

Correlation between Outer Nuclear Layer Thickness and Visual Acuity with Duration of Retinal Detachment

Taw Dipu¹, Thakar Meenakshi², Bansal Pooja³, Gautam Akanksha⁴, Gupta Priyadarshi⁵, Pavitra Banu⁶, Dacruz Russel⁷

¹M. S, FAICO (Retina and Vitreous), Senior Resident Gurunanak eye Centre
Corresponding Author Email - taw.anne[at]yahoo.com

²M. S, Director Professor Gurunanak Eye Centre

³M. S, Assistant Professor Gurunanak Eye Centre

⁴M. S, DNB, Senior Resident Gurunanak Eye Centre

⁵MBBS, Senior Resident Gurunanak Eye Centre

⁶MBBS, Post Graduate Gurunanak Eye Centre

⁷MBBS, Post Graduate Gurunanak Eye Centre

Abstract: Purpose: To correlate outer nuclear layer thickness and visual acuity with duration of detachment. Design: It was a prospective interventional study. Method: The population consisted of patients treated for rhegmatogenous retinal detachment. Post RRD repair 45 patients were divided into three groups. Group A operated within 1 month of RRD, Group B within 1 - 3 months, and Group C after 3 months. ONL Thickness and Best corrected visual acuity was compared at 4 months. Statistical analysis: The variables were compared using unpaired t - test. These variables were correlated with duration of retinal detachment using Pearson's correlation coefficient and ANOVA. Results: The difference in ONL thickness was significant between Group A and C ($p < 0.001$), Group B and C ($p = 0.049$) but insignificant between Group A and B ($p = 0.246$). The difference in BCVA was significant between Group A and B ($p = 0.028$), between Group A and C ($p < 0.001$) and insignificant between Group B and C ($p = 0.052$). With each day of RD there was 0.004 logMAR loss of vision. Inner Segment - Outer segment disruption and External limiting layer disruption was significant between Group A and B and Group A and C and insignificant between Group B and C. Conclusions: ONL restoration were better if operated within 3 months but BCVA was significantly better when operated within 1 month of retinal detachment. Other OCT parameters like IS - OS disruption, ELM disruption, intraretinal and sub retinal fluid post RD repair were associated with poorer BCVA and found more with longer duration of retinal detachment.

Keywords: outernuclear layer, retinal detachment, optical coherence tomography

Abbreviation

RRD: Rhegmatogenous Retinal detachment

RD: Retinal detachment

ONL: Outer nuclear layer

BCVA: Best corrected visual acuity

IS - OS: Inner segment - outer segment

ELM: External limiting membrane

OCT: Optical coherence tomography

ERM: Epiretinal membrane

1. Introduction

Rhegmatogenous retinal detachment (RRD) is a sight threatening disease. It is caused due to full thickness defect in the neurosensory retina, which permits fluid derived from the liquefied vitreous to gain access into the subretinal space. RRD occurs in approximately 1 in 10, 000 of general population and has bilateral involvement in 10% of patients¹. Risk factors for RRD are peripheral lattice degeneration, snail tract degeneration, white without pressure areas, atrophic holes, myopia, retinoschisis and cystic tufts²⁻⁴. RRD is associated with systemic diseases like Wagner's

syndrome, Stickler syndrome, Marfan syndrome and Down syndrome⁵⁻⁷. RRD can also occur post trauma, post cataract surgery and post Nd - YAG laser capsulotomy^{8, 9}. Infectious conditions like CMV retinitis, HIV retinitis and ocular toxoplasmosis can also lead to RRD due to retinal necrosis and hole^{10, 11}. It has been postulated that the first insult to the retinal structure is the photoreceptor outer segment loss and is followed by reduction in outer nuclear layer thickness which is gradually restored after repair over next few months². The outer nuclear layer consists of the nuclei of photoreceptors. Recent advances enable us to visualize structures of retina with high resolution owing to OCT. Spectral domain optical coherence tomography is a

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non - contact, non - invasive tool which provides high - resolution cross - sectional images of the retina and enables visualization of the microscopic anatomy of the retina and outer nuclear layer thickness. Studying OCT factors like ONL thickness, IS - OS and ELM disruption, ERM, intraretinal edema, sub retinal fluid and foveal thinning helps to prognosticate visual outcome after anatomically successful retinal detachment surgery^{12 - 14}.

In Indian scenario where patients present late due to lack of resources and expertise, we wish to find out how delay in surgery affects the prognosis. The purpose of the study was to compare outer nuclear layer thickness, other structural OCT findings and visual acuity with duration of detachment after retinal detachment surgery in anatomically successful RRD repair. we are unaware of previous reports on oct finding and correlation with duration of detachment in Indian population. There are similar studies conducted on other population but no such study was conducted in Indian population.

2. Methods

Study design: it was a prospective, interventional and comparative study conducted. A written informed consent was taken from each patient.

Inclusion criteria:

Individual with anatomically successful rhegmatogenous retinal detachment repair with normal macula on funduscopy and normal healthy fellow eye for comparison

Exclusion criteria:

- 1) Associated retinal pathology like diabeticretinopathy, hypertensive retinopathy involving the macula
- 2) Media opacities
- 3) Proliferative vitreoretinal changes involving the macula
- 4) Macula on RRD.
- 5) Age <18yrs of age
- 6) Anisometropia

Patients were divided into three Groups, Group A - patients operated within 1 month of RRD, Group B - RRD repaired 1 - 3 months and Group C - RRD repaired after 3 months. Each group had 15 patients with total of 45 patients (90 eyes). The OCT parameters and BCVA were noted 4 months post - operative.

To measure the mean ONL thickness, we chose the OCT image with the steepest foveal excavation from the radial scans across the fovea. The outernuclear layer thickness was calculated as the distance between the inner limiting membrane and the external limiting membrane at the central fovea. This was compared with patient's normal eye to give ONL restoration in percentage.

Preoperative evaluation: all patients underwent general physical and ocular examination including, BCVA, slit lamp examination, IOP and fundus examination

Surgical technique: patients underwent either scleral buckling (SB) or primary parsplana vitrectomy (PPV) depending on indication for either surgery under local

anesthesia. The patients with PPV had silicone oil removal done at 3 months post - operative.

Postoperative evaluation: patients with anatomically successful RD repair underwent thorough evaluation. OCT parameters like ONL Thickness, ONL restoration, ELM disruption, IS - OS disruption, ERM, subretinal and intraretinal fluid was observed. BCVA was noted in standard logMAR notation at 4 months post - operative.

Outcome measures:

Primary outcome measure was ONL thickness and ONL restoration post RRD repair and correlation with duration of detachment.

Secondary outcome measure were other structural changes seen such as IS - OS disruption, ELM disruption, persistent sub retinal fluid and correlation of above with duration of detachment. Correlation of BCVA with ONL and duration of detachment

Statistical analysis

The quantitative variables were expressed as mean±SD and compared using unpaired t - test. Also, these variables were correlated with duration of RD before surgery using Pearson's correlation coefficient and ANOVA. A p - value <0.05 was considered statistically significant

3. Results

The patients were age between 18 to 66 years, with mean age of 40.02 years.34 patients were male and 11 females, male preponderance was observed.26 patients had right eye involved and rest 19 had left eye involved. The mean duration of detachment was 19.33 days in Group A, 57.33 days Group B and 70.67 days in Group C.

Relationship between ONL thickness and duration of detachment

At the final follow up at 4 months, the mean outer nuclear layer thickness was 106.27µm in Group A, 95.47µm in Group B and 76.14µm in Group C. The difference was statistically significant between Group A and Group C (p<0.001), Group B and Group C (p=0.049). The difference was statistically insignificant between Group A and Group B (p=0.246). There was a negative correlation between the duration of detachment and outer nuclear layer thickness. Figure 1

Relationship between ONL restoration and duration of detachment

The mean percentage of ONL restored in Group A was 86.49%, Group B 79.24% and Group C 64.82%. The difference was statistically significant between Group A and C (p<0.001), Group B and C (p=0.025) but insignificant between Group A and B (p=0.197). There was a negative correlation between duration of detachment and ONL restoration with a linear trend which is statistically significant (p<0.001). Figure 2

Relationship between BCVA and duration of detachment

The mean BCVA (logMAR) was 0.57 in Group A, 0.84 in Group B and 1.06 in Group C. The difference is statistically

significant between Group A and C ($p < 0.001$) and Group A and B ($P = 0.028$). The difference was statistically insignificant between Group B and C ($p = 0.052$). The visual outcome was measured as good ($\geq 6/18$), moderate ($6/24 - 6/36$) and poor ($\leq 6/60$) according to ICD - 10 recommended by International council of ophthalmology. Good visual outcome was seen in 46.66% of patients in Group A, 13.33% in Group B and none in Group C. Moderate visual outcome was seen in 46.66% of patients in Group A, 40% in Group B and 26.67% in Group C. Poor visual outcome was seen in 6.67% of patients in Group A, 46.67% in Group B and 73.33% in Group C. There was a negative correlation between the duration of detachment and final BCVA with a linear trend which is statistically significant ($p < 0.001$). **We also observed that with each day of detachment there was 0.004 logMAR unit loss of vision, hence the need for early repair of RRD.** Figure 3 and figure 4

Relationship of BCVA with ONL thickness

We also compared ONL thickness and ONL restoration with BCVA at 4 months. We found a positive correlation between ONL thickness and ONL percentage restoration with BCVA with Pearson correlation $r = 0.557$, which was statistically significant $p < 0.001$

Relationship with structural OCT changes and duration of detachment

Other structural OCT changes were also compared. IS - OS disruption was seen in 13.33% of patients in Group A, 53.33% in Group B and 86.67% in Group C. The difference was statistically significant between Group A and B ($p = 0.02$), Group A and C ($P = 0.001$) and insignificant between Group B and C ($p = 0.05$). ELM disruption was seen in 20% of patients in Group A, 60% in Group B and 86.67% of patients in Group C. the difference in ELM disruption was significant between Group A and B ($p = 0.027$), Group A and C ($p < 0.001$) and insignificant between Group B and C ($p = 0.104$). Intraretinal cysts were seen in 6.67% in Group B and 13.33% in Group C and none in Group A. The frequency of patients with residual SRF were equal (20%) in each Group. ERM was seen in only 1 patient in Group C. table 1

4. Discussion

Rhegmatogenous retinal detachment causes complex cellular responses including photoreceptor degeneration, remodeling of synapses, hypertrophy and proliferation of muller cells causing subretinal fibrosis and proliferative vitreoretinopathy¹⁵. RD induces apoptosis of photoreceptors in the early stage of the process. Apoptosis was identified within hours, peaked at 2 days and dropped after 1 week^{15 - 17}.

In RRD with macular involvement, the volume of photoreceptors has shown to be reduced compared to RRD with no macular involvement. Several studies have shown gradual recovery of outer nuclear layer of retina after RRD surgery^{18, 19}.

In our study, we found that ONL gradually restores over time in all cases after successful RRD surgery. Complete (100%) ONL thickness restoration was seen in 6 patients

operated within 3 months, in which 4 patients were operated within 1 month and 2 patients operated 3 months and none in patients operated beyond 3 months.

In a multivariate study by Ghabriya et al¹³, they found that ONL thickness was significantly lower in macula involved patients than macula uninvolved. Similar to our study they also found gradual increase in the ONL thickness over the course of 6 months, they had a mean interval between symptoms and surgery of 8.7 days (1 - 30 days) and patients were followed up till 6 months post operatively. In another study by Dooley et al⁽²¹⁾, they found that ONL thickness at presentation is significantly and positively correlated with the final ONL thickness. Menke et al¹⁸ analyzed the thickness of various retinal layers following successful macula off retinal detachment surgery. There was significant correlation between ONL thicknesses, ONL restoration with duration of detachment. Similar result was seen between restoration of inner nuclear layer - outer plexiform layer (INL - OPL) and ellipsoid zone - retinal pigment epithelium complex (EZ - RPE) with time of surgery.

In our study we found positive correlation between ONL thickness and ONL restoration with BCVA at 4 months post - operative. Similar finding was seen in study by Gharbiya et al, they found that ONL thickness and status of intermediate line were the most important predictors of post - operative BCVA among OCT parameters. Dooley et al²⁰ found ONL thickness correlated with BCVA at 6 weeks post - operative. Maruko and Associates²¹ found the BCVA correlated with the thickness of ONL post - operative and the height of retinal detachment preoperative. In study by Takkar et al²², they found that % Central foveal thickness (CFT) change were not significantly associated with final BCVA.

Visual recovery after Rhegmatogenous retinal detachment is associated with several factors, although the most important prognosticating factor has consistently been macular involvement and duration of detachment. Studies have found poorer visual outcome with longer duration of detachment specially if operated beyond 1 month. We are unaware of previous studies giving amount of vision loss with each day of detachment and could find no references to it in a computerized search such as PubMed. We found that with each day of detachment there was **0.004 logMAR** unit of loss of vision. We also found a negative correlation between the duration of detachment and final BCVA with a linear trend. Similar results were seen in study by Salicone et al²³, They found that BCVA were worse with duration of detachment > 30 days. In patients with visual outcome of $> 20/40$ mean duration of detachment was 10.9 days, 11.9 days in patients with BCVA 20/50 - 20/100 and 30.7 days in patients with $< 20/200$ vision. While comparing the vision with duration of detachment it was significant between detachment > 1 month and < 1 month. It was insignificant between different groups within 1 month of detachment. Study by Takkar et al²² also found that mean duration of RD was significantly lower in group with better visual outcome (17.5 days vs 29.0 days). Similarly Tani et al²⁴ found 41% patients had favorable visual outcome of 20/50 in patients operated within 1 month and only 28% in patients operated > 1 month of detachment. Matsui et al¹² found that BCVA at 6 months showed no significant difference between the

group operated within 10 days and > 10days (10 - 120days). Hasan et al²⁴ found a significant worsening of BVCA in patients operated after 6 weeks of detachment but not so when compared between patients operated < 10days and 10days to 6weeks of detachment. In another study by Ross et al²⁵, they found no visual benefit from earlier surgery when operated within 1 week. The variation among patients repaired within 7days of detachment has been attributed to the height of macular detachment.

We also evaluated other OCT parameters and found continuity of IS - OS junction and ELM to be the most important predictors of post - operative BCVA. Similar findings were seen in Ghabriya et al¹³ study, they found that other than ONL thickness, status of ELM, IS - OS junction, ILM disruption and intraretinal fluid showed correlation with BCVA and retinal sensitivities. They also found that neither the presences of SRF nor ERM was correlated with final visual outcome. Wakabayashi et al²⁶, stated that the postoperative BCVA of eyes with macular detachment was significantly correlated with IS - OS junction and ELM continuity. ELM is the boundary between the outer nuclear layer which contains the nuclei of the photoreceptor cells and the inner segment of the photoreceptor cell layer, the disruption of ELM, IS - OS junction influence the nuclei of the photoreceptor cell layer. Similarly kawashima et al²⁷, suggested that the improvement of vision was associated with intact IS - OS junction and ELM. Restoration of ELM was prerequisite for the restoration of IS - OS junction. Roohipur et al²⁸ found that in SB group, correlation between the final BCVA with ELM and IS - OS junction disruption was significant. The BCVA was significantly better in eyes with intact ELM. They also found that the final BCVA was not correlated with presence of SRF which was similar to our study. Zghal et al¹⁴ found that discontinuity or absences of ELM, and IS - OS junction continuity <90um were associated with poor visual outcome. Others factors associated with poorer visual outcome were ONL (<90um), foveal thinning of <250 um, central foveal thickness <160um, photoreceptor outer segment <18um. Matsui et al¹² found that BCVA was significantly correlated with IS - OS and ELM continuity at 3 months. The visual acuity at 6 months was significantly better when persistent foveal SRF resolved within 3months than which resolved after 3 months of surgery. They also found that the preoperative VA and the final BCVA at 6 months were significantly better in patients who had height of retinal detachment (HRD) <1000µm and compared to HRD >1000µm. These studies and others have evaluated the Outer retinal layers using OCT and correlated with duration of detachment and visual outcome. However, to the best of our knowledge none have studied the effect of duration of detachment within 1 month, 1 - 3 months and >3 months prior to RD surgery in Indian scenario.

The limitation of our studies was short follow up period of 4 months as it has been seen that outer retinal layers restore till 12 - month post operatively. Sample size was insufficient to establish any demographic profile of RRD in the population

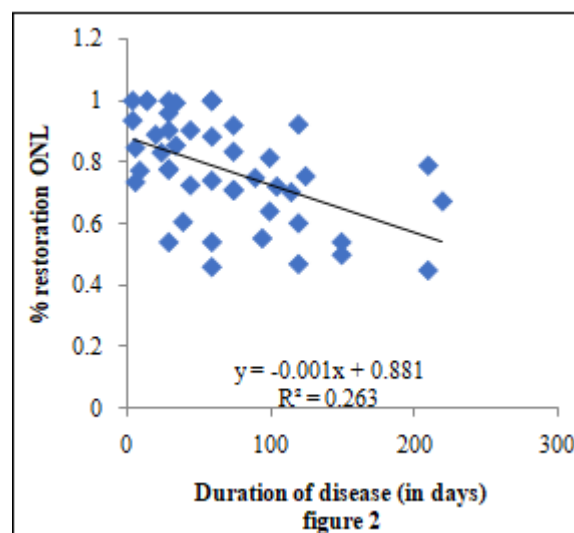
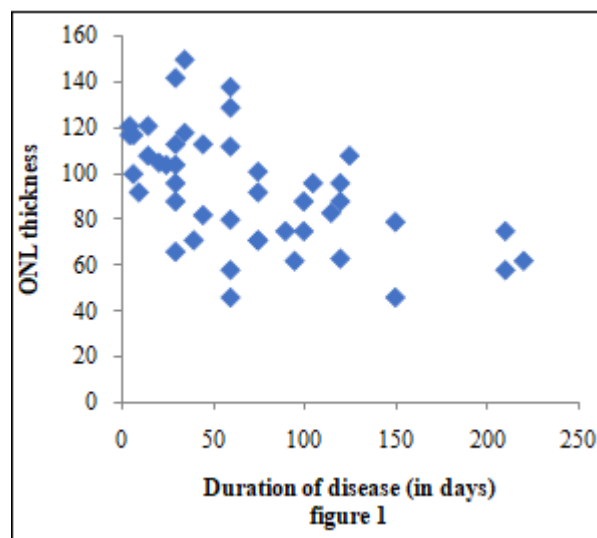
5. Conclusion

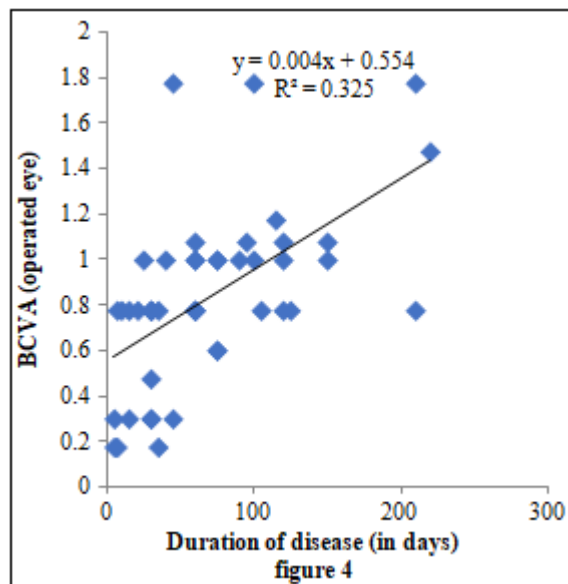
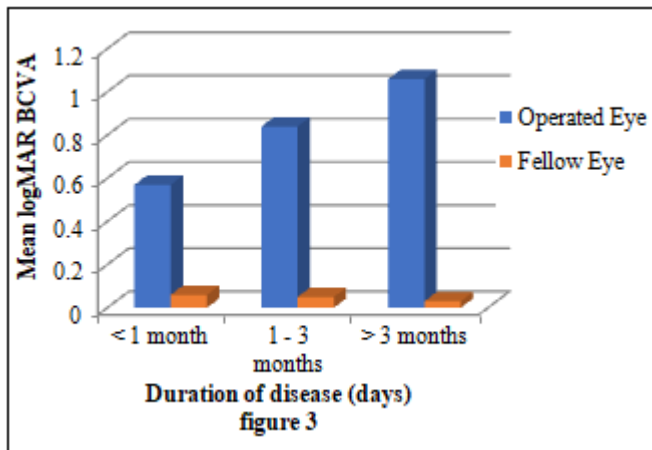
Our study reemphasis the need of early repair of RRD within 1 month. Beyond 1 month, though ONL restoration occurred

in group B (1 - 3 months) the BCVA was worse than in patients operated within 1 month. Most microstructural changes go hand in hand with the chronicity of detachment. With an increase in duration of detachment a greater number of patients had IS - OS junction disruption and ELM disruption. However, ERM, persistent SRF and intraretinal fluid had no correlation with duration of detachment and final BCVA. Longer duration of follow up is required to give better idea about the ONL restoration, and other OCT parameters like IS - OS junction disruption, ELM disruption, intraretinal and sub retinal fluid, ERM formation.

Table 1: OCT changes in each group.

	Group A		Group B		Group C		p - value
	n	%	n	%	n	%	
IS - OS disruption	2	13.33%	8	53.33%	13	86.67%	<0.001
ELM disruption	3	20.00%	9	60.00%	13	86.67%	0.001
Residual SRF	3	20.00%	3	20.00%	3	20.00%	1.000
Intra Retinal Cyst	0	0.00%	1	6.67%	2	13.33%	0.343
ERM	0	0.00%	0	0.00%	1	6.67%	0.360
ONL Thickness	15	106.27um	15	95.47um	15	76.14um	
ONL restoration	15	86.49%	15	79.24%	15	64.82%	
BCVA logMAR	15	0.57	15	0.84	15	1.06	





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The manuscript has been read and approved by all authors.

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