Original Article

Retinal Nerve Fiber Layer Changes Following Primary Retinal Detachment Repair with Silicone Oil Tamponade and Subsequent Oil Removal

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Abstract

Purpose: To evaluate the correlation between the retinal nerve fiber layer (RNFL), particularly the temporal RNFL (TRNFL), and visual outcomes following surgery for rhegmatogenous retinal detachment (RRD).
Methods: This retrospective study was performed at a tertiary center; 32 patients underwent single and successful vitrectomy for total RRD using silicone oil as tamponade. Data were collected after oil removal. RNFL thickness and central foveal thickness (CFT) were measured using spectral domain optical coherence tomography. RNFL thickness and CFT of normal eyes were acquired as a control to calculate percentage changes in the affected eyes. The correlation between postoperative best-corrected visual acuity (BCVA) and TRNFL changes was the primary outcome measure.
Results: Postoperative BCVA correlated negatively with retinal detachment (RD) duration (Pearson coefficient 0.56, $P = 0.001$) and percentage loss in TRNFL thickness (Pearson Coefficient 0.41, $P = 0.02$). The macula lost the maximum RNFL thickness (26%). The mean percentage loss of TRNFL was significantly higher in patients with postoperative BCVA <6/60 (42.63% vs. 24.06%, $P = 0.009$). Patients with postoperative BCVA <6/60 had a significantly longer mean RD duration (29 days) than those with postoperative BCVA >6/60 (17.5 days) ($P = 0.026$).
Conclusion: When eyes with RRD are successfully repaired using silicone oil tamponade, the thickness of the RNFL decreases, particularly in the macula, and less macular neuronal loss is associated with better visual outcomes.

Keywords: Retinal Detachment; Retinal Nerve Fiber Layer; Vitrectomy

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INTRODUCTION

Recent advances in vitreoretinal surgery have markedly improved the anatomical prognoses following these surgeries. However, a good functional outcome still depends on the retinal tissue.[1,2] Various factors, including the height of macular detachment on ultrasound[3] and sub foveal outer retinal changes, like the integrity of inner segment/outer segment (IS/OS) and external limiting membrane (ELM) on optical coherence tomography (OCT), have been evaluated in relation

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to poor visual outcomes in rhegmatogenous retinal detachment (RRD).[4,5] In contrast, very few studies have evaluated the impact of inner retinal changes on the functional success of retinal detachment (RD).[1,2]

Changes in the peripapillary retinal nerve fiber layer (RNFL) have been previously assessed in patients who were operated for RD, without exploring its influence on visual outcome.[1,2] In the current study, we aimed to determine the association between RNFL changes at the optic disc with postoperative visual acuity, particularly analyzing the temporal RNFL (TRNFL) as an anatomical representative of the inner retinal layers of the fovea.

METHODS

The study conformed to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board. This retrospective study was performed at a tertiary care center in northern India. Thirty-two patients who had undergone primary vitrectomy, with successful retinal reattachment for total RRD, with proliferative vitreoretinopathy (PVR) of less than grade C2 (Silicone Oil Study classification), were included. All patients had undergone comprehensive ophthalmological examination. The duration of visual loss, LogMAR of best-corrected visual acuity (BCVA), intraocular pressure (IOP), and axial length were noted. Patients with axial anisometropia (on clinical examination or a previous known difference of >0.3 mm on A-scan sonography) were excluded. Cases with a PVR grade >C2, epiretinal macular membranes, macular holes, or cases requiring internal limiting membrane (ILM) peeling were excluded. Patients with traumatic RD, glaucoma (previous or preoperative/during follow up), and a duration of vision loss of more than 30 days were also excluded from the study.

All patients underwent single successful primary vitrectomy, with or without scleral buckling. After complete vitrectomy, fluid air exchange was performed for retinal reattachment. Posterior retinotomy was performed in all cases to facilitate sub-retinal fluid drainage. Although the site of retinotomy depended on the anatomy of the RRD, the superonasal location was preferred. Laser around the breaks along with an additional 360º barrage laser was performed, followed by silicone oil injection (Aurosil Oil- 1000 ct, Aurolabs, India). Silicone Oil was removed within 3–6 months of primary surgery. LogMAR BCVA and IOP were recorded 12 months after vitrectomy. All patients had either nearly clear central crystalline lens or were pseudophakic at the time of evaluation. All OCT imaging was performed 6–9 months after silicone oil removal. The central foveal thickness (CFT) was recorded manually for both eyes using spectral domain OCT (Cirrus; Zeiss Meditec, Inc., Dublin, CA). After acquiring high-definition five-line raster OCT scans, the measurement line was drawn manually at the center most point of the foveal dip, from the ILM to retinal pigment epithelium (RPE). Optic disc RNFL measurements were recorded using the fast RNFL thickness scanning protocol. The average RNFL thickness was measured globally and separately for the superior, inferior, temporal, and nasal quadrants. The RNFL thickness and CFT of the normal eye was acquired as control RNFL and CFT for the affected eye with RD (see discussion). Percentage changes in RNFL thickness (%RNFL) and CFT (%CFT) were calculated accordingly.

The correlation between RNFL changes and BCVA was the main outcome measure. The correlation between BCVA, and CFT and RD duration were secondary measures. Four age-based groups were defined as follows: <20 years, 20–40 years, 40–60 years, and >60 years. Patients were also divided in two groups based on the duration of vision loss at the time of RD. Group 1 had vision loss of less than 15 days, whereas Group 2 had vision loss between 15 and 30 days. Data were entered into Microsoft excel sheets. Statistical analyses were performed using SPSS software (version: 16, IBM Corporation, New York, United States). Statistical significance was set at $P < 0.05$. A two-tailed Chi-squared test was used to compare parametric variables. A paired *t*-test was used to analyze visual gain. Pearson's coefficient of correlation was used to establish association between continuous variables. The correlations between preoperative BCVA, postoperative BCVA, CFT, RNFL thickness, and RD duration were analyzed. The correlations between TRNFL thickness (measured using the fast RNFL thickness protocol) and other variants were also analyzed. A comparison was also done to analyze factors associated with a postoperative BCVA better than 1 LogMAR unit (Snellen 6/60). Visual gain was defined as the difference between pre- and postoperative LogMAR visual acuity. TRNFL measures were a particular focus during the analysis.

RESULTS

A total of 32 eyes of 32 patients were included in the current study. Mean age was 39.6 ± 17.9 years (15-67 years). Most of the patients were aged between 20–40 years (n = 18, 56%); only two patients were ages <20 years or > 60 years. The study cohort included 21 male patients. The right eye was more commonly affected (18 cases). The mean duration of vision loss amongst all patients was 19.06 ± 17.5 days. Fourteen patients were pseudophakic. Both group 1 (vision loss of <15 days) and group 2 (vision loss of 15–30 days) had 16 patients. Data are summarized in Tables 1 and 2.

Visual Acuity

The mean pre-operative and postoperative visual acuity (LogMAR) was 2.16 ± 0.7 (3–0.8) and

Table 1. Vision and changes in optical coherence tomography (OCT) parameters in different age groups

	<20 years	20-40 years	40-60 years	>60 years	*P*
n	2	18	10	2	
Mean Pre BCVA	2.48	1.84	2.19	3	0.119*
Mean Post BCVA	1.78	0.79	0.9	1.18	0.007*
Mean AE CFT change (%)	8.15	8.46	18.47	22.72	0.045*
Mean AE TRNFL change (%)	57.41	20.75	32.5	35.32	0.001*

*Analyzed using *t*-test. AE, Affected eye; BCVA, best-corrected visual acuity; CFT, central foveal thickness; TRNFL, temporal retinal nerve fiber layer

Table 2. Variation of vision and change in optical coherence tomography parameters with duration of retinal detachment

	<15 days	15-30 days	*P*
n	16	16	
Mean Pre BCVA	1.69	2.44	0.002*
Mean Post BCVA	0.72	1.09	0.012*
Mean AE CFT change (%)	13.01	11.91	0.782*
Mean AE TRNFL change (%)	25.51	27.25	0.975*

*Analyzed using *t*-test. AE, affected eye; BCVA, best-corrected visual acuity; CFT, central foveal thickness; TRNFL, temporal retinal nerve fiber layer

0.9 ± 0.4 (1.8–0.3), respectively. There was significant visual gain (*P* = 0.001). Tables 1 and 2 outline the variation of visual outcomes, with age groups and RD duration. Table 3 presents the correlation between postoperative BCVA and all the parameters. When comparing duration of vision loss [Table 2], Group 1 had significantly better pre-and postoperative BCVA. There was no significant correlation between age of patients and postoperative visual acuity (*R* = 0.298, *P* = 0.09). Postoperative visual gain correlated negatively with the duration of RD (Pearson's coefficient, −0.505; *P* = 0.004). There was also a significant positive correlation between postoperative vision (in LogMAR units) and duration of RD (Pearson's coefficient, +0.56; *P* = 0.001).

Central Foveolar Thickness

The final mean postoperative CFT in the affected eyes was 208.81 ± 42.1 μm, while that of the normal eyes was 239.1 ± 39.1 μm. This difference was statistically significant (*P* = 0.001). The normal eye CFT was similar across all groups. When considering quantitative decrease in macular thickness after surgery, in comparison to baseline CFT, the mean percentage decrease in CFT was 12.5%. There was significant negative correlation between the CFT of the affected eye and patient age (−0.40; *P* = 0.01). The %CFT change in the affected eye, however, was significantly positively correlated with patient's age (0.45; *P* = 0.01). The %CFT change of the affected eye did not correlate significantly with either pre- or postoperative vision [Table 3], or duration of RD (*R* = 0.075, *P* = 0.69).

RNFL Thickness – Inner Retinal Changes

The final mean postoperative RNFL at the optic nerve head of the affected eye was the least in temporal quadrant (nearly 51 μm), followed by the nasal (65 μm), superior (85 μm), and inferior (94 μm) quadrants. The distribution was similar in the normal eyes. In terms of %RNFL thickness change, the temporal (26%) and inferior (21%) regions had higher changes than the superior (19%) and nasal (18%) quadrants. Table 1 presents the variation of TRNFL with patient age. There was no significant difference in %TRNFL change, based on duration of RD. Postoperative BCVA (in LogMAR units) was significantly correlated with the drop in %TRNFL change (Pearson's coefficient, +0.41; *P* = 0.02) [Table 3].

Factors Associated with Postoperative BCVA >6/60

Factors associated with a final BCVA better than 1 LogMAR unit (i.e., Snellen 6/60) were analyzed. Age and %CFT change were not significantly associated with a final BCVA >6/60. The mean duration of RD was significantly lower in the group with better visual outcome (17.5 days vs. 29.0 days, *P* = 0.026). Similarly, the %TRNFL change was significantly lower in the group with better visual outcome (24.06% vs. 42.63%, *P* = 0.009) [Table 4].

DISCUSSION

The aim of the current study was to determine the association between RNFL changes and visual outcomes in eyes affected with RRD managed with vitrectomy and silicone oil tamponade. We also evaluated the impact of duration of RD, patient age, and CFT on visual outcomes, and their relation to peripapillary RNFL thickness. We used OCT parameters (i.e. CFT and RNFL thickness) of the fellow normal eye as control parameters for the index eye, after excluding axial anisometropia. There is a high degree of symmetry in normal eyes that are matched for axial length in terms of both RNFL and CFT readings by OCT[6,7] and, inter-ocular differences should be considered a mono-ocular disorder.[6,7] We assumed that this method was more accurate than

Table 3. Correlation of postoperative LogMAR best-corrected visual acuity (BCVA) with other variables

Variable	Coefficient of correlation	*P*
Age	+0.298	0.09*
Duration of RD	+0.56	0.001*
AE CFT change (%)	+0.039	0.84*
AE TRNFL change (%)	+0.41	0.02*

*Analyzed using Pearson's coefficient of correlation. AE, affected eye; CFT, central foveal thickness; RD, retinal detachment; TRNFL, temporal retinal nerve fiber layer

Table 4. Factors affecting postoperative best-corrected visual acuity (BCVA)

	BCVA >6/60	BCVA <6/60	*P*
n	24	8	
Mean age (years)	40	39	0.92*
Duration of symptoms (days)	17.5	29.0	0.026*
AE CFT change (%)	11.96	15.91	0.51*
AE TRNFL change (%)	24.06	42.63	0.009*

*Analyzed using *t*-test. AE, affected eye; BCVA, best-corrected visual acuity; CFT, central foveal thickness; TRNFL, temporal retinal nerve fiber layer

using the baseline parameters of the affected eye, since eyes with RD have poor fixation and can have retinal edema, leading to inaccurate measurements. Half of the patients in the current study presented with 15–30 days of vision loss. Although it was desirable to have a group of patients with duration of RD of more than 30 days, this could not be done due to the low number of patients with the required characteristics as macular puckers occur in many of the eyes with longstanding detachment, which necessitate more than one surgery for successful reattachment.

Outer retinal degeneration occurs after experimentally induced RD.[8] Following retinal reattachment, the photoreceptor layer regenerates and re-establish connections with RPE.[9] Duration of RD is a well-established predictor of visual gain after surgery.[10] In the current study, postoperative visual acuity correlated negatively with the duration of visual symptoms. However, there was no significant association between age and postoperative BCVA [Table 3].

Changes in the outer retina, such as regeneration of photoreceptors in the outer segment, as previously discussed, involves changes in the outer segment lengths.[11] In acute experimental RD, the size of outer retina is normalized by 150 days after reattachment.[11] Prolonged RD causes apoptosis[12] and necrosis[13] of the photo receptor-outer nuclear layer complex. These changes are irreversible. Thus, one would expect CFT to reduce and correlate well with BCVA, duration of RD, etc., However, Muller cells are known to grow and even invaginate the sub-retinal space to form scars in prolonged detachments,[14] which would counteract the decrease in retinal thickness. Considering that the photoreceptor layer, where the majority of these changes occur, contributes only approximately 60 µm or a quarter of the total foveal thickness, these changes may not have a significant impact on the CFT itself. Alterations of this outer layer in particular, rather than the whole foveolar thickness may correlate better with visual acuity and other parameters, as proven in other studies.[15] In the current study, the mean CFT of the normal eye was approximately 240 µm, which is close to the normal range of CFT on spectral domain OCT. Hence, it can be considered to be representative of a normal population.[16] The mean CFT of affected eyes was nearly 30 µm less, demonstrating a mean reduction of 12.5%. There was a weak negative, but significant, correlation of approximately 0.4, between age and CFT of the affected eye. There was also a positive correlation of 0.45 between age and %CFT change of affected eyes. CFT of the affected eyes were not correlated with duration of RD and postoperative BCVA. Findings like ELM discontinuity and IS-OS junction anomalies may better correlate with functional success, as previously documented.[17]

In the current study, the distribution of RNFL at the optic disc was in accordance with the ISNT rule established for glaucoma.[18] The %RNFL change was highest for the temporal quadrant. It does seem interesting that the %RNFL thickness reduction mostly affected the macula, which by far is the most active region of retina. This may reflect that the most active part is the most vulnerable to injury and microenvironmental changes induced by RD. The outer retinal layers are dominated in the foveola, which mainly depends on the choroidal vasculature for its oxygen and nutrient supply.[19] In highly compromised situations, like macular detachment, antegrade neuronal degeneration (like lower motor neuronal degeneration following upper motor neuronal loss) may affect the second and third order neurons in the relay. This could consequently be reflected as a reduction in RNFL thickness at the optic disc. This finding corroborated well with the poor visual outcomes in those patients, but not with the negative %CFT change, which reflects only outer retinal changes. Thus far a few studies have evaluated RNFL loss in patients following vitrectomy for RD.[1] In a longitudinal study, Lee et al[1] compared the average of the detached "clock hours" with the mirror image of the other eye, and found significant differences at 12 and 24 months post-primary surgery. They demonstrated a mean loss of only 8% at 1 year, compared to the 26% loss in the temporal quadrant in the current study. However, since Lee et al[1] used gas for tamponade and did not analyzed the RD duration, the two studies cannot be adequately compared.

Assessment of RNFL thickness with older OCT models has not been found to be reproducible in silicone-oil-filled eyes in comparison to normal eyes.[20] Therefore, in the current study, the protocol using OCT for measuring RNFL after removal of oil from the eyes may be better than that for in eyes filled with silicone oil. A previous study performing OCT (with a machine similar to that used in the current study), with oil *in situ*, found increased RNFL thickness after vitrectomy and oil tamponade for RD.[2] That study was conducted prospectively in 60 eyes and included eyes with postoperative ocular hypertension. Although the study found a significant increase in RNFL thickness (compared to fellow eyes) in each follow-up until 6 months, there was no indication that the eyes were matched for axial length. However, the authors did note that initial RNFL changes "may be partly caused by surgical manipulation and early postoperative retinal readjustment." Therefore, differences in the results of that study, compared to the current study, could be attributed to a different timeline of OCT image acquisition and different optical media. Another study found significant thinning in ganglion cell layers of the macula after oil tamponade, even in cases without macular involvement prior to the surgery.[21] The authors of the study suggested retinal accumulation of potassium and subsequent neuronal degeneration as a possible cause. *In vitro* studies have demonstrated reduction in the number of viable retinal cells after exposure to silicone oil.[22] One study comparing the effect of gas vs. oil tamponade in macula on RD, reported poor visual outcomes and inner macular thinning with oil.[23] Similar to the results of current study, Shalchi et al[24] demonstrated the loss of foveal RNFL in patients with unexplained visual loss following silicone oil tamponade for RD. Therefore, the loss of papillofoveal projection is a matter of crucial concern when employing silicone oil for tamponade in eyes with RD. Recently, a study with automated retinal layer segmentation by the OCT software following silicone oil tamponade for RD demonstrated that ganglion cell layer thinning had a strong relationship with visual outcomes.[25] Further, the impact of oil tamponade in causing unexplained vision loss in macula on RD has also been proven with micro-perimetry.[26] Therefore, most studies, including the current one, are indicative of a reduction in RNFL thickness following surgery with silicone oil tamponade.

Finally, as functional success is of paramount importance, we also investigated factors associated with postoperative BCVA less than 6/60. We chose this cutoff as it represents the visual potential of the outer 10º of a well-functioning macula and should reflect the contribution of the TRNFL to BCVA. The mean TRNFL was significantly higher and the %TRNFL loss was lower in the group with BCVA > 6/60. The mean loss was as high as 42% in patients with BCVA < 6/60 [Table 4].

Some limitations of the current study must be noted. The relatively small sample size and unequal distribution amongst age groups precluded effective comparisons between age groups. Further, removal of the oil could have variably affected RNFL. Unfortunately, however, the impact of duration of exposure of retina to silicone oil, gauge of surgical instruments, and use of scleral buckle on RNFL loss could not be assessed in this study.

In conclusion, the RNFL thickness decreased in eyes with RRD successfully repaired using silicone oil as tamponade. These changes were not related to the duration of RD and the macula had the highest neuronal loss, which correlated with worse visual outcome. In patients with RD, changes in TRNFL may be better correlated with functional outcome than CFT.

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Nil.

Conflicts of Interest

There are no conflicts of interest.

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