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

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Abstract: Rhegmatogenous retinal detachment (RRD) is a serious and emergency condition that may cause visual disturbance. Treatment include pars plana vitrectomy with tamponade such as intraocular gas or silicone oil (SO). In many countries, silicone oil is still favorable compared to intraocular gases as 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 and difficulties in taking images. 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 respectively. The results showed that the changes in RNFL thickness were significantly decreased in the group of ≤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. Improved visual acuity is associated with decreased of RNFL and central macular thickness after SO removal.

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

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1. Introduction

Rhegmatogenous retinal detachment (RRD) is the separation of neurosensory layer retina from the retinal pigmen epithelium (RPE) with full thickness break in the retina. In most cases, these breaks are brought about by vitreous traction on the retina, which also makes it possible for fluid to accumulate in the subretinal region.[1] This pathologic condition is devastating and need for immediate treatment as it may result vision loss. The number of cases with a prevalence of 1 in 10,000 cases per year.[2] Age, gender, history of cataract surgery, and myopic status are all variables that might increase the likelihood of developing rhegmatogenous retinal detachment. There is an increased risk of RRD in myopic patients by a factor of ten for every three dioptres. In Asia, the rate of high myopia among school-aged children is as high as 80%.[3] The risk of RRD varies not just by myopic status but also male gender and race Caucasian and Asians having a relatively higher risk than other groups.[4]

The treatment of RRD including surgery of pneumatic retinopexy (PnR), scleral buckling (SB), and pars plana vitrectomy (PPV). Pneumatic retinopexy is a non-incisional, minimally invasive surgical surgery that was initially reported by Rosengren in 1938.[5] It is used to cure rhegmatogenous retinal detachment with the location of superior breaks. In PnR, the fundamental surgical processes include retinopexy of retinal break by using cryotherapy or laser photocoagulation, intraocular gas injection either before or after retinopexy, and the maintenance of an appropriate head position for the required amount of time following surgery.[6,7]

Scleral buckling is a surgical procedure that repairs retinal breaks and reduces vitreous stress on retinal tears. Since the 1950s, SB has been used as either the primary or secondary treatment for RRD repair. This approach was inspired by Jules Gonin's [8], and until now SB is still the choice of option the treatment for phakic eyes with localized RRD accompanied with small anterior holes or retinal dialysis, especially when the sign of proliferative vitreoretinopathy (PVR) is not present. The buckle creates a depression in the sclera, to reattach the retinal separation of the neurosensory retinal (NSR) layer to the retinal pigmen epithelium (RPE). The surgery is based on two key principles: the closing of retinal tears and the creation of a lasting chorioretinal adhesion.[9] Both of these principles are essential to the success of the operation. It has been shown that scleral buckling provides better morphological and functional results in phakic eyes when compared to vitrectomy, when the separation is simple or relatively less complicated.[10,11]

In some circumstances, RRD are associated with vitreous opacities that obscure the retinal view, giant retinal breaks, posterior retinal breaks that cannot be easily reached by buckling or any related condition with vitreoretinal traction that cannot be relieved by SB.[12] In cases of retinal detachment requiring PPV, tamponade agents such as intraocular gases or silicone oils (SO) are used to restore intraocular volume and apply surface tension to the entire detached retinal surface.[13] In contrast to PnR, which makes use of intraocular gases that are not diluted and expand, tamponade in PPV is typically achieved by completely filling the vitreous cavity with non-expanding gases that have been diluted in air at isovolumetric concentrations (for example, 20% SF6 or 14% C3F8). This is done in order to prevent the vitreous cavity from being displaced. [14,15]

The application of SO provides a higher anatomical success rate, especially in cases of PVR that were previously considered untreatable.[16,17] SO must displace retinal aqueous humor to work as an internal tamponade. This function depends on four physical parameters, including specific gravitation, buoyancy, interfacial tension, and viscosity.[18] Silicone oil floats in vitreous cavity because the specific gravity is 0.97, its bubbles' surface tension may change after injection into the eye. Higher viscosity silicone oils may emulsify less. In the vitreous cavity, buoyancy and gravity operate on an intraocular tamponade agent that presses against the retina as downward force. Moreover, the interfacial tension is the interaction between two immiscible chemicals, such silicone oil and aqueous humor. Current silicone oils have viscosities ranging from one thousand (MW 37 kDa) to five thousand cSt (MW 65 kDa).[18,19]

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. The objective assessment of retinal nerve fiber layer (RNFL) in the eyes with intraocular SO tamponade is difficult due to imaging limitations. Optical coherence tomography

(OCT) is a non-contact and non-invasive technology used to describe and monitor retinal layers and optic nerve morphology. It can detect retinal nerve tissue loss by quantitatively measuring RNFL thickness at high resolution.[20–23] Meanwhile, recent advances in vitreoretinal surgery have improved surgical outcomes.[24] Various factors including the height of the macular detachment and outer retinal subfoveal changes, have been evaluated for visual acuity outcomes in RRD.[25]

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

2. Materials and Methods

This study was a prospective cohort study that conducted at Hasanuddin University Hospital and JEC-ORBITA eye clinic, Makassar, Indonesia, to evaluate the changes in retinal nerve fiber layer thickness and central macular thickness in patients of rhegmatogenous retinal detachment using intraocular tamponade silicone oil and after its removal.

A total of 35 patients fulfilled the inclusion criterias and underwent pars plana vitrectomy followed by silicone oil as intraocular tamponade. The range of patient age was 15 – 60 years old as well as willing to participate in the study and signed the informed consent. Meanwhile, the exclusion criterias were the presence of macular abnormalities such as epiretinal membrane (ERM), macular hole, and all cases requiring internal limiting membrane (ILM) or ERM peeling, glaucomatous optic neuropathy, and non-cooperative patients. Others with a history of ocular trauma and retinal vascular disease were also excluded. Patients are declared dropouts when they did not follow up according to the time schedule and experienced retinal redetachment after the removal of silicone oil.

The silicone oils used were SO 1300 and 5000 cSt with the duration of intraocular tamponade ranging from 3 to 12 months. Silicone oil removal was performed when complete retinal attachment status was achieved or there were any signs of silicone oil emulsification. All patients who fulfilled the inclusion criterias were examined for visual acuity, anterior segment of the eye, intraocular pressure, indirect funduscopy, and OCT (*Heidelberg engineering, HRA OCT Spectralis®)* for the examination of RNFL and CMT using three circular scans with a diameter of 3.4 mm for each eye, as well as macula. This examination was carried out serially before removal (group 1) and after SO removal in 1 week (group 2), 4 weeks (group 3), and 8 weeks (group 4). All results were recorded and analyzed using paired t-test and repeated ANOVA followed by post-hoc Bonferroni test, sig. $p<0.05$.

3. Results

The mean difference in retinal nerve fiber layer thickness, central macular thickness, intraocular pressure, and best corrected visual acuity before and after SO removal is shown in table 1. In figure 1, the data was divided based on intraocular tamponade SO duration (≤ 6 months and >6 months). Statistical analysis found that there were significant difference between RNFL thickness ≤6 months in the areas of superior ($p<0.001$) and temporal ($p<0.001$), CMT ≤6 months ($p<0.001$), and BCVA measurements ≤6 and >6 months ($p<0.001$). Therefore, a post-hoc analysis was performed on RNFL thickness, CMT, and

BCVA based on the duration of silicone oil was displayed in table 2. Moreover, the correlation of significant value of RNFL (superior and temporal) thickness and CMT with BCVA was shown in figure 2.

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				p-value
	Pre SO removal	1 wk Post SO removal	4 wk Post SO removal	8 wk Post SO removal	
RNFL (μm)					
Inferior	154,31 ± 44,05	142,23 ± 38,46	138,34 ± 35,66	139,69 ± 36,38	0,17
Superior	139,31 ± 34,71	142,86 ± 42,86	128,91 ± 27,16	121,94 ± 25,47	<0,001*
Nasal	98,97 ± 34,50	91,37 ± 28,54	89,77 ± 32,79	90,40 ± 31,43	0,34
Temporal	109,20 ± 44,92	109,43 ± 42,85	102,11 ± 31,79	97,86 ± 31,23	0,02*
CMT (μm)	265,91 ± 20,01	269,46 ± 18,52	263,14 ± 22,14	257,14 ± 22,17	<0,001*
IOP (mmHg)	14,94 ± 2,74	14,46 ± 2,72	14,06 ± 2,51	14,06 ± 2,87	0,08
BCVA (LogMAR)	0,75 ± 0,33	0,69 ± 0,29	0,61 ± 0,29	0,58 ± 0,27	<0,001*

Description: IOP: Intraocular pressure; BCVA: Best corrected visual acuity; *sig., $p<0.05$

SO: Silicone oil; OCT: Optical coherence tomography, LogMAR: Logarithm of the minimum angle of resolution; RNFL: Retinal nerve fiber layer; CMT: Central macular thickness.

Based on the table 1, it can be seen that RNFL thickness were significantly decreased at 4 and 8 weeks after SO removal compared to pre SO removal ($p<0.05$). Similar result was found in CMT that the thickness of central macular was significantly decreased post SO removal ($p<0.001$). The IOP did not show any significant difference between pre- and post SO removal ($p>0.05$). Meanwhile, BCVA showed increased value after SO removal ($p<0.001$).

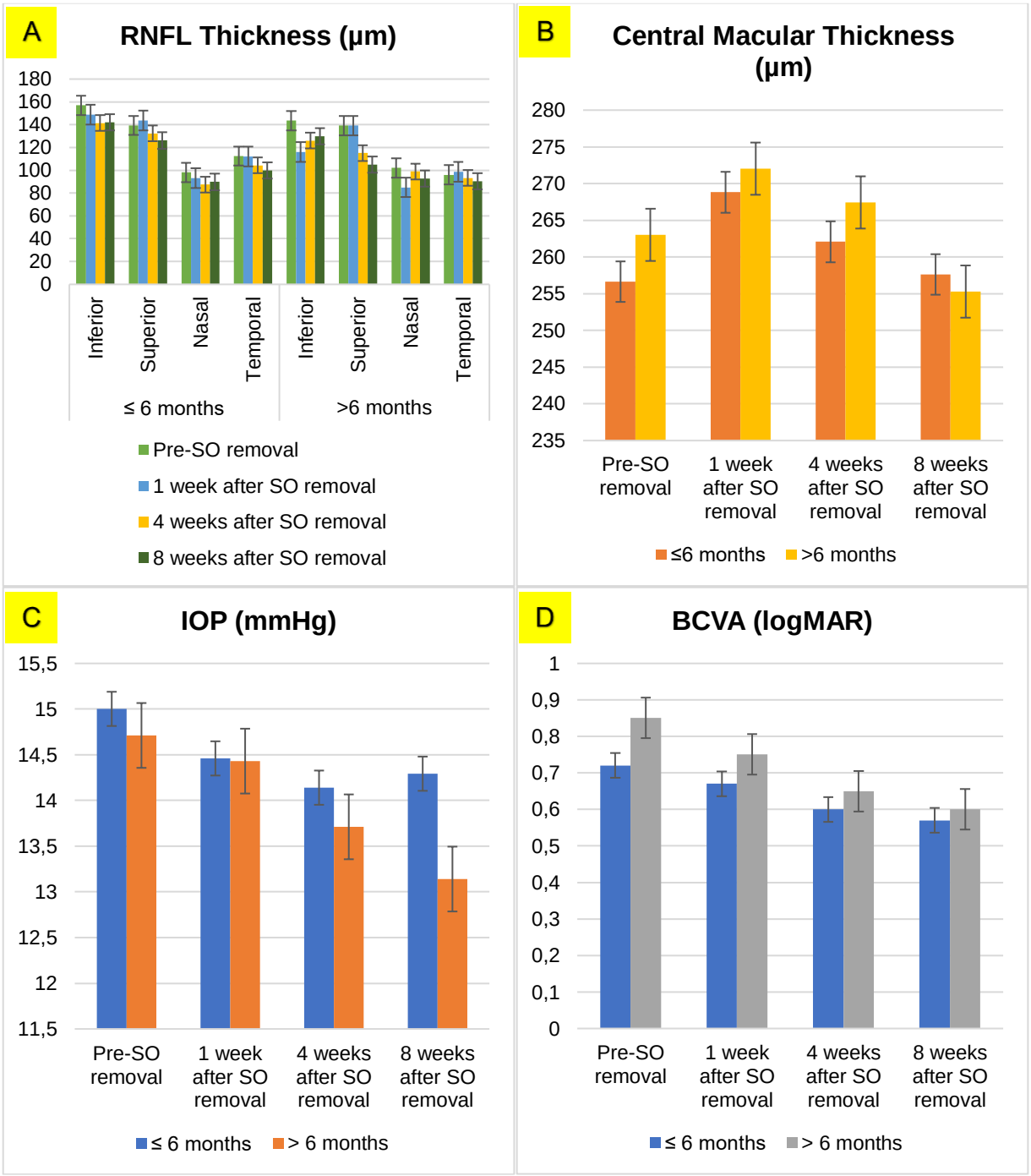

Figure 1. Average value of (A) RNFL thickness, (B) CMT, (C) IOP, and (D) BCVA based on duration of use SO on measurement time of pre and post silicone oil removal in rhegmatogenous retinal detachment patients.

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		*Mean Difference*	*p-value*	95% *CI*	
					Lower	*Upper*
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
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 Superior <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 Temporal <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

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), *sig., p<0.05.

Table 2 shows post-hoc analysis of best corrective visual acuity, central macular thickness, and retinal nerve fiber layer thickness, there are significant difference among groups with group 4 (8 weeks post SO removal) was the most significant improvement in all variables (p<0.05).

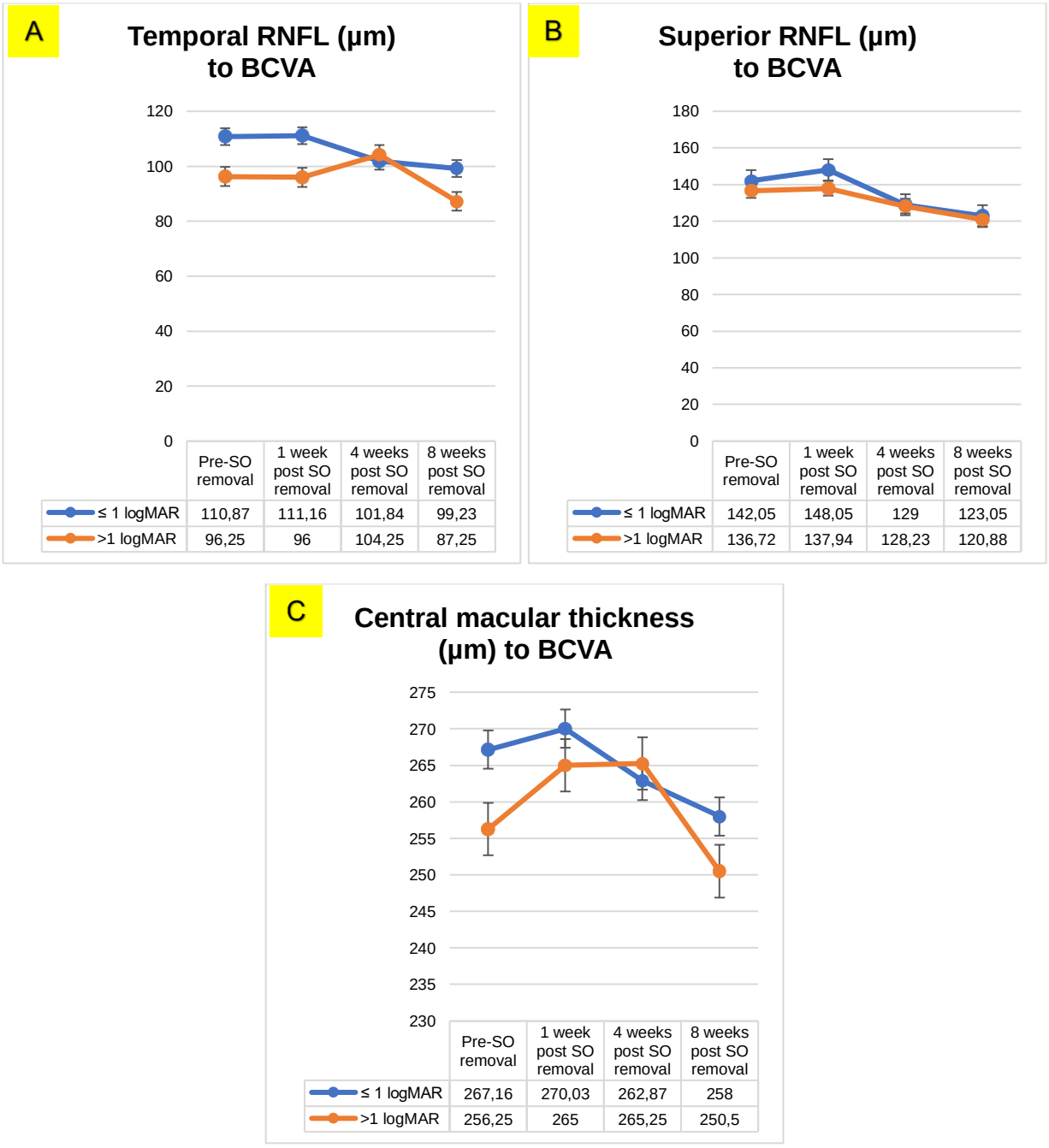

Figure 2. (A)Temporal RNFL thickness, (B) Superior RNFL thickness and (C) Central Macular thickness to BCVA in rhegmatogenous retinal detachment patients pre- and post SO removal.

Figure 2 shows the relationship between retinal nerve fiber layer thickness and CMT with BCVA. In Figures 2A and 2B it can be seen that there is a decrease in the thickness of the retinal nerve fiber layer both on the superior and temporal sides before and after SO removal. Similar results were also shown by the comparison of CMT and BCVA (2C) that macular thickness decreased with the duration of follow-up.

4. Discussion

In this study, the viscosity of silicone oil 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.[26] A study by Kartasasmita et al. (2017) found that SO 1,000 emulsified more than SO 5,000.[27] 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.[28]

In this study, the mean BCVA before silicone oil removal was 0.75 LogMAR, but afterward it improved to 0.69, 0.61, and 0.58 at 1, 4, and 8 weeks post SO removal 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, consecutively.[29] A study by Nassar et al. (2019) also reported that 6 months or >6 months of SO application affected BCVA. Increased of IOP may damage the fovea through mechanical stress, and can caused loss of outer nuclear layer cell bodies. Increased IOP may mechanically stress the fovea, causing outer nuclear layer cell body loss. Thus, this drop in IOP may have improved retinal sensitivity. In a recent macula-on retinal detachment research, higher IOP during SO endotamponade was the biggest risk factor for vision loss.[30] 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 ($p<0.05$) and the mean IOP before and after 4 weeks of removal were 20.18 mmHg and 14.18 mmHg ($p=0.025$).[31]

Our study found that IOP was not Similar result was reported by Nassar et al (2019), Increased of IOP may damage the fovea through mechanical stress, and can caused loss of outer nuclear layer cell bodies. Increased IOP may mechanically stress the fovea, causing outer nuclear layer cell body loss. Thus, this drop in IOP may have improved retinal sensitivity. In a recent macula-on retinal detachment research, higher IOP during SO endotamponade was the biggest risk factor for vision loss significantly different at pre- and post SO removal ($p=0.08$). This result is similar to the study by Brănişteanu et al (2017) that report of a decrease in IOP post SO removal.[32]

Saleh et al (2020) reported a different result which IOP was significantly increased from the baseline value when 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 $p<0.001$.[33] Several reports also showed that the first sign 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.[32,33] 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±14mmHg after 6 months.[34–36]

In this study, the mean of CMT was 265.91±20.01 μm. In the first week post- SO removal, it was 269.46±18.52 μm, then gradually decreased to 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 central macular edema (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.[37]

Because of the wide disparity in CMT values depending on several factors such as age, gender, and ethnicity, it is possible to get more consistent findings by comparing the CMT values of both eyes belonging to the same person.[38] Following tamponade with silicone oil, Bae et al. (2019) found that the structure of the participants' macular tissue was altered in 46 patients. Epiretinal membrane (26.1% of cases), cystoid macular edema (19.6% of cases), and a decrease in the thickness of the central macular area were changed that occurred in the retinal structure. Once the silicone oil was removed, these alterations were able to be recovered.[39]

In the most recent study conducted by Rabina et al. (2020) that reported 41 patients, showed a temporary decrease in retinal thickness, particularly in the inner retinal layers. However, after the silicone oil was removed from their eyes, these patients' retinas regained the thickness levels of the healthy structure.[40] Another study that included 10 people and their eyes found that a tamponade of silicone oil caused the fovea to become flatter. Following the removal of the silicone oil, the phenomenon reverted, and the fovea reclaimed the thickness as it had before to the operation.[38]

The thickness of the subfoveal choroidal layer and the retinal layer both reduced noticeably as a result of the SO tamponade. According to the findings of study conducted by Kheir WJ et al. (2018), CMT levels dropped when the SO tamponade was applied, but they increased when the SO was withdrawn. Nevertheless, these changes did not reach the level of statistical significance ($p = 0.44$).[42] In addition, the inner retinal layers were shown to be much thinner in the presence of SO tamponade in comparison to healthy eyes in two separate tests that were carried out by Purtskhvanidze et al. and Caramoy et al.[43,44]

During tamponade, the RNFL thickness was measured and continuously evaluated until 8 weeks after SO removal. After 8 weeks of removal, the RNFL thickened in the nasal quadrant from 98,97 ± 34,50 μm to 90,40 ± 31,43 μm, in the temporal area 109,20 ± 44,92μm to 97,86 ± 31,23μm, in superior area 139,31 ± 34,71 μm to 121,94 ± 25,47μm and in the inferior area 154,31 ± 44,05 μm to 139,69 ± 36,38 μm. In this study, superior and temporal nerve fiber layer thickness was significantly decreased at the 8 weeks after SO removal ($p<0.001$). 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.[45] Another study found that RNFL thickness increased in all quadrants after SO removal compared to pre-removal. In the area of inferior and superior, RNFL thickness decreased after 2 years of SO removal.[46] 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.[24] Takkar et al (2018) stated that potassium accumulation and nerve degeneration cause retinal thinning, while Sebastian et al (2003) stated that it may caused by mechanical stress. SO toxicity and dehydration are also hypothesized as potential retinal thinning mechanisms.[36,45]

Raczynska et al. (2018) reported the effects of silicone oil on ganglion cell complex (GCC) and compare it to other endotamponades like sulfur hexafluoride gas (SF6) and perfluoropropane gas (C3F8). Spectral domain (SD) OCT showed a significant reduction in average GCC thickness in practically all sectors in the silicone oil endotamponade group at all follow-up visits, despite no visual complaints or scotomas. After surgery, macula status did not change the mean of GCC.[47]

Silicone oil intraocular tamponades are safe and widely used. Several studies recommended carefully monitor SD-OCT patients with silicone oil tamponade to identify early changes in inner retinal layer thickness.[48,49] During SO application and its removal, BCVA correlated with central macular thickness and RNFL thickness. In RRD patients with pre-removal, BCVA ≤1 and >1 LogMAR, temporal RNFL thickness was 110.87 μm and 96.25 μm respectively. The value dropped to 99.23 μm for ≤1 LogMAR and 87.25 μm for >1 LogMAR in 8 weeks after SO removal.

Temporal RNFL thickness changes correspond to the macula, 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.[45] Rabina et al (2020) 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.[40] Doslak (1988) stated the electroretinogram (ERG) declined rapidly in silicone oil filled eye, the ERG (with a functional retina) was severely reduced to 15% of normal, and even with the most extreme variations of the other parameters there was still a reduction (60%) of the ERG.[50] Christou et al. (2022) reported the amplitudes of the a- and b-waves were significantly higher after SO removal than those before SO removal, which means the photoreceptors should have recovered after silicone oil was removed.[51]

5. Conclusions

There were statistically significant decrease in retinal nerve fiber layer thickness and central macular thickness in postoperative rhegmatogenous retinal detachment patients after silicone oil removal, particularly in the inferior and superior quadrants. This result may correlated with the improvement of best corrected visual acuity.

Supplementary Materials: None

Author Contributions: Conception and design: FAC, AMI; Provision of study materials or patients: AMI, HSM, BD; Collection and assembly of data: FAC, BD; Data analysis and interpretation: JH, ICI; Administrative support: ICI; Manuscript writing: All authors; Final approval of manuscript: All authors.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study, including consent to publish this paper.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

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Conflicts of Interest: The authors declare no conflict of interest.

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

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Abstract: Rhegmatogenous retinal detachment (RRD) is a serious and emergency condition that may cause visual disturbance. Treatment include pars plana vitrectomy with tamponade such as intraocular gas or silicone oil (SO). In many countries, silicone oil is still favorable compared to intraocular gases as 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 and difficulties in taking images. 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 respectively. The results showed that the changes in RNFL thickness were significantly decreased in the group of ≤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. Improved visual acuity is associated with decreased of RNFL and central macular thickness after SO removal.

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

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1. Introduction

Rhegmatogenous retinal detachment (RRD) is the separation of neurosensory layer retina from the retinal pigmen epithelium (RPE) with full thickness break in the retina. In most cases, these breaks are brought about by vitreous traction on the retina, which also makes it possible for fluid to accumulate in the subretinal region.[1] This pathologic condition is devastating and need for immediate treatment as it may result vision loss. The number of cases with a prevalence of 1 in 10,000 cases per year.[2] Age, gender, history of cataract surgery, and myopic status are all variables that might increase the likelihood of developing rhegmatogenous retinal detachment. There is an increased risk of RRD in myopic patients by a factor of ten for every three dioptres. In Asia, the rate of high myopia among school-aged children is as high as 80%.[3] The risk of RRD varies not just by myopic status but also male gender and race Caucasian and Asians having a relatively higher risk than other groups.[4]

The treatment of RRD including surgery of pneumatic retinopexy (PnR), scleral buckling (SB), and pars plana vitrectomy (PPV). Pneumatic retinopexy is a non-incisional, minimally invasive surgical surgery that was initially reported by Rosengren in 1938.[5] It is used to cure rhegmatogenous retinal detachment with the location of superior breaks. In PnR, the fundamental surgical processes include retinopexy of retinal break by using cryotherapy or laser photocoagulation, intraocular gas injection either before or after retinopexy, and the maintenance of an appropriate head position for the required amount of time following surgery.[6,7]

Scleral buckling is a surgical procedure that repairs retinal breaks and reduces vitreous stress on retinal tears. Since the 1950s, SB has been used as either the primary or secondary treatment for RRD repair. This approach was inspired by Jules Gonin's [8], and until now SB is still the choice of option the treatment for phakic eyes with localized RRD accompanied with small anterior holes or retinal dialysis, especially when the sign of proliferative vitreoretinopathy (PVR) is not present. The buckle creates a depression in the sclera, to reattach the retinal separation of the neurosensory retinal (NSR) layer to the retinal pigmen epithelium (RPE). The surgery is based on two key principles: the closing of retinal tears and the creation of a lasting chorioretinal adhesion.[9] Both of these principles are essential to the success of the operation. It has been shown that scleral buckling provides better morphological and functional results in phakic eyes when compared to vitrectomy, when the separation is simple or relatively less complicated.[10,11]

In some circumstances, RRD are associated with vitreous opacities that obscure the retinal view, giant retinal breaks, posterior retinal breaks that cannot be easily reached by buckling or any related condition with vitreoretinal traction that cannot be relieved by SB.[12] In cases of retinal detachment requiring PPV, tamponade agents such as intraocular gases or silicone oils (SO) are used to restore intraocular volume and apply surface tension to the entire detached retinal surface.[13] In contrast to PnR, which makes use of intraocular gases that are not diluted and expand, tamponade in PPV is typically achieved by completely filling the vitreous cavity with non-expanding gases that have been diluted in air at isovolumetric concentrations (for example, 20% SF6 or 14% C3F8). This is done in order to prevent the vitreous cavity from being displaced. [14,15]

The application of SO provides a higher anatomical success rate, especially in cases of PVR that were previously considered untreatable.[16,17] SO must displace retinal aqueous humor to work as an internal tamponade. This function depends on four physical parameters, including specific gravitation, buoyancy, interfacial tension, and viscosity.[18] Silicone oil floats in vitreous cavity because the specific gravity is 0.97, its bubbles' surface tension may change after injection into the eye. Higher viscosity silicone oils may emulsify less. In the vitreous cavity, buoyancy and gravity operate on an intraocular tamponade agent that presses against the retina as downward force. Moreover, the interfacial tension is the interaction between two immiscible chemicals, such silicone oil and aqueous humor. Current silicone oils have viscosities ranging from one thousand (MW 37 kDa) to five thousand cSt (MW 65 kDa).[18,19]

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. The objective assessment of retinal nerve fiber layer (RNFL) in the eyes with intraocular SO tamponade is difficult due to imaging limitations. Optical coherence tomography

(OCT) is a non-contact and non-invasive technology used to describe and monitor retinal layers and optic nerve morphology. It can detect retinal nerve tissue loss by quantitatively measuring RNFL thickness at high resolution.[20–23] Meanwhile, recent advances in vitreoretinal surgery have improved surgical outcomes.[24] Various factors including the height of the macular detachment and outer retinal subfoveal changes, have been evaluated for visual acuity outcomes in RRD.[25]

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

2. Materials and Methods

This study was a prospective cohort study that conducted at Hasanuddin University Hospital and JEC-ORBITA eye clinic, Makassar, Indonesia, to evaluate the changes in retinal nerve fiber layer thickness and central macular thickness in patients of rhegmatogenous retinal detachment using intraocular tamponade silicone oil and after its removal.

A total of 35 patients fulfilled the inclusion criterias and underwent pars plana vitrectomy followed by silicone oil as intraocular tamponade. The range of patient age was 15 – 60 years old as well as willing to participate in the study and signed the informed consent. Meanwhile, the exclusion criterias were the presence of macular abnormalities such as epiretinal membrane (ERM), macular hole, and all cases requiring internal limiting membrane (ILM) or ERM peeling, glaucomatous optic neuropathy, and non-cooperative patients. Others with a history of ocular trauma and retinal vascular disease were also excluded. Patients are declared dropouts when they did not follow up according to the time schedule and experienced retinal redetachment after the removal of silicone oil.

The silicone oils used were SO 1300 and 5000 cSt with the duration of intraocular tamponade ranging from 3 to 12 months. Silicone oil removal was performed when complete retinal attachment status was achieved or there were any signs of silicone oil emulsification. All patients who fulfilled the inclusion criterias were examined for visual acuity, anterior segment of the eye, intraocular pressure, indirect funduscopy, and OCT (*Heidelberg engineering, HRA OCT Spectralis®)* for the examination of RNFL and CMT using three circular scans with a diameter of 3.4 mm for each eye, as well as macula. This examination was carried out serially before removal (group 1) and after SO removal in 1 week (group 2), 4 weeks (group 3), and 8 weeks (group 4). All results were recorded and analyzed using paired t-test and repeated ANOVA followed by post-hoc Bonferroni test, sig. $p<0.05$.

3. Results

The mean difference in retinal nerve fiber layer thickness, central macular thickness, intraocular pressure, and best corrected visual acuity before and after SO removal is shown in table 1. In figure 1, the data was divided based on intraocular tamponade SO duration (≤ 6 months and >6 months). Statistical analysis found that there were significant difference between RNFL thickness ≤6 months in the areas of superior ($p<0.001$) and temporal ($p<0.001$), CMT ≤6 months ($p<0.001$), and BCVA measurements ≤6 and >6 months ($p<0.001$). Therefore, a post-hoc analysis was performed on RNFL thickness, CMT, and

BCVA based on the duration of silicone oil was displayed in table 2. Moreover, the correlation of significant value of RNFL (superior and temporal) thickness and CMT with BCVA was shown in figure 2.

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				p-value
	Pre SO removal	1 wk Post SO removal	4 wk Post SO removal	8 wk Post SO removal	
RNFL (μm)					
Inferior	154,31 ± 44,05	142,23 ± 38,46	138,34 ± 35,66	139,69 ± 36,38	0,17
Superior	139,31 ± 34,71	142,86 ± 42,86	128,91 ± 27,16	121,94 ± 25,47	<0,001*
Nasal	98,97 ± 34,50	91,37 ± 28,54	89,77 ± 32,79	90,40 ± 31,43	0,34
Temporal	109,20 ± 44,92	109,43 ± 42,85	102,11 ± 31,79	97,86 ± 31,23	0,02*
CMT (μm)	265,91 ± 20,01	269,46 ± 18,52	263,14 ± 22,14	257,14 ± 22,17	<0,001*
IOP (mmHg)	14,94 ± 2,74	14,46 ± 2,72	14,06 ± 2,51	14,06 ± 2,87	0,08
BCVA (LogMAR)	0,75 ± 0,33	0,69 ± 0,29	0,61 ± 0,29	0,58 ± 0,27	<0,001*

Description: IOP: Intraocular pressure; BCVA: Best corrected visual acuity; *sig., $p<0.05$

SO: Silicone oil; OCT: Optical coherence tomography, LogMAR: Logarithm of the minimum angle of resolution; RNFL: Retinal nerve fiber layer; CMT: Central macular thickness.

Based on the table 1, it can be seen that RNFL thickness were significantly decreased at 4 and 8 weeks after SO removal compared to pre SO removal ($p<0.05$). Similar result was found in CMT that the thickness of central macular was significantly decreased post SO removal ($p<0.001$). The IOP did not show any significant difference between pre- and post SO removal ($p>0.05$). Meanwhile, BCVA showed increased value after SO removal ($p<0.001$).

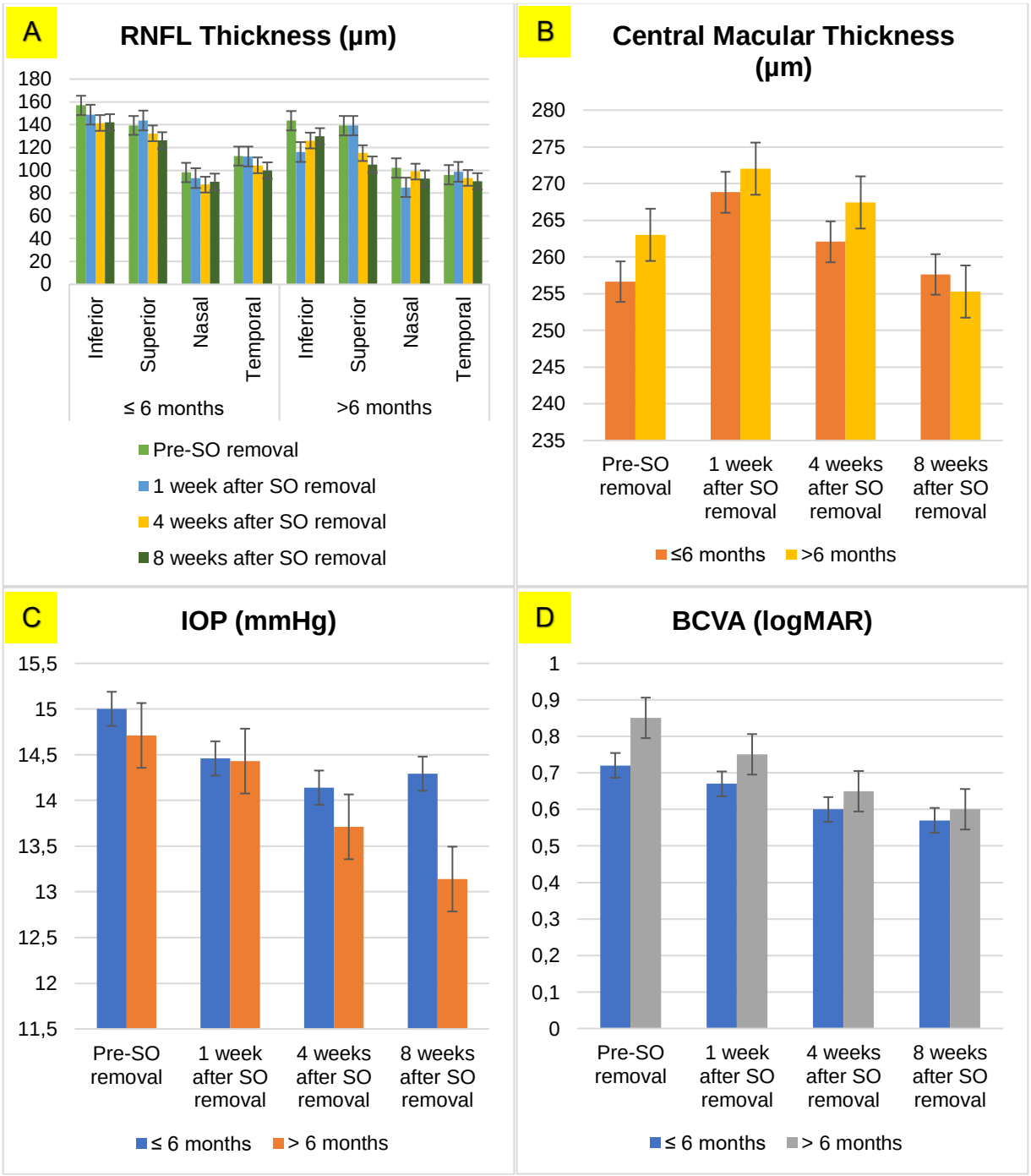

Figure 1. Average value of (A) RNFL thickness, (B) CMT, (C) IOP, and (D) BCVA based on duration of use SO on measurement time of pre and post silicone oil removal in rhegmatogenous retinal detachment patients.

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		*Mean Difference*	*p-value*	95% *CI*	
					Lower	*Upper*
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
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 Superior <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 Temporal <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

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), *sig., p<0.05.

Table 2 shows post-hoc analysis of best corrective visual acuity, central macular thickness, and retinal nerve fiber layer thickness, there are significant difference among groups with group 4 (8 weeks post SO removal) was the most significant improvement in all variables (p<0.05).

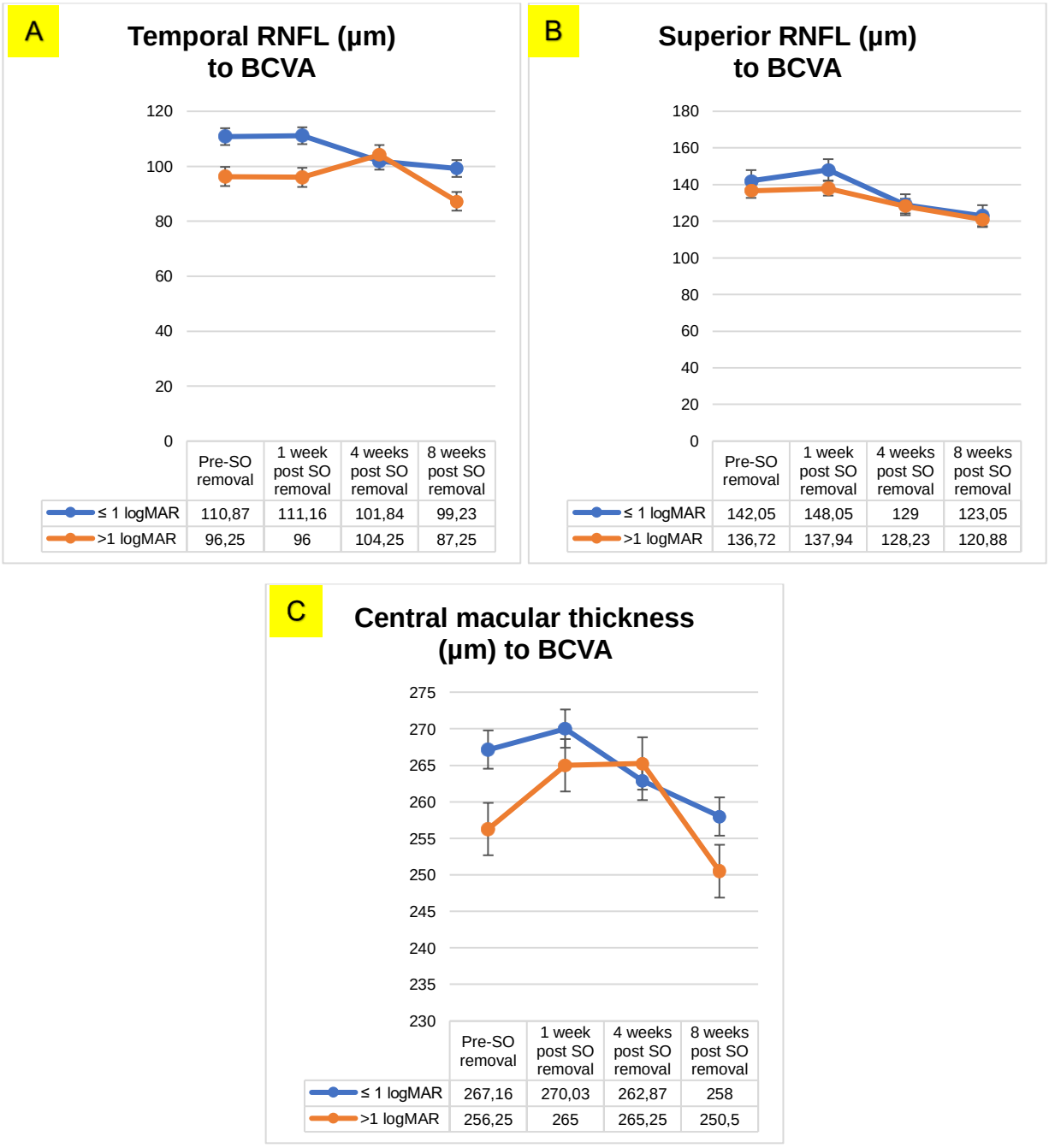

Figure 2. (A)Temporal RNFL thickness, (B) Superior RNFL thickness and (C) Central Macular thickness to BCVA in rhegmatogenous retinal detachment patients pre- and post SO removal.

Figure 2 shows the relationship between retinal nerve fiber layer thickness and CMT with BCVA. In Figures 2A and 2B it can be seen that there is a decrease in the thickness of the retinal nerve fiber layer both on the superior and temporal sides before and after SO removal. Similar results were also shown by the comparison of CMT and BCVA (2C) that macular thickness decreased with the duration of follow-up.

4. Discussion

In this study, the viscosity of silicone oil 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.[26] A study by Kartasasmita et al. (2017) found that SO 1,000 emulsified more than SO 5,000.[27] 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.[28]

In this study, the mean BCVA before silicone oil removal was 0.75 LogMAR, but afterward it improved to 0.69, 0.61, and 0.58 at 1, 4, and 8 weeks post SO removal 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, consecutively.[29] A study by Nassar et al. (2019) also reported that 6 months or >6 months of SO application affected BCVA. Increased of IOP may damage the fovea through mechanical stress, and can caused loss of outer nuclear layer cell bodies. Increased IOP may mechanically stress the fovea, causing outer nuclear layer cell body loss. Thus, this drop in IOP may have improved retinal sensitivity. In a recent macula-on retinal detachment research, higher IOP during SO endotamponade was the biggest risk factor for vision loss.[30] 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 ($p<0.05$) and the mean IOP before and after 4 weeks of removal were 20.18 mmHg and 14.18 mmHg ($p=0.025$).[31]

Our study found that IOP was not Similar result was reported by Nassar et al (2019), Increased of IOP may damage the fovea through mechanical stress, and can caused loss of outer nuclear layer cell bodies. Increased IOP may mechanically stress the fovea, causing outer nuclear layer cell body loss. Thus, this drop in IOP may have improved retinal sensitivity. In a recent macula-on retinal detachment research, higher IOP during SO endotamponade was the biggest risk factor for vision loss significantly different at pre- and post SO removal ($p=0.08$). This result is similar to the study by Brănişteanu et al (2017) that report of a decrease in IOP post SO removal.[32]

Saleh et al (2020) reported a different result which IOP was significantly increased from the baseline value when 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 $p<0.001$.[33] Several reports also showed that the first sign 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.[32,33] 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±14mmHg after 6 months.[34–36]

In this study, the mean of CMT was 265.91±20.01 μm. In the first week post- SO removal, it was 269.46±18.52 μm, then gradually decreased to 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 central macular edema (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.[37]

Because of the wide disparity in CMT values depending on several factors such as age, gender, and ethnicity, it is possible to get more consistent findings by comparing the CMT values of both eyes belonging to the same person.[38] Following tamponade with silicone oil, Bae et al. (2019) found that the structure of the participants' macular tissue was altered in 46 patients. Epiretinal membrane (26.1% of cases), cystoid macular edema (19.6% of cases), and a decrease in the thickness of the central macular area were changed that occurred in the retinal structure. Once the silicone oil was removed, these alterations were able to be recovered.[39]

In the most recent study conducted by Rabina et al. (2020) that reported 41 patients, showed a temporary decrease in retinal thickness, particularly in the inner retinal layers. However, after the silicone oil was removed from their eyes, these patients' retinas regained the thickness levels of the healthy structure.[40] Another study that included 10 people and their eyes found that a tamponade of silicone oil caused the fovea to become flatter. Following the removal of the silicone oil, the phenomenon reverted, and the fovea reclaimed the thickness as it had before to the operation.[38]

The thickness of the subfoveal choroidal layer and the retinal layer both reduced noticeably as a result of the SO tamponade. According to the findings of study conducted by Kheir WJ et al. (2018), CMT levels dropped when the SO tamponade was applied, but they increased when the SO was withdrawn. Nevertheless, these changes did not reach the level of statistical significance ($p = 0.44$).[42] In addition, the inner retinal layers were shown to be much thinner in the presence of SO tamponade in comparison to healthy eyes in two separate tests that were carried out by Purtskhvanidze et al. and Caramoy et al.[43,44]

During tamponade, the RNFL thickness was measured and continuously evaluated until 8 weeks after SO removal. After 8 weeks of removal, the RNFL thickened in the nasal quadrant from 98,97 ± 34,50 μm to 90,40 ± 31,43 μm, in the temporal area 109,20 ± 44,92μm to 97,86 ± 31,23μm, in superior area 139,31 ± 34,71 μm to 121,94 ± 25,47μm and in the inferior area 154,31 ± 44,05 μm to 139,69 ± 36,38 μm. In this study, superior and temporal nerve fiber layer thickness was significantly decreased at the 8 weeks after SO removal ($p<0.001$). 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.[45] Another study found that RNFL thickness increased in all quadrants after SO removal compared to pre-removal. In the area of inferior and superior, RNFL thickness decreased after 2 years of SO removal.[46] 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.[24] Takkar et al (2018) stated that potassium accumulation and nerve degeneration cause retinal thinning, while Sebastian et al (2003) stated that it may caused by mechanical stress. SO toxicity and dehydration are also hypothesized as potential retinal thinning mechanisms.[36,45]

Raczynska et al. (2018) reported the effects of silicone oil on ganglion cell complex (GCC) and compare it to other endotamponades like sulfur hexafluoride gas (SF6) and perfluoropropane gas (C3F8). Spectral domain (SD) OCT showed a significant reduction in average GCC thickness in practically all sectors in the silicone oil endotamponade group at all follow-up visits, despite no visual complaints or scotomas. After surgery, macula status did not change the mean of GCC.[47]

Silicone oil intraocular tamponades are safe and widely used. Several studies recommended carefully monitor SD-OCT patients with silicone oil tamponade to identify early changes in inner retinal layer thickness.[48,49] During SO application and its removal, BCVA correlated with central macular thickness and RNFL thickness. In RRD patients with pre-removal, BCVA ≤1 and >1 LogMAR, temporal RNFL thickness was 110.87 μm and 96.25 μm respectively. The value dropped to 99.23 μm for ≤1 LogMAR and 87.25 μm for >1 LogMAR in 8 weeks after SO removal.

Temporal RNFL thickness changes correspond to the macula, 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.[45] Rabina et al (2020) 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.[40] Doslak (1988) stated the electroretinogram (ERG) declined rapidly in silicone oil filled eye, the ERG (with a functional retina) was severely reduced to 15% of normal, and even with the most extreme variations of the other parameters there was still a reduction (60%) of the ERG.[50] Christou et al. (2022) reported the amplitudes of the a- and b-waves were significantly higher after SO removal than those before SO removal, which means the photoreceptors should have recovered after silicone oil was removed.[51]

5. Conclusions

There were statistically significant decrease in retinal nerve fiber layer thickness and central macular thickness in postoperative rhegmatogenous retinal detachment patients after silicone oil removal, particularly in the inferior and superior quadrants. This result may correlated with the improvement of best corrected visual acuity.

Supplementary Materials: None

Author Contributions: Conception and design: FAC, AMI; Provision of study materials or patients: AMI, HSM, BD; Collection and assembly of data: FAC, BD; Data analysis and interpretation: JH, ICI; Administrative support: ICI; Manuscript writing: All authors; Final approval of manuscript: All authors.

Funding: None

Institutional Review Board 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.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study, including consent to publish this paper.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

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Conflicts of Interest: The authors declare no conflict of interest.

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FIGURES

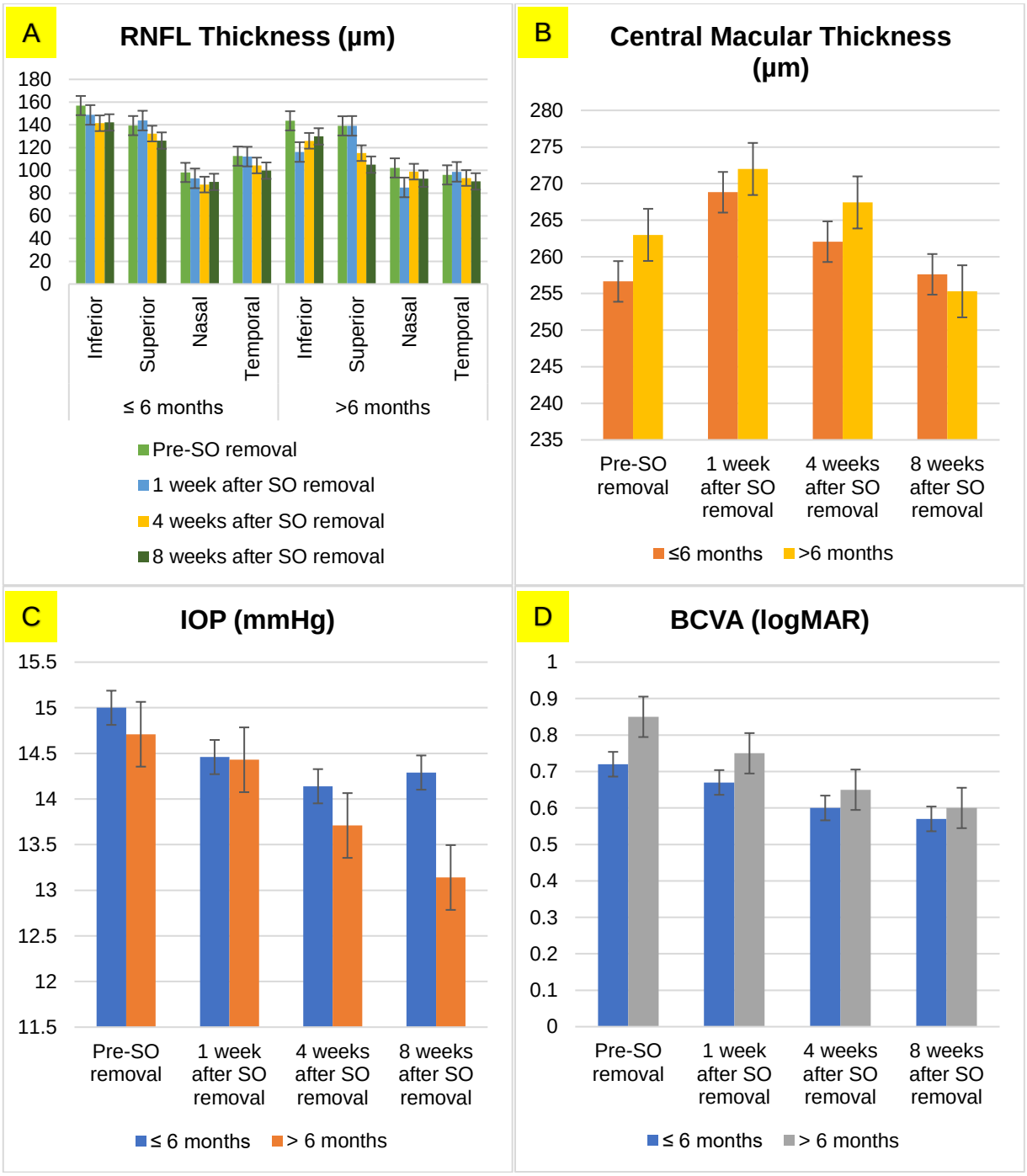

Figure 1. Average value of (A) RNFL thickness, (B) CMT, (C) IOP, and (D) BCVA based on duration of use SO on measurement time of pre and post silicone oil removal in rhegmatogenous retinal detachment patients.

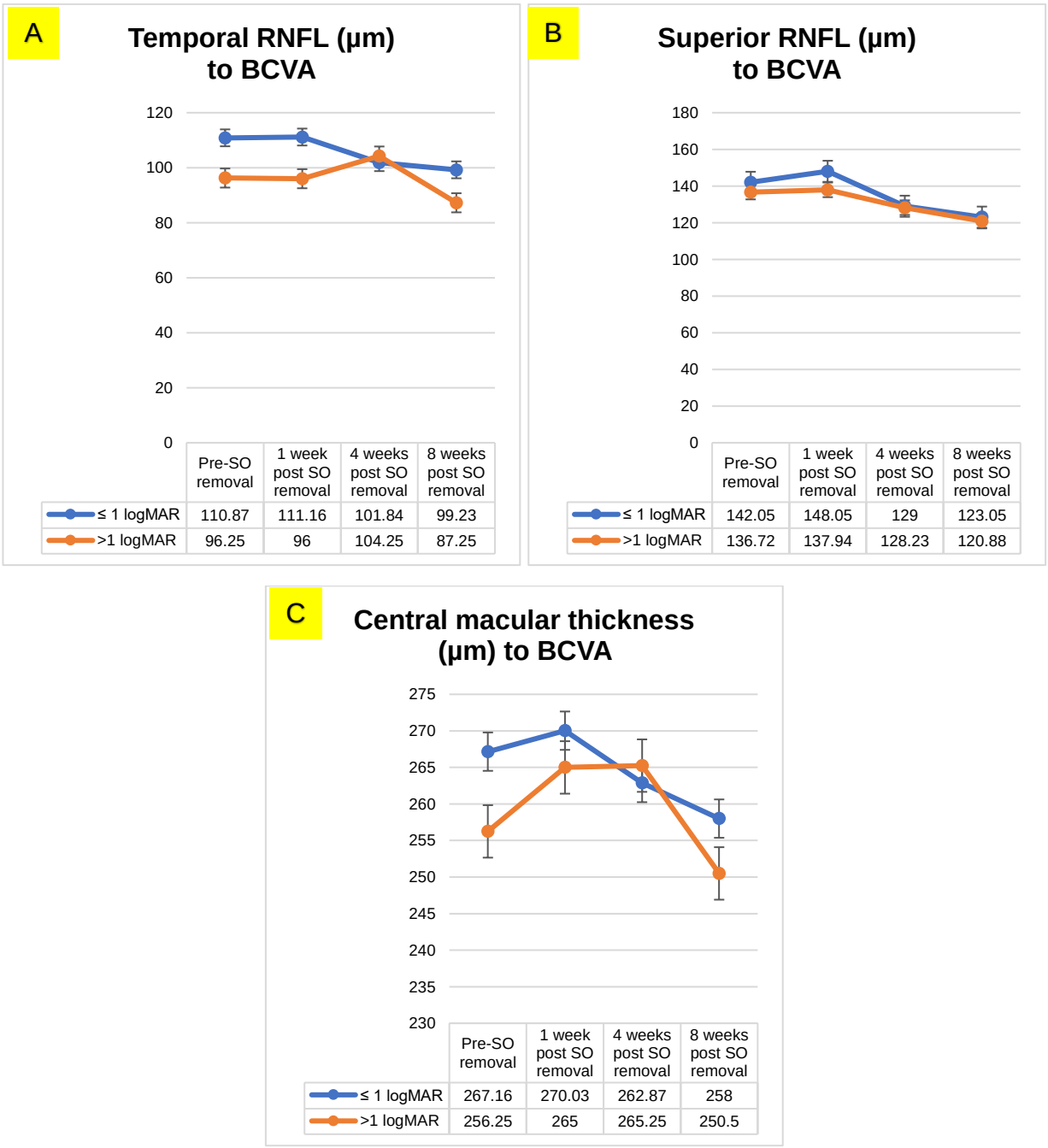

Figure 2. (A)Temporal RNFL thickness, (B) Superior RNFL thickness and (C) Central Macular thickness to BCVA in rhegmatogenous retinal detachment patients pre- and post-SO removal.

COVER LETTER

Date: 09th February 2023

To
The Editor,
Vision

I am enclosing herewith of revised 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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REVIEWER 3

1. Authors presented an interesting analysis of INTRA-OCULAR SILICONE OIL TAMPONADE treatment. However, I feel figures are not clearly presented.

   Response:

   We have already added some explanations about the figures and tables in our manuscript (manuscript line 152-169).

2. Average values should be presented with standard deviation bars on figure 1.

   Response:

   Based on your suggestion, we have already added the standard deviation bars on all figures (manuscript line 152-169).

3. The groups in the table 2 (x vs y) are not clear, please present groups in more comprehensible way.

   Response:

   We have already removed the "X vs Y" statement from table 2. Basically, the meaning of x and y previously was to explain the comparison between each groups (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). It shown in manuscript line 155-164.

REVIEWER 2

It would be useful to supplement the discussion with electrophysiological findings (ERG) after SO application → Invest Ophthalmol Vis Sci. 1988 Dec;29(12):1881-4.

Response:

Thank you for your kind suggestion and information, we agree to your suggestion that ERG examination after silicone oil removal is may increase the value of this study, but unfortunately, we did not perform the ERG examination due to the lack of equipment facility in our hospital.
So, we added the ERG information in our discussion section (manuscript line 288-294).

REVIEWER 1

Comments on the article: Changes in the retinal nerve fiber layer after intraocular tamponade with silicone oil in rhegmatogenous retinal detachment.

1. The work analyzes preoperative ocular variables and after silicone oil removal; in addition to measuring intraocular pressure, best corrected visual acuity, macular thickness, and nerve fiber layer thickness; The clinical characteristics of rhegmatogenous retinal detachments should be included for analysis, such as their location, extension, macular involvement, anteroposterior diameter of the eye, and mechanism of production of the detachment, since these factors could modify the outcome of the variables studied.

   Response:

   Thank you for your kind suggestion, our study did not measure the clinical characteristic of the RRD as mention above, because some of the characteristics already became our exclusion criteria. We realized that BCVA outcome is closely related to status of macula. Unfortunately, this study did not measure the relation between macular status on the baseline (pre-op) with the visual outcome. The purpose of our study is just to assess RNFL thickness changes in rhegmatogenous retinal detachment patients using SO tamponade and subsequent its removal, so we excluded any unrelated conditions that may cause bias for the measurement of RNFL thickness such as that have macular off or any kind of involvement of macula, traumatic history, etc (manuscript line 98-101 and 108-116) .

2. What was the medical criteria to indicate the removal of intraocular silicone oil?

   Response:

   The criteria for oil removal in our study were:

   1. Complete retinal attachment
   2. Any signs of silicone oil emulsification

   These statements are already written in our main manuscript line 117-120.

3. What clinical characteristics did the patients treated with silicone for more than 6 months have?

   Response:

   Decision for silicone oil removal based on the reattachment status of the retina. Most of patients were removed SO less than 6 months, but some of patients have prolong SO removal due to covid-19 lockdown regulation.