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Clinical Variables Associated with Failure of Retinal Detachment Repair

The European Vitreo-Retinal Society Retinal Detachment Study Report Number 4

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Objective: To identify risk factors associated with failure of anatomic reattachment in primary rhegmatogenous retinal detachment repair.

Design: Nonrandomized, multicenter, collaborative study.

Participants: Primary procedures for 7678 rhegmatogenous retinal detachments reported by 176 surgeons from 48 countries.

Methods: We recorded specific preoperative clinical findings, repair method, and outcome after intervention. We performed univariate, bivariate, and multivariate analyses to identify variables associated with surgical failure.

Main Outcome Measures: Final failure of retinal detachment repair (level 1), remaining silicone oil at study conclusion (level 2), and need for additional procedures to repair the detachment (level 3).

Results: We analyzed 7678 cases of rhegmatogenous retinal detachment repair. Presence of choroidal detachment or significant hypotony was associated with significantly higher level 1 failure rates when grade 0 or B proliferative vitreoretinopathy (PVR) was present and higher level 2 failure rates, regardless of PVR status ($P<0.05$). Excluding cases with choroidal detachment or hypotony, increasing PVR was associated with increasing level 1 failure rates. The difference between grade B and C-1 PVR was significant ($P = 2 \times 10^{-6}$). No difference was observed in level 1 failure rates when operated eyes were phakic versus pseudophakic. Level 1 failure was significantly higher when all 4 quadrants of retina (4.4%) were detached than when only 1 quadrant (0.8%) had subretinal fluid. With grade B or C-1 PVR, cases with large or giant tears had significantly higher level 1 failure rates. No association was observed between number of retinal breaks and failure rates. Multivariate analysis showed grade C-1 PVR, 4 detached quadrants, and presence of choroidal detachment or significant hypotony were independently linked with a greater level 1 failure rate; the presence of a smaller retinal break was associated with a lesser level 1 failure rate.

Conclusions: Choroidal detachment, significant hypotony, grade C-1 PVR, 4 detached quadrants, and large or giant retinal breaks were independent explanatory variables of retinal detachment repair failure. In contrast to earlier studies, the significance of phakic versus pseudophakic status was not confirmed. *Ophthalmology 2014;121:1715-1719 © 2014 by the American Academy of Ophthalmology.*

*Supplemental material is available at www.aaojournal.org.

The identification of variables associated with the failure of retinal detachment repair is integral to prognosis and decisions regarding management. A clear understanding of specific factors that usually lead to a greater or lesser likelihood of success is valuable when deciding on a procedure. Awareness of adverse clinical findings can not only allow the surgeon to better prepare for the surgery ahead, but also to prepare the patient for the possibility of a suboptimal outcome.

Additional information regarding risk factors for retinal detachment repair failure is desirable. Recently, the Scleral Buckling versus Primary Vitrectomy in Rhegmatogenous Retinal Detachment (SPR) study reported results from a multivariate analysis to identify risk factors associated with failure of anatomic reattachment.[1] Overall, an increased number of retinal breaks was associated with failure, whereas in the group of phakic eyes, larger breaks and intraoperative use of cryotherapy were negative indicators. Prior analyses from the SPR study demonstrated that the extent of the detachment, inferior location, lack of intraoperative laser photocoagulation, and duration of symptoms can all lead to poorer outcomes.[2,3] Several investigations have noted the presence of proliferative vitreoretinopathy (PVR) as a significant factor in failure of repair.[4–9] In addition, hypotony has been cited as a risk factor for reoperation.[3,10]

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Table 1. Baseline Demographic Patient Data

Lens Status	Level of Proliferative Vitreoretinopathy, n			
	Grade 0	*Grade A*	*Grade B*	*Grade C-1*
Phakic	1504	1779	858	642
Pseudophakic	810	1030	516	431

In this investigation, members of the European Vitreo-Retinal Society (EVRS) reported their cases of rhegmatogenous retinal detachment (RRD) repair. In all, 176 surgeons from 5 continents provided information on 7678 RRDs. Prior published reports have provided information regarding the strategy for detachment repair in these cases.[11–13] Herein we have analyzed preoperative clinical findings, risk factors, and their varying association with failure of anatomic reattachment.

Methods

The EVRS Retinal Detachment Study, a nonrandomized, collaborative, multicenter study, collected pre- and postoperative information regarding cases of retinal detachment and their repair. Members of the society reported the RRDs they operated on from April 2010 to April 2011. We gathered specific preoperative clinical findings, repair method, and anatomic outcome after intervention. Participants reported 7678 RRD repairs, with follow-up ranging from 3 months to 1 year. The EVRS Retinal Detachment Reports Numbers 1 and 2 include a more specific description of the methodologies used and limitations of the study.[11,12] Institutional review board regulations differed by location; therefore, each investigator was responsible for following the specific requirements within each country and institution. Study design and ethical aspects of the investigation were approved by EVRS Committees. The French National Institute of Statistics and Economic Studies analyzed the results independent from the investigators. We analyzed the influence of the following factors on anatomic outcome: lens status, PVR grade, number of detached quadrants, type of retinal break, size of retinal break, number of retinal breaks, hypotony, choroidal detachment, and vitreous hemorrhage. Anatomic outcome of repair was reported in terms of 3 categories of failure rates. Level 1 failure rate represents the true failure rate, where the detached retina was determined to be irreparable at the conclusion of the study. Level 2 failure rate is the proportion of eyes with silicone oil remaining in the eye at the study's conclusion. Level 3 failure rate is the number of eyes that had a recurrent detachment or a complication after the initial procedure, necessitating additional surgery.

The National Institute of Statistics and Economic Studies performed univariate and then bivariate analyses using the entire database. A graphical representation of the results was produced. These initial steps identified some factors associated with each of the failure rates. A multivariate analysis with a step-by-step logistic regression was performed on the entire database to further identify those preoperative findings independently linked with the failure of detachment repair. For this evaluation, statistical significance was defined as a 2-tailed $P<0.05$.

Table 2. Procedure Performed with Regard to Lens Status, Excluding Cases with Choroidal Detachment or Significant Hypotony

Lens Status	Scleral Buckle Alone, n (%)	Vitrectomy with or without Scleral Buckle, n (%)
Phakic	1606 (36)	2855 (64)
Pseudophakic	285 (11)	2310 (89)

Results

In total, 176 surgeons from 48 countries on 5 continents provided information on the clinical findings and primary procedures performed for 7678 patients with RRDs. Baseline demographic data including level of PVR and lens status are displayed in Table 1. Information on the procedure performed with regard to lens status is displayed in Table 2.

Initial univariate and bivariate analyses were performed to identify major independent explanatory variables of the failure rate. Cases with choroidal detachment or significant hypotony (intraocular pressure <6 mmHg) were separated based on level of PVR and each group was analyzed (Table 3, available at www.aaojournal.org). Choroidal detachment and significant hypotony were associated with a significantly higher level 1 failure rate in those cases with grade 0 or B PVR ($P = 10^{-7}$ and 0.006, respectively). These aggravating factors were associated with a higher level 2 failure rate, regardless of the extent of PVR ($P<0.05$). Given this, choroidal detachment and significant hypotony were determined to be major independent explanatory variables of the failure rate.

Vitreous hemorrhage coexisted with retinal detachment in 647 cases. The presence of vitreous hemorrhage, not quantity of blood, was reported by the surgeons. Earlier studies suggested that vitreous hemorrhage may be associated with a worse prognosis.[14,15] The bivariate analysis performed in our study showed that vitreous hemorrhage was not an independent explanatory variable of the failure rate.

Next, the association of PVR with the failure rate was examined. Cases of choroidal detachment and hypotony were excluded from this analysis considering their determined independent association with the failure rate. Cases with grade B PVR similarly had higher level 2 and 3 failure rates than eyes with grade A PVR (Table 4, available at www.aaojournal.org). Finally, when cases with grade C-1 PVR were compared with those with grade B PVR, higher level 1 and 2 failure rates were associated with the eyes with more severe PVR (Table 5, available at www.aaojournal.org).

Lens status was then analyzed as a possible factor influencing the failure rate. In a comparison of the level 1 failure rates when the operated eyes were phakic versus pseudophakic, there was no difference observed ($P = 0.84$; Table 6). However, there were significantly higher level 2 and 3 failure rates in the group with pseudophakic eyes.

The relationship between the number of detached quadrants at preoperative examination with the subsequent failure rates after treatment is shown in Table 7. The level 1 failure rate was significantly greater when all 4 quadrants of the retina were detached than when only 1 quadrant had subretinal fluid (4.4% vs 0.8%). This pattern held true for the level 2 and 3 failure rates. Table 8 displays the correlation between PVR, choroidal detachment, and significant hypotony with number of detached quadrants. A greater number of detached quadrants was

Table 6. Failure Rates According to Lens Status

Level of Failure	Phakic (%)	Pseudophakic (%)	*P* Value
1	2.1	2.1	0.84
2	4.3	7.3	2×10^{-6}
3	14.7	16.3	4×10^{-6}

Table 7. Failure Rates According to Number of Detached Quadrants

Level of Failure	No. of Detached Quadrants (%)			
	1	*2*	*3*	*4*
1	0.8	1.5	2.2	4.4
2	3.0	3.4	7.0	11.8
3	13.8	14.8	14.1	18.5

P values for level 1 failure: 1 quadrant vs. 2 quadrants: 0.08; 2 quadrants vs. 3 quadrants: 0.07; 3 quadrants vs. 4 quadrants: 0.0006.
P values for level 2 failure: 1 quadrant vs. 2 quadrants: 0.007; 2 quadrants vs. 3 quadrants: 5×10^{-9}; 3 quadrants vs. 4 quadrants: 4×10^{-9}.
P values for level 3 failure: 1 quadrant vs. 2 quadrants: 0.03; 2 quadrants vs. 3 quadrants: 0.004; 3 quadrants vs. 4 quadrants: 10×10^{-9}.
The numbers are the percent of cases with Level 1, 2, or 3 failure in the setting of 1, 2, 3, or 4 detached quadrants.

associated with significantly higher rates of PVR, hypotony, and choroidal detachment ($P<10^{-10}$).

We then analyzed the association between the size of the retinal breaks and the failure rates. Detachments were classified based on the size of the largest break present; cases of choroidal detachment and hypotony were excluded, and the groups were further separated by level of preoperative PVR. Small and medium breaks were defined as <1 clock-hour in size, whereas breaks between 1 and 3 clock-hours were considered to be large. Those >3 clock-hours were labeled giant. Large and giant tears were grouped together and compared with small and medium tears. When grade B or C-1 PVR was present, cases with large or giant tears had significantly higher level 1 failure rates ($P = 0.047$ and 9×10^{-4}, respectively; Table 9).

We analyzed the correlation of the number of retinal breaks and the failure rate. The mean number of retinal breaks was 1.98 (range, 1−6). No obvious relationships were discernable between the number of retinal breaks and PVR or the failure rate. Thus, the number of retinal breaks did not seem to be a major explanatory factor of the failure rate (Table 10).

Finally, we conducted a multivariate analysis to isolate independent variables that have an influence on the level 1 failure rate. This was performed with a logistic regression, based on a step-by-step approach. Grade C-1 PVR, 4 detached quadrants, and the presence of choroidal detachment or significant hypotony were all independently linked with a greater level 1 failure rate (Table 11). The presence of a smaller retinal break, versus a large or giant tear, was associated with a lesser level 1 failure rate.

Discussion

Considering the numerous factors influencing outcome and prognosis in retinal detachment repair, it is important to carefully investigate initial clinical findings that portend a positive or negative result. Herein, our goal was to identify major independent explanatory variables of retinal detachment repair failure. Although visual acuity is arguably a good metric of success, our study was based on anatomic outcome.

Table 8. Correlation between Proliferative Vitreoretinopathy (PVR), Choroidal Detachment, and Significant Hypotony with Number of Detached Quadrants

Variable	No. of Detached Quadrants (%)			
	1	*2*	*3*	*4*
PVR	4.4	8.8	14.2	35.7
Choroidal detachment	0.4	0.5	0.8	3.7
Hypotony	2.0	3.5	9.4	14.0

P values for PVR all $P < 10^{-10}$.

Table 9. Level 1 Failure Rates According to Size of the Retinal Break and Level of Proliferative Vitreoretinopathy (PVR), Excluding Choroidal Detachment or Significant Hypotony

Type of Retinal Break	Level of PVR (%)		
	Grade A	*Grade B*	*Grade C-1*
Normal	1.4	1.0	3.3
Large or giant	1.5	2.7	9.2
	$P = 0.82$	$P = 0.047$	$P = 9 \times 10^{-4}$

Based on earlier analysis, aggravating factors of choroidal detachment and significant hypotony were the first to be analyzed. The role of choroidal detachment as a negative predictive factor of final anatomic success was postulated by Girard et al,[9] who analyzed 290 eyes operated on for RRD. Hypotony was estimated as a major negative prognostic factor of retinal detachment in a series of 302 eyes with complex retinal detachment operated with vitrectomy and retinectomy.[16] Considering the higher level 1 and 2 failure rates observed when choroidal detachment or hypotony was present, regardless of the degree of PVR, these factors were determined to be independently associated with failure of reattachment. Multivariate analysis subsequently confirmed this assertion to be true no matter which operative technique was used.

It is a reasonable assumption, based on the literature, that an increasing level of PVR will correspond with an increasing surgical failure rate, and the results here certainly support this expectation.[4,9,17–21] When analyzing PVR and failure rates without the impact of choroidal detachment and hypotony, we can conclude that PVR is associated with the failure rate. Even though the number of subjects in this study is very large, some of the subgroups are relatively small in number. Thus, some subgroup analyses may not attain significance. Taking the multivariate analysis into account, these results further clarify that grade C-1 PVR or greater is a major independent variable of the effective failure rate.

Turning to the extent of the retinal detachment, there was a trend toward an increasing failure rate with an increasing number of detached quadrants. When choroidal detachment, hypotony, and PVR were taken into account, these aggravating factors were found to present at greater rates when

Table 10. Failure Rates According to Number of Small and Medium Retinal Breaks, Large and Giant Retinal Breaks Excluded

Level of Failure	No. of Retinal Breaks (%)					
	1	*2*	*3*	*4*	*5 or 6*	*>6*
1	1.5	0.9	0.9	2.6	0.6	3.2
2	3.2	4.6	5.8	4.8	6.1	5.2
3	13.5	16.4	17.9	18.2	19.0	15.8

Table 11. Multivariate Analysis Displaying Variables Independently Linked to the Level 1 Failure Rate

Variable	β Coefficient	*P* value
Grade C-1 proliferative vitreoretinopathy	0.45	0.0227
4 Detached quadrants	1.11	$<10^{-5}$
Choroidal detachment or hypotony	0.88	2×10^{-4}
Smaller retinal break	−0.49	0.0232

more quadrants were detached. Therefore, when analyzing the failure rate after excluding these aggravating factors, the influence of the number of detached quadrants decreases. To reconcile this, we can turn to the final multivariate analysis and confirm that 4 detached quadrants is a major independent explanatory variable of the failure rate. These data confirm earlier suggestions from smaller studies that less extensive retinal detachments have a better prognosis.[9,14]

This study confirms earlier data from smaller studies that the presence of hypotony, choroidal detachment, higher PVR grade, and 4 detached quadrants are negative prognostic factors for final anatomic outcome. However, previous smaller studies have suggested risk factors for poor outcomes, which were not confirmed with multivariate analysis here. Among them were lens status and the number of retinal breaks.[1]

With regard to lens status, there was no difference observed in the level 1 failure rates between phakic and pseudophakic eyes. However, pseudophakic eyes seemed to have a higher level 2 failure, or a higher rate of remaining silicone oil. This can be explained by the fact that pseudophakic eyes were far more likely to receive a vitrectomy compared with phakic eyes. This is not surprising because most surgeons likely made their decision in accordance with the literature available during the period of patient enrollment. According to the SPR study, pseudophakic patients needed more surgeries to achieve final success when their initial surgery was scleral buckling compared with primary vitrectomy.[1] Although randomization is the best method for investigating the efficacy of medications, randomization may be difficult in studying the efficacy of different operative procedures. The creation of homogenous groups is extremely difficult in retinal detachment cases because the size of the retinal break, PVR, number of detached quadrants, and many other factors differ among patients. With univariate, bivariate, and multivariate analyses, lens status does not seem to be an independent explanatory variable of the level 1 failure rate.

Last, the number, size, and type of retinal breaks leading to the detachments were examined. From the bivariate and multivariate analyses, there is no apparent link between the number of breaks and the failure rate. As for retinal break size, the presence of a large or giant tear is a major independent explanatory variable of the failure rate. This was supported by the multivariate analysis, which showed that a smaller break tends to decrease the risk of failure in comparison with a larger tear.

In conclusion, in this large-scale, multicenter study, choroidal detachment, significant hypotony, grade C-1 PVR, 4 detached quadrants, and a large or giant retinal break were all independent explanatory variables of retinal detachment repair failure. In contrast with earlier studies, the significance of phakic versus pseudophakic status, vitreous hemorrhage, and the number of retinal tears in predicting the final anatomic outcome were not confirmed.

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Abbreviations and Acronyms:
EVRS = European Vitreo-Retinal Society; **PVR** = proliferative vitreoretinopathy; **RRD** = rhegmatogenous retinal detachment; **SPR** = Scleral Buckling versus Primary Vitrectomy in Rhegmatogenous Retinal Detachment Study.

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