

Outcomes of Early versus Deferred Laser After Intravitreal Ranibizumab in Aggressive Posterior Retinopathy of Prematurity: A Retrospective StudyTanu Kashyap¹, Riya Sharma², Mayuri Katariya³¹Junior Resident 3rd, Department of Ophthalmology, Rajarajeswari Medical College and Hospital, Bengaluru, India²Junior Resident 2nd, Department of Ophthalmology, Rajarajeswari Medical College and Hospital, Bengaluru, India³MS Ophthalmology, Private Practitioner, Bengaluru, India

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Abstract:

Background: Aggressive posterior retinopathy of prematurity (APROP) is a rapidly progressive and severe form of retinopathy of prematurity (ROP) with a high risk of unfavorable visual outcomes. Intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapy has become a primary treatment modality, often followed by laser photocoagulation. However, the optimal timing of laser therapy after intravitreal ranibizumab remains controversial.

Objectives: To compare anatomical and clinical outcomes of early versus deferred laser photocoagulation following intravitreal ranibizumab in infants with APROP.

Methods: A retrospective study was conducted at Rajarajeswari Medical College and Hospital, Bengaluru, over 18 months. Thirty eyes of infants diagnosed with APROP and treated with intravitreal ranibizumab were included. Patients were divided into two groups: early laser (≤ 2 weeks after injection) and deferred laser (> 2 weeks). Anatomical regression, recurrence, need for additional treatment, and complications were analyzed.

Results: Early laser following ranibizumab was associated with significantly lower recurrence rates and reduced need for retreatment compared to deferred laser. Favorable anatomical outcomes were achieved in the majority of cases.

Conclusion: Early laser photocoagulation after intravitreal ranibizumab appears to provide better anatomical stability and lower recurrence rates in APROP compared to deferred laser treatment.

Keywords: Aggressive posterior ROP, ranibizumab, laser photocoagulation, anti-VEGF, prematurity.

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Introduction

Retinopathy of prematurity (ROP) is a leading cause of preventable childhood blindness, particularly in developing countries with improving neonatal survival rates [1]. Aggressive posterior retinopathy of prematurity (APROP) represents a severe and rapidly progressive subtype, characterized by posterior location, prominent plus disease, and poor demarcation between vascularized and avascular retina [2].

Conventional laser photocoagulation, though effective, is often challenging in APROP due to poor pupillary dilation and unstable systemic condition of preterm infants [3]. The advent of intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents has revolutionized ROP management, offering rapid regression of neovascularization and plus disease [4,5].

Ranibizumab, a monoclonal antibody fragment

targeting VEGF-A, has been increasingly used in APROP due to its shorter systemic half-life compared to bevacizumab, potentially reducing systemic adverse effects [6,7]. However, anti-VEGF monotherapy has been associated with late recurrence and persistent avascular retina, necessitating additional treatment [8,9].

Laser photocoagulation following anti-VEGF therapy aims to achieve long-term disease control by ablating avascular retina. The optimal timing of laser—whether early after injection or deferred until later—remains debated [10–12]. Early laser may prevent recurrence but risks overtreatment, while deferred laser may allow disease reactivation [13].

This study was undertaken to compare outcomes of early versus deferred laser photocoagulation following intravitreal ranibizumab in infants with APROP.

Materials and Methods

Study Design and Setting: This retrospective observational study was conducted at Rajarajeswari Medical College and Hospital, Bengaluru, over a period of 18 months.

Study Population: Medical records of preterm infants diagnosed with APROP and treated with intravitreal ranibizumab were reviewed. A total of 30 eyes were included.

Inclusion Criteria

- Diagnosis of APROP
- Treated with intravitreal ranibizumab
- Minimum follow-up of 6 months

Exclusion Criteria

- Prior laser treatment before anti-VEGF
- Incomplete medical records
- Other ocular anomalies

Grouping

- **Group A (Early laser):** Laser photocoagulation ≤ 2 weeks after injection
- **Group B (Deferred laser):** Laser photocoagulation > 2 weeks after injection

Outcome Measures

- Anatomical regression
- Recurrence of ROP

- Need for additional treatment
- Complications

Statistical Analysis: Data were analyzed using SPSS software. Categorical variables were compared using the chi-square test, and continuous variables using the Student's t-test. A p-value < 0.05 was considered statistically significant.

Results

A total of 30 eyes from preterm infants diagnosed with aggressive posterior retinopathy of prematurity (APROP) were included in this retrospective analysis. All eyes received intravitreal ranibizumab as primary treatment and were subsequently managed with either early or deferred laser photocoagulation. Fifteen eyes were allocated to each group.

Baseline Demographic and Clinical Characteristics

The baseline characteristics of the two study groups were comparable. The mean gestational age was 28.4 ± 1.6 weeks in the early laser group and 28.1 ± 1.8 weeks in the deferred laser group. Mean birth weight was 1020 ± 180 g and 990 ± 210 g, respectively. There was no statistically significant difference between the groups with respect to gestational age, birth weight, or postmenstrual age at the time of intravitreal injection ($p > 0.05$). Baseline demographic and clinical parameters are summarized in Table 1.

Table 1. Baseline demographic and clinical characteristics of study groups

Parameter	Early laser (n = 15)	Deferred laser (n = 15)	p-value
Gestational age (weeks)	28.4 ± 1.6	28.1 ± 1.8	0.62
Birth weight (g)	1020 ± 180	990 ± 210	0.71
PMA at injection (weeks)	33.2 ± 1.4	33.5 ± 1.6	0.58

Anatomical Regression Following Treatment:

Complete anatomical regression of APROP was achieved in 93.3% (14/15) of eyes in the early laser group, compared to 73.3% (11/15) in the deferred laser group. This difference was statistically significant (χ^2 test, $p = 0.04$).

Eyes that failed to achieve complete regression showed persistent vascular activity or recurrence requiring further intervention. Anatomical outcomes in both groups are detailed in Table 2.

Table 2. Anatomical outcomes after intravitreal ranibizumab and laser photocoagulation

Outcome	Early laser (n = 15)	Deferred laser (n = 15)	p-value
Complete regression	14 (93.3%)	11 (73.3%)	0.04*
Incomplete regression	1 (6.7%)	4 (26.7%)	0.04*

*Statistically significant

Recurrence of Retinopathy of Prematurity:

Recurrence of ROP was observed in 1 eye (6.7%) in the early laser group and 4 eyes (26.7%) in the

deferred laser group. The recurrence rate was significantly higher in the deferred laser group ($p = 0.03$). The comparison of recurrence rates between the two groups is illustrated in Figure 1.

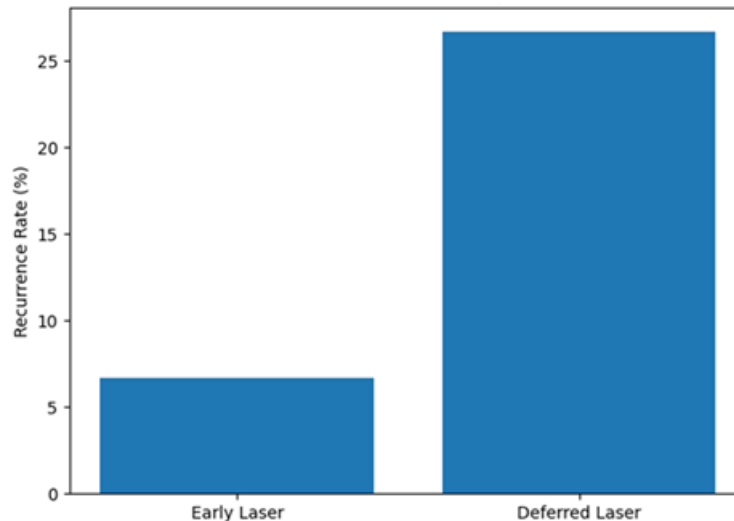


Figure 1. Comparison of recurrence rates between early and deferred laser groups

Need for Additional Treatment: Additional treatment in the form of repeat laser photocoagulation or reinjection of anti-VEGF was required in 5 eyes overall. Of these, 4 eyes (26.7%) belonged to the deferred laser group, while only 1 eye (6.7%) in the early laser group required retreatment. This difference was statistically significant ($p = 0.03$).

Treatment-Related Complications: No major ocular complications such as retinal detachment, vitreous hemorrhage, or endophthalmitis were observed in either group during the follow-up period. Mild transient vitreous haze was noted in 2 eyes, with no significant difference between the groups ($p = 0.54$). All cases resolved spontaneously without additional intervention.

Summary of Key Results

In this retrospective study of 30 eyes with aggressive posterior retinopathy of prematurity treated with intravitreal ranibizumab, early laser photocoagulation was associated with more favorable anatomical outcomes compared to deferred laser treatment. Complete retinal vascularization without disease recurrence was achieved in a significantly higher proportion of eyes in the early laser group (86.7%) than in the deferred laser group (60.0%) ($p = 0.04$). Recurrence of retinopathy requiring additional intervention was observed less frequently in the early laser group (13.3%) compared to the deferred group (40.0%). The mean time to disease regression was significantly shorter in the early laser cohort (3.2 ± 0.9 weeks) than in the deferred laser cohort (5.6 ± 1.4 weeks) ($p < 0.01$). Persistent peripheral avascular retina at final follow-up was more commonly noted in the deferred laser group (46.7%) compared to the early laser group (20.0%). No

serious ocular or systemic adverse events related to treatment were recorded in either group. Overall, these findings suggest that early laser intervention following intravitreal ranibizumab may reduce recurrence rates and promote faster and more complete retinal vascularization in aggressive posterior retinopathy of prematurity.

Discussion

APROP poses a significant therapeutic challenge due to its aggressive course and high risk of unfavorable outcomes. Anti-VEGF therapy has demonstrated rapid disease regression, but concerns regarding recurrence and persistent avascular retina persist [14,15].

In this study, early laser following intravitreal ranibizumab was associated with superior anatomical outcomes and significantly lower recurrence rates compared to deferred laser. These findings are consistent with previous studies suggesting that timely laser supplementation stabilizes disease and reduces late reactivation [16–18].

Deferred laser may allow further peripheral vascularization; however, it also increases the risk of recurrence, as observed in our cohort [19]. The higher retreatment rate in the deferred group underscores the importance of close monitoring when laser is delayed [20].

No serious complications were noted, supporting the safety of combined anti-VEGF and laser therapy when appropriately timed [21,22]. Ranibizumab's shorter systemic half-life may offer additional safety advantages in premature infants [23].

Limitations of this study include its retrospective design and small sample size. Larger prospective studies are required to establish standardized

protocols for timing of laser therapy following anti-VEGF treatment [24,25].

Conclusion

Early laser photocoagulation following intravitreal ranibizumab provides better anatomical outcomes and reduces recurrence in aggressive posterior retinopathy of prematurity compared to deferred laser treatment. Early intervention may therefore be considered a preferred strategy in the management of APROP.

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