· Clinical Research ·

Outcomes and predictors of vitrectomy and silicone oil tamponade in retinal detachments complicated by proliferative vitreoretinopathy

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Abstract

● **AIM:** To evaluate outcomes and determine factors influencing the outcomes of vitrectomy with silicone oil (SO) endotamponade for the management of rhegmatogenous retinal detachment (RRD) complicated by advanced proliferative vitreoretinopathy (PVR).

● **METHODS:** This is a retrospective, interventional case series of eyes with PVR grade C associated RRD with or without prior surgery that underwent vitreoretinal surgery and SO tamponade. Eyes with a minimum follow-up of 6mo after SO extraction were included. Eyes were classified into three PVR subgroups according to severity and extension of proliferation. The influence of several preoperative, intraoperative and postoperative factors upon the functional and anatomical outcomes was assessed using multivariate logistic regression analysis.

● **RESULTS:** A hundred and one eyes of 101 patients that met the inclusion criteria were studied. Seventy-five of 101 eyes (74.3%) had successful retinal reattachment after one operation. Increased aqueous cell and flare at the first week exam had a statistically significant association with redetachment, recurrent membrane proliferation and keratopathy. Visual acuity improvement was significantly associated with faint postoperative aqueous inflammation values, primary vitrectomy and PVR outside of the posterior pole.

● **CONCLUSION:** Although encouraging anatomical and functional outcomes are achieved after vitrectomy and SO tamponade in eyes with RRD complicated by PVR, an increase in aqueous flare or cells at the first week follow-up is most likely to result in postoperative late complications. Primary vitrectomy, PVR associated with minimal posterior pole extension and absent to mild postoperative aqueous inflammation are associated with improved post-operative final visual acuity.

● **KEYWORDS:** proliferative vitreoretinopathy; aqueous inflammation; silicone oil tamponade; vitrectomy; predictors

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INTRODUCTION

Rhegmatogenous retinal detachments (RRD) are managed with a variety of methods and the success rate for primary repair is over 80%[1-3]. The major cause of failure in retinal detachment repair is proliferative vitreoretinopathy (PVR)[4-5]. The key factor triggering PVR development seems to be partial dedifferentiation, migration, and proliferation of retinal pigment epithelial (RPE) cells, resulting in the formation of fibrocellular membrane[5-7]. The formation of these membranes may lead to traction on both surfaces of the retina and cause fixed retinal folds, new retinal breaks and re-opening of treated breaks. PVR occurs postoperatively in 5%-10% of all RRD[8-9]. It usually occurs after surgical repair or after penetrating ocular trauma, but it may occur in a significant number of untreated eyes with retinal detachment[10-11].

In this study, we examined the anatomical and functional outcomes and complications of vitreoretinal surgery with silicone oil (SO) endotamponade in a series of patients with advanced PVR associated with RRD. We also assessed the influence of several preoperative, intraoperative and postoperative factors upon the functional and anatomical outcomes. To the best of our knowledge, this is the first study evaluating the effects of postoperative aqueous inflammation values on functional outcomes in patients undergoing vitrectomy for PVR-associated RRD.

SUBJECTS AND METHODS

Ethical Approval This study was approved by the Ethics Committee of Ankara Research and Training Hospital, Turkey. The authors are responsible for the content and writing of the papers. Before surgery, informed consent was obtained from each patient following an explanation of the vitrectomy procedures and potential adverse effects of the procedure. For the retrospective study, formal consent is not required. This paper was written in accordance with the 1964 Declaration of Helsinki and its later amendments. Clinical and operative records of patients undergoing 23 or 25-gauge pars plana vitrectomy (PPV) with SO endotamponade for RRD complicated by PVR at Ulucanlar Eye Training and Research Hospital, University of Health Science, between April 2008 and April 2017 were reviewed after the Institutional Review Board had approved the study.

Study Design and Patient Selection Eyes with PVR greater than grade CP1 (C: grade, P: posterior, 1: 1 quadrant) and/or CA1 (C: grade, A: anterior, 1: 1 quadrant) with or without prior vitrectomy surgery were included in the study. The PVR grading in this series followed the Silicone Study Classification System[12]. The eyes were classified into 3 subgroups. Group 1 consisted of eyes with grade C PVR, with total proliferation that extended more than one quadrant anterior to the equator and equal to or less than one quadrant posterior to the equator (>CA1+≤CP1). Group 2 included eyes with grade C PVR in which the total proliferation extended more than one quadrant posterior to the equator and equal to or less than one quadrant anterior to the equator (>CP1+≤CA1). Group 3 had grade C PVR with total proliferation that extended more than one quadrant both anterior and posterior to the equator (>CA1+>CP1). Patients with a minimum of 6mo follow-up after SO extraction were included in the analysis. Patients with a history of trauma, recurrent uveitis, proliferative diabetic retinopathy, RRD attributable to retinopathy of prematurity and eyes that had gas as long-term tamponade after surgery were excluded.

Functional success was defined as at least 3 lines improvement in best-corrected visual acuity (BCVA) or defined as a visual acuity of 20/400 or better. Anatomic success was defined as complete retinal attachment posterior to the buckle or edge of the retinectomy for a minimum of 6mo after SO removal. If the retina redetached after single operation, then the anatomic success rate of the subsequent surgical intervention was also assessed.

Pre-operative, Intra-operative, and Post-operative Parameters and Measurements Pre-operative data obtained including age, gender, symptoms, BCVA, number of previous vitreoretinal surgeries, presence of an encircling scleral buckle, extent and location of the RRD (quadrant), macular status (macula attached/detached), and grade of PVR. Surgical data obtained including placement of an encircling scleral buckle, and relaxing retinectomy. Post-operative variables examined were anatomic status of the retina, final BCVA, number of lines of visual improvement, intraocular pressure (IOP), recurrent membrane proliferation either in the posterior pole or in the periphery, corneal findings and the presence of cells or flare in the anterior chamber.

The numbers of cells in the anterior chamber were counted and graded at the 1×1 mm^2 slit beam according to the Standardized Uveitis Nomenclature (SUN) schema at the first postoperative week examination as follows: Grade 0: no cell, grade 0.5+: 1-5 cells, grade 1+: 6-15 cells, grade 2+: 16-25 cells, grade 3+: 26-50 cells, grade 4+: >50 cells[13]. Aqueous flare caused by increased protein count from breakdown of blood ocular barrier was graded by using a 1×1 mm^2 slit beam as follows: Grade 0: undetectable, grade 1+ (faint): just detectable, grade 2+ (moderate): iris and lens details clear, grade 3+ (marked): iris and lens details hazy and grade 4+ (intense): fibrin clot[13]. Increased IOP was defined as 25 mm Hg or greater, measured at any time during follow-up, as defined in the Silicone Study reports[14]. Chronic hypotony was defined as an IOP of 5 mm Hg or less on more than two visits greater than 1mo apart[15]. Corneal findings were taken into consideration after the one month follow-up and included stromal and epithelial edema, persistent corneal epithelial defects, pigmented keratic precipitates (KP) and corneal opacities including localized and band keratopathy.

Surgical Procedure In all cases, a standard three-port 23 or 25 gauge PPV using intraoperative perfluorocarbon liquid (PFCL) and subsequent with SO endotamponade (5000 centistokes) was performed by a single surgeon (Sonmez K). In addition to vitrectomy combined cataract surgery was also performed in patients with phakic eyes. An encircling scleral buckle (2.5 or 3.5 mm width silicone band) was placed in some eyes that did not flatten after meticulous membrane dissection. Relaxing retinotomies/retinectomies were performed in eyes with retinal shortening and in eyes with residual anterior membranes that were anticipated to lead to recurrent retinal detachment.

Statistical Methods We used multivariate logistic regression analysis to evaluate associations between preoperative, intraoperative, and early postoperative variables and late postoperative complications in all eyes and visual acuity in eyes with success after one operation. In order to compare preoperative and postoperative visual acuities, Snellen visual acuities with a skewed distribution were converted to a logarithmic scale (logMAR) to obtain a normal distribution.

Four postoperative complications (retinal detachment, keratopathy, recurrent membrane proliferation, and recurrent peripheral membrane proliferation) were included as dependent variables in the multivariate logistic regression analysis. Nine independent variables were included in the analysis: age, gender, primary vitrectomy versus vitrectomy after one or more previous failed vitrectomy surgeries, groups 1-3 as previously defined, retinal detachment involving less than or equal to 3 quadrants or greater than 3 quadrants, vitrectomy alone or vitrectomy with retinectomy, presence of an encircling scleral buckle versus nonbuckle, aqueous cells less than 2+ or ≥2+ at first postoperative week and aqueous flare less than 2+ or ≥2+ at first postoperative week. Age was treated as a continuous variable, while the others were treated as categorical variables. The associations between a similar set of independent variables and dependent variables including 3 or more visual acuity lines improvement and final visual acuity of 20/400 or better after one successful operation were evaluated with a multivariate logistic regression analysis. Since the number of lines improvement in visual acuity (logMAR) is a quantitative measurement, dichotomization may lead to a loss of information. Therefore, visual acuity was treated as a quantitative variable and the association between the number of lines improvement in visual acuity (logMAR) and the independent variables were evaluated further with a multivariate generalized linear model regression. Descriptive statistics were given as mean, range and standard deviation. The odds ratio (OR) and 95% confidence intervals (CI) were calculated for all of the categorical variables. Statistical analysis was conducted using the SAS software 9.0 (SAS, Cary, NC, USA). A *P*-value less than 0.05 was considered statistically significant.

RESULTS

One hundred and one eyes of 101 patients (50 females and 51 males) who met the inclusion criteria were included in the study. The mean age was 57.9±16.4y (range, 16-81). The mean duration of follow-up was 23.1±17.5mo (range, 7-79). Of 101 eyes, 75 (74.3%) developed PVR detachment after failed previous vitreoretinal surgery and 26 (25.7%) had preoperative PVR without prior surgery. For the eyes with failed prior surgery, the mean number of previous PPV was 1.84±0.5 (range, 1-3). All eyes had macula-involving retinal detachments encompassing more than 2 quadrants, and the extent of the detachments was greater than 3 quadrants in 77 eyes (76.2%). Among the 101 eyes, 45 (44.6%) eyes were in group 1 (>CA1+≤CP1), 37 (36.6%) eyes were in group 2 (≤CA1+>CP1) and 19 (18.8%) eyes were in group 3 (>CA1+>CP1). At the initial examination, 52 eyes were phakic, 49 eyes were pseudophakic (Table 1).

We placed an encircling scleral buckle during surgery in 17 eyes. Among the eyes with failed previous vitreoretinal surgery, 10 eyes (13.3%) had encircling scleral buckle. To relieve retinal contraction and to reattach the retina, we performed relaxing retinotomies/retinectomies in 24 (23.8%) of the 101 eyes.

Table 1 Clinical and demographic data of participants

Items	Data
Number of eyes	101
Gender (F/M)	50/51
Age (y)	57.9±16.4 (16-81)
Mean follow-up time (mo)	23.1±17.5 (7-79)
PVR status	
Previous vitreoretinal surgery (*n*)	75
Primary vitrectomy (*n*)	26
Number of previous vitrectomy	1.84±0.5 (1-3)
Detachment status	
≥2 quadrants	101
≥3 quadrants	77
Group	
1 (>CA1+≤CP1)	45 (44.6%)
2 (≤CA1+>CP1)	37 (36.6%)
3 (>CA1+>CP1)	19 (18.8%)
Lens status	
Phakic	52 (51.5%)
Pseudophakic	49 (48.5%)

CA1: Grade, Anterior, One quadrant; CP1: Grade, Posterior, One quadrant; F: Female; M: Male; PVR: Proliferative vitreoretinopathy.

We recorded anterior chamber cell and flare. At first week follow-up, 28 eyes (27.7%) had 2+ or greater anterior chamber cells, while 15 eyes (14.9%) had 2+ or greater anterior chamber flare.

SO was subsequently removed from eyes and patients were followed up for a minimum duration of 6mo after SO removal. The mean duration of silicone tamponade prior to removal was 4.9±2.2mo (range, 3-11mo).

We obtained long-term retinal reattachment in 75 eyes (74.3%) following a single PPV with SO tamponade operation and subsequent removal of SO (ROSO). In 26 eyes (25.7%), retinal redetachment occurred following ROSO with a mean period of 5.8±3.9wk (range, 1-14wk). The important causes of redetachment were a combination of newly diagnosed breaks associated with or without recurrent membrane formation in 10 eyes (38.5%), tractional membranes causing opening of the retinotomy site in 7 eyes (26.9%), re-opening of pre-existing retinal breaks from recurrent membranes in 5 (19.2%) eyes, and tractional detachments without breaks in 4 eyes (15.4%).

Twenty of the redetached patients underwent repeat vitrectomy with SO injection and 16 eyes (80%) were successfully reattached 6 or more months after ROSO. In the six remaining patients, 3 patients refused further operation, while we did not feel that three patients would benefit from further intervention due to severe macular ischemia with intrinsic retinal contraction and did not recommend surgery. The final retinal reattachment rate in this series was 90.1% (91 out of 101 eyes) after one or two surgeries.

The intra-operative, immediate and late post-operative complications are listed in Table 2. The most common intra-operative complication was bleeding from the retinectomy site (11.9%) which was easily controlled by raising the infusion pressure and diathermizing the offending tissue. The most common postoperative complication was recurrent membrane proliferation, seen in 34 eyes (33.7%) and followed by redetachment (25.7%) and keratopathy (21.8%), respectively.

Preoperative, intraoperative and early postoperative variables were analyzed with multivariate logistic regression to assess whether they were associated with four complications: retinal re-detachment, recurrent membrane formation, recurrent peripheral membrane formation and keratopathy (Table 3). There was no significant difference in the prevalence of these four post-operative complications among the three PVR groups. Eyes that underwent retinectomy were more likely to develop recurrent membrane formation (P=0.025; OR, 9.12; 95%CI, 1.41-21.30). Among the 34 eyes developing recurrent membrane formation, 16 (47%) eyes were treated with relaxing retinectomy. Also, there was a statistically significant association between the eyes that underwent relaxing retinectomy and peripheral membrane formation (P=0.0019; OR, 17.88; 95%CI, 3.03-52.21). Among the 26 eyes having peripheral membrane formation, 17 eyes (65.4%) underwent relaxing retinectomy. The presence of greater than or equal to 2+ cells in anterior chamber at the first-week exam was significantly associated with four following complications; retinal redetachment (P=0.0025; OR, 12.85; 95%CI, 2.72-65.51), recurrent membrane formation (P=0.012; OR, 7.28; 95%CI, 2.16-24.01), peripheral membrane formation (P=0.007; OR, 7.99, 95%CI, 1.96-32.18) and keratopathy (P=0.004; OR, 8.92; 95%CI, 2.11-34.24). There were 28 eyes (27.7%) with 2+ or greater cells at the first week examination. In addition, if the presence of aqueous flare was greater than or equal to 2+ at the first week examination, the vitreoretinal surgery was significantly associated with similar late postoperative complications: retinal re-detachment (P=0.0032; OR, 12.53; 95%CI, 3.33-61.32), recurrent membrane formation (P=0.012; OR, 5.75; 95%CI, 1.44-24.91), peripheral membrane formation (P=0.019; OR, 4.48; 95%CI, 1.18-16.92) and keratopathy (P=0.005; OR, 7.35; 95%CI, 2.04-36.91) respectively.

Visual acuity improvement was evaluated in 75 eyes with long-term retinal reattachment following one operation. The mean follow-up of these eyes was 18.4±16.9mo (range, 8-79). Pre-operative and post-operative BCVA at final follow-up data is shown in Figure 1. Postoperative visual acuity was between hand motion and 20/25. BCVA was improved in 69 eyes (92%), remained the same in 6 eyes (8%). BCVA was equal to or better than 20/400 in 48 eyes (64%) with reattached retinas. At the final post-operative visit, 50 eyes (66.7%) had an increase 3 or more lines. There was a noticeable difference in visual acuity improvement between eyes in group 1 and eyes in group 3 (Figure 2). Among the 50 eyes that showed three or more lines

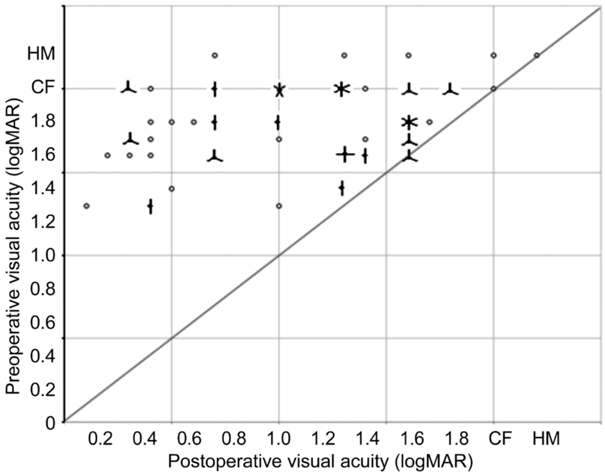

Figure 1 Conventional sunflower plot of logMAR visual acuity in successfully attached eyes Presenting visual acuity is compared to postoperative visual acuity at the final follow-up available for each eye. CF: Counting fingers; HM: Hand motion; Each sunflower petal represents one eye.

Table 2 Intraoperative, immediate and late postoperative complications

Complications	*n* (%)
Intraoperative	
Hemorrhage at the retinotomy site	12 (11.9)
Subretinal PFCL	4 (3.9)
Postoperative	
REMP	
Peripheral retina	19 (18.8)
Epimacular	8 (7.9)
Epimacular + peripherial	7 (6.9)
Redetachment	26 (25.7)
Keratopathy	
Edema	11 (10.9)
FKP	5 (4.9)
PCED	3 (3)
Opacity	2 (2)
Opacity and edema	1 (1)
IOP increase	11 (10.9)
Hypotony[a]	6 (5.9)
SO in A/C	5 (4.9)
CME	2 (2)
Optic nerve atrophy	1(1)

[a]Among the eyes successfully attached at the final follow-up. A/C: Anterior chamber; CME: Cystic macular edema; FKP: Fine pigmented keratic precipitates; IOP: Intraocular pressure; PCED: Persistent corneal epithelial defects; PFCL: Perfluorocarbon Liquid; REMP: Recurrent epiretinal membrane proliferation; SO: Silicone oil.

Table 3 Preoperative, intraoperative and early postoperative parameters and their relationship to development of redetachment, recurrent membrane proliferation, recurrent peripheral membrane proliferation, and keratopathy after pars plana vitrectomy and SO injection

Parameters	*n*=101	Redetachment			Recurrent membrane proliferation			Peripheral membrane proliferation			Kerathopathy		
		n (%)	OR (95%CI)	*P*	*n* (%)	OR (95%CI)	*P*	*n* (%)	OR (95%CI)	*P*	*n* (%)	OR (95%CI)	*P*
Age (y)		NA	NA	0.90	NA	NA	0.20	NA	NA	0.09	NA	NA	0.23
Gender			0.47 (0.12, 1.87)	0.29		1.13 (0.37, 3.50)	0.83		0.80 (0.22, 2.86)	0.44		0.65 (0.22, 2.16)	0.72
Male	51	14 (27)			19 (37)			15 (29)			10 (20)		
Female	50	12 (24)			15 (30)			11 (22)			12 (24)		
Retinectomy			0.99 (0.17, 5.59)	0.99		9.12 (1.41, 21.30)	0.025		17.88 (3.03, 52.21)	0.0019		0.45 (0.11, 1.77)	0.25
Yes	24	7 (29)			16 (67)			17 (71)			7 (29)		
No	77	19 (25)			18 (23)			9 (12)			15 (19)		
No. of previous surgeries			0.28 (0.14, 1.73)	0.22		0.54 (0.17, 1.76)	0.31		0.39 (0.11, 1.39)	0.15		2.35 (0.58, 3.18)	0.08
>1	75	19 (25)			25 (33)			19 (25)			19 (25)		
Primary vitrectomy	26	7 (27)			9 (35)			7 (27)			3 (12)		
Preoperative PVR													
CA>1 & CP≤1 (group1)	45	11 (24)	1.02 (0.05, 6.97)	0.79[a]	13 (29)	1.01 (0.02, 7.88)	0.86[a]	10 (22)	1.01 (0.01, 5.43)	0.65[a]	8 (18)	1.72 (0.21, 3.03)	0.36[a]
CA≤1 & CP>1 (group2)	37	9 (24)	1.78 (0.33, 9.45)	0.50[b]	12 (32)	1.51 (0.39, 5.84)	0.55[b]	10 (27)	1.52 (0.28, 6.85)	0.51[b]	9 (24)	1.81 (0.61, 3.12)	0.28[b]
CA>1 & CP>1 (group3)	19	6 (32)	1.03 (0.18, 5.89)	0.98[c]	9 (47)	1.20 (0.30, 4.79)	0.80[c]	6 (32)	1.21 (0.26, 4.01)	0.78[c]	5 (26)	0.98 (0.51, 1.83)	0.65[c]
Size of detachment (quadrants)			0.51 (0.11, 2.35)	0.19		0.58 (0.18, 1.83)	0.35		1.01 (0.36, 3.28)	0.85		1.53 (0.45, 5.14)	0.49
>3	77	19 (25)			25 (32)			19 (24)			17 (22)		
≤3	24	7 (29)			9 (38)			7 (29)			5 (21)		
Presence of cell after surgery in A/C			12.85 (2.72, 65.51)	0.0025		7.28 (2.16, 24.01)	0.012		7.99 (1.96, 32.18)	0.007		8.92 (2.11, 34.24)	0.004
≥2 cells	28	17 (61)			18 (64)			17 (61)			14 (50)		
<2 cells	73	9 (12)			16 (22)			9 (12)			8 (11)		
Aqueous flare			12.53 (3.33, 61.32)	0.0032		5.75 (1.44, 24.91)	0.012		4.48 (1.18, 16.92)	0.019		7.35 (2.04, 36.91)	0.005
≥2	15	11 (73)			11 (73)			12 (67)			11 (73)		
<2	86	15 (17)			23 (27)			24 (30)			11 (13)		
Scleral buckle placement			0.57 (0.16, 2.02)	0.38		0.58 (0.21, 1.58)	0.89		0.88 (0.25, 1.89)	0.72		1.64 (0.49, 4.06)	0.16
Yes	27	6 (22)			9 (33)			6 (22)			8 (30)		
No	74	20 (27)			25 (34)			20 (27)			14 (19)		

CA1: Grade, anterior, one quadrant; CP1: Grade, posterior, one quadrant; CI: Confidence interval; OR: Odds ratio; PVR: Proliferative vitreoretinopathy; SO: Silicone oil. [a]Comparison between group 1 *vs* group 2, [b]comparison between group 1 *vs* group 3, [c]comparison between group 2 *vs* group 3.

Table 4 Preoperative, intraoperative and early postoperative parameters and their relationship to functional outcomes in the 75 eyes with successfully reattached retinas after a single pars plana vitrectomy and SO injection

Parameters	*n*=75	≥3 lines improvement in logMAR			Snellen VA≥20/400			No.of lines improvement on logMAR, *P*
		n (%)	OR (95%CI)	*P*	*n* (%)	OR (95%CI)	*P*	
Age (y)		NA	NA	0.43	NA	NA	0.33	0.56
Gender			0.72 (0.14, 3.27)	0.69		0.88 (0.21, 5.18)	0.94	0.96
Male	37	27 (73)			26 (70)			
Female	38	23 (61)			22 (58)			
Retinectomy			3.29 (0.32, 12.38)	0.16		2.18 (0.33, 10.94)	0.38	0.24
Yes	17	11 (65)			11 (65)			
No	58	39 (67)			37 (64)			
No. of previous surgeries			5.76 (0.65, 17.89)	0.04		4.63 (0.57, 15.96)	0.05	0.03
≥1	19	13 (93)			12 (86)			
Primary vitrectomy	56	37 (65)			36 (63)			
Preoperative PVR								
CA>1 & CP≤1 (group 1)	33	29 (87)	1.38 (0.26, 16.02)	0.26[a]	28 (85)	1.11 (0.09, 13.82)	0.37[a]	0.43[a]
CA≤1 & CP>1 (group 2)	29	16 (55)	12.28 (1.26, 98.15)	0.028[b]	15 (52)	9.67 (0.93, 95.03)	0.035[b]	0.02[b]
CA>1 & CP>1 (group 3)	13	5 (38)	1.41 (0.19, 13.72)	0.22[c]	5 (38)	1.29 (0.16, 15.00)	0.33[c]	0.80[c]
Size of detachment (quadrants)			1.44 (0.34, 6.31)	0.56		2.08 (0.44, 9.80)	0.35	0.33
>3	58	39 (67)			38 (66)			
≤3	17	11 (65)			10 (59)			
Aqueous cell			9.06 (0.97, 21.7)	0.014		4.9 (1.03, 14.3)	0.044	0.06
≥2 cells	11	4 (36)			5 (46)			
<2 cells	64	46 (72)			43 (67)			

CA1: Grade, anterior, one quadrant; CP1: Grade, posterior, one quadrant; CI: Confidence interval; OR: Odds ratio; PVR: Proliferative vitreoretinopathy; SO: Silicone oil. [a]Comparison between group 1 *vs* group 2, [b]comparison between group 1 *vs* group 3, [c]comparison between group 2 *vs* group 3.

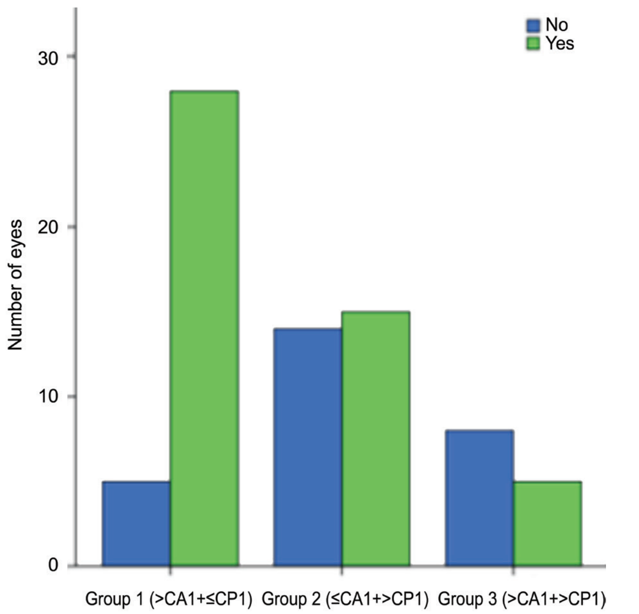

Figure 2 Eyes showing 3 or more lines (logMAR) improvement in visual acuity for the three PVR groups in the successfully reattached eyes after a single vitreoretinal surgery.

of visual improvement, 29 (58%) were in group 1, 16 (32%) were in Groups 2 and 5 (10%) were in Group 3.

To evaluate the visual acuity improvement, the association between the similar independent variables and visual acuity improvement was examined in 75 eyes (Table 4). Multivariate logistic regression revealed that three or more lines improvement in vision (logMAR) was significantly more frequent in Group 1 eyes compared with Group 3 eyes (*P*=0.028; OR, 12.28; 95%CI, 1.26-98.25). In addition, the percentage of eyes with a visual acuity of equal to or better than 20/400 and number of lines improvement in vision after surgery were also significantly higher in Group 1 eyes compared with Group 3 eyes (*P*=0.035; OR, 9.67; 95%CI, 0.93-95.03 and *P*=0.02, respectively).

Eyes with the postoperative aqueous cell of grade <2+ at the first-week exam were significantly more likely have postoperative BCVA≥20/400 (*P*=0.044; OR, 4.9; 95%CI, 1.03-14.3) and three or more lines improvement in vision (*P*=0.014; OR, 9.06; 95%CI, 0.97-21.7). Also, there was a trend among eyes that had less than grade 2+ aqueous cells toward having more logMAR lines improvement (*P*=0.06).

By examining the number of lines improvement in vision and three or more lines improvement in vision after multivariate generalized linear model regression analysis, the eyes that underwent primary vitrectomy responded to surgery significantly better than the eyes with failed prior vitreoretinal surgery (*P*=0.04; OR, 5.76; 95%CI, 0.65-17.89 and *P*=0.03, respectively). Also, there was a trend among eyes that underwent primary vitrectomy toward having a visual acuity of 20/400 or better (*P*=0.05; OR, 4.63; 95%CI, 0.57-15.96).

DISCUSSION

SO has been commonly used as an intraocular tamponade in the management of complex retinal detachments due to severe PVR. Although the Silicone Study concluded that the effectiveness of the SO is roughly equivalent to perfluoropropane (C_3F_8) gas in the management of the retinal detachment with severe PVR[14], in some conditions such as in eyes with severe anterior PVR and in eyes undergoing retinectomy, eyes treated with SO achieved better anatomical and functional success[16-17].

Surgical reattachment rate for PVR-associated retinal detachment repair varies between studies. In the present study, recurrent retinal detachment developed in 26 of 101 eyes (25%) post-operatively after a single surgery. Our reattachment rate was 75% after a single operation and 91% following one or two operations. In 1985, McCuen *et al*[18] examined a series of 44 eyes with recurrent retinal detachment and severe PVR, and found that 48% were reattached after one operation and 64% were reattached after multiple re-operations. In their study, more than half of the eyes (52%) included had either a narrow or closed funnel, which was higher than in our series. In addition to the differences in preexisting proliferations of the included eyes between the two studies, advances in the surgical techniques and instrumentation over the last twenty years likely may also play a role in the different outcomes between studies. Recently, Narala *et al*[19] reported anatomical success in 84.3% of eyes that underwent repeat PPV after failed previous surgery for PVR-associated retinal detachment and was comparable to our study, presenting rates of 91% after multiple re-operation. Similarly, Tranos *et al*[20] reported final complete anatomical success rate as 84% in eyes that underwent repeat PPV after failed previous surgery for PVR-associated retinal detachment. In contrast to our study, they studied only the eyes with recurrent retinal detachment after vitrectomy for PVR[18-20]. Recently, Lumi *et al*[21] reported anatomical success in 92% of eyes that underwent primary PPV for the treatment of PVR-associated retinal detachment. More recently, Foveau *et al*[22] reported anatomical success in 95% of eyes that underwent vitrectomy for primary macula off retinal detachment complicated by PVR. Thus, most of the recent published studies reported their final retinal reattachment rates roughly similar although there were some differences in the PVR severity of the studied eyes between the studies.

In this present study, we assessed the anatomical success of eyes undergoing primary PVR surgery and the eyes that underwent vitrectomy for PVR-associated retinal detachment after history of failed vitrectomy. We found a reattachment rate of 73% and 75% of eyes that underwent a primary vitrectomy and eyes that had already undergone at least one vitrectomy for PVR-associated retinal detachment, respectively, and no significant difference in the recurrent retinal detachment rate was found between two groups. Our findings are consistence with those reported by the Silicone Study Group[23]. The Silicone Study Group also assessed the anatomical success of eyes undergoing primary PVR surgery and the eyes that underwent vitrectomy for PVR-associated retinal detachment after history of failed vitrectomy[23]. They found a reattachement rate of 64% and 61% of eyes that underwent SO tamponade in both groups, respectively and there was no significant difference in achieving complete retinal reattachment or observing recurrent retinal detachment between two groups. Similarly, Narala *et al*[19] found no significant difference between the successful and unsuccessful groups regarding the number of total operations. In contrast to these studies, Falkner *et al*[24] found a mean of total operations in the redetached group higher than in the attached group. These conflicting results between the studies may be explained by differences in studied eyes or in residue immature membranes leading to a higher rate of reproliferation and recurrent detachment following the surgery.

In the present study, our retinal detachment rate after ROSO was 25.7% and nearly half of these redetachments occurred within the first 3mo. Falkner *et al*[24] reported a similar result in which the retinal redetachment after ROSO mainly occurred within 3mo with a rate of 16.5%. In the present study, new retinal breaks associated with or without reproliferation is found to be the major factor for detachment after ROSO. Heimann *et al*[25] also reported that the major cause for recurrent retinal detachment was the development of new breaks in eyes with retinal detachment after vitrectomy. While their findings were consistent with this study, their group studied only the eyes with primary retinal detachment.

IOP abnormalities are a common postoperative complication in eyes that have undergone vitrectomy for PVR and the rates of hypotony vary between 3.5% and 39%[14,18-19,26]. In the present study, hypotony occurred in 6% of the eyes, which was similar to the Silicone Study Group which also had hypotony in 7% of eyes[14]. Similarly, Narala *et al*[19] and Falkner *et al*[24] reported their hypotony rate as 5.8% and 3.5%, respectively, after

ROSO. In contrast to these lower reported rate of hypotony, the incidence of hypotony was over 18% in some other studies[18,26]. Likely, the differences in the severity of anterior PVR in the studied eyes, study groups, definition of hypotony and surgical success between the studies may account for these variable hypotony rates.

To evaluate the role of the breakdown of blood-aqueous barrier in the recurrence of the proliferation, we evaluated the anterior chamber reaction at one week of surgery. Since Shah and Spalton[27] reported an increase in either flare and cells or flare alone during the first postoperative week, which was associated with a delayed recovery of the blood-aqueous barrier, we evaluated the activity of the anterior chamber inflammation at the postoperative week 1. Significant reaction which was the presence of flare ≥2+ or aqueous cells ≥2+ likely paralleled blood-ocular breakdown. We observed that eyes with postoperative flare ≥2+ and aqueous cells ≥2+ were significantly associated with development of recurrent and peripheral membrane formation. It was reported that flare in the aqueous was significantly higher in eyes with grade B and grade C PVR (PVR-C) than in eyes without significant PVR (non-PVR and PVR-A)[28]. Total protein concentration in the vitreous was investigated in eyes with retinal detachment and higher vitreous protein levels were found in eyes with PVR[29]. Our result is accordance with those reported by Mudler *et al*[30] showing a significant association between the higher flare values at both 2 and 6wk postoperatively and the development of postoperative PVR in eyes undergoing PPV for RRD. Recently, Narala *et al*[19] reported a significant association between the preoperative flare of grade ≥2+ and postoperative failure in eyes undergoing vitrectomy for PVR. Also, Young-Zvandasara *et al*[31] reported that both preoperative and postoperative PVR occurred frequently in uveitis eyes with rhegmatogenous retinal detachment. The breakdown of the blood-ocular barrier may allow the invasion of macrophages and cytokines into the vitreous cavity contributing to the proliferation and metaplasia of the RPE cells, resulting in the development of PVR[6]. In an experimental animal study, Baudouin *et al*[32] demonstrated that the existence of inflammation preceded cell proliferation and migration, and had a role in PVR. As inflammatory cells such as macrophages and lymphocytes are involved in PVR development[6-7], examination of the anterior chamber might be a predictive factor for proliferation in retinal detachment cases after the vitreoretinal surgery. Indeed, both postoperative flare ≥2+ and aqueous cells ≥2+ were significantly associated with recurrent and peripheral membrane proliferation and possible treatment intervention with potent anti-inflammatory medication at this point may also decrease the risk of complications associated with blood ocular breakdown.

Since all eyes in this study had a preoperative Grade C PVR involving one or more quadrants at least anteriorly or posteriorly, we could evaluate the postoperative recurrence of PVR instead of the role of early PVR development. In our series, postoperative recurrent membrane proliferation developed in 34 eyes: 13 of the 45 eyes (29%) in Group 1, 12 of the 37 eyes (32%) in Group 2 and 9 of the 19 eyes (47%) in Group 3. Although the postoperative proliferation rate was higher in group 3 PVR eyes, we did not find a significant association for development of postoperative PVR among three PVR groups. Similar to the findings reported previously by Kon *et al*[29], the postoperative PVR recurrence rate was seen higher in more advanced cases (Group 3) in this study. Indeed, it is not unexpected to observe the postoperative membrane proliferation more frequent in advance PVR cases, as the excessive surgical procedures which may induce breakdown of the blood-ocular barrier is necessitated for reattaching the retina in these eyes. In addition, as the pre-operative PVR was often severe, a retinotomy/retinectomy was needed to reattach the retina in 24% of our cases. We also found recurrent membrane reproliferation (peripheral and macular) was significantly more frequent in eyes undergoing retinectomy than eyes not undergoing retinectomy. Areas of quiescent RPE exposed to the vitreous cavity increase the chance for membrane proliferation[7]. Also, as the inflammatory mediators and RPE cells are likely to be higher in the remaining fluid of eyes that undergo retinotomy, a higher rate of peripheral membrane proliferation would be expected. In corresponding to this hypothesis, in the present study, the development of postoperative membrane proliferation at the peripheral retina was found to be significantly prevalent in the eyes undergoing retinectomy than the eyes not undergoing retinectomy.

In the present study, we found that the visual outcomes were worse in eyes undergoing vitrectomy for PVR-associated retinal detachment after failed previous vitrectomy than in the eyes undergoing primary vitrectomy. This is in keeping with previous studies, indicating that the number of previous surgeries was associated with decreased visual outcome and decreased improvement in the BCVA in eyes undergoing vitrectomy for RRD[4,33]. In our current study, the visual outcome in eyes with anatomical success after the first vitrectomy operation was significantly better as was also found in the National Eye Institute (NEI) SO Studies[23,34]. The cell death in the photoreceptor cell layer is likely to be a significant factor in visual recovery after reattachment[35-36] and recurrent retinal detachment induces higher level of photoreceptor cell loss compared to primary retinal detachment[37]. Thus, poorer visual prognosis is expected in eyes requiring multiple vitrectomy surgery to achieve reattachment. In contrast to these findings, Pournaras *et al*[38] reported that there was no effect of multiple surgeries on visual outcome. However, Pournaras *et al*[38] found that the existence of PVR worsened the visual outcome. Since the existence of PVR not only affects the success rates of further surgery but also disrupts the retinal architecture[39], finding a significant deterioration in visual acuity after repeat retinal detachment surgery due to PVR is not surprising.

Corneal abnormalities induced by pars plana vitrectomy and SO use were defined as epithelial and/or stromal edema, corneal opacity including localized or band keratopathy and corneal epithelial defects in most of the studies[40-41]. In this study, in addition to these corneal abnormalities, eyes having keratic precipitates postoperatively were also included in the keratopathy group as the increasement of aqueous protein concentration was observed in eyes that underwent vitrectomy, which indicates that the blood-aquoeus barrier function was disturbed after surgery due to mechanical damage and/or thermal injury[42]. Similarly, in a study reported by Narala *et al*[19], corneal changes including corneal edema, band keratopathy, corneal striae, superficial punctate keratitis, endothelial pigment, or corneal opacification were defined as corneal abnormality in eyes that underwent repeat PPV after failed previous surgery. Keratopathy occurred in 22% of eyes in this study, which was similar to previous studies[34,40]. However, lower incidences of keratopathy were reported in other studies[24,43]. Differences in the severity of PVR, operative techniques to reattach the retina and criteria used to define corneal abnormality between studies might lead to these different rates. In our study, the presence of aqueous cell and flare, graded equal or greater than 2+ at the first postoperative week were found to be significantly associated with presence of the corneal abnormalities. Similarly, the Silicone Study Group reported a significant association between the presence of aqueous cells grade 3+ or greater and the occurrence of keratopathy[40]. They also showed marginal significance between the presence of aqueous flare 3+ or greater and the development of keratopathy. This association might be due to an increase at the levels of inflammatory cytokines inducing apoptosis of corneal endothelial cells[44-45] and/or increase at the levels of fibrin and fibrin associated factors causing corneal endothelial cell damage[46].

There are some limitations to this study. First, the major limiting factor of our study was its retrospective nature. Therefore, the method and contents of documentation could not be standardized as prospective nature. However, inconsistency in documentation may lessen due to the fact that all the operations and follow-up examinations were performed by a single ophthalmologist. Second, we had relatively small sample sizes (101 eyes with PVR-associated RRD and 75 eyes with successfully reattached retinas after one operation), which may be underpowered to detect the significant difference with a larger sample size. Third, the duration of surgeries that may contribute to the development of postoperative inflammation may need to be considered in the analysis. However, duration of surgery was not available in patients' charts. Another drawback of this study is that SUN grading scheme used for the evaluation of anterior chamber cells and flare remains subjective with large intra-observer and inter-observer variations. Finally, duration of retinal detachment, presence of preoperative inflammation, and general medical conditions such as diabetes mellitus and hypertension that may also contribute to the development of postoperative complications also need to be considered in the analysis. However, since reliable assessment of these factors are not always possible in a retrospective study, they were not included in the analysis.

In conclusion, although encouraging anatomical and functional outcomes were achieved after vitrectomy and SO tamponade in eyes with RRD complicated by PVR, an increase in aqueous flare or cells at the first week follow-up seems to be a significant finding influencing the chance for postoperative success. Likely the breakdown of the blood-aqueous barrier resulted in increased cell and flare and was related to several late postoperative complications such as redetachment, recurrent membrane proliferations and keratopathy. Primary vitrectomy, PVR associated with minimal posterior pole extension, and absent to mild postoperative aqueous inflammation seem to have a favorable influence on the visual acuity improvements in the successfully attached eyes. Further studies including large sample size will be needed to validate these results.

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