Original Article

Surgical Outcomes of Rhegmatogenous Retinal Detachment Associated with Regressed Retinopathy of Prematurity

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Abstract

Objectives: To evaluate the characteristics and surgical outcomes of late-onset rhegmatogenous retinal detachment (RRD) associated with regressed retinopathy of prematurity (ROP) and the status of fellow eyes.

Materials and Methods: Retrospective review of consecutive cases undergoing surgery for regressed ROP-related RRD and the fellow eyes between 2012-2022. Demographic data, fundus findings, retinal detachment characteristics, surgical procedures, and anatomic and functional outcomes were analyzed. Anatomic success was defined as retinal attachment after silicone oil removal at final follow-up.

Results: Fifteen eyes of 14 patients with a history of regressed ROP underwent surgical repair for RRD at a mean age of 12 (range, 3-26) years. Primary surgical intervention yielded a 53% failure rate overall. This rate was 33% for scleral buckling (SB), 100% for pars plana vitrectomy (PPV), and 40% for combined SB-PPV surgery. Eyes with posterior cicatricial changes and/or proliferative vitreoretinopathy (PVR) demonstrated a higher tendency for recurrence. The final anatomic success rate was 73% after a mean number of 2.3 (range, 1-5) surgeries. The chances of restoring useful vision diminished with repeated surgery despite the improvement in anatomic success. In the fellow eyes, peripheral retinal pathologies were universally observed, with posterior cicatricial changes noted in 33%.

Conclusion: The study reveals a significant initial failure rate in surgical treatment of cases with late-onset RRD associated with regressed ROP, particularly in eyes with posterior cicatricial changes or PVR, suggesting the need for a combined surgical approach as an initial strategy in such high-risk cases. The consistent presence of retinal abnormalities in fellow eyes calls for proactive monitoring and potential prophylactic intervention.

Keywords: Retinopathy of prematurity, ROP, retinal detachment, regressed ROP, cicatricial ROP

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Introduction

Retinopathy of prematurity (ROP) is a developmental vasoproliferative disorder of the retina that affects premature infants. As a result of advances in neonatal care and improved survival rates of extremely premature infants with low birth weights, the incidence of ROP has markedly increased over recent decades.[1] Most cases of ROP regress either spontaneously or after treatment with laser photocoagulation, anti-vascular endothelial growth factor (VEGF) injections, or vitreoretinal surgery.[2] Following the resolution of the acute phase of ROP, premature retinas generally undergo regression stages.[2,3] However, until recently, the classification and treatment of ROP have predominantly concentrated on the acute phase, with limited attention given to regression. The third edition of the International Classification of ROP recently provided a comprehensive delineation of the long-term sequelae associated with regressed ROP, including retinal detachment (RD), retinoschisis, and peripheral avascular retina, which is predisposed to lattice-like retinal degenerations and tears.[4] Previous large-scale studies have reported retinal tear rates ranging from 11% to 31% and RD rates from 15% to 39% in ROP survivors.[5,6,7] Once a rhegmatogenous RD (RRD) occurs, it brings unique challenges to the surgeon because of the nature of the disease, which involves a thinned, avascular, and hence fragile retina, and the pathological vitreoretinal interface in these eyes. Management strategies include scleral buckling (SB), pars plana vitrectomy (PPV), or a combination of both. Nevertheless, the prognosis remains guarded, with success rates typically lower than those observed in adult RRD without a history of ROP.[5]

In this report, we present the characteristics and surgical outcomes of eyes with spontaneous or treatment-induced regressed ROP that developed late RRD, also providing an overview of the status of fellow eyes. Herein, we aim to investigate the optimal surgical strategy in these eyes, specifically exploring the efficacy of PPV, SB, or combined surgery (SB and PPV) based on fundus characteristics.

Materials and Methods

We conducted a retrospective review of medical records at Gazi University Medical Faculty Hospital from 2012 to 2022. The focus of the investigation was on individuals who underwent vitreoretinal surgery for late RRD associated with a history of regressed ROP, whether spontaneously or following laser treatment. The study received approval from the Gazi University Local Ethics Committee with a protocol number of E.867614 (meeting date: 23.01.2024) and was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients or their parents.

Patients were excluded if their gestational age at birth exceeded 32 weeks, birth weight was over 2000 grams, or if they presented clinical findings or had a family history indicative of familial exudative vitreoretinopathy, incontinentia pigmenti, or other Wnt-associated vitreoretinopathies.

Data collected for each case included patient demographics (age and sex), gestational age and weight at birth, duration of postnatal incubation, systemic and ocular comorbidities, any previous treatment for ROP during the neonatal period, RD details with descriptions and age at onset, type and size of retinal tear(s), surgical procedure(s) performed, tamponade used, anatomical and functional results, and follow-up periods. To objectively analyze cicatricial findings in each eye, we utilized the staging system previously described by Kaiser et al.[5] Eyes without posterior cicatricial changes but with peripheral retinal abnormalities such as lattice-like degeneration, vitreoretinal abnormalities at the former ridge area, or peripheral avascular retina were classified as stage 1. Those with changes in the posterior pole, particularly macular dragging and ectopia, were classified as stage 2. The presence of a retinal fold indicated stage 3, tractional RD or retinoschisis indicated stage 4, and phthisis was classified as stage 5. The condition of the fellow eyes was also investigated, focusing on fundus findings, prophylaxis administered, and spherical equivalent refraction. Anatomic success was defined as retinal attachment at the final follow-up after silicone oil removal.

Statistical Analysis

Statistical analyses were conducted using the Statistical Package for Social Sciences v22.0 (IBM Corp.; Armonk, NY, USA) and statistical significance was set as a 2-tailed p value <0.05. Snellen visual acuities were converted to logarithm of the minimum angle of resolution (logMAR) units for analyses. Continuous data were tested for normality using the Shapiro-Wilk test. The Wilcoxon signed ranks test was used to compare paired non-parametric data when evaluating the significance of differences in initial and final visual acuity.

Results

Twenty-eight eyes of 14 patients were included in the study. Ten (71%) were male, 4 (29%) were female. The patients' birth weights ranged from 720 to 2000 g, with a mean of 1324 g. Their gestational ages at birth ranged from 24 to 32 weeks, with a mean of 28.6 weeks. All patients had a history of incubator care with oxygen therapy ranging from 1 week to 3 months. Half of the patients had intellectual disabilities, accompanied by varying degrees of motor disturbance and a tendency toward self-mutilation in some patients. Two patients had a history of laser photocoagulation treatment in both eyes for type 1 ROP, while the remaining eyes did not receive any treatment in the neonatal period.

Fifteen eyes developed late RRD, with 13 patients experiencing RRD in one eye and one patient having bilateral RRD with a 5-year interval between eyes. The age at RD development ranged from 3 to 26 years, with an average of 12 years. Two eyes had prior prophylactic treatment with SB. Two eyes had prior phacoemulsification and intraocular lens implantation an average of 3 years (30 and 42 months) before RD development.

In terms of RD characteristics, all eyes presented with macula-off RD. Nine eyes (60%) had total RD, while 6 eyes (40%) had subtotal RD, mainly involving the temporal and inferior quadrants. Types of retinal breaks included multiple retinal holes and tears (n=10, 67%), dialysis (n=3, 20%), giant retinal tear (n=1, 7%), and a tear that could not be visualized in one eye (7%). Six eyes (40%) had peripheral retinal pathologies only, such as peripheral avascular retina, lattice-like degeneration, and vitreoretinal interface abnormalities at the former ridge area, without apparent cicatricial changes. Three eyes (20%) had stage 2 cicatricial changes, showing macular ectopia without apparent peripheral retinal traction. The remaining 6 eyes (40%) had a significant tractional component, including retinal folds or tractional RD, consistent with stage 3 and 4 fundus changes. Two-thirds of the eyes (n=10, 67%) had proliferative vitreoretinopathy (PVR) on presentation.

Six eyes (40%) underwent primary SB surgery, 6 eyes (40%) underwent PPV (including 2 eyes that had prior prophylactic SB), and the remaining 3 eyes (20%) underwent combined SB and PPV surgery. Additional procedures during the primary surgery included lensectomy (n=6, 40%) and retinotomy-retinectomy procedures (n=3, 20%). Silicone oil tamponade was employed in all eyes where vitrectomy was performed.

Overall, 8 eyes (53%) had failure of the primary repair, necessitating further surgery. Specifically, the primary failure rate was 33% in eyes treated solely with SB surgery. This subgroup comprised eyes with stage 1 (n=4) and 2 (n=2) fundus changes without a significant tractional component. Two eyes experiencing repair failure after SB had PVR (n=1) or posterior cicatrization (n=1). Notably, the remaining 4 eyes had no posterior pole pathology or PVR and did not show recurrence after primary SB surgery.

In contrast, eyes treated with primary PPV showed a 100% primary failure rate. All eyes in this subgroup presented with PVR at baseline. Among them, 2 eyes (25%) had stage 3-4, 1 eye (25%) had stage 2, and 1 eye (25%) had stage 1 fundus changes.

Among eyes treated with combined surgery, including the 2 eyes previously treated with prophylactic buckle, the primary failure rate was 40%. Of these 5 eyes, 4 (80%) displayed stage

3-4 cicatrization with significant peripheral traction, and 4 (80%) had PVR.

In the entire cohort, RD recurrence was more common in eyes with PVR (70%) than in those without PVR (20%) and in eyes with posterior cicatricial changes with or without peripheral traction (67%) compared to those with peripheral abnormalities only (33%). However, these differences did not reach statistical significance because of the low number of patients (p=0.06 and p=0.44, respectively). In two eyes, RD recurrence was related to macular holes secondary to posterior tractional membranes, and they were successfully repaired with an amniotic membrane graft (Figure 1).

Following repeat surgeries, the final anatomical success rate reached 73% (n=11), with an average of 2.3 surgeries (range: 1-5) required per eye. The mean follow-up time was 47 months, ranging from 10 to 126 months. At the final follow-up, 3 eyes (20%) retained silicone oil, while 1 eye (7%) developed hypotonia and phthisis bulbi. Overall, there was a significant improvement in visual acuity after surgery (p=0.011), with an initial mean visual acuity of 2.1±0.6 logMAR (equivalent to 20/2500 Snellen) and subsequent improvement to a final mean visual acuity of 1.4±0.8 logMAR (equivalent to 20/500 Snellen). Further investigation of the visual outcomes based on the recurrence of RD revealed notable differences. In eyes that did not experience a recurrence and were successfully treated with primary surgery, the improvement in functional vision was statistically significant (-0.89 logMAR, p=0.04). Conversely, in eyes that did experience recurrent RD, despite achieving anatomic reattachment by the final follow-up, the improvement in visual acuity was not statistically significant (-0.31 logMAR, p=0.1).

Fellow Eyes

Of the 14 patients, one patient had bilateral late-onset RD and the fellow eye of another patient was already in a phthisic state. Among the remaining 12 fellow eyes, peripheral avascular retina was noted in 4 eyes (33%), visible vitreous membranes and interface abnormalities at the former ridge area in 3 eyes (25%), lattice peripheral retinal degeneration in 6 eyes (50%), atrophic retinal holes in 4 eyes (33%), macular ectopia and dragging in 3 eyes (25%), macular fold in 1 eye (7%), and tractional retinoschisis in 1 eye (7%). To address these conditions, prophylactic 360-degree laser photocoagulation was performed in 8 of these eyes. Furthermore, a prophylactic encircling buckle was placed in 2 eyes. Refraction data, available for 8 of these eyes, revealed a mean spherical equivalent error of -3.2 diopters with a range of -6.50 to +1.00 diopters.

Discussion

The management of ROP extends beyond the treatment of acute disease, demanding lifelong attention. Our study adds to the growing evidence highlighting the imminent threat to useful vision in ROP survivors due to late rhegmatogenous complications, particularly RD. Previous research has documented concerning rates of surgical failure (23% to 60%) in this population, coupled with a generally poor visual prognosis once a RRD occurs.[3,5,6,8,9] Consistent with these findings, we observed a high rate of reoperation (53%) and poor visual outcomes.

Previously, Kaiser et al.[5] revealed a susceptibility to RRD even in patients without severe retinal cicatrization. Subsequent research has corroborated this, demonstrating a higher-than-expected prevalence of peripheral degenerations (54%), atrophic holes (35%), and tears (31%) in the peripheral avascular retina, significantly contributing to late RRD.[6,7] Our findings align, with half of the fellow eyes exhibiting lattice-like degenerations,

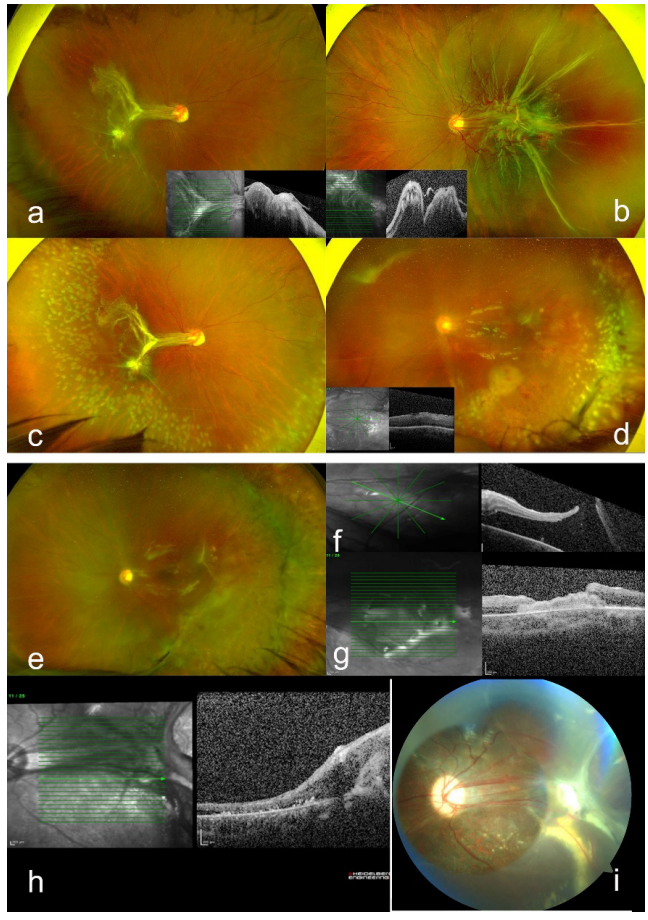

Figure 1. A 12-year-old male patient born at 32 weeks of gestation with a birth weight of 2000 grams who did not receive any treatment for retinopathy of prematurity as an infant was referred with sudden decline in vision in his left eye. His visual acuity was 20/400 in the right eye and counting fingers at a distance of 1 meter in the left eye. The baseline examination revealed bilateral macular dragging and peripheral avascular retina (a, b), along with rhegmatogenous retinal detachment in the left eye caused by a retinal break in the upper temporal quadrant (b). Prophylactic laser photocoagulation was applied to the pigmented lattice degenerations present in the avascular retina of the right eye (c). Combined surgery involving scleral buckling and pars plana vitrectomy was performed in the left eye (d). One month postoperatively, the retina was successfully reattached (e). However, a subsequent recurrent retinal detachment occurred due to the formation of a secondary macular hole within a period of one month (f). This complication was managed by the placement of an amniotic membrane graft, which facilitated the closure of the hole (g). After the third surgical intervention, anatomic success was confirmed, with the retina remaining attached during an 8-month follow-up period after silicone oil removal (h, i). The patient's visual acuity in the left eye remained counting fingers at 1 meter despite anatomic reattachment

and one-third presenting with retinal holes or tears, indicating a sustained risk.

Notably, the mean age for RD development in our cohort (12 years) echoes the findings of Tufail et al.[10] and Sen et al.[9] who observed RRD predominantly in the first to third decades of life (Table 1). While RRD more commonly occurred in late childhood to adolescence, it is crucial to consider the high prevalence of mental retardation and intellectual disabilities in this demographic, as seen in our cohort where half of the patients presented with these conditions, often leading to delayed detection of RD. Furthermore, self-mutilation behavior, commonly observed in this group, heightens the risk of trauma-induced RRD, emphasizing the critical need for proactive preventative strategies to protect these vulnerable eyes. Given the risks, prophylactic treatments such as laser ablation of the persistent avascular retina, or SB in rare cases with significant peripheral retinal pathologies or evident traction, can be considered. Notably, in our cohort, two eyes treated with prophylactic buckle still developed late-stage RRD. This suggests that wider buckles supporting more posteriorly located degenerations or tractions may be necessary to effectively protect areas at risk. The need for further research is evident, particularly to determine the indications and benefits of prophylactic treatment for high-risk eyes and to better understand the implications of persistent avascular retina.

Beyond the challenges of delayed recognition, the inherent complexity of RD within the context of ROP significantly impacts surgical outcomes and complicates the choice of an optimal surgical approach. Existing literature indicates a higher success rate for SB over PPV or combined approaches.[6,9,10] Tufail et al.[10] reported a single surgery success rate of 73% with SB in ROP patients with late RRD, compared to 57% with PPV. Similarly, Hamad et al.[6] reported a primary success rate of 64% with SB, as opposed to 36% with PPV or combined procedures. In our cohort, the primary success rate after SB was 67%, which was higher than PPV or combined surgery (0% and 60%, respectively). This disparity likely stems from the careful patient selection for each technique. SB appears to be particularly effective for isolated RRD in phakic eyes when the retinal break(s) are identifiable and located in mid-zone 2 or anterior zones. However, its efficacy as a stand-alone procedure decreases in the presence of significant posterior cicatrization and tractional components such as retinal folds or tractional RD, which were observed in 40% of our cases. These eyes typically presented retinal tears near areas of traction, where a regressed fibrovascular ridge created a taut vitreoretinal interface with fibrotic membranes. Our experience shows that PPV poses its own set of challenges in such eyes, particularly the difficulty in separating the vitreous cortex, which tends to adhere strongly to both the detached retina and the former ridge area. Achieving complete vitreous removal up to the periphery is often elusive, making an encircling band a useful adjunct to PPV for supporting the residual peripheral vitreous. Notably, while all eyes in the primary PPV group initially failed in our cohort, only 40% in the combined PPV and SB group required further surgery. Despite the high prevalence of PVR (80%) and tractional component (80%) in the combined surgery group, the primary failure rate was nearly comparable to those with milder cicatricial changes who underwent primary SB repair (33%). However, it is important to note that while surgery often more effectively releases anteroposterior traction, it may not fully alleviate tangential traction. The persistence of this traction can lead to recurrences and the formation of new breaks, necessitating repeat surgeries, including relaxing retinectomies in some instances, or the use of some novel sealing materials such as amniotic membrane grafts, as demonstrated in Figure 1.

Study Limitations

There are several limitations to this study. The retrospective nature and the small patient cohort limit its scope, preventing the derivation of incidence or prevalence data. Additionally, referral selection bias is inherent, as the research was conducted at a tertiary institution, which typically attracts more severe

Table 1. Literature review of ROP-related RRD outcomes

Author[ref]	Year	N of cases	Mean GA at birth (weeks)	Mean birth weight (g)	Age at RD development (years)	Mean number of surgeries	Primary anatomic success (%)*			Final anatomical success (%)**
							Primary SB	Primary PPV	Combined SB-PPV	
Kaiser et al.[5]	2001	31	27.9	1136	26.6	1.25	73	100	100	96
Park et al.[3]	2004	5	29.8	1252	8.2	1.6	0	0	100	20
Tufail et al.[10]	2004	40	28.8	1100	22.3	-	72	57	75	97
Sen et al.[9]	2019	22	29.6	1300	10.4	1.4	71	47	-	73
Hamad et al.[6]	2019	88	26.2	832	35	1.5	86	75	26	76
Our study	2024	15	28.6	1324	12	2.3	67	0	60	73

*Primary anatomic success is defined as complete retinal reattachment following the initial surgical procedure, without additional interventions, **Final anatomic success is defined as retinal attachment maintained after silicone oil removal, as assessed at the final follow-up. ROP: Retinopathy of prematurity, RRD: Rhegmatogenous retinal detachment, GA: Gestational age, SB: Scleral buckling; PPV: Pars plana vitrectomy

and complex cases. This may lead to an observation of a disproportionately high rate of primary failure compared to the general population. Despite these constraints, the study gathered long-term follow-up data on ROP-related late RRD and fellow eyes, contributing valuable insights to the relatively sparse literature on late complications in regressed ROP and its management strategies. Overall, our findings support the use of SB as the initial approach for isolated RRD with limited posterior cicatrization. For cases involving significant posterior cicatrization, along with considerable traction and/or posterior breaks, a combination of PPV and SB appears to be the most effective initial approach. While anatomic success can be achieved even after multiple surgeries, the chances of restoring useful vision diminish correspondingly.

Conclusion

As we confront the growing global challenge of ROP due to increased survival rates of extremely premature neonates and the use of anti-VEGF therapy, our focus should pivot towards a deeper understanding, proactive prevention, and effective management of its late complications. It is imperative to establish a rigorous lifelong examination schedule, particularly for non-verbal patients, to timely identify and address potential complications. Further research is essential not only to determine effective prophylactic and surgical strategies but also to customize these approaches for the unique risk profiles of individual patients.

Ethics

Ethics Committee Approval: The study received approval from the Gazi University Local Ethics Committee with a protocol number of E.867614 (meeting date: 23.01.2024) and was conducted in accordance with the Declaration of Helsinki.

Informed Consent: Obtained.

Authorship Contributions

Surgical and Medical Practices: Ş.Ö., Concept: Ş.Ö., E.Ö.Z., Design: Ş.Ö., E.Ö.Z., Data Collection or Processing: T.K., E.Ö.Z., Analysis or Interpretation: Ş.Ö., E.Ö.Z., T.K., Literature Search: T.K., E.Ö.Z., Writing: E.Ö.Z.

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