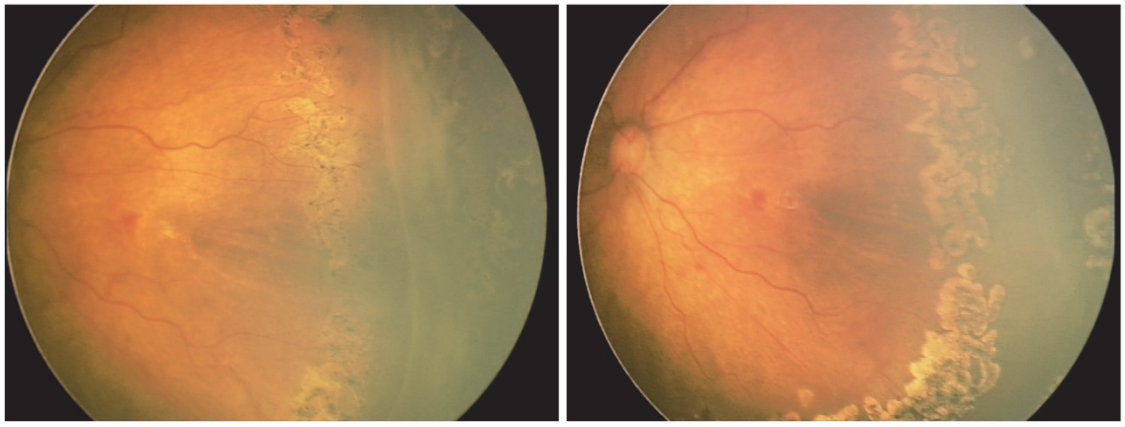

Figure 3 Preoperative-(left panel) and 2-week postoperative (right panel) fundus view of stage 4A ROP. Postoperatively, the retina is completely reattached.

Surgical technique

In eyes with stage 4 ROP, if the fibrovascular tissue is located posterior to the equator, the lens can be spared with a high probability. Maguire and Trese [14] originally described the surgical technique of a 2-port, lens-sparing vitrectomy using 20-gauge instruments. This technique may be useful for avoiding lens damage by the infusion port. However, it requires special 20-gauge instruments, such as an infusion light pipe and infusion spatula, that are not widely used today. Instead, many surgeons adapt a standard 3-port, small-gauge system, such as 23-, 25-, and 27-gauge systems.

In vitrectomy for ROP, special caution should be exercised, owing to the unique anatomical features of infant eyes, such as a short pars plana [16] and relatively large lens size. After conjunctival

peritomy, sclerotomies are made at 0.5 to 1 mm from the limbus. In addition, as the lens is relatively large in infants, the direction of sclerotomy should be more posterior to avoid lens damage [17]. Cannulas can then be inserted either by a one-step technique (sclerotomy by trocars) or a two-step technique (sclerotomy by V-lance followed by trocar insertion). As the sclera of infants is thin and soft, it is difficult to achieve self-sealing, even using a small-gauge system. Therefore, I prefer the two-step technique and suturing every wound. For a fundus view, I use a wide-angle viewing system, such as Resight (Zeiss, Germany) or BIOM (Oculus, Germany). Other surgeons use floating lenses with smaller diameters than the conventional ones for adult surgery.

In eyes with stage 4A ROP, tractions to the fibrous tissue are created in various directions, including tractions between the lens and FVMs, between the peripheral retina and fibrous tissue, between the posterior retina and fibrous tissue, and loop traction on the fibrous tissue. The purpose of vitrectomy is to release these tractions, which can lead to gradual reattachment of the retina postoperatively. Use of horizontal and/or vertical scissors should be minimized to avoid intraoperative bleeding, formation of an iatrogenic retinal hole, or both. Fibrous tissue can be left untouched unless the loop traction by fibrous tissue is so severe that retinal reattachment cannot be expected.

If the ridge is anterior to the equator, the distance between the lens and fibrous tissue is too close to dissect without removing the lens, or both, lensectomy should be performed. If an iatrogenic retinal hole develops, fibrous tissue around the retinal break should be meticulously dissected, followed by fluid/air exchange, and laser photocoagulation. Either long-acting gas or silicone oil is injected at the end of the procedure.

Surgical results

Surgical results of vitrectomy for stage 4 ROP are much better than those for stage 5 ROP. According to previous reports, the anatomical success rates for stage 4A and 4B ROP range from 84 to 100% and 73 to 92%, respectively [17-22], and the mean postoperative visual acuities of stage 4A and 4B ROP range from 20/550 to 20/58, and 20/1600 to 20/200, respectively.[22-24]

Vitrectomy for Stage 5 ROP

Owing to the improvement of neonatal care, widespread use of appropriate screening, laser treatment, and the introduction of anti-VEGF therapy, the number of eyes with stage 5 ROP appears to be decreasing in developed countries. However, there are many eyes with stage 5 ROP (figure 4) in developing countries.

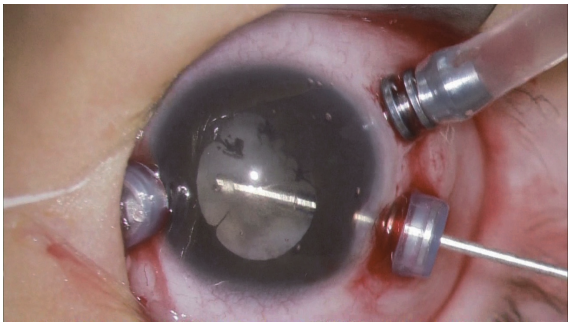

Figure 4 Intraoperative view of lensectomy and vitrectomy for stage 5 ROP.
The lens is being removed using a 27-gauge vitrectomy cutter. Retrolental, white membrane, posterior synechiae, and total retinal detachment can be observed.

Surgical technique

In most eyes with stage 5 ROP, lensectomy is required to approach the membranes. Prior to surgery, where to make surgical incisions should be carefully determined. If the retrolental membranes exist adjacent to the ciliary body, surgical wounds should be made at the limbus to avoid an iatrogenic retinal break or dialysis. If there is some space between the ciliary body and membranes, sclerotomy wounds may be created 0.5 to 1 mm from the limbus, which allows for better visibility during vitrectomy. A mixture of limbal and pars plicata incisions can be employed, depending on the space between the ciliary body and membranes. Lensectomy should be performed thoroughly, including the entire lens capsule, as remnants of the lens capsule can adhere to the iris and/or remaining retrolental membrane after surgery. Dissection of the membranes is usually performed via forceps and scissors or a spatula using the bimanual technique (Figure 5). Dissection can be started in the center of the membranes and extended peripherally in a concentric and/or circumferential manner. To increase the chance of retinal reattachment, membranes should be removed as much as possi-

ble. Special care should be taken to avoid introducing any iatrogenic retinal breaks, especially in the peripheral region, where distinction between the thin membrane and avascular retina is difficult. To avoid dialysis, care should be taken to avoid pulling the membranes too far in the peripheral region. The presence of a retinal break is closely associated with surgical failure in stage 5 ROP surgery. If most membranes can be removed, the retina is gradually reattached within several weeks (Figure 6). Otherwise, reoperation to remove residual membranes should be considered.

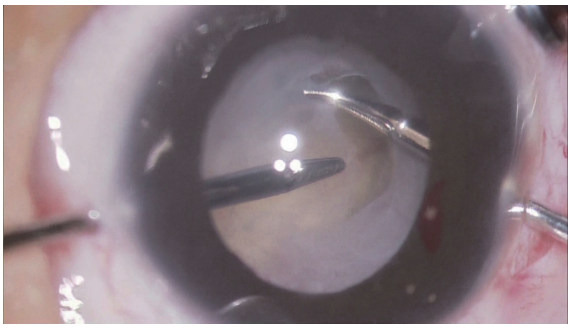

Figure 5 Intraoperative view of vitrectomy for stage 5 ROP. After lens removal, membrane peeling and delamination are performed.

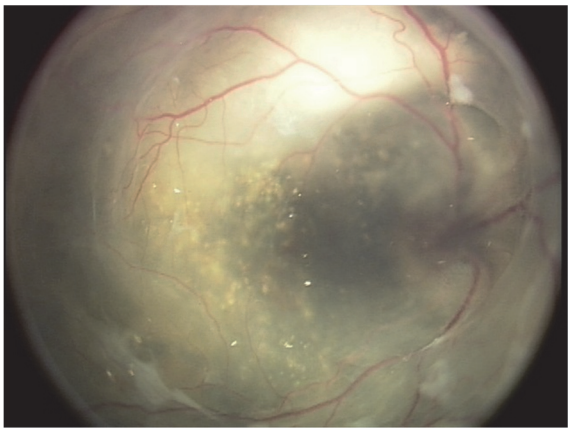

Figure 6 Stage 5 ROP (OD). Five days after the operation. The retina is still detached, but the subretinal fluid has already markedly reduced.

Surgical results

Surgical results of vitrectomy for stage 5 ROP are generally poor. The Cryotherapy for Retinopathy Cooperative Group (CRYO-ROP) [25] reported that at least a portion of the retina was reattached in 11 out of 52 eyes (21%), and visual acuity was limited to light perception or no light perception in all but one eye after vitrectomy for stage 5 ROP at 5.5 years of age. Cusick et al.[26] reported that at least partial retinal reattachment was achieved in 33% of 956 eyes of 601 infants, with a visual acuity of better than 5/200 in 8 out of 183 eyes. In my case series of 48 eyes with stage 5 ROPs evaluated 6 months postoperatively, 20 (42.6%) and 5 (10.6%) eyes had total and partial reattachment of the retina, respectively (unpublished data). Similar results have been reported with retinal reattachment rates of approximately 40 to 60% [26-31,35-37], and limited functional outcomes [26-34] (Table 1). Regarding factors related to anatomical success, a closed shape of the funnel, the presence of subretinal hemorrhage and vascularized membranes, and the age at vitrectomy may be associated with poor surgical outcomes.[26,27,31]

Conclusions

Appropriate care of premature infants by neonatologists and screening with appropriate timing and methods by ophthalmologists are key to reducing severe ROP that requires treatment. Interventions, such as laser ablation or anti-VEGF therapy, are critical for preventing the development of tractional retinal detachment, which is directly associated with poor anatomical and functional results. If tractional detachment occurs, vitrectomy should be performed at stage 4A, before the macula is detached, to achieve favorable outcomes.

Table 1 Summary of previous reports on vitrectomy for stage 5 ROP

Authors	Number of Eyes	RA rate (%)	Functional results (%)	Birth Weight (g)	Length of gestation at birth (wks)	Publication
Trese	85	48	F&F:44, grasp object: 38, shape recognition: 15	640～1,400	24～32	1986 [35]
Tasman, et al. (Open-sky Vtx)	23	35	NA	1,038 (539～1,950)	26 (24～32)	1987 [36]
Zilis, et al.	121	TRA: 9 PRA: 31	fix and follow or greater: 11%, LP: 56% NLP: 25%	955 (560～1,850)	26.3 (22～32)	1990 [37]
Fuchino, et al.	51	59	NLP:5, LP:19, HM:14, > 20/2000： 62	948 (515～1,760)	27 (23～33)	1995 [28]
Cusick,et al.	608	TRA: 25 PRA: 7	NLP:26, LP:59, HM:10, >20/2000: 4	871 (340～2,750)	26 (20～35)	2006 [26]

RA: retinal attachment, g: gram, wks: weeks, Vtx: vitrectomy, F&F: fix and follow, NA: not available, TRA: total retinal attachment, PRA: partial retinal attachment, LP: light perception, NLP: no light perception, HM: hand movement, inc.: including

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