Persistent subfoveolar fluid following retinal detachment surgery: an SD-OCT guided study on the incidence, aetiological associations, and natural history

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Abstract

Purpose To investigate the incidence and natural history of persistent subfoveolar fluid (PSF) following surgery for macular off rhegmatogenous retinal detachment and the effect of PSF on photoreceptor structure and final visual acuity.

Methods Retrospective study of 61 cases with post-operative optical coherence tomography (OCT) performed within 12 weeks of surgery. Based on aetiology, cases were categorized into tractional retinal tears (TRT) group or atrophic round holes and dialyses (RHD) group to investigate the incidence and duration of PSF. A Kaplan–Meier graph was plotted to compare survival time of subfoveolar fluid for both groups. Following secondary reclassification of cases into those with and without PSF, the effect of PSF on final visual acuity and photoreceptor structure was investigated with Mann–Whitney *U*-test used for comparison. Spearman's correlation testing was used to probe associations between time to recorded resolution of PSF with final visual acuity and photoreceptor structure.

Results Incidence of PSF was greater in the RHD group and persisted for longer compared with TRT group. No detectable adverse effect of PSF on final visual acuity was seen however an individual case of severe photoreceptor atrophy was observed. No significant correlation was found between the time to recorded resolution of PSF and the final visual acuity or to photoreceptor grading scores.

Conclusions A difference in incidence of PSF was detected between the aetiological

groups. PSF was ubiquitous and slow to resolve in the RHD group. Most cases of PSF resolve without adverse sequelae; however, progressive photoreceptor atrophy and sub-optimal visual outcome may result in a minority.

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Introduction

Persistent subfoveolar fluid (PSF) as seen on optical coherence tomography (OCT) is a recognized complication of otherwise anatomically successful surgery for macula involving retinal detachments, with reported prevalence between 0 and 94%.^{1–7}

The aetiology, associations, natural history, and visual outcome of PSF are incompletely understood. Previous reports have associated PSF with scleral buckling surgery. There are, however, potentially important differences such as break type and absence of a posterior vitreous detachment (PVD) in cases that undergo scleral buckling compared with vitrectomy. These differences, instead of treatment received, may be important determinants of PSF.

The aims of this study were to investigate: (1) incidence, aetiological associations, and relationship of PSF to causative retinal breaks; (2) time taken for fluid absorption; and (3) PSF effect on photoreceptor structure and final visual acuity.

Materials and methods

Ethics approval was not required as data from clinical information previously collected for

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routine care was used. A retrospective review of patient records and the surgical database was conducted to identify cases of macula involving rhegmatogenous retinal detachments that underwent surgical repair from 2009 to 2013 at St Thomas' Hospital, London, UK. Macula involvement was defined as subretinal fluid extending to or beyond the foveal centre. Cases with anatomical success following a single procedure and OCT imaging performed within 12 weeks of surgery were selected for the study inclusion.

To investigate the associations and duration of PSF, cases were primarily categorized into two groups as per causative breaks: those secondary to atrophic retinal round holes and retinal dialyses (RHD group) and those secondary to tractional retinal tears (TRT group).

To investigate the effect of PSF on visual function and photoreceptor structure, cases were secondarily reclassified into those that demonstrated PSF on their initial post-operative OCT and those that did not.

Follow-up intervals were for at least 3 months and three to four monthly, thereafter, until the fluid had fully absorbed. The following demographic and clinical data were abstracted for use in this study: age, pre-operative clinic visual acuity, PVD status, causative break, extent of retinal detachment, type of surgery performed, post-operative habitually corrected visual acuity at each visit, anatomical status of retina on subsequent clinical examination, and OCT findings.

Scans were obtained with Topcon 1000 Mark II spectral-domain OCT scanner (Tokyo, Japan) with images taken in a 6 mm by 6 mm format centred on the macula. Scans were reviewed in grey scale with the following definitions applied for analyses: Foveal centre was located by observing the point where outer nuclear layer reached inner retinal surface. The foveola was defined as the area

within a 175 microns radius of the foveal centre. PSF was defined as subretinal fluid present within the central 350 microns. Foveola ellipsoid zone (EZ) and external limiting membrane (ELM) layer integrity were quantified on the final follow-up scans of eyes in which PSF had either absorbed or never been found post-operatively. Proportional integrity of the ELM and EZ layers were graded from 0 to 5 on the central horizontal line scan. Grade 0: line absent; Grade 1: $\leq \frac{1}{4}$ line present; Grade 2: $> \frac{1}{4}$ but $\leq \frac{1}{2}$ line present; Grade 3: $> \frac{1}{2}$ but $\leq \frac{3}{4}$ line present; Grade 4: $> \frac{3}{4}$ line present; Grade 5: full line present. This was an adaptation of a published method for quantitative assessment of the OCT photoreceptor layer.⁸

Statistical analysis was performed with XLSTAT version 2014.6.02 (Addinsoft, New York, NY, USA) software. A Kaplan-Meier graph comparing survival time of subfoveal blebs for the RHD and TRT groups was plotted. The Mann-Whitney *U*-test was used to compare final visual acuity between PSF and non-PSF groups, and to compare the foveola EZ and ELM layers between PSF and non-PSF groups. Spearman's correlation was used to investigate the association between time to recorded resolution of PSF and final visual acuity, ELM, and EZ grades.

Results

Sixty-one eyes of 61 patients were included in this study, 27 in the RHD group and 34 in the TRT group. Table 1 shows demographic and pre-operative data. 23/27 patients in the RHD group were treated with cryotherapy and scleral buckling. 3/27 cases underwent external drainage of subretinal fluid as part of the buckling procedure. Four cases in this group underwent vitrectomy and gas with internal drainage of subretinal fluid. All cases in the TRT group underwent a 23-gauge

Table 1 Patient demographics for atrophic retinal round holes and dialyses (RHD) group and tractional retinal tears (TRT) group

	<i>Atrophic RHD group</i>	<i>TRT group</i>
<i>N</i>	27	34
Median age	32 (range 11–71)	58.5 (range 37–77)
<i>Pre-operative PVD status</i>		
PVD present	4	34
PVD not present	21	
Unspecified	2	
Causative break	22 round holes 5 retinal dialyses	34 tractional tears
Median extent of detachment (circumferential clock hours)	5 (range 3–9)	5 (range 3–12)
Median duration of symptoms prior to surgery (days)	10 (range 1–180)	6.5 (range 2–120)
Median VA at presentation (logMAR)	0.48 (range 0–2.3)	1.90 (range 0.18–2.60)
<i>Type of surgery</i>		
Scleral buckling	23	0
Vitrectomy and gas	4	34
Median duration of follow-up from surgery (weeks)	32 (range 7–132)	29.5 (range 6–124)

vitrectomy, internal drainage of subretinal fluid, retinopexy with laser or cryotherapy as deemed appropriate by the operating surgeon and fluid-air-gas exchange. 14/34 patients in the TRT group were pseudophakic pre-operatively as were 2/4 of the patients in the RHD group treated with vitrectomy.

Table 2 shows the number of patients in both groups with PSF on their first OCT scan at differing time points. 15/24 patients found to have PSF were followed until resolution. The other 9 were lost to follow-up prior to PSF resolution. The longest duration of PSF noted in the RHD group was in a patient scanned at 56 weeks with resolution at 80 weeks. Another patient in the TRT group had PSF at 56 weeks with resolution at 79 weeks post-operatively. Patient data were used to plot the Kaplan–Meier graph to provide an estimate of the rate of persistence of subfoveolar fluid in each group, as shown in Figure 1.

Table 3 shows a comparison of the final acuity and scans of patients in whom PSF was present but subsequently absorbed, and those in whom PSF was not identified on their first post-operative scan. One patient from the TRT group developed a full-thickness macular hole and was excluded from structural grading and visual acuity analysis.

No statistically significant correlation was demonstrated between time to recorded resolution of PSF and final acuity (Spearman's $r = 0.147$, $P = 0.595$); or to EZ (Spearman's $r = -0.084$, $P = 0.768$); or ELM scores (Spearman's $r = 0.342$, $P = 0.209$) for the 15 patients with resolved PSF. Median change in acuity between the last assessment on which PSF was identified and the final recorded acuity was an improvement of 0.18 logMAR (range -0.03 to 0.5 logMAR). Median acuity of the nine patients with PSF on final follow-up was 0.43 logMAR (range -0.1 to 0.5 logMAR). Only 1 of 15 patients with resolved PSF had a final post-operative acuity that was worse than at presentation (decline of 0.7 logMAR during follow-up) with complete loss of foveola EZ and ELM layers. This patient had evidence of a very chronic peripheral retinal detachment secondary to round holes that had acutely progressed to involve the macula. The

features of chronicity in this case were extensive retinal pigment epithelial degeneration and formation of multiple subretinal bands. Figure 2a shows an OCT scan taken 2 weeks post-operatively on this subject. Figure 2b was taken more than 2 years later for this patient and demonstrates progressive photoreceptor layer atrophy.

Discussion

The incidence of persistent 'blebs' or 'clefts' of subretinal fluid on OCT following macroscopically successful retinal detachment surgery is reported to vary from 0 to 94%, with first post-operative OCTs performed from 1 month to 6 weeks.^{1–7} Various terminologies have been used to describe this entity, for example, subfoveal detachment, subfoveolar fluid, subretinal fluid, and submacular fluid. In our study, we specifically studied subfoveolar fluid

Figure 1 Kaplan–Meier graph illustrating the rate of subfoveolar fluid persistence against time for both atrophic retinal round hole and dialyses (RHD) group and tractional retinal tears (TRT) group.

Table 2 The number of patients in the atrophic retinal round holes and dialyses (RHD) group and tractional retinal tears (TRT) group found to have persistent subfoveolar fluid on the first post-operative OCT scan

Timing of first post-operative OCT scan	RHD group Number of patients with persistent subfoveolar fluid on first post-operative OCT/total number of patients with first post-operative scan within stated period	%	TRT group Number of patients with persistent subfoveolar fluid on first post-operative OCT/total number of patients with first post-operative scan within stated period	%
≤ 4 weeks	18/20	90	3/10	30
5–8 weeks	3/5	60	0/10	0
> 8 and ≤ 12 weeks	0/2	0	0/14	0
Total	21/27	78	3/34	9

Table 3 Final visual acuities, foveola ellipsoid zone (EZ), and external limiting membrane (ELM) scores for patients in whom PSF was found on OCT and subsequently absorbed (resolved PSF group), compared with patients in whom subfoveolar fluid was not found on the first post-operative OCT scan (non-PSF group)

	Resolved PSF group n = 15 (median, range, interquartile range (IQR))	Non-PSF group n = 36 (median, range, IQR)	Mann–Whitney U-test P-value
Foveola EZ grading score	4, 0 to 5, IQR 1	4, 0 to 5, IQR 1.5	0.239
Foveola ELM grading score	4, 0 to 5, IQR 1.5	3, 0 to 4, IQR 3	0.083
LogMAR visual acuity	0.07, –0.08 to 1.18, IQR 0.24	0.18, –0.08 to 1.00, IQR 0.20	0.043

Figure 2 (a and b) OCT scans for the same patient with chronic retinal detachment secondary to round holes that was treated with scleral buckling. (a) The scan taken at 2 weeks post-operatively demonstrating persistent subfoveolar fluid with a height of 231 microns. (b) Taken at 2 years and 7 months following surgery shows resolution of subfoveolar fluid and central photoreceptor atrophy.

that was present under the foveal centre as defined above. The aetiology and natural history of this condition is not fully understood. Despite this several treatment options have been described.^{9–12}

Several aetiological or associated factors have been identified: type of surgery performed, pre-operative macula involvement, position, extent, and duration of the retinal detachment. In one series it was reported that persistent submacular fluid was found in 36% of cases that were clinically considered to have a fully attached macula prior to surgery; which raised the possibility that the fluid is exudative rather than persistent subretinal fluid from the retinal detachment.³ It has been suggested that PSF may be associated with choroidal leakage following cryotherapy;¹³ however, the use of laser retinopexy as a substitute for cryotherapy did not exclude PSF occurrence.¹⁴ In addition, despite extensive angiographic study, no signs of leakage were ever found in many cases of PSF.

The incidence of persistent subretinal fluid following scleral buckling surgery has been reported to be 53–94% compared with 0–40% when patients undergo vitrectomy.^{1–7} It is unclear whether this arises from the treatment received or systematic differences in the cases treated with vitrectomy or buckling. For example, in our unit, we generally perform scleral buckling surgery on retinal detachments secondary to RHD, and vitrectomy surgery for PVD-related retinal detachments secondary to tractional tears. PSF has been reported to persist for many months following surgery. Studies have identified subretinal fluid persisting in 25–55% of cases at 6 months following scleral buckling surgery.^{1,3,4,7} A study of six patients with a mean age of 31 years with PSF at 6 months following scleral buckling surgery for inferior macula-off detachments raised the suggestion of ‘marginally liquefied vitreous’ and delayed fluid reabsorption; however, the type of causative break was not mentioned.¹⁵

In our study, we primarily grouped patients according to the causative breaks rather than by the treatment received. To our knowledge, no previous studies have related PSF to causative break type. PSF was both more prevalent and persisted for longer in patients with detachments due to atrophic breaks or dialyses (RHD group) compared with those caused by tractional tears (TRT group; Table 2 and Figure 1): the incidence on first scans performed within a month of surgery was 90% in the RHD group and 30% in the TRT group. The Kaplan–Meier graph shows that 50% of cases of PSF will still persist at 34 weeks (95% CI, 18–50 weeks) in the RHD group compared with 8 weeks (95% CI, 7–11 weeks) in the TRT group. For a 25% rate of persistence, the corresponding figures are 52 weeks (95% CI, 34–54 weeks) and 12 weeks (95% CI, 9–12 weeks).

PSF content has been reported to be viscous with high cellularity. In one study, subretinal fluid samples were obtained at time of surgery; high concentration of rhodopsin-containing cells were found in viscous samples, corresponding to eyes with PSF at 6 weeks post-operative OCT. The authors hypothesized that PSF occurs as a result of fluid composition in relation to the absence of PVD and chronicity of the detachment.¹⁴ In another study, optical density ratios from OCT scans were used as a surrogate measure of SRF composition

following surgery.¹⁶ This ratio increased in conjunction with a decrease in height of subretinal fluid and was suggested to reflect an increasing particulate concentration of subretinal fluid during the process of subretinal fluid absorption.¹⁶

Retinal detachments secondary to atrophic holes and dialyses are not dependent upon development of a PVD.¹⁷ They frequently present when acute symptomatic progression of a chronic asymptomatic peripheral detachment occurs.¹⁸ Retinal detachments due to TRT are typically acute phenomena with rapid recruitment of relatively acellular, low viscosity fluid from the vitreous cavity into the subretinal space.

We hypothesize from these data and previous studies that a systematic chronicity and fluid current induced difference in the viscosity, protein, and cellular content of the subretinal fluid explains our observation of a threefold greater incidence of PSF in the RHD rather than TRT group, and the greater duration of persistence. Our data do not, however, allow us to discount the hypothesis that it is the treatment received (scleral buckling as opposed to vitrectomy), which underlies the difference in the incidence and the persistence of subretinal fluid. Only 4/27 patients in the RHD group underwent a vitrectomy and none of the 34 patients in the TRT group were buckled. Two of these four patients demonstrated PSF.

The third aim of this study was to investigate the effect of PSF on macula structure and visual function. In this respect, the comparisons were performed between patients who had demonstrated PSF on a first post-operative scan performed within 3 months and those in whom the first scan showed absorption of the subfoveolar fluid (the inclusion criteria specified a retinal detachment with central foveal involvement so all cases would have had subfoveolar fluid at presentation).

Structural integrity of photoreceptor cells on OCT is associated with visual acuity in a wide variety of retinal diseases. OCT studies following successful surgery have reported the recovery of outer retinal layers with the presence of an intact or improved EZ layer correlating with visual acuity.^{6,19–22} The integrity of the ELM layer has also been reported to be important for visual recovery.^{20–22}

The retrospective observational design and limited size of this study gives rise to potential confounders regarding the interpretation of the acuity outcome, most notably, duration of foveal involvement prior to surgical repair, the development if any of secondary cataract and non-systematic final follow-up. The two groups are also different in age with the TRT group being a median of 26 years older. These caveats are, however, common to all previous studies in this field.

PSF while present was found to be associated with an impaired visual acuity. The median acuity of patients in whom PSF was present at final follow-up was 0.43 logMAR. Patients in whom PSF was present but subsequently resolved had an improvement in acuity of 0.18 logMAR (range –0.03 to 0.50 logMAR) noted between clinical assessments during which the PSF resolved and a median final acuity of 0.07 logMAR. This is better than the median final acuity of 0.18 logMAR in the group in whom no PSF was identified ($P=0.04$). As a confirmation of the absence of obvious generalized loss of structure and function in association with PSF, we did not find in the group as a whole that PSF was associated with incremental photoreceptor damage: there was no significant difference between the EZ and ELM grades of patients who did or did not demonstrate PSF. We were also unable to demonstrate a statistically significant association between the duration of PSF persistence and either final acuity or EZ or ELM grades.

This study was performed at a time of increasing but not systematic use of OCT during post-operative assessment of patients treated for retinal detachment and it is possible that some cases of PSF went undetected, for example, in patients demonstrating good post-operative visual recovery. This study was insufficiently powered to detect a difference in visual acuity between the groups, however, we report a trend in improvement of visual acuity following PSF resolution. A future prospective study is needed with prior sample size determination to address these issues.

The nine patients lost to follow-up before resolution of PSF were from the RHD group and their final OCT was performed at a median of 15 weeks (range 1 to 32 weeks) following surgery. In contrast, 12 patients from the RHD group were followed up until resolution of PSF. The timing of assessments and last recorded visual acuities in the 9 patients lost to follow-up were similar to that of the penultimate assessments of the 12 patients who were followed until the resolution of PSF (weeks compared with weeks and visual acuity compared with visual acuity). This data suggest the series was not obviously biased by loss to follow-up.

Some patients with PSF did, however, end up with sub-optimal visual outcome once the fluid has absorbed: 7.7% or four patients with absorbed PSF (including the 'never PSFs') had a final acuity worse than 0.6 logMAR. Apart from one patient with an amblyopic eye there was no other identifiable cause for impaired acuity here. The acuity of one patient (2%) declined during follow-up from 0.48 logMAR to 1.18 logMAR over a period of 2 years and 7 months. Figures 2a and b show the immediate post-operative and final OCT scans of this patient. There is progressive atrophy of the photoreceptor cells that may have been an idiosyncratic response, there

may, however, be systematic differences in the subretinal fluid that underlie this 'toxic' response. Based on the data there does not appear to be a universal requirement for treatment to hasten the absorption of PSF, but we cannot at present identify those at risk of central vision loss.

In summary, PSF is virtually ubiquitous in patients with macula involving retinal detachments secondary to atrophic round holes or dialyses. It can be found in around a third of patients with similar macula involving retinal detachments due to tractional tears. The fluid when present may persist for up to a year. Our data support previous hypotheses¹⁴ that PSF arises from the chronicity and viscosity of the subretinal fluid rather than the treatment received, but cannot prove that with this study. Most cases of PSF resolve slowly without adverse sequelae but in a small proportion of cases it is associated with progressive foveal photoreceptor atrophy and loss of visual acuity.

Summary

What was known before

- Persistent subfoveal fluid (PSF) is a complication of otherwise anatomically successful retinal detachment repair.
- PSF can persist for months following retinal detachment repair.

What this study adds

- Incidence of PSF following surgery is greater in retinal detachments that occur secondary to atrophic holes or dialyses, compared with retinal detachments secondary to tractional tears.
- Most cases of PSF resolve slowly without adverse sequelae, however, in a small proportion of cases it is associated with progressive foveal photoreceptor atrophy and loss of visual acuity.

Conflict of interest

The authors declare no conflict of interest.

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