Risk of complications of vitrectomy for floaters,based on presence or absence of posterior vitreous detachment.

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Authorship and contribuationship:

1. R Rahman: Conception and design of study, acquisition and analysis of data, revising article critically and approval of the version to be published.
2. J Gormley: Preparation of manuscript.
3. J Stephenson: Statistical analysis of the data,revising the article and final approval of published version.

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Abstract

Purpose: To ascertain whether vitreous status (attached versus detached) affects the risk of intraoperative retinal breaks and number of operations in patients undergoing vitrectomy for floaters.

Methods: Consecutive, comparative single-surgeon case series. All patients undergoing vitrectomy for visually disabling floaters between July 2003 and June 2016 were included in this study. Data was collected prospectively into a vitreo-retinal database and reviewed retrospectively for the purpose of the study.The following data was collected on each patient: Age in years, sex, axial length (mm), presence of myopia, pre and post-operative visual acuity in LogMAR. The status of the posterior hyaloid face was ascertained using preoperative clinical and OCT assessment which was confirmed intraoperatively. The primary outcome measure was considered to be the presence or absence of a retinal tear. Significant visual loss (Reduction in ≥ log units visual acuity), number of operations and time from surgery to discharge were considered to be secondary outcomes. Sequential multiple logistic and Cox regression analyses were conducted.

Results: Data was collected on 97 patients (55 males, 42 females). Indications for surgery were Fuchs heterochromic cyclitis (9 patients); asteroid hyalosis (12 patients); vitreous syneresis (76 patients). 21 patients were pseudophakic on presentation, while 76 underwent combined phacovitrectomy. Vitreous status was significantly associated with retinal tears/breaks (p=0.010). Controlling for other parameters, the odds of a retinal break in patients with vitreous attached were about 5.5 times those in patients with vitreous detached (95% confidence interval [CI] 1.52 to 20.4). Number of operations was also significantly associated with this outcome (p=0.027); the odds of a retinal tear increase by 6.28 times (95% CI 1.23 to 32.1).

A substantive difference in the proportion of patients with retinal breaks was observed between the two groups, with a 50% prevalence rate in the attached group and a 9~~0~~.9<u>1</u>% prevalence rate in the detached group<u>.</u> ~~**(to change this line).**~~

Controlling for other parameters, the odds of a retinal tear or break in patients with vitreous attached were about 5.5 times those in patients with vitreous detached (95% confidence interval [CI] 1.52 to 20.4). Number of operations was also significantly associated with this outcome (p=0.027); the odds of a retinal break increase by 6.28 times (95% CI 1.23 to 32.1).

Vitreous status was not associated with either secondary outcome measure. Number of operations was also significantly associated with improvement in visual acuity (p=0.017; odds ratio 15.8 [95% CI 1.65 to 151]) in a multiple logistic regression model; and with time to discharge (p=0.008; hazard ratio 2.78 [95% CI 1.30 to 5.91]) in a multiple Cox model. Hence an increasing number of operations is associated with higher odds of visual improvement; and with longer time to discharge. Was there any association with Axial length or presence or absence of myopia?

Conclusion: The analysis has found evidence to link vitreous status with the primary outcome of the presence of a retinal break. However, the risk of retinal detachment was zero in both groups. Number of operations is of substantive importance with respect to all measured outcomes.

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Introduction

The human vitreous undergoes significant macroscopic changes with age, namely liquefaction (synchesis) and collapse (syneresis). [1] As a result, posterior vitreous detachment (PVD) occurs causing visually significant floaters. [1, 2] However, visually debilitating floaters can occur in the absence of a PVD, due to age-related liquefaction which is accelerated in myopia. PVD, followed by myopic vitreoretinopathy and asteroid hyalosis are the most common cause of floaters. [3, 4]

Recent studies suggest that floaters can have a negative impact on quality of life and are perceived by patients as a significant health problem. [5, 2] While treatment options are limited to Nd:YAG (Yttrium aluminium garnet)vitreolysis or vitrectomy,[6] primary vitrectomy is increasing in popularity. [7]

Patients undergoing this procedure have given good satisfaction scores (85% satisfied / very satisfied) as measured using QOLVFQ (Quality of Life visual function questionnaire) suggesting that it can enhance quality of life. [7]

With the more widespread use of transconjunctival small gauge vitrectomy, reports have declared the improved safety profile of pars plana vitrectomy for floaters, [4, 7, 8] encouraging surgeons to offer it to patients more readily.

Performing pars plana vitrectomy for floaters is associated with certain risks, such as iatrogenic retinal breaks, retinal detachment and cataract formation. These risks have been reported to occur at rates between 0 – 16.4% for breaks, 0 - 10.9% for detachment and 22 - 60% for cataract [2, 7-10]. It has been identified that induction of PVD during surgery is associated with higher complications, especially of retinal breaks and detachment [9, 11]. Preoperative OCT analysis provides accurate visualisation of vitreous status at the optic disc, hence enabling surgeons to plan surgery and counsel patients appropriately. [12]

In this study we aimed to examine the outcomes in patients undergoing combined phacovitrectomy/vitrectomy for floaters. We compared two similar groups varying in vitreous status: attached versus detached; and reported their outcomes in terms of retinal break/tears, posterior segment complications, significant visual deterioration and time to discharge.

Materials and Methods

This study was a comparative, single surgeon series. Data was collected prospectively in a vitreo-retinal database and reviewed retrospectively. All patients presenting with visually disabling floaters requiring vitrectomy between July 2003 and June 2016 at Calderdale Royal Hospital, UK were included. The local Research and Development department confirmed that no ethical approval was required as there was no deviation from the usual standard of care.

The surgical procedure was a standard 23 gauge transconjunctival sutureless vitrectomy (TSV) +/- combined phacoemulsification and IOL insertion. From July 2015, 27g TSV was used. In all cases a three port pars plana approach was used with sclerostomies 3.5 mm from the limbus. For patients with an intact posterior hyaloid face (PHF), separation was induced with a 23 or 27-gauge cutter probe using suction.

Baseline demographics including sex, age and indication for surgery (asteroid hyalosis, Fuchs heterochromic cyclitis or floaters) were recorded. Posterior hyaloid status was assessed using OCT (Optovue RTVue – 100 with V. 4.0 software, Freemont, California, USA) and slit lamp biomicroscopy; this was confirmed intraoperativley with the use of the BIOM viewing system

(Oculus, Wetzlar, Germany). In addition to demographic data, we recorded axial length, and pre-operative visual acuity in LogMAR. We recorded the number and type of operation (vitrectomy or phacovitrectomy), tamponade used (none, air, C_2F_6, SF_6 or Silicone oil.We also recorded whether the vitreous was attached or detached (*Vitreous*); considered to be the explanatory variable of primary interest. The primary outcome measure was whether or not the patient experienced a retinal break (*Break*) as a direct consequence of intra-operative separation of posterior hyaloid face. The secondary outcome measures were time from surgery to discharge in days (*Time*) and any significant visual loss (2 or more logmar units loss from pre-operative level). Other variables were considered to be controlling variables. Some levels of categorical variables were combined before analysis due to low frequencies.

The sample was summarised descriptively. Sequential logistic regression analysis was conducted on the primary outcome measure of *Break*. All controlling variables were entered in the first block, with a parsimonious subset of variables derived using backward elimination. These were added to the key *Vitreous* variable which was forced entered in the second block. A second sequential logistic regression analysis was conducted on the secondary outcome measure of *Improvement*, utilising the same modelling strategy. Semi-parametric time-to-event analyses (Cox regression) were conducted on the secondary outcome of *Time*, again utilising the same modelling strategy.

Odds ratios (logistic regression analyses) or hazard ratios (Cox regression analyses), with associated confidence intervals; and p-values were reported for all analyses. For the logistic regression analyses, model goodness-of-fit was assessed using Nagelkerke's pseudo-R^2 statistic and classification tables, and model calibration was assessed using Hosmer and Lemeshow's test statistic.

All statistical analysis was conducted using SPSS statistical software (Version 22.0).

Results

A total of 97 patients were included in the study. 42 patients (43.3%) had vitreous attached; 55 patients (56.7%) had vitreous detached. Majority of the patients undergoing simultaneous cataract surgery had non-clinically significant cataracts. The age range of the analysed patients was 23-94 years, with a mean age of 60.1 years (SD 13.2 years). 55 patients were male (56.7%). Both groups were similarly matched in terms of gender and age, and type of surgery performed (vitrectomy versus phacovitrectomy). Vitreous syneresis was a more common indication for surgery in the vitreous detached patient group. Other indications were more common in the vitreous attached patient group.

Tamponade agents varied between the two groups, with a higher number of patients with vitreous detached requiring air (46 out of 55 patients (83.6%) detached versus 24 out of 42 patients (57.1%) attached); with higher rates of ulitization of other agents in the attached group. The association between agent and vitreous staus was statistically significant at the 5% significance level ($\chi^2_{(1)}=8.32$, $p=0.004$). The magnitude of the effect was medium ($\varphi=0.293$). **~~Was this statistically significant?~~** An imbalance between groups was also noted needed, with 100% of patients with detached vitreous needing only a single posterior segment surgery—; compared with 76.9% in patients with attached vitreous needing only a single (5 patients (17.9%) ~~(5)~~ needing 2 surgeries and ~~(~~2 patients~~)~~ (5.1%) needing 3 surgeries).

The outcomes of time from surgery to discharge and changes in visual acuity were very similar between the two groups. A substantive difference in the proportion of patients with retinal tears or breaks was observed between the two groups, with a 50% prevalence rate in the attached group and a 9~~0.9~~.1% prevalence rate in the detached group.

A small amount of missing data was recorded for the variables corresponding to number of operations and improvement in vision after surgery. Missing values were not imputed.

A full descriptive summary of the sample is provided in Table 1.

Table 1: Descriptive summary of data

Categorical Variable	**All (n=97)**	**Vitreous attached (valid%) (n=42)**	**Vitreous detached (valid%) (n=55)**
	Frequency (valid %)	**Frequency (valid %)**	**Frequency (valid %)**
Gender			
Male	55 (56.7%)	23 (54.8%)	32 (58.2%)
Female	42 (43.3%)	19 (43.3%)	23 (41.8%)
Indications for surgery			
Vitreous syneresis	76 (78.4%)	30 (71.4%)	46 (83.6%)
Asteroid hyalosis	12 (12.4%)	7 (16.7%)	5 (9.1%)
Fuchs heterochromic cyclitis	9 (9.3%)	5 (11.9%)	4 (7.3%)
Type of operation			
Vitrectomy	21 (21.6%)	7 (16.7%)	14 (25.5%)
Phacovitrectomy	76 (78.4%)	35 (83.3%)	41 (74.5%)
Tamponade medium			
None reported	7 (7.2%)	1 (2.4%)	6 (10.9%)
Air	70 (72.2%)	24 (57.1%)	46 (83.6%)
C_2F_6	2 (2.1%)	2 (4.8%)	0 (0.0%)
SF_6	13 (13.4%)	10 (23.8%)	3 (5.5%)
SO	5 (5.2%)	5 (11.9%)	0 (0.0%)
Number of posterior segment operations (*n*=94)			
1	83 (88.3%)	30 (~~76.9~~76.9%)	5~~3~~ (~~96.4~~96.4%)
2	~~0~~5(~~9.6~~9.3%)	~~5~~ 7 (~~17.9~~17.9%)	~~2~~0 (~~3.6~~3.6%)
3	2 (2.1%)	2 (5.~~1~~1%)	0 (0.0%)
Vision after surgery (*n*=95)			
Improved		19 (47.5%)	26 (47.3%)
Stayed the same	~~4~~5 (47.4%)	18 (45.0%)	28 (50.9%)
Worsened	46 (48.4%)	3 (7.5%)	1 (1.8%)
	4 (4.2%)		
Retinal tear or break			
No tear or break	71 (73.2%)	21 (50.0%)	~~3~~50 (9~~0~~.9~~1~~%)
Tear or break	26 (26.8%)	21 (50.0%)	5~~2~~ (9~~0~~.1~~9~~%) ~~No break~~

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Covariate	Mean (SD)	Mean (SD)	Mean (SD)
Age (years)	60.1 (13.2) Range: (23, 94)	59.1 (14.9) Range: (31, 94)	60.8 (9.09) Range: (38, 80)
Pre-operative visual acuity (LogMAR)	0.202 (0.231 Range:(-0.10, 1.0)	0.230 (0.250) Range: (-0.10, 1.00)	0.188 (0.238) Range: (-0.10, 1.00)
Time from surgery to discharge or last observation[1] days	125 (88) Range: (0, 60)	124 (75.2) Range: (0, 360)	126 (107) Range: (0, 600)
Axial length (mm)	24.9 (1.82) Range: (20.1, 29.0)	24.6 (2.01) Range: (20.1, 29.0)	25.2 (1.74) Range: (21.7, 28.6)

Five patients required two surgeries for removal of silicone oil (ROSO) ~~a~~, as they had multiple retinal breaks, including inferior breaks on PVD induction initial surgery, which necessitated use of silicone oil.

Of these 2 patients required a further operation, one for a symptomatic epiretinal membrane (ERM) and another for a post ROSO vitreous haemorrhage wash out.

Those requiring further surgery often had ocular comorbidities (lattice degeneration, myopia, diabetic retinopathy).

A sequential logistic regression analysis conducted on the *Break* outcome retained age and number of operations from the block of controlling variables. Number of operations, plus the primary vitreous status variable, were found to be significantly associated at the 5% significance level with retinal breaks or tears in a final parsimonious multiple model (p=0.027 for number of operations; p=0.010 for vitre~~u~~ous status). Age was substantively associated with the outcome but was not statistically significant at the 5% significance level (p=0.128).

Controlling for other parameters, the odds of a retinal tear or break in patients increase by about 6.3 times with each additional operation conducted. Controlling for other parameters, the odds of a retinal tear or break in patients with vitreous attached were about 5.5 times the odds of a retinal tear or break in patients with vitreous detached.

Nagelkerke's pseudo-R^2 statistic for the final model was 0.366; indicating that the model was a good fit to the data. A classification table revealed that 80.5% of cases were correctly classified. Hosmer and Lemeshow's test for calibration revealed no evidence that the final model was not well calibrated ($\chi^2_{(8)}$=3.50, p=0.899).

Full model parameters are given in Table 2 below.

Table 2: Model parameters of parsimonious logisitic regression model of retinal break

Variable	**Odds ratio**	**95% CI**	***p*-value**
Age (years)	0.96	(0.91, 1.01)	0.128
Number of operations	6.28	(1.23, 32.1)	0.027
Vitreous status (reference category *Detached*)	5.56	(1.52, 20.4)	0.010

A sequential logistic regression analysis conducted on the *Improvement* outcome retained indications for surgery and number of operations from the block of controlling variables. Number of operations was found to be significantly associated at the 5% significance level with improvement in visual acuity in a final parsimonious multiple model (p=0.017). Indications for surgery was substantively associated with the outcome but was not statistically significant at the 5% significance level (p=0.056). There was no evidence for any association between vitreous status and the outcome (p=0.793). Controlling for other parameters, the odds of improvement in visual acuity increases by about 15.8 times with each additional operation conducted.

Nagelkerke's pseudo-R^2 statistic for the final model was 0.219; indicating that the model is a fairly good fit to the data. A classification table revealed that 63.8% of cases were correctly classified. Hosmer and Lemeshow's test for calibration revealed no evidence that the final model was not well calibrated ($\chi^2_{(3)}$=1.62, p=0.655).

Full model parameters are given in Table 3 below.

Table 3: Model parameters of parsimonious logisitic regression model of visual improvement

Variable	Odds ratio	95% CI	*p*-value
Indications for surgery	3.93	(0.97, 15.9)	0.056
Number of operations	15.8	(1.65, 151)	0.017
Vitreous status (reference category *Detached*)	0.87	(0.31, 2.43)	0.793

A sequential Cox regression analysis conducted on the *Time* outcome retained number of operations from the block of controlling variables. Number of operations was found to be significantly associated at the 5% significance level with time to discharge in a final parsimonious multiple model (p=0.008). There was no evidence for any association between vitreous status and the outcome (p=0.934). Controlling for other parameters, the "hazard" of discharge increases by about 2.8 times with each additional operation conducted.

Full model parameters are given in Table 4 below.

Table 4: Model parameters of parsimonious Cox regression model of time to discharge

Variable	Hazard ratio	95% CI	*p*-value
Number of operations	2.78	(1.30, 5.91)	0.008
Vitreous status (reference category *Detached*)	0.87	(0.61, 1.58)	0.934

Discussion:

Research suggests that patient satisfaction from vitrectomy for floaters is high, with the majority of patients being satisfied and very satisfied. [6, 10] While there is significant data available on satisfaction, there is limited and variable data available on complication rates and visual outcomes. [9]

This study aimed to investigate the incidence of complications such as retinal tear/detachment following PPV for floaters, to ascertain if there was any difference between patients with vitreous attached or detached prior to surgery. Additionally we looked at the post-operative complications and time to discharge in these two groups.

A large proportion of patients (47.5% vitreous attached; 47.3% vitreous detached) had an improvement of vision after surgery. There were also a large proportion of patients (45.0% vitreous attached; 50.9% vitreous detached) for whom vision was unchanged. These outcomes were expected, as most patients undergoing surgery had normal or near normal visual acuity on Snellen's chart, the standard clinical test for visual function. Improvement in the visual disability secondary to floaters is best determined by QOLVFQ as patients' distress does not correlate with visual acuity. [10]

16.7% of the vitreous attached group and 25.5% with vitreous detached group were already pseudophakic. All patients were pseudophakic following vitrectomy; therefore the visual outcome were not cofounded by post-operative cataract which has been reported in high proportions (22.5-75%) in other studies. [4, 7-10]

A major concern following vitrectomy is iatrogenic retinal breaks leading to rhegmetogenous retinal detachment if missed. In our series of 97 eyes there were no cases of post-operative

retinal detachment (both vitreous attached or detached); this is similar to Mason et al. 2014 (168 eyes) and Sebag et al. 2014 (49 eyes). In contrast to other studies [8, 9] however, we had a high proportion of intra-operative retinal breaks requiring retinopexy 36.2% (25 eyes). This was much higher in the group with vitreous attached (51.4%) than in the group with vitreous detached (21.2%). (to mention proportion requiring retinopexy and gas tamponade) This difference has been noted previously by Rahman et al. 2013 who studied 137 patients undergoing PPV and PHF separation; iatrogenic retinal breaks were found in 18.2%. Tan et al. 2011 found a statistically significant relationship between retinal breaks and PVD induction. Where PVD was induced, breaks were found in 30.5% of cases and only 11.6% of cases where PVD pre-existed (P =0.019). Better intraoperative detection of breaks due to excellent peripheral view afforded by combined phakovitrectomy and prospective data collection may have contributed to a higher incidence of peripheral breaks in this study.

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The analysis has revealed strong evidence for a link between vitreous status and the ocrruence of retain breaks or tear, with no evidence revealed to link vitreous status with any of the secondary outcomes. All available patients were included in the analysis; no formal power calculation was undertaken. However, it is unlikely that findings would be substantively different from a larger sample.

Conclusion

This study suggests that when offering PPV as a treatment for floaters, surgeons must be mindful of vitreous status. Having to induce a PVD as part of the vitrectomy is associated with increased retinal breaks, post-operative complications and potentially a worse visual outcome. Patients should therefore be made aware of this and be counselled appropriately about the possibility of retinopexy and a longer acting tamponade when considering treatment.

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Summary Box

What was known before:

- Transconjunctival sutureless vitrectomy (TSV) is an effective treatment for floaters
- TSV is associated with high patient satisfaction scores on QOLVFQ
- Induction of PVD during vitrectomy is associated with an increased risk of iatrogenic retinal breaks.

What this study adds:

- Retinal breaks are significantly likely in patients with vitreous attached, however they do not lead to postoperative retinal detachment, if properly managed at the time of surgery.
- Patient with vitreous detachmed are more likely to undergo retinopexy and tamponade compared to vitreous detached.

- There is no significant difference in time to discharge or levels of improvement of VA between those with vitreous attached or detached before surgery

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