• Clinical Research •

Nomogram for predicting non-proliferative vitreoretinopathy probability after vitrectomy in eyes with rhegmatogenous retinal detachment

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Abstract

● **AIM:** To identify the risk factors for postoperative proliferative vitreoretinopathy (PVR) in patients with primary rhegmatogenous retinal detachment (RRD) and develop a nomogram for predicting postoperative PVR-free probability.

● **METHODS:** A total of 741 patients (741 eyes) diagnosed with primary RRD who underwent first surgery in the same hospital were retrospectively reviewed and randomly assigned with 521 to the training set and 220 to the validation set. Univariate and multivariate logistic regression analyses were performed in the training cohort to determine risk factors to construct a nomogram for predicting the 3-, 4-, 5-, and 6-month postoperative PVR-free probabilities. Nomogram performance was estimated by the concordance index (C-index), calibration plot, and the area receiver operating characteristic (ROC) curve.

● **RESULTS:** A nomogram was constructed based on the preoperative PVR, silicone oil tamponade time (SOTT), photocoagulation energy (PE), retinal tear size (RTS), and hypertension. In the training set, the C-index of the nomogram was 0.896, 0.936, 0.961, and 0.972 at 3, 4, 5, and 6mo, respectively. The C-index values in the validation set were 0.860, 0.936, 0.951, and 0.965 at 3, 4, 5, and 6mo, respectively. Decision-curve analysis indicated that only the 4-, 5-, and 6-month nomograms had significant net benefits over a large threshold probabilities interval.

● **CONCLUSION:** Preoperative PVR, SOTT, PE, RTS, and hypertension are significant risk factors for postoperative PVR formation in patients with primary RRD. The proposed nomogram can effectively predict the 4-, 5-, and 6-month PVR-free probabilities after surgery and assist in making clinical decisions during follow-up.

● **KEYWORDS:** nomogram; proliferative vitreoretinopathy; rhegmatogenous retinal detachment; risk factor

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INTRODUCTION

With decades of advances in vitreoretinal surgery, the primary success rate of surgery for rhegmatogenous retinal detachment (RRD) has increased to over 90%[1-2]. Among RRD surgeries that fail, development of proliferative vitreoretinopathy (PVR) is the most common cause[3-4]. The incidence of postoperative PVR ranged from 4% to 34% in prospective studies[5]. Reduction of the incidence of PVR by surgical techniques or agents has always been a challenge for vitreoretinal surgeons[6]. A key step in achieving this is to identify patients at high risk for PVR development because they would benefit the most.

Previous studies have reported multiple clinical risk factors for PVR through univariate and multiple regression analyses, including preoperative PVR, preoperative vitreous hemorrhage, silicone oil (SO) tamponade, large retinal hiatus, choroidal detachment (CD), and excessive cryotherapy[7-8]. However, the results of these studies were frequently inconsistent and

contradictory. Some researchers have used these risk factors to devise formulas to predict the risk for PVR development[9-12]. Nevertheless, these formulas are complex, have low sensitivity and specificity, and external validation showed that they are not reliable for clinical application[13]. This prompted us to devise a more convenient, accurate, and clinically applicable method for predicting PVR occurrence.

A nomogram is a popular tool for predicting survival prognosis of cancer, including mortality and recurrence. It can construct a concise numerical estimation model to predict the probability of an event and effectively simplify complex statistical prediction models which contain a large number of factors[14]. The nomogram is an easy to master form of graphical interface for clinical decision-making, which is a graphical representation of a complex mathematical formula[15]. In the same way, a nomogram can also be applied to eye diseases research to obtain statistical predictive models to predict the prognosis of eye diseases.

The purpose of this study was to identify the risk factors for postoperative PVR in patients with primary RRD. Furthermore, a nomogram was generated to predict the probability of being PVR-free in patients with primary RRD at different time points after vitrectomy.

SUBJECTS AND METHODS

Ethical Approval The retrospective study protocol was approved by the Eye Hospital and School of Ophthalmology and Optometry Ethics Committee of Wenzhou Medical University (MEC numbers: 2021-083-K-72). All clinical procedures were performed in accordance with the Helsinki Declaration. The informed consent was obtained from the subjects.

Patients The patients who underwent first vitrectomy surgery to repair primary RRD in our hospital from January 2016 to January 2020 were reviewed. Surgical procedures included 23-G vitrectomy (Constellation vision system, Alcon, Fort Worth, TX, USA) combined with SO (SO, RT SIL-OL 5000cs; Carl Zeiss Meditec AG company, Germany) or perfluoropropane (C_3F_8) tamponade, and all patients underwent phacoemulsification and intraocular lens (IOL) implantation during the first operation. The exclusion criteria were previous intraocular surgery (*e.g.*, vitreoretinal surgery, glaucoma surgery, or crystalline lens surgery), pseudophakia or aphakia, diabetic retinopathy, type 1 diabetes, history of trauma, history of severe intraocular infections or inflammatory disease, a follow-up time less than 6mo, or severe data loss.

Data Collection Patients' clinical data were obtained from hospital medical records, including age, sex, medical history, systemic disease, diagnosis, time from onset to surgery (TOS), lens status, surgical procedures, PVR grade, intraocular pressure, preoperative and postoperative routine examinations, perioperative complications, and follow-up time.

The following factors of postoperative PVR were evaluated: age, sex, silicone oil tamponade time (SOTT), cryotherapy, photocoagulation energy (PE), number of photocoagulation points (NOPP), electric coagulation (EC), type 2 diabetes (T2D), hypertension, retinal tear size (RTS), retinal detachment (RD) extension, SO or C_3F_8 tamponade, preoperative CD, and preoperative PVR. The type of tamponade is chosen by the surgeon depended on experience and patient preference[16]. All operations were performed by an experienced vitreoretinal surgeon under retrobulbar block anesthesia.

PVR was graded according to the 1983 International Retinal Association Classification Guidelines[17]. The SOTT was divided into five grades according to the length of time: grade I, 2–3mo; grade II, 4–6mo; grade III, 7–9mo; grade IV, 10–12mo; and grade V, >12mo. The PE was divided into four grades according to the energy used during the first surgery: grade I, 120–165 mV; grade II, 166–210 mV; grade III, 211–255 mV; and grade V, 256–300 mV. The long diameter of a retinal tear was evaluated according to the diameter of the optic papilla (PD).

Statistical Analysis Kolmogorov-Smirnov inspection of continuous numerical variables was used to test for normal distribution. Chi-square test or Fisher's exact test was applied for univariate analysis of categorical variables. Wilcoxon rank sum test was used for univariate analysis of rank variables and Student's normal *t*-test was used to compare the mean values of normal distribution variables. The differences between groups with and without postoperative PVR were compared. Logistic regression analysis was applied to identify the risk factors for postoperative PVR. Stepwise regression analysis was used to further determine the risk factors which were used to establish the model. Based on the results of multivariate analysis, a nomogram was constructed to predict the 3-, 4-, 5-, and 6-month postoperative PVR-free probabilities. We developed the model in the training set and then validated it in the validation set to ensure the prediction accuracy of the nomogram. Harrell's consistency index (C-index) and the area under the time-dependent receiver operating characteristic (ROC) curve were used to estimate the prediction accuracy of the constructed nomogram. The calibration curves were used to compare the predicted probability and the actual results, using a 45-degree line as the optimal model. Finally, decision-curve analysis (DCA) was applied to evaluate the clinical nomogram application by quantifying the net improvement benefits under different threshold probabilities. Statistical analyses were performed using SPSS (version 24.0, SPSS Inc., Chicago, IL, USA) and R version 3.4.2 software (The R Foundation for Statistical Computing, Vienna, Austria. http://www.r-project.org). A $P<0.05$ was considered statistically significant.

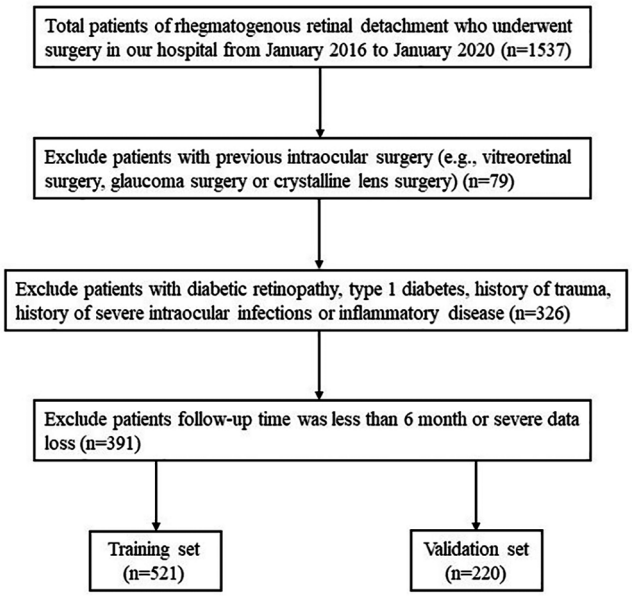

Figure 1 Flow diagram of the data screening process.

RESULTS

Patient Characteristics A total of 1537 eyes with primary RRD in 1537 patients were reviewed. Finally, 741 patients were included after screening with the exclusion criteria, and 521 were randomly assigned to the training set and 220 to the validation set (Figure 1). In the training group, most patients were aged <70y (94.7%) and male (56.2%), while 6% had T2D and 28.6% were hypertensive.

The TOS of patients was usually <7d (84.5% of 521). The most common primary RTS was <1 PD (77.9% of 521). RD extension in most patients was ≤2 quadrants (86.2% of 521). Preoperative CD was present in 51 (9.8% of 521) patients. There were 180 (34.5% of 521) patients with preoperative PVR, including 25 (13.9% of 180) with grade B and 155 (86.1% of 180) with grade C (Table 1). Following surgery, 117 (22.5% of 521) patients eventually developed postoperative PVR, including 15 (13.3% of 113) grade B and 98 (86.7% of 113) grade C (Table 2). In this study, patients in the training and validation sets were comparable in all clinical characteristics (Table 1).

Univariate and Multivariate Logistic Regression Analyses of Effects of Factors on Postoperative PVR In the training cohort, univariate analysis showed that eleven variables of the characteristics were significantly associated with postoperative PVR, which were the SOTT, PE, NOPP, EC, cryotherapy, T2D, hypertension, RTS, SO tamponade, preoperative CD, and preoperative PVR (Table 2). However, only the SOTT, PE, hypertension, RTS, and preoperative PVR were identified as significantly associated with postoperative PVR in the multivariate logistic regression analysis (P<0.05; Table 3).

Nomogram Construction All five significant independent risk factors for postoperative PVR identified by multivariate logistic regression analysis were integrated to develop the nomogram. Figure 2 demonstrates the nomogram to predict the 3-, 4-, 5-, and 6-month postoperative PVR-free probabilities in the training set. By summing up the scores for each variable, it is convenient to calculate a patient's individual postoperative PVR-free probability at different points in time.

Table 1 Characteristics of the training and validation cohorts *n* (%)

Variables	Total (*n*=741)	Training cohort (*n*=521)	Validation cohort (*n*=220)	*P*
Age (y)				0.303
I ≤40	155 (20.9)	101 (19.4)	54 (24.5)	
II 41-50	126 (17.0)	93 (17.9)	33 (15.0)	
III 51-60	215 (29.0)	139 (18.8)	76 (34.5)	
IV 61-70	197 (26.6)	149 (28.6)	48 (21.9)	
V >70	48 (6.5)	39 (5.3)	9 (4.1)	
Sex				0.054
Female	318 (42.9)	228 (43.8)	90 (40.9)	
Male	423 (57.1)	293 (56.2)	130 (59.1)	
T2D				0.467
Yes	46 (6.2)	31 (6.0)	15 (6.8)	
No	695 (93.8)	490 (94.0)	205 (93.2)	
Hypertension				0.652
Yes	205 (27.7)	149 (28.6)	56 (25.5)	
No	536 (72.3)	372 (71.4)	164 (74.5)	
TOS (d)				0.568
I (1-7)	562 (75.8)	440 (84.5)	122 (55.5)	
II (8-30)	154 (20.8)	68 (13.1)	86 (39.1)	
III (31-90)	20 (2.7)	10 (1.9)	10 (4.5)	
IV (>90)	5 (0.7)	3 (0.5)	2 (0.9)	
RTS				0.659
<1 PD	579 (78.1)	406 (77.9)	173 (78.6)	
≥1 PD, <2 PD	90 (12.2)	66 (12.7)	24 (10.9)	
≥2 PD, <3 PD	62 (8.4)	42 (8.1)	20 (9.1)	
≥3 PD	10 (1.3)	7 (1.3)	3 (1.4)	
RD extension				0.237
1 quadrant	330 (44.5)	212 (40.7)	118 (53.6)	
2 quadrants	317 (42.8)	237 (45.5)	80 (36.4)	
3 quadrants	86 (11.6)	68 (13.1)	18 (8.2)	
4 quadrants	8 (1.1)	4 (0.7)	4 (1.8)	
Preop. CD				0.522
Yes	65 (8.8)	51 (9.8)	14 (6.4)	
No	676 (91.2)	470 (90.2)	206 (93.6)	
Preop. PVR				0.932
No	491 (66.3)	341 (65.5)	150 (68.2)	
PVR (A)	0	0	0	
PVR (B)	30 (4.0)	25 (4.8)	5 (2.3)	
PVR (C)	220 (29.7)	155 (29.7)	65 (29.5)	

T2D: Type 2 diabetes; TOS: Time from onset to surgery; RTS: Retinal tear size; PD: The diameter of the optic papilla; RD: Retinal detachment; CD: Choroidal detachment; PVR: Proliferative vitreoretinopathy.

Table 2 Univariable association analyses in the training and validation cohorts

Category	Training cohort				*P*	Validation cohort				*P*
	Postop. PVR (*n*=117)		Without postop. PVR (*n*=404)			Postop. PVR (*n*=45)		Without postop. PVR (*n*=175)		
Gender	*n*	%	*n*	%	0.521	*n*	%	*n*	%	0.841
Male	48	41.0	180	44.6		19	42.2	71	40.6	
Female	69	59.0	224	55.4		26	57.8	104	59.4	
Age (y)					0.211					0.807
I ≤40	20	17.1	81	20.1		10	22.2	44	25.1	
II 41-50	23	19.7	70	17.3		7	15.6	26	14.9	
III 51-60	31	26.4	108	26.7		17	37.8	59	33.7	
IV 61-70	23	19.7	126	31.2		8	17.7	40	22.9	
V >70	20	17.1	19	4.7		3	6.7	6	3.4	
Follow-up time (mo, median±IQR)	12±6.3		12±6.1		0.633	12±5.8		12±5.9		0.853
TOS (d)					0.277					0.126
I (1-7)	62	53.0	378	93.6		20	44.5	102	58.3	
II (8-30)	45	38.5	23	5.7		16	35.6	70	40.0	
III (31-90)	8	6.8	2	0.5		8	17.8	2	1.1	
IV (>90)	2	1.7	1	0.2		1	2.1	1	0.6	
SOTT (mo)					<0.001					<0.001
No	28	23.9	167	41.3		12	26.7	68	38.9	
I (2-3)	17	14.5	152	37.7		7	15.6	83	47.4	
II (4-6)	41	35.1	78	19.3		17	37.8	21	12.0	
III (6-9)	14	12.0	5	1.2		5	11.1	2	1.1	
IV (9-12)	9	7.7	2	0.5		3	6.7	1	0.6	
V (>12)	8	6.8	0	0		1	2.1	0	0	
PE (mV)					<0.001					0.198
No	0	0	161	39.9		0	0	66	37.7	
I (120-165)	4	3.4	77	19.1		0	0	33	18.9	
II (166-210)	85	72.6	165	40.8		24	53.3	75	42.9	
III (211-255)	25	21.4	0	0		16	35.6	0	0	
IV (256-300)	3	2.6	1	0.2		5	11.1	1	0.6	
NOPP (*n*)					<0.001					<0.001
No	0	0	159	39.4		0	0	66	37.7	
I (120-200)	15	12.8	36	8.9		8	17.8	15	8.6	
II (201-400)	19	16.2	70	17.3		5	11.1	32	18.3	
III (401-600)	19	16.2	58	14.4		3	6.7	37	21.1	
IV (601-800)	8	6.8	37	9.2		5	11.1	13	7.4	
V (>800)	56	47.9	44	10.9		24	53.3	12	6.9	
Cryotherapy					<0.001					0.003
Yes	26	2.2	193	47.8		12	26.7	91	52.0	
No	91	77.8	211	52.2		33	73.3	84	48.0	
EC					<0.001					0.050
Yes	40	34.2	74	18.3		14	31.1	31	17.7	
No	77	65.8	330	81.7		31	68.9	144	82.3	
T2D					<0.001					<0.001
Yes	27	23.1	4	1.0		15	33.3	0	0	
No	90	76.9	400	99.0		30	66.7	175	100	
Hypertension					0.008					0.001
Yes	45	38.5	104	25.7		20	44.4	36	20.6	
No	72	61.5	300	74.3		25	55.6	139	79.4	
RTS					<0.001					<0.001
<1 PD	30	25.6	376	93.1		11	24.4	162	92.6	
≥1 PD, <2 PD	52	44.4	14	3.5		15	33.3	9	5.1	
≥2 PD, <3 PD	32	27.4	10	2.5		17	37.8	3	1.7	
≥3 PD	3	2.6	4	1.0		2	4.4	1	0.6	
RD extension					0.238					0.717
1 quadrant	77	65.8	135	33.4		21	46.7	97	55.4	
2 quadrants	21	17.9	216	53.5		15	33.3	65	37.1	
3 quadrants	16	13.8	52	12.9		5	11.1	13	7.5	
4 quadrants	3	2.5	1	0.2		4	8.9	0	0	
SO tamponade					0.005					<0.001
Yes	89	76.1	237	58.7		33	73.3	107	61.1	
No	28	23.9	167	41.3		12	26.7	68	38.9	
Preop. CD					0.003					0.002
Yes	12	10.3	127	31.4		29	64.4	123	70.3	
No	105	89.7	277	68.6		16	35.6	52	29.7	
Preop. PVR					<0.001					<0.001
No	4	3.4	337	83.4		1	2.2	150	85.7	
Yes	113	96.6	67	16.6		44	97.8	25	14.3	
PVR (A)	0		0			0		0		
PVR (B)	15	13.3	11	16.4		7	15.9	3	12.0	
PVR (C)	98	86.7	56	83.6		37	84.1	22	88.0	

PVR: Proliferative vitreoretinopathy; TOS: Time from onset to surgery; SOTT: Silicone oil tamponade time; PE: Photocoagulation energy; NOPP: Number of photocoagulation points; EC: Electric coagulation; T2D: Type 2 diabetes; RTS: Retinal tear size; PD: The diameter of the optic papilla; RD: Retinal detachment; SO: Silicone oil; CD: Choroidal detachment.

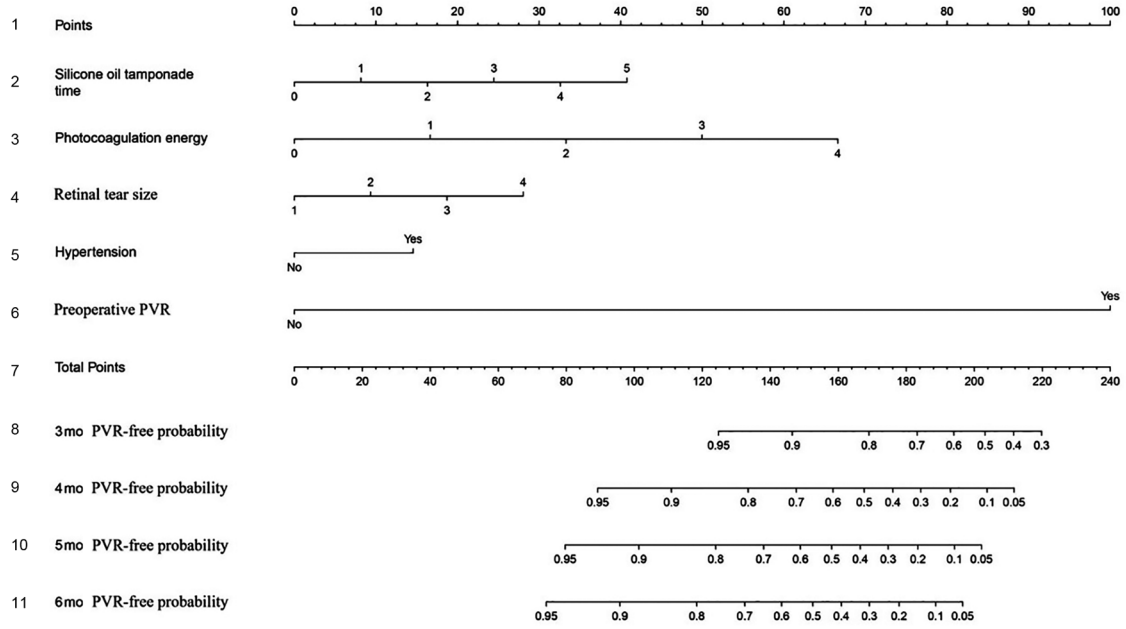

Figure 2 Nomogram predicting the 3-, 4-, 5-, and 6-month PVR-free probabilities after surgery of patients with primary RRD The row 1 shows the point assignment for each predictor. Rows 2–6 show the five predictors included in the nomogram. For each patient, each predictor is assigned a point value based on individual characteristics. The sum of these point values is located on the "Total Points" row. The rows 8-11 show the 3-, 4-, 5-, and 6-month PVR-free probabilities of patients with primary RRD after surgery. PVR: Proliferative vitreoretinopathy, RRD: Rhegmatogenous retinal detachment.

Table 3 Multivariate logistic regression analysis to identify risk factors of postoperative PVR in patients with primary RRD in training cohort

Category	Univariate analysis		Multi-factor analysis	
	OR (95%CI)	*P*	OR (95%CI)	*P*
Gender	0.886 (0.613, 1.281)	0.521	0.894 (0.605, 1.322)	0.574
Age	1.101 (0.946, 1.282)	0.211	0.925 (0.783, 1.093)	0.358
TOS	0.782 (0.628, 0.881)	0.479	0.694 (0.705, 1.122)	0.437
SOTT	2.291 (2.051, 2.557)	<0.001	1.319 (1.135, 1.533)	<0.001
PE	3.737 (3.024, 4.619)	<0.001	1.688 (1.171, 2.431)	<0.001
NOPP	1.656 (1.478, 1.854)	<0.001	0.938 (0.810, 1.086)	0.390
Cryotherapy	0.355 (0.230, 0.550)	<0.001	1.236 (0.777, 1.967)	0.370
EC	2.010 (1.433, 3.077)	<0.001	1.079 (0.722, 1.611)	0.711
T2D	8.181 (5.280, 12.676)	<0.001	1.219 (0.690, 2.152)	0.495
Hypertension	1.657 (1.141, 2.405)	0.008	1.495 (0.999, 2.236)	0.012
RTS	2.857 (2.440, 3.346)	<0.001	1.345 (1.013, 1.785)	0.012
RD extension	1.221 (0.991, 1.297)	0.892	1.287 (0.896, 1.385)	0.749
SO tamponade	33.134 (8.187, 134.101)	<0.001	0.564 (0.059, 5.404)	0.619
Preop. CD	0.608 (0.483, 0.754)	0.003	0.608 (0.583, 0.754)	0.652
Preop. PVR	82.458 (30.381, 223.807)	<0.001	31.573 (10.168, 98.036)	<0.001

PVR: Proliferative vitreoretinopathy; RRD: Rhegmatogenous retinal detachment; TOS: Time from onset to surgery; SOTT: Silicone oil tamponade time; PE: Photocoagulation energy; NOPP: Number of photocoagulation points; EC: Electric coagulation; T2D: Type 2 diabetes; RTS: Retinal tear size; RD: Retinal detachment; SO: Silicone oil; CD: Choroidal detachment.

Internal and External Validation of the Nomogram The nomogram displayed good accuracy for predicting the postoperative PVR-free probability in both internal and external validation. In the training set, the C-index of the nomogram was 0.896, 0.936, 0.961, and 0.972 for the 3-, 4-, 5-, and 6-month postoperative PVR-free probabilities, respectively. Additionally, the C-index values in the validation set were 0.860, 0.936, 0.951, and 0.965 for the 3-, 4-, 5-, and 6-month postoperative PVR-free probabilities, respectively (Figure 3). The calibration curves of nomogram at the different time points all indicated good agreement between the nomogram prediction and the actual observation in the validation cohort (Figure 4).

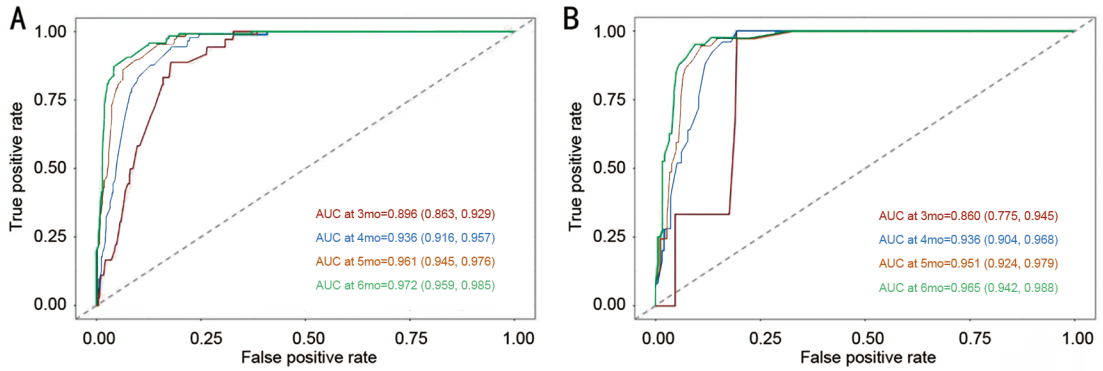

Figure 3 The ROC curves of the nomogram for the postoperative 3-, 4-, 5-, and 6-month PVR-free probability predictions of the training cohort (A) and validation cohort (B) The discrimination of the model is measured by the AUC. ROC: Receiver operating characteristic; AUC: Area under the curve.

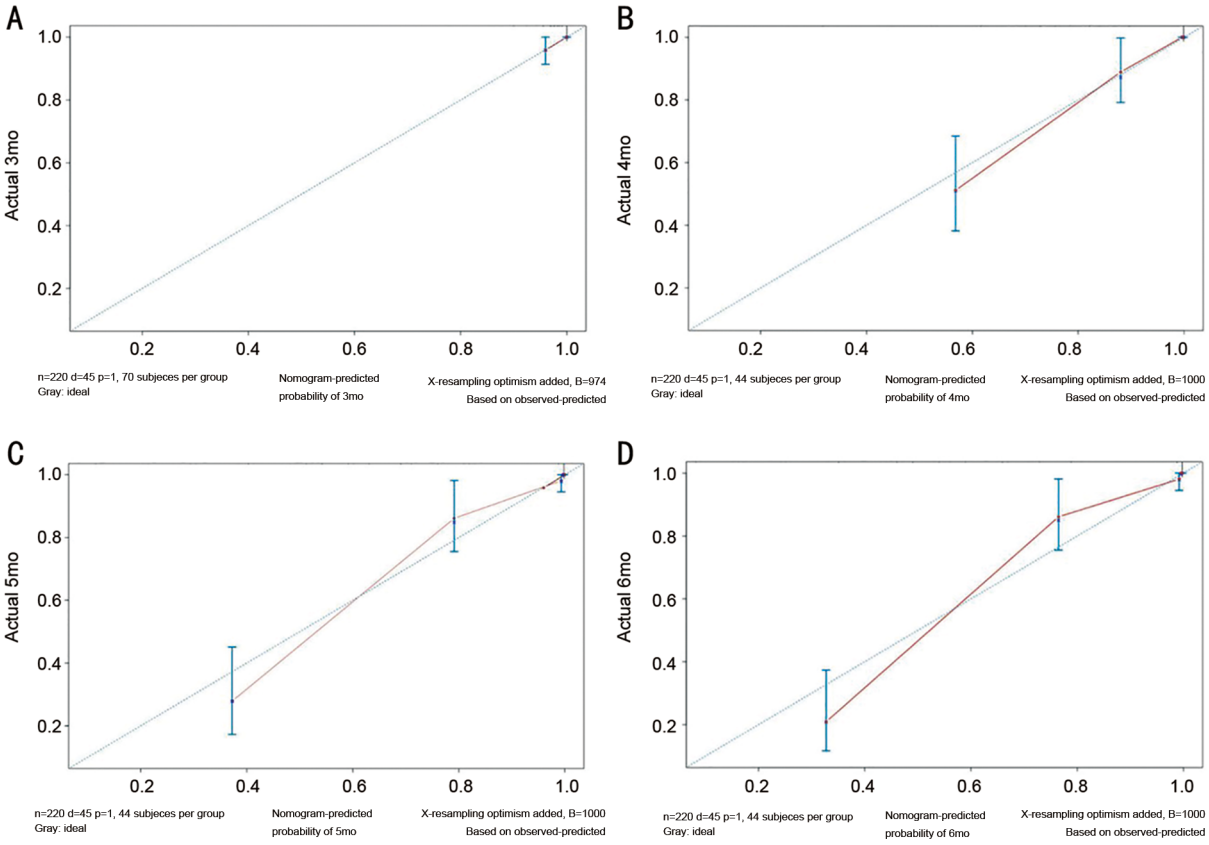

Figure 4 Calibration plots of the nomogram for the postoperative 3-, 4-, 5-, and 6-month PVR-free probability predictions in the validation cohort.

Decision-Curve Analysis DCA of the nomogram for predicting the postoperative PVR-free probability at 3, 4, 5, and 6mo in the training and validation sets are depicted in Figure 5. The 4-, 5-, and 6-month DCA of the nomogram from the training and validation cohorts all showed significant net benefits over a large threshold probabilities interval. However, the 3-month DCA of the nomogram from the training and validation cohorts were both close to the zero net benefit horizontal line, which indicated that the nomogram at 3mo had limited value for clinical decision-making.

DISCUSSION

PVR is the most common cause of failure of RRD repositioning, which always requires further surgery and means a worse prognosis[3-4]. The development of PVR is a complex process involving inflammation and cell migration and proliferation, which has many similarities with the wound healing response[18]. A large number of previous studies have reported numerous risk factors for PVR, but their results were frequently inconsistent and contradictory, and could not accurately predict or calculate a patient's individual postoperative PVR probability[19]. In this study, we identified risk factors for postoperative PVR in cases of primary RRD repair and established a well-calibrated prognostic nomogram to predict the PVR-free probability at different time points after surgery.

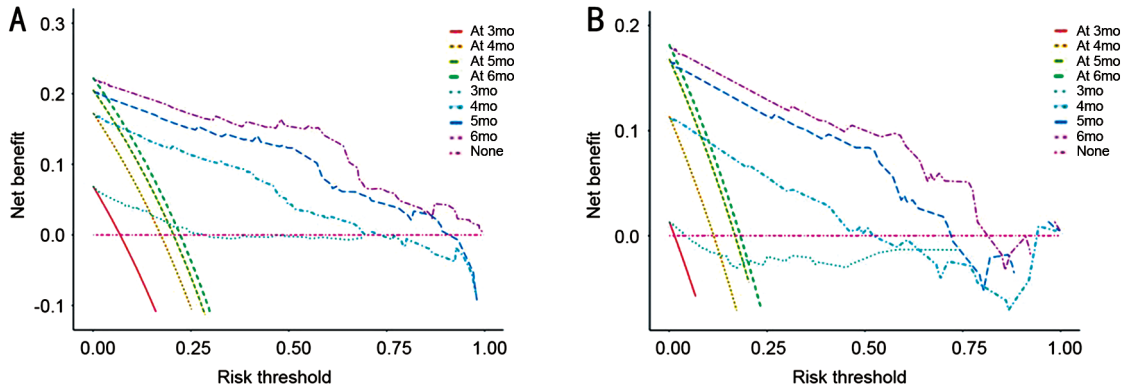

Figure 5 DCA for the nomogram in the prediction of the PVR-free probability of patients with primary RRD at the 3-, 4-, 5-, and 6-month time points after surgery in the training cohort (A) and validation cohort (B) The X-axis is the threshold probability and the Y-axis is the net benefit rate. The horizontal line indicates that all samples are negative and untreated, with zero net benefit. The oblique curve indicates that all samples are positive, and the net benefit is a backslash with a negative slope. PVR: Proliferative vitreoretinopathy; RRD: Rhegmatogenous retinal detachment; DCA: Decision-curve analysis.

To our best knowledge, the proposed nomogram is the first for predicting PVR in primary RRD patients after vitrectomy. In 2005, Pastor *et al*[10] devised a statistical model specifically for patients with RD repair surgery to assess the probability of PVR. Although the sensitivity and specificity of this model were higher than those of previous studies[9,11], the optimal values were still only 78.0% and 75.6%, respectively. Later, Wickham *et al*[12] developed a simplified formula to predict the risk for PVR in patients with primary RD after vitrectomy using preoperative clinical data. The area under the ROC curve of this model was 0.86. However, the sensitivity and specificity of these formulas were not high enough for routine clinical use. In the present study, the C-index of the nomogram exceeded 0.9 at 4, 5, and 6mo in both the internal and external validations, demonstrating favorable discrimination. Additionally, the calibration curves confirmed the validity of the nomogram. This indicated that our innovative nomogram is reliable for predicting the 4-, 5-, and 6-month PVR-free probabilities of RRD patients after surgery.

The proposed nomogram in the present study included several independent prognostic factors—preoperative PVR, SOTT, PE, RTS, and hypertension. These factors were all identified by forward and backward stepwise selection methods in a Cox regression model. Previous studies have indicated that preoperative PVR is a significant predictor and risk factor for postoperative PVR[6,12,19-20]. For RD patients with preoperative PVR, the incidences of postoperative PVR and recurrent RD were reported to be significantly increased[21-22]. Consistent with these reports, our study additionally found that preoperative PVR had the highest risk score of all the prognostic factors in the nomograms. In the present study, the incidence of postoperative PVR in the training group was 22.5%, which was higher than that previously reported[3,20]. This may be because of the higher proportion of patients (34.4%) who presented with preoperative PVR in the training group compared with previous studies[3,20]. Postoperative PVR formation may be a continuation of previous proliferative diseases. In addition, the majority of postoperative PVR were grade B (94.0%), which was less serious and did not affect the final surgical success rate.

Previous studies reported different results on whether tamponade (SO or gas) was a risk factor for PVR[11,19,23-24]. In the present study, the type of tamponade (SO or C_3F_8) was not associated with postoperative PVR. By contrast, multivariate analysis showed that a longer SOTT was associated with a greater incidence of postoperative PVR. Prolonged tamponade will cause SO droplets to migrate into the retina and other ocular tissues, leading to inflammation[25-26]. Furthermore, SO bubbles can occupy a large part of the vitreous cavity and may promote cell proliferation by aggregating active factors near the retina[22,27]. Moreover, a prolonged SOTT leads to a greater abundance of retinal pigment epithelial and glial cells, thus increasing the possibility of PVR formation[24]. Combined with our outcomes, we propose that SO removal at a suitable time (*e.g.*, ≤3mo after tamponade) may reduce the risk for PVR.

Of note, we found that hypertension is also an independent risk factor for PVR, which has to our best knowledge not been reported in previous studies. Farioli *et al*[28] reported an association between blood pressure levels and RRD risk among non-myopic populations, but the causality has not been confirmed. How hypertension affects PVR remains unclear. We suspect that it may be related to the oxidative and inflammatory mechanisms of the excessive production of reactive oxygen species in hypertensive patients, but further verification is needed[29]. Retinal tear characteristics and excessive endolaser have been reported to be associated with PVR development in

several studies[8,10,30]. Similarly, our findings demonstrated that PVR formation is positively associated with both PE and RTS. Furthermore, the risk factors included in our proposed nomogram prediction model can be readily obtained from clinical medical records. By inputting these readily accessible clinical variables into the nomogram, clinicians will be able to estimate the PVR-free probability for individual patients at postoperative 4, 5, and 6mo to assist in making clinical decisions during follow-up.

The main strengths of this study were its large sample size and is probably the first application of a nomogram to predict the PVR-free probability after primary RRD repair. There were several limitations in this study. First, the nomogram was constructed based on retrospective data from a single hospital, which might present selection bias. Second, many other factors associated with PVR, including retinal tear number, duration of the operation, intensity of retinal laser spot and pigment release during endodrainage, were not analyzed because of lack of data. Our future research will incorporate these factors. Third, a small number of patients with postoperatively late-onset PVR may have been missed because of the short follow-up time.

In conclusion, we identified preoperative PVR, SOTT, PE, RTS, and hypertension as risk factors associated with PVR formation. Based on the currently identified risk factors, we constructed and validated a novel nomogram to predict the PVR-free probability in patients with primary RRD at 4, 5, and 6mo after surgery. This nomogram, with its good discrimination and calibration, will be beneficial for personalized PVR prediction and facilitating clinical decision-making during follow-up.

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