

RETINAL NERVE FIBER LAYER CHANGES AFTER INTRAOCULAR SILICONE OIL TAMPONADE IN RHEGMATOGENOUS RETINAL DETACHMENT

INTRODUCTION

In cases of retinal detachment requiring pars plana vitrectomy (PPV), tamponade agents are used to restore intraocular volume and apply surface tension to the entire detached retinal surface.¹ The application of SO provides a higher anatomical success rate, especially in cases of PVR that were previously considered untreatable.^{2,3} Meanwhile, RRD is an emergency cause of vision loss with a prevalence of 1 in 10,000 cases per year.⁴ Recent advances in vitreoretinal surgery have improved surgical outcomes.⁵ Various factors including the height of the macular detachment and outer retinal subfoveal changes, have been evaluated for visual acuity outcomes in RRD.⁶

A study of SO tamponade in rabbit eyes showed a significant reduction in myelinated optic nerve fibers. Human and animal studies report silicone oil migration to ocular tissues, including the optic nerve, and macrophage-mediated inflammatory responses. RNFL objective assessment using intraocular SO tamponade is difficult due to imaging limitations. OCT is a non-contact and non-invasive technology used to describe and monitor retinal and optic nerve diseases. It can detect retinal nerve tissue loss by quantitatively measuring RNFL thickness at high resolution.⁷⁻¹⁰

OBJECTIVE

This study aims to assess the best corrected visual acuity, intraocular pressure, central macular thickness, and retinal nerve fiber layer thickness changes in rhegmatogenous retinal detachment patients using silicone oil tamponade and subsequent its removal.

METHOD

This study was a prospective cohort study that conducted at Hasanuddin University Hospital and JEC-ORBITA eye clinic, Makassar, Indonesia. A total of 35 patients aged 15-60 years were examined for visual acuity, anterior segment, eye pressure, funduscopy, and OCT RNFL using three circular scans with a diameter of 3.4 mm for each eye as consider fulfilled the inclusion criteria and underwent vitrectomy using SO as tamponade of 1,300 and 5,000 centistoke (cSt) for 3-12 months. This examination was carried out serially before and after SO removal in 1, 4, and 8 weeks. All results were recorded and analyzed using Paired t-test and repeated ANOVA followed by post-hoc Bonferroni test, sig. $p < 0.05$.

RESULTS

The mean difference in BCVA, IOP, CMT, and RNFL before and after SO removal are shown in table 1 and figure 1. Statistical analysis found that there were significant difference between BCVA measurements ≤ 6 and > 6 months ($p < 0.001$), CMT ≤ 6 months ($p = 0.04$) and RNFL thickness ≤ 6 months in the areas of inferior ($p = 0.03$) and superior ($p < 0.001$). Therefore, a post-hoc analysis was performed on BCVA, CMT, RNFL thickness based on the duration of silicone oil, and CMT on BCVA in RRD patients that displayed in table 2 and figure 2.

DISCUSSION

In this study, the SO type that mostly used were SO 1,300 cSt for the primary reattachment surgery and 5,000 cSt for the redetachment patients. It is similar with a

study by Soheilian et al (2006) reported that the use of SO 5,000 cSt was associated with a high incidence of retinal redetachment after SO removal.¹¹ A study by Kartasasmita et al. (2017) found that SO 1,000 emulsified more than SO 5,000.¹² A retrospective study by Scott et al (2006) on 325 eyes with complex retinal detachment with anatomic success rates and visual acuity had no significant difference between SO 1,300 and 5,000 cSt.¹³

In this study, the mean BCVA before SO removal was 0.75 LogMAR, but afterward it was 0.69, 0.61, and 0.58 after 1, 4, and 8 weeks respectively. Similar results were found by Selim et al. (2019), who assessed BCVA before and 8 weeks after removal, the BCVA was 0.05 dec and 0.05-0.8 dec, respectively. SO removal reduces subfoveal choroidal thickness.¹⁴ Another study also reported that 6 months or >6 months of SO application affected BCVA.¹⁵ Abu Al Naga et al. (2019) and Ghada et al (2019) reported BCVA improves 4 weeks after removal by 1.06-2.1 folds higher ($p<0.05$).¹⁶

In this study, mean IOP before and after 4 weeks of removal were 20.18 mmHg and 14.18 mmHg ($p=0.025$). This result is similar to Brănișteanu et al (2017) report of a decrease in IOP post SO removal. Saleh et al (2020) reported a contra situation where IOP significantly increased from the baseline value while using endotamponade, from 15 ± 5 mmHg to 20 ± 11 mmHg ($p<0.001$). However, after removal, it significantly reduced to 15 ± 6 mmHg at the last visit with $p<0.001$.¹⁷ Several reports also showed that the first signs of SO emulsification can be found within the first 3 months postoperatively, or even 4 weeks after endotamponade. Due to a large number of cases of SO emulsification within 1 year, the consensus recommended that removal must be carried out within this time interval.^{17,18}

The mean IOP for all age groups and duration of SO application did not affect pre-removal measurements or follow-up. According to Issa et al (2020), who studied post- SO removal complications, IOP pre-removal was 15.7 ± 5.1 mmHg and decreased to 15.0 ± 5.8 mmHg at the second month of follow-up. Jawad et al (2016) observed changes in IOP during SO tamponade and after removal. The mean of IOP measurements in pre-SO removal was 27.35 ± 9.20 mmHg, but it decreased to 16.10 ± 14 mmHg after 6 months.¹⁹⁻²¹

In this study, the mean of CMT was 265.91 ± 20.01 μm . In the first week post-removal, it was 269.46 ± 18.52 μm , then became 263.14 ± 22.14 μm and 257.16 ± 22.17 μm after 4 and 8 weeks. Dugyu et al (2021) reported that there was an increase in CMT values after 1 month SO removal. This is presumably associated with inflammation and the incidence of CME. The inflammatory response to SO tends to continue until post-SO removal. The CMT area reduces as the decreases of inflammatory response, and this will in turn improve the visual acuity.²²

During tamponade, the temporal RNFL thickness compared to the control eye. After 4 weeks of removal, the RNFL thickened in the nasal quadrant 87.84 ± 22.27 μm vs 78.38 ± 15.23 μm ($p=0.01$), and temporal 103.46 ± 46.67 μm vs 79.08 ± 38.89 μm ($p=0.004$). In this study, superior and inferior nerve fiber layer thickness was statistically significant, but it decreased after removal. Takkar et al. (2018) reported similar results, with the temporal quadrant had the lowest mean RNFL thickness after removal at 51 μm , followed by nasal 65 μm , superior 85 μm , and inferior 94 μm . The temporal and inferior quadrants increased before and after removal, at 26% and 21%, respectively.²³ Another study found that RNFL thickness increased in all quadrants after SO removal compared to pre-removal. After 2 years, inferior and superior RNFL thickness decreased. This is likely due to axonal loss from panretinal photocoagulation (PRP). Lee et al. (2012) described RNFL thickness in RRD patients with retinal

detachment. At 6,12, and 24 months after endotamponade, values were 113.9 ± 13.5 μm , 108.8 ± 15.1 μm , and 104.5 ± 14.2 μm . The results showed decreased value during the follow-up period, but there were no post-removal measurements. SO tamponade can affect retinal structure, and several hypotheses have been proposed. Takkar et al (2018) stated that potassium accumulation and nerve degeneration cause retinal thinning, while Sebastian et al (2003) stated that it may be caused by mechanical stress. SO toxicity and dehydration are also hypothesized as potential retinal thinning mechanisms.^{5,21,23}

During SO application and removal, central macular thickness correlated with temporal. In RRD patients with pre-removal BCVA 1 and >1 LogMAR, temporal RNFL thickness was $118.87\mu\text{m}$ and $96.25\mu\text{m}$ respectively. The value dropped to $99.23\mu\text{m}$ for 1 LogMAR and $87.25\mu\text{m}$ for 1 LogMAR 8 weeks after removal. Macula activity is affected by temporal RNFL thickness changes. This means that the most active sites are more susceptible to retinal detachment injury and microenvironmental changes. The foveola relies on choroidal blood vessels for oxygen and nutrition. Macular detachment and antegrade neuronal degeneration can affect the second and third neurons in the relay. Reduced RNFL thickness in the optic disc reflects the description.²³ Rabina et al (2019) reported a transient reduction in central macular thickness. SO thins the retinal component without affecting BCVA. Because the mechanical effect only affects the inner retinal layer and does not permanently damage the photoreceptors, visual acuity is minimally affected.²⁴

STUDY LIMITATION

In this study, there was no long-term observation after SO removal until when the thickness of RNFL layer reached a stable value.

CONCLUSION

There was a statistically significant decrease in retinal nerve fiber layer thickness in postoperative rhegmatogenous retinal detachment patients before and after silicone oil removal, particularly in the inferior and superior quadrants, this result followed by the improvement of best corrected visual acuity.

ETHICAL STATEMENT

This study was carried out in accordance to the declaration of Helsinki 1964, that obtained from the Biomedical Research Ethics Commission, Faculty of Medicine, Hasanuddin University with approval number: 280/UN4.6.4.5.31/ PP36/2021.

The 'Author contributions' section should be presented as follows:

- (I) Conception and design: FAC, AMI.
- (II) Administrative support: ICI.
- (III) Provision of study materials or patients: AMI, HSM, BD.
- (IV) Collection and assembly of data: FAC, BD.
- (V) Data analysis and interpretation: JH, ICI.
- (VI) Manuscript writing: All authors.
- (VII) Final approval of manuscript: All authors.

FIGURES CAPTIONS

Figure 1. Average value of (a) BCVA, (b) IOP, (c) CMT, and (d) RNFL thickness based on duration of use SO on measurement time of pre and post SO removal in RRD patients.

Figure 2. Temporal RNFL thickness and mean CMT to BCVA in RRD patient pre and post SO removal.

TABLES

Table 1. The mean difference in best corrected visual acuity, intraocular pressure, central macular thickness, and retinal nerve fiber layer thickness between pre and post silicone oil removal.

Variables	Measurement time			
	Pre-SO evacuation	1 wk Post-SO evacuation	4 wk Post-SO evacuation	8 wk Post-SO evacuation
BCVA (LogMAR)	0,75 ± 0,33	0,69 ± 0,29	0,61 ± 0,29	0,58 ± 0,27
IOP (mmHg)	14,94 ± 2,74	14,46 ± 2,72	14,06 ± 2,51	14,06 ± 2,87
CMT (µm)	265,91 ± 20,01	269,46 ± 18,52	263,14 ± 22,14	257,14 ± 22,17
RNFL (µm)				
<i>Inferior</i>	154,31 ± 44,05	142,23 ± 38,46	138,34 ± 35,66	139,69 ± 36,38
<i>Superior</i>	139,31 ± 34,71	142,86 ± 42,86	128,91 ± 27,16	121,94 ± 25,47
<i>Nasal</i>	98,97 ± 34,50	91,37 ± 28,54	89,77 ± 32,79	90,40 ± 31,43
<i>Temporal</i>	109,20 ± 44,92	109,43 ± 42,85	102,11 ± 31,79	97,86 ± 31,23

Description: IOP: Intraocular pressure; BCVA: Best corrected visual acuity; SO: Silicone oil; OCT: Optical coherence tomography, LogMAR: Logarithm of the minimum angle of resolution; RNFL: Retinal nerve fiber layer; CMT: Central macular thickness.

Table 2. Post-Hoc analysis on best corrected visual acuity, central macular thickness, retinal nerve fiber layer thickness based on the duration of silicone oil, and central macular thickness on best corrected visual acuity in rhegmatogenous retinal detachment patients

Variables	Group (x vs y)	Mean Difference	p value	95% CI		
				Lower	Upper	
Best corrected visual acuity						
BCVA ≤6 mos group	1	2	0,04	0,57	-0,03	0,12
		3	0,11	<0,001*	0,04	0,19
		4	0,14	<0,001*	0,06	0,23
	2	3	0,07	0,04	0,00	0,14
		4	0,10	<0,001*	0,02	0,17
	3	4	0,02	0,37	-0,01	0,07
BCVA >6 mos group	1	2	0,10	0,90	-0,13	0,34
		3	0,19	0,01*	0,04	0,35
		4	0,25	0,07	-0,02	0,52
	2	3	0,09	0,39	-0,06	0,25
		4	0,14	0,08	-0,01	0,31
	3	4	0,05	1,00	-0,11	0,21
Central Macular Thickness						
CMT >6 mos group	1	2	-2,17	1,00	-14,63	10,27
		3	4,57	1,00	-9,25	18,39
		4	9,03	0,43	-4,70	22,77
	2	3	6,75	0,15	-1,40	14,90
		4	11,21	0,04*	0,26	22,16
	3	4	4,46	0,57	-2,91	11,84
RNFL thickness						
RNFL Inferior <6 mos group	1	2	8,25	0,06	-0,53	17,03
		3	15,57	0,04*	0,76	30,38
		4	14,85	0,02*	2,00	27,70
	2	3	7,32	0,16	-3,13	17,78
		4	6,60	0,19	-3,50	16,72
	3	4	-0,71	0,87	-9,56	8,13
RNFL Superior <6 mos group	1	2	-4,42	1,00	-13,53	4,67
		3	7,00	1,00	-7,54	2154
		4	13,17	0,05*	-0,30	26,65
	2	3	11,42	0,19	-2,96	25,82
		4	17,60	0,01*	3,06	31,15
	3	4	6,17	0,03*	0,25	12,10
Central Macular Thickness on BCVA						
Macular Thickness in visual acuity ≤1 logMAR	1	2	-2,87	1,00	-14,81	9,07
		3	4,29	1,00	-8,32	16,90
		4	9,16	0,23	-2,88	21,20
	2	3	7,16	0,18	-1,79	16,12
		4	12,03	0,02*	1,36	22,70
	3	4	4,87	0,41	-2,43	12,17

Group 1: Pre-SO removal; Group 2: 1 week post SO removal; Group 3: 4 weeks post SO removal; Group 4: 8 weeks post SO removal. *Post hoc test (Bonferroni)

FIGURES

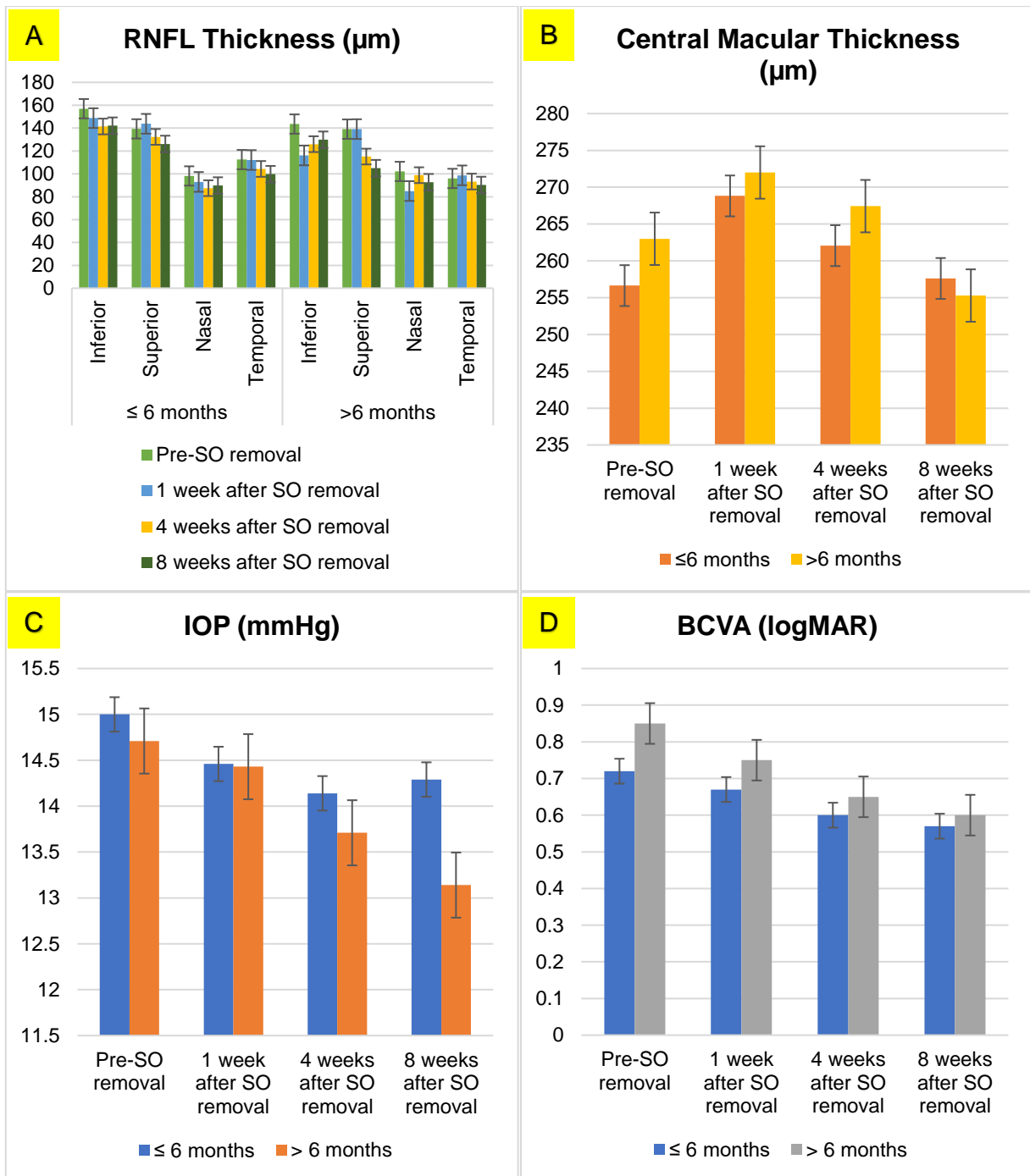


Figure 1. Average value of (A) RNFL thickness, (B) CMT, (C) IOP, and (D) BCVA based on duration of use SO on measurement time of pre and post silicone oil removal in rhegmatogenous retinal detachment patients.

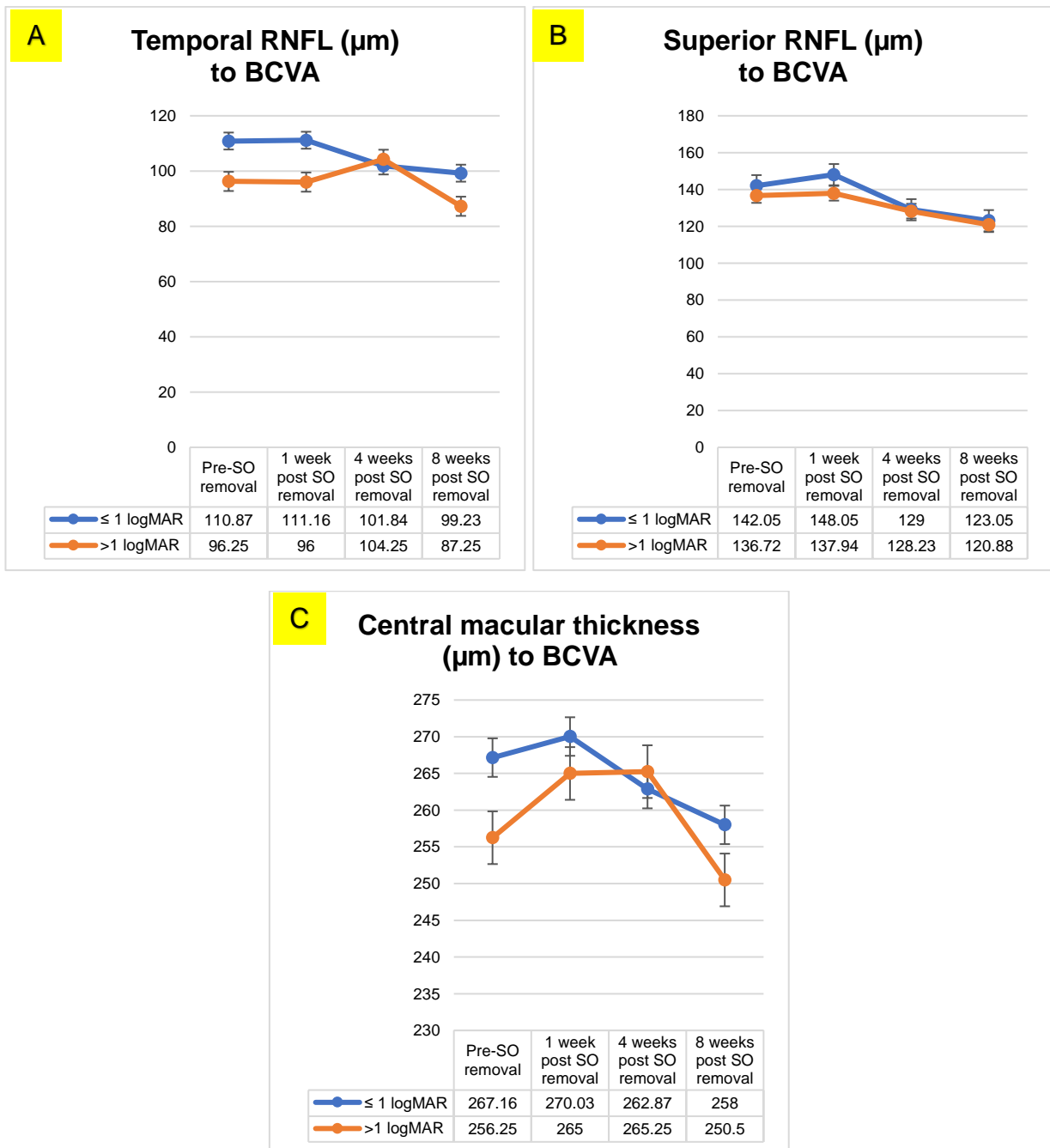


Figure 2. (A) Temporal RNFL thickness, (B) Superior RNFL thickness and (C) Central Macular thickness to BCVA in rhegmatogenous retinal detachment patients pre- and post-SO removal.

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COVER LETTER

Date: 19th February 2023

To
The Editor,
Vision

I am enclosing herewith of our final proofreading manuscript entitled:

RETINAL NERVE FIBER LAYER CHANGES AFTER INTRAOCULAR SILICONE OIL TAMPONADE IN RHEGMATOGENOUS RETINAL DETACHMENT

We are looking for possible evaluation and publication in VISION. The aim of this paper is to assess retinal nerve fibre layer thickness changes in rhegmatogenous retinal detachment (RRD) patients using silicone oil (SO) tamponade and subsequent evacuation.

Submitted manuscript is a **research letter**.

The corresponding author of this manuscript is **Andi Muhammad Ichsan** (am_ichsan@med.unhas.ac.id) and contribution of the authors as mentioned below:

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With the submission of this manuscript, I would like to undertake that:

1. All authors of this paper have directly participated in the planning, execution, or analysis of this study;
2. All authors of this paper have read and approved the final version submitted;
3. The contents of this manuscript have not been copyrighted or published previously;
4. The contents of this manuscript are not now under consideration for publication elsewhere;
5. The contents of this manuscript will not be copyrighted, submitted, or published elsewhere, while acceptance by the Journal is under consideration;
6. There are no directly related manuscripts or abstracts, published or unpublished, by any authors of this paper;
7. My Institute's Department of Ophthalmology, Hasanuddin University, Makassar, Indonesia representative is fully aware of this submission.

Best regards,

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ABSTRACT

Rhegmatogenous retinal detachment (RRD) is a serious condition that may cause visual disturbance. Treatment include pars plana vitrectomy with tamponade such as intraocular gas or silicone oil (SO). Silicone oil is favorable as an intraocular tamponade for reattachment of retinal detachment surgery. The application provides a higher anatomical success rate, especially in cases of proliferative vitreoretinopathy (PVR) that were previously considered untreatable. Objective assessment of the retinal nerve fiber layer (RNFL) using optical coherence tomography (OCT) in the eye with silicone oil tamponade is a challenge because of the limitations in imaging. This study aims to assess RNFL thickness changes in rhegmatogenous retinal detachment patients using SO tamponade and subsequent its removal that conducted on a total of 35 postoperative RRD patients. Central macular and RNFL thickness, as well as best-corrected visual acuity (BCVA) were recorded at the time of tamponade and after removal of SO on 1 week, 4, and 8 weeks. The results showed that the changes in RNFL thickness were significantly decreased after ≤ 6 month, especially in the superior and inferior quadrants, and BCVA increased after SO removal ($p < 0.05$). Central macular thickness was significant ($p = 0.02$) at the end of the visit. Based on the results, improved visual acuity is associated with decreased of RNFL and central macular thickness.

Keywords: Silicone oil tamponade, rhegmatogenous retinal detachment, retinal nerve fiber layer, central macular thickness.

TITLE:

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