• Clinical Research •

Comparison of persistent submacular fluid in different preoperative macular status after vitrectomy for rhegmatogenous retinal detachment

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Abstract

• AIM: To compare the incidence of persistent submacular fluid (SMF) and visual outcome after pars plana vitrectomy (PPV) for rhegmatogenous retinal detachment (RRD) in different preoperative macular status according to optical coherence tomography (OCT).

• METHODS: A non-randomized, retrospective review was performed for patients who underwent successful PPV for RRD. OCT exams were taken preoperatively and 1mo after surgery, until SMF disappeared. According to the preoperative macular status on OCT, patients were divided into two groups: macula-off RRD (Group A) and macula-on RRD (Group B). In Group A, there were two subgroups: macula partly detached (Group A1) and macula totally detached (Group A2). The main outcome measures were the presence of SMF on OCT 1mo after surgery, and the preoperative and postoperative best corrected visual acuities (BCVA), among the different groups and depending on the presence or absence of persistent SMF.

• RESULTS: A total of 139 eyes of 139 patients were included in the study. Persistent SMF at 1mo after surgery was 15.8% (22/139), all occurring in Group A (22/101); Group B had no SMF at 1mo after surgery (0/38, *P*=0.002). The incidence of persistent SMF at 1mo after surgery in Group A1 was 50% (14/28), and in Group A2 was 11.0% (8/73, *P*<0.001). Significant differences were shown between the presence and absence of persistent SMF on foveola-off RRD, the preoperative BCVA, the 1mo postoperative BCVA, and the degree of the BCVA improvement from 1mo postoperatively to the final follow-up (*P*<0.05). However, there were no significant differences in the final BCVA (*P*>0.05).

• CONCLUSION: Persistent SMF after PPV for retinal detachment is associated with preoperative macular status. Macula-uninvolving RRD shows no persistent SMF after PPV. Macular partly detached RRD has a higher incidence of SMF than macula totally detached RRD after PPV. The persistence of SMF may be responsible for the delayed visual recovery, whereas there were no significant differences in the final visual acuity.

• KEYWORDS: submacular fluid; rhegmatogenous retinal detachment; optical coherence tomography; vitrectomy; macula

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INTRODUCTION

Optical coherence tomography (OCT) is a useful noninvasive tool for detecting macular pathologic features, many of which cannot be seen on clinical examination[1]. Subclinical submacular fluid (SMF) has often been identified on OCT and was shown to persist for months (up to 18mo) after successful retinal detachment (RD) surgery, without being recognized by ophthalmoscopy or fluorescein angiography[2-8]. Previous reports mainly studied patients undergoing scleral buckling (SB) procedures, with few about vitrectomy for RD[2,5,7].

The causes of the persistent SMF are still unclear. The incidence of the persistent SMF varies after pars plana vitrectomy (PPV). Wolfensberger and Gonvers[2] reported 24 patients who underwent PPV with no persistent SMF on OCT for 1mo after PPV. Benson *et al*[3] reported that in 100 patients who underwent PPV, 15 were found to have persistent subretinal fluid (SRF) on OCT at 6wk after surgery, and there were no significant differences in the persistence of SRF between the macula-on RD group and macula-off RD group after PPV. However, in Benson *et al*'s study[3], the preoperative macular status was defined by clinical examination alone, rather

than by OCT scan. And, no studies showed the relationship between macular status preoperatively and persistent SMF postoperatively.

The influence of persistent SMF on visual outcomes is still controversial. Recent studies[8-10] have showed that persistent SMF may delay the visual recovery, did not injury the final visual outcomes.

This study was undertaken to compare by OCT imaging the incidence of persistent SMF after primary PPV for rhegmatogenous retinal detachment (RRD) in different preoperative macular conditions, and to investigate the relationship between SMF and visual outcome.

SUBJECTS AND METHODS

A non-randomized, retrospective review was performed for patients who underwent successful PPV surgery for RRD in the Affiliated Eye Hospital of Wenzhou Medical College from June, 2012 to June, 2016. All investigations followed the tenets of the Declaration of Helsinki. Informed consents were obtained from the patients and subjects after explanation of the nature and possible consequences of the study.

Inclusions for analysis were restricted to: 1) patients who completed a follow-up examination at least six months postoperatively; 2) patients who completed OCT exam preoperative and 1mo postoperative. Exclusion criteria were: 1) patients with proliferative vitreoretinopathy (above C1); 2) patients with primary surgical failure; 3) patients with a history of ocular surgery, other than an uncomplicated cataract operation; 4) patients with a trauma history; 5) patients with a preexisting macular pathology, such as age-related macular degeneration, macular hole; 6) patients with a condition likely to influence retinal flattening after RRD surgery, such as epiretinal membrane, and combined traction detachment attributable to diabetes.

Patients underwent best corrected visual acuity (BCVA, the Snellen VA chart) assessment, anterior segment examination, and retinal examination with indirect and slit-lamp biomicroscopy using a Volk super field NC lens and OCT scan preoperative and 1mo after surgery. The 6×6-mm^2 radial line scan protocol was performed using Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany). Those patients who had an abnormality on OCT scan would undergo follow-up repeated check-up until the SMF disappeared. All the patients completed a follow-up examination at least six months postoperatively.

All surgeries were performed by an experienced retinal surgeon (Shen LJ). Perfluorocarbon was used or not after vitrectomy to flatten the detached retina. C3F8 or silicon was selected based on the surgeon's decision. All patients were required to be face down for 2wk at least postoperatively. If a visually significant cataract developed during the follow-up, cataract surgery would be performed. And the visual acuity (VA) at that point was adopted from the VA at 1mo after cataract surgery.

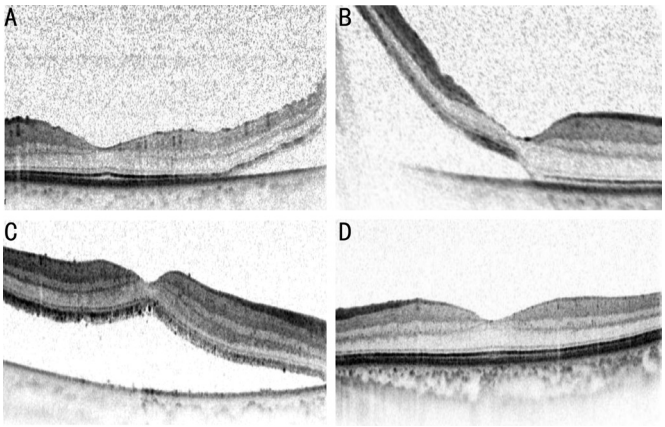

Figure 1 Different macular status preoperatively A: Macula partly detached RRD (Group A1, foveola-on); B: Macula partly detached RRD (Group A1, foveola-off); C: Macula totally detached RRD (Group A2, foveola-off); D: Macula-on RRD (Group B).

The definition of macula was a round area at the posterior pole measuring appropriately 5.5 mm in diameter[11]. SMF was defined as the fluid between the sensory retina and retinal pigment epithelium (RPE) in macula area.

Patients were classified into two groups showing in the OCT findings preoperatively. Those who showed macula-involving RRD by OCT were assigned to Group A (Figure 1A-1C), and those who showed macula-uninvolving RRD were assigned to Group B (Figure 1D). Relying on the different range of detachment in macula, we further subdivided Group A into subgroups A1 and A2. Group A1 (Figure 1A, 1B), macula was partly detached; Group A2 (Figure 1C), macula was totally detached. Those who showed SMF on OCT 1mo after surgery were assigned to group SMF (+), while the others were assigned to group SMF (-). We continued follow-up examination until SMF disappeared. Final VA was defined as BCVA at least 6mo after surgery.

For statistical comparison, VA was expressed as a logarithm of the minimum angle of resolution (logMAR) equivalents. The Mann-Whitney *U* test, *t* test, Chi-square test, and Fisher's exact test were used to assess the significance of observed associations. A P value <0.05 was considered significant. All analyses were conducted using SPSS 20.

RESULTS

A total of 139 patients (139 eyes) were recruited in this study. The mean follow-up time was 10.74mo (range 6-56mo). Table 1 showed the patients' demographic data. Group A consisted of 101 (72.7%) patients, and Group B consisted of 38 (27.3%) patients. Twenty-two (15.8%) patients had persistent SMF on OCT at 1mo after surgery. As shown in Table 1, no patient had persistent SMF on OCT at 1mo after surgery in Group B, whereas 22 (21.8%) patients in Group A had persistent SMF on OCT at 1mo after surgery (χ^2=9.83, P=0.002). Macula-uninvolved RRD patients had better VA (Z=-7.02, P<0.001) and fewer clock hours of detachment than macula-involved

Table 1 Demographic and clinical characteristics of Group A and Group B

Characteristics	Group A (*n*=101)	Group B (*n*=38)	Statistical value	*P*
Age (y)	53.77±12.61	54.74±10.81	*t*=-0.42	0.68
Gender (male/female)	52/49	16/22	χ^2=0.97	0.32
Duration of symptoms (d)	16.28±15.59	13.24±13.11	*Z*=-1.30	0.19
High myopia eyes	25	11	Fisher exact test	0.67
Perfluorocarbon	94	33	χ^2=1.36	0.31
Gas tamponade used (C3F8/silicon)	43/58	12/26	Fisher exact test	0.25
Clock hours of detachment	7.15±2.73	5.61±2.44	*Z*=-3.31	0.001
Follow-up (mo)	11.30±10.43	9.26±8.91	*Z*=-0.91	0.36
Submacular fluid	22 (21.8%)	0 (0)	χ^2=9.83	0.002
Preoperative BCVA	0.89±0.59	0.28±0.32	*Z*=-7.02	<0.001

BCVA: Best corrected visual acuity.

Table 2 Demographic and clinical characteristics of Group A1 and Group A2

Characteristics	Group A1 (*n*=28)	Group A2 (*n*=73)	Statistical value	*P*
Age	54.96±11.89	53.70±13.22	*t*=-0.31	0.76
Duration of symptoms (d)	19.59±19.29	15.00±13.86	*Z*=-1.04	0.30
C3F8/silicon	20/8	38/35	χ^2=3.11	0.08
Preoperative BCVA	0.66±0.54	1.52±0.64	*Z*=-5.32	<0.001
SMF (+)	14 (50%)	7 (10.0%)	χ^2=18.11	<0.001

BCVA: Best corrected visual acuity; SMF: Submacular fluid.

Table 3 Comparison of preoperative and postoperative BCVA between SMF (+) group and SMF (-) group for foveola-on RRD

Foveola-on RRD	SMF(+) Group (*n*=3)	SMF(-) Group (*n*=43)	Statistical value	*P*
Preoperative BCVA	0.19±0.13	0.22±0.25	*t*=0.46	0.76
Postoperative BCVA in 1 mo	0.28±0.10	0.32±0.32	*Z*=-0.38	0.30
Final BCVA	0.16±0.10	0.21±0.25	*Z*=-0.23	0.08

RRD: Rhegmatogenous retinal detachment; SMF: Submacular fluid; BCVA: Best corrected visual acuity.

Table 4 Comparison of preoperative and postoperative BCVA and degree of change in BCVA between SMF (+) group and SMF (-) group for foveola-off RRD

Foveola-off RRD	SMF (+) Group (*n*=19)	SMF (-) Group (*n*=74)	Statistical value	*P*
Preoperative BCVA	1.06±0.61	1.45±0.68	*Z*=-2.40	0.02
Postoperative BCVA in 1mo	0.56±0.32	0.86±0.48	*Z*=-2.49	0.013
Final BCVA	0.48±0.35	0.63±0.47	*Z*=-1.19	0.24
Change in BCVA				
1mo	0.50±0.58	0.60±0.74	*t*=0.51	0.61
From 1mo to final	-0.23±0.38	-0.08±0.17	*Z*=-2.71	0.007
Final	0.58±0.58	0.82±0.71	*t*=1.39	0.17

RRD: Rhegmatogenous retinal detachment; SMF: Submacular fluid; BCVA: Best corrected visual acuity.

RRD patients preoperatively (*Z*=-3.31, *P*=0.001). There was no difference in age, gender, duration of symptoms, number of high myopia eyes, the use of perfluorocarbon, different tamponades, or follow-up time between the two groups.

In Group A (macula-off group), persistent SMF 1mo after surgery was more frequent in the macula partly detached group (Group A1, 14/28, 50%) than in the macula totally detached group (Group A2, 8/73, 11.0%, χ^2=18.105, *P*<0.001). And, the macula partly detached group had better preoperative BCVA than did the macula totally detached group (*Z*=-5.32, *P*<0.001). But, there were no significant differences between the two groups in age or duration of detachment, nor was it associated with the use of C3F8 or silicon (Table 2).

There were two foveola statuses in the macular partly detached RRD group before surgery: foveola-on RRD and foveola-off RRD. Figure 1A, 1D were included in foveola-on RRD whereas Figure 1B, 1C were foveola-off RRD. The visual outcomes were compared between the SMF (+) and SMF (-) groups in foveola-on and foveola-off RRD, respectively (Tables 3, 4). There were no significant preoperative or postoperative BCVA difference between the SMF (+) and SMF (-) groups in the foveola-on RRD during the follow-up times. However, in the foveola-off

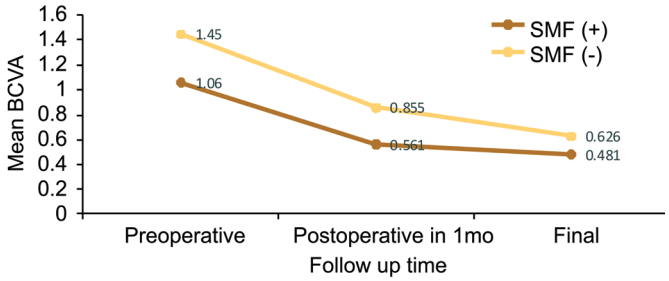

Figure 2 Comparison of preoperative and postoperative BCVA between SMF (+) group and SMF (-) group for foveola-off RRD.

RRD, the SMF (+) group had significantly higher preoperative BCVA (Z=-2.40, P=0.017), postoperative BCVA at 1mo (Z=-2.49, P=0.013), and improvement from 1mo BCVA to the final BCVA than did the SMF (-) group (Z=-2.71, P=0.007; Figure 2). The final VA outcomes, along with the change in BCVA at other time points, showed no significant difference between the two groups.

DISCUSSION

OCT is widely used in detecting SMF after surgery. The OCT images are able to show shallow SRF, even when all retinal breaks are closed and the retina appears fully attached on ophthalmoscopy.

Quintyn and Brasseur[12] reported that the SRF of the RRD contained hyaluronic acid, various proteins (globulin, plasmin, apoprotein, fibronectin), lipids, and glucides, and assumed that the osmotic pressure (which was linked to the protein content) would be the main cause of SRF accumulation. Veckeneer *et al*[13] further hypothesized that the persistent SRF after surgery may be mostly related with the conditions of high cellularity and viscosity in the subretinal space. Then, in PPV, after water is largely excluded, the residual SRF is left much more concentrated in hyaluronic acid, protein, and other components. The osmotic pressure would increase and be reabsorbed through the outer blood-retinal barrier, which would explain the persistent SMF after the surgery. Chen *et al*[14] recently used a prospective study showing that completely exchanging SRF with balanced salt solution would diminish the SMF after the surgery, if there was no RPE damage. Kim *et al*[15] also showed evidence that delayed absorption of SMF after surgery was associated with high choroidal permeation. Nonetheless, Kim *et al*[16] studied the periphery SRF blebs and proposed that there was a horizontal power parallel with the interface of PRE-photoreceptor cells, and this power resulted in the changes of the blebs features.

In our study, 22 of 139 eyes had SMF detected by OCT at 1mo after surgery. The incidence (15.8%) of SMF at 1mo after PPV was almost the same as that in Benson *et al*'s study[17] (15.0%), who described 100 RD patients who underwent PPV; SRF was seen in 15 of 100 patients at 6wk. However, Kim *et al*[18] described only 1 of 16 (6.3%) RD patients who underwent PPV showed persistent SMF 1mo after surgery,

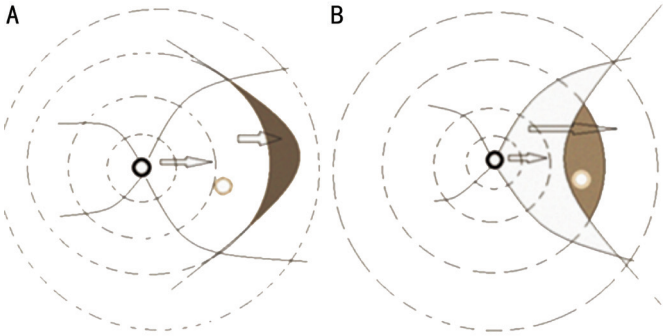

Figure 3 Edge effect Two statuses of the edge of the detached retina. A: Macula totally detached; B: Macula partly detached.

and Wolfensberger and Gonvers[2] described no one in 24 RD patients who underwent PPV showed persistent SMF 1mo after surgery. The small sample in these studies and short duration of the symtoms[5,18] may contribute to the lower incidence of persistent SMF. Both Benson *et al*[17] and Theodossiadis *et al*[5] had reported that macular-uninvolving RRD patients had a higher prevalence of persistent SMF after the surgery, which conflicted with our result (0/28). Thus, we speculated three reasons for the difference, as follows: 1) low-resolution OCT missed the shallow SMF preoperatively; 2) the OCT was performed earlier than just before the surgery, which did not take the progress of RRD into account; and 3) the supine position during the surgery contributed to the SMF.

Our study was the first to discover the relationship between the preoperative macular status and the incidence of persistent SMF after PPV. According to the preoperative macular status, patients were divided into three groups. And, we surprisingly found that the incidence of persistent SMF after PPV for RD was 50% in the macula partly detached RRD patients, which was higher than that in macula-on RRD patients (0, P<0.001), or the macula totally detached RRD patients (11%, P<0.001). Taking the the former results into account, we considered that the residual SMF may be the most important source of persistent SMF after RRD surgery. And, the residual SMF was highly associated with the preoperative macular status.

We hypothesized there was an edge effect. Figure 3 shows two statuses of the edge of detached retina: the arc face to the discus opticus or the arc back to the discus opticus. In the first status, SRF is enclosed by perfluorocarbon or air. The edge of the detached retina is unable to be excluded (the left picture). In the second status, the SRF on the edge is pushed forward and begins to accelerate from zero speed. The speed of the SRF on the edge may be slower than perfluorocarbon or tamponade. Then, the perfluorocarbon or tamponade will stop the SRF from moving forward under gravity. Furthermore, the position of the edge may be the reason that the macular partly detached RRD group had a higher rate of SMF after surgery: as none of our patients' hole was located on the posterior pole, the edge effect would more frequently happen in macular partly RRD,

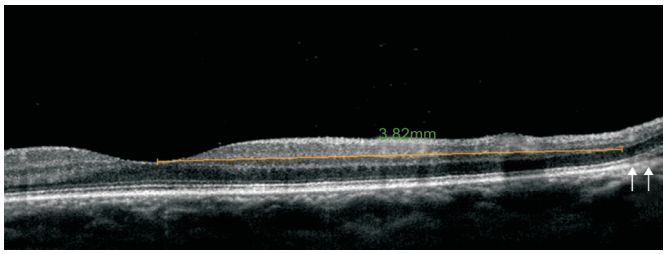

Figure 4 A macular-on RRD patient postoperative OCT image in 1mo The SRF (double right arrow) was 3.82 mm away from the foveola.

especially with the temporal holes, than in the macula area in macular totally detached RRD or macula-on RRD. We infer that there will be SRF on the edge in patients with macular totally detached RRD or macula-on RRD. Figure 4 shows the SRF that was 3.82 mm away from the center of the macula 1mo after surgery in a macular-on RRD patient. Kang *et al*[19] showed OCT and fundus photograph findings of SRF away from the macula area as well.

For the VA, previous studies had produced contrary conclusions. Most of the studies concluded that the persistent SMF after surgery did not correlate with final VA[20]. Some studies that concluded differently were limited by the small sample sizes or the short follow-up period. Whereas Benson *et al*[3] reported that RD patients with SRF 6wk after PPV had worse VA. However, 50 in 157 were macula-on whereas 107 in 157 were macula-off RD patients. When visual outcomes were compared between the presence or the absence of persistent SRF groups, they calculated the VA of macula-on and macula-off patients together. It is well known that VA in foveola-on RD patients is better than that in foveola-off RD patients preoperatively or postoperatively. And, almost all macula-on patients did not have SRF after PPV. It turned out that the more macular-on patients there were, the better the visual outcome of the absence of persistent SRF group. Thus, in our study, when comparing VA among SMF (+) and SMF (-) groups, we divided all patients into foveola-on and foveola-off RRD groups. Futhermore, there were 46 foveola-on RRD patients, and only 3 had persistent SMF. Considering such a small number of patients in the SMF (+) group, we excluded the foveola-on RRD patients.

In the foveola-off RRD group (Table 4), just as we presumed, the largest portion of the SMF (+) group were macular partly detached patients (A1), whereas the SMF (-) group was derived from nearly all the macular detached patients (A2). So, it explained why the SMF (+) group had significantly higher preoperative VA and postoperative VA along a short time-period (P<0.05). In our study, there was no significant evidence that SMF influences the final visual outcomes. All the patients had gradually recovered VA (Figure 2). But, when comparing the speed or the extent of the improvement of VA between the two groups, obviously the SMF (+) group was slower and smaller during the follow-up period. There was a significant difference in the change of BCVA from 1 to 6mo. We concluded that, among the foveola-off RRD patients, the persistence of SMF after the surgery may be responsible for the delayed visual recovery.

In conclusion, persistent SMF after PPV for RD was associated with preoperative macular status. The grouup of patients with macula partly detached RRD had a higher incidence of SMF than did the patients with macula totally detached or those with macula-on RRD after PPV surgery. The edge effect may be an explanation for this phenomenon. The persistence of SMF may disturb the recovery of the VA in the short term, whereas it has no influence on the final visual outcome.

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