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ORIGINAL RESEARCH

A Prediction Nomogram for Recurrent Retinal Detachment

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Purpose: Recurrent retinal detachment (re-RD) is one of the complications in rhegmatogenous retinal detachment patients who underwent surgical treatment. We investigated the risk factors for re-RD and developed a nomogram for estimating clinical risk.

Methods: Univariate and multivariable logistic regression models were performed to determine the association between variables and re-RD, and a nomogram was then developed for re-RD. The nomogram performance was assessed based on its discrimination, calibration, and clinical usefulness.

Results: This study analyzed 15 potential variables of re-RD in 403 rhegmatogenous retinal detachment patients who underwent initial surgical treatment. Axial length, inferior breaks, retinal break diameter, and surgical methods were independent risk factors for re-RD. A clinical nomogram incorporating these four independent risk factors was constructed. The diagnostic performance of the nomogram was excellent (area under the curve = 0.892, 95% CI: 0.831–0.953). Our study further validated this nomogram by bootstrapping for 500 repetitions. The area under the curve of the bootstrap model was 0.797 (95% CI: 0.712–0.881). This model showed good calibration curve fitting and a positive net benefit in decision curve analysis.

Conclusion: Axial length, inferior breaks, retinal break diameter, and surgical methods could be risk factors for re-RD. We have developed a prediction nomogram of re-RD for rhegmatogenous retinal detachment following initial surgical treatment.

Keywords: recurrent retinal detachment, nomogram, risk factors

Introduction

Rhegmatogenous retinal detachment (RRD) is the most common form of retinal detachment. In the treatment of RRD, the most commonly used techniques are scleral buckling (SB), pars plana vitrectomy (PPV), and pneumatic retinopexy (PR). Some surgeons prefer a combination of these interventions to treat RRD. Previous studies on the safety and efficacy of these interventions found that the primary reattachment rate and final visual acuity were similar between SB and PPV.[1,2] Compared with standalone PPV, PPV with supplemental SB did not improve primary reattachment rates or vision.[3] Likewise, in the comparison of PR to SB, there was no difference between the initial and final reattachment rates.[2]

Although substantial progress has been made in surgical techniques and devices to reduce recurrent retinal detachment (re-RD), up to 10–40% of cases require more than one intervention to repair retinal detachment; even as many as 5% of eyes may sustain permanent anatomic failure.[4,5] In addition, the reported incidence of RRD ranges from 6.3 to 17.9 per 100,000 population,[6] and the increasing number of patients have brought with it a greater number of recurrences. Therefore, re-RD remains a significant challenge for vitreoretinal surgeons and patients, considering the economic and emotional burden of undergoing multiple interventions.

Comprehensive analysis of risk factors for re-RD in RRD patients who underwent surgical treatment was reported previously in several articles, including the development of proliferative vitreoretinopathy (PVR),[7] retinal break diameters,[8] subretinal fluid (SRF),[9] high myopia,[10] posterior staphyloma,[11] multiple surgeries,[12] and silicone oil removal

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before silicone oil emulsification.[13] However, thus far, few reports have combined these factors to establish a risk prediction model to predict re-RD occurrence in RRD patients following surgical treatment.

Prediction models are tools that combine multiple predictors by assigning relative weights to each predictor to obtain a risk or probability.[14] Prediction model studies can broadly be divided into model development, model validation, or both.[15] Studies developing new prediction models should always include some form of internal validation or external validation to quantify the predictive performance of the developed model.[16] Besides, nomograms are commonly used to visualize prediction models. As a simple statistical visual tool, the nomogram has been widely used to predict disease occurrence, development, prognosis, and survival.[17,18]

This study sought to investigate the risk factors and establish a prediction nomogram for re-RD in RRD patients. The model mainly focuses on the early prediction of re-RD caused by preoperative risk factors and surgical methods.

Materials and Methods

Patients

The Institutional Ethics Committee of the First Affiliated Hospital of Soochow University approved this retrospective study in compliance with the principles of the Declaration of Helsinki and obtained informed consent from the patients. Seven hundred sixty-five patients with retinal detachment underwent their first surgery intervention at the First Affiliated Hospital of Soochow University (Suzhou, Jiangsu, China) between October 2020 and April 2022. Patients were excluded from the final analysis for the following reasons: traction retinal detachment, exudative retinal detachment, macular hole retinal detachment, open globe injury-induced RD, PVR grade > B, combined with other fundus diseases: diabetic retinopathy, retinal vein occlusion, and history of any intraocular vitreoretinal procedure. Finally, 403 RRD patients were included in the final analysis.

Baseline characteristics of the patients included age, sex, hypertension, diabetes, laterality, trauma history, contralateral eyes, duration of central vision loss, preceding surgeries, lens status, axial length, location of retinal breaks, the diameter of breaks, macular status, and surgical methods.

Surgical Procedures

The retinal breaks were identified and treated for SB surgery by transscleral cryotherapy. Mattress sutures were placed 7.0 to 7.5 mm apart with 4–0 supramid for the circumferential segmental buckle, and a silicone sponge was sutured as an explant in all cases. The SRF was drained if necessary. For the PPV surgery, a 3-port 23-gauge pars plana vitrectomy was performed, and subretinal fluid was internally aspirated. Fluid-air exchange was followed by retinopexy using endophotocoagulation and cryotherapy. Then, the sterile gas or silicone oil (SO) was injected into the vitreous completion of the PPV. Cataract surgery was implemented during PPV if the cataract was visually significant. None of the patients had any PPV supplements with SB. Only patients who achieved anatomical success in primary surgery were included in the study. PPV or SB was selected according to individual condition assessment and surgeons' clinical experience.

Developing and Validating the Model

Univariate and multivariable logistic regression models were used to detect the relationship between variables and re-RD. A crude analysis was conducted to identify possible risk factors in the univariate analysis. All variables having a bivariate association with re-RD with $P < 0.05$ were included in the multivariable model. Backward stepwise selection using the Akaike information criterion was applied to select the independent predictors for constructing the prediction model in the multivariate logistic regression. We developed a nomogram based on the multivariate logistic regression results. The area under the curve (AUC) of the receiver operator characteristic (ROC) was used to evaluate the model's discrimination. Calibration was assessed with a calibration plot to evaluate the goodness-of-fit of the nomogram. A bootstrap validation was also performed using simple random sampling with the replacement for 500 repetitions to verify the accuracy of our model. Finally, the clinical usefulness of our model was evaluated using the decision curve analysis (DCA) by calculating the net benefits at different threshold probabilities.

Statistical Analysis

The statistical analyses were performed using R statistical software, version 4.1.3, and SPSS, version 26.0. A logistic regression algorithm was conducted using the "plyr" package. Nomogram construction was conducted using the "rms" package. ROC curves were generated using the "pROC", "tidyverse" and "rms" package. Calibration plots were conducted using the "gbm", "rlang", "magrittr" and "rms" packages. DCA was performed with the "rmda" package. Mean + standard deviation (SD) or median (min-max) are used for continuous variables, and categorical variables are expressed as percentages or numbers. Based on χ^2 tests, Fisher exact tests, and logistic regression models, associations were assessed between re-RD and variables. Statistical analyses were two-tailed with 95% confidence intervals (CI). In all statistical tests, $P < 0.05$ was considered significant.

Results

Patient Characteristics

The final study cohort was composed of 403 patients. The characteristics of the patients with RDD are summarized in Table 1. The mean age was 52.5 ± 13.65 years, and 205 (50.90%) patients were men. 8.2% of patients previously underwent closed ocular trauma, and 5.2% had a previous retinal detachment in the contralateral eye. More than half of the patients (65.5%) had central vision loss for more than seven days. Besides, the lens status of patients was almost in Phakic (92.6%). The axial length of 32.2% of patients was more than 26.00mm. The rate of inferior breaks in patients was 27.0%, while retinal break diameter ≥ 3PD was 21.3%. Moreover, 55.1% of patients were treated with PPV+SO, while only 8.7% underwent SB. Of 403 patients, re-RD occurred in 34 (8.4%) patients.

Risk Factors for Recurrent Retinal Detachment

Univariate and multivariate logistic regression analyses performed to determine the relationship between variables and re-RD are shown in Table 2. Only 4 out of 15 candidate variables were associated with re-RD in the univariate logistic regression analyses with a $P < 0.05$. These were axial length (AL), inferior breaks, the diameter of retinal breaks, and surgical methods. The risk of re-RD among patients with AL ≥ 26.00mm was higher than that of patients with AL< 26.00mm (OR= 4.43, 95% CI: 2.12–9.28, $P < 0.0001$). Compared with the SB group, more patients in the PPV+ gas group developed re-RD, with a significantly increased risk (OR= 3.38, 95% CI: 0.93–12.29, $P = 0.065$). Patients with inferior breaks were more likely to suffer from re-RD than those with superior breaks (OR= 3.93, 95% CI: 1.92–8.05, P <0.0001). Besides, patients with a diameter of retinal breaks ≥ 3PD increased the risk of re-RD (OR= 2.51, 95% CI: 1.20–5.25, P =0.014). In addition, the incidence of re-RD did not differ significantly based on sex, age, diabetes, hypertension, laterality, history of eye trauma, surgical history, duration of central vision loss, lens status, or macular status. Multivariate logistic regression was conducted using all variables with a bivariate association with re-RD with $P <$ 0.05, resulting in the adjusted odds ratios shown in Table 2. The significant predictors of re-RD in the multivariate model were: AL ≥ 26.00mm (OR= 4.25, 95% CI:1.79–10.1, $P = 0.001$), the diameter of retinal breaks ≥3PD (OR= 3.47, 95% CI:1.33–9.06, $P = 0.011$), inferior breaks (OR= 7.19, 95% CI:2.85–18.18, P <0.0001), and surgical methods (OR= 9.04, 95% CI:2.02–40.43, $P = 0.004$). All possible two-way interactions between variables were examined in the multivariable model, but no statistically significant interaction was found ($P > 0.05$).

Nomogram for Recurrent Retinal Detachment

Fifteen clinical variables were analyzed to determine their association with re-RD. Four of the initial 15 variables were screened out: axial length, inferior breaks, the diameter of retinal breaks, and surgical methods. In this study, the backward stepwise selected model was computed as follows: −4.809+1.447×(axial length ≥ 26mm) +1.244×(diameter of retinal breaks ≥ 3PD) +1.973×(inferior breaks = yes) +2.202×(PPV+ gas) −1.900 (PPV+SO) + 0.957 (PPV+SO +SOR). The probability of re-RD can be estimated using the nomogram, as described in Figure 1. Based on the ROC curve analysis of this nomogram, the AUC was 0.892, indicating an excellent diagnostic performance (Figure 2) with a sensitivity of 79.4% and a specificity of 87.3% at the optimal cut-off value.

Table 1 Baseline Characteristics of the Investigated Patients (n = 403)

Characteristics	Category	n = 403	Percentage (%)
Sex (n, %)	Female	198	49.1
	Male	205	50.9
Age (years)	Range 13–82	–	–
	Mean 52.50, median 55.00	–	–
Diabetes (n, %)	Yes	26	6.5
	No	377	93.5
Hypertension (n, %)	Yes	100	24.8
	No	303	75.2
Laterality (n, %)	Right	208	51.6
	Left	195	48.4
History of eye trauma (n, %)	Yes	33	8.2
	No	370	91.8
Surgical history (n, %)	Myopia surgery	8	2.0
	Retinal photocoagulation	11	2.7
	Cataract surgery	28	6.9
	No	356	88.3
History of the contralateral eye (n, %)	Retinal detachment	21	5.2
	No-retinal detachment	382	94.8
Duration of central vision loss (days, n, %)	£7	139	34.5
	>7	264	65.5
Lens status (n, %)	Phakic	373	92.6
	Pseudophakic	28	6.9
	Aphakia	2	0.5
Axial length (mm, n, %)	<26.00	273	67.7
	≥26.00	130	32.3
Inferior breaks (n, %)	Yes	109	27.0
	No	294	73.0
Diameter of retinal breaks, (PD, n, %)	<3	317	78.7
	≥3	86	21.3
Macular status (n, %)	On	75	18.6
	Off	328	81.4
Surgical methods (n, %)	SB	35	8.7
	PPV+ gas	79	19.6
	PPV+ SO	222	55.1
	PPV+SO+SOR	67	16.6
Recurrent retinal detachment	Yes	34	8.4
	No	369	91.6

Note: Data are presented as the number of patients unless indicated otherwise.
Abbreviations: PPV, pars plana vitrectomy; PPV+ gas, PPV+ vitreous sterile air tamponade; PPV+ SO, PPV+ vitreous silicone oil tamponade; PPV+SO+SOR, PPV+ vitreous silicone oil tamponade + silicone oil removal; SB, scleral buckling.

Model Validation

We further validated the nomogram using internal bootstrapping. Based on bootstrapping for 500 repetitions, the AUC of the bootstrap model was 0.797 (95% CI: 0.712–0.881), with similar statistical power to the original model (Figure 3). A calibration curve derived from internal bootstrap validation demonstrated that our model had excellent fitting and calibration with the ideal curve (Figure 4). Moreover, the internal bootstrap decision curve analysis revealed net positive benefits in the predictive model under a threshold probability of 0.85, indicating the predictive model's favorable potential clinical effect (Figure 5).

Discussion

Artificial intelligence has received increasing attention in ophthalmology, and diagnostics for diabetic retinopathy, age-related macular degeneration, glaucoma, and proliferative vitreoretinopathy have demonstrated expert-level accuracy.[19–21] However,

Table 2 Univariate and Multivariate Logistic Regression Analysis of Clinical Candidate Predictors

Variable	Univariate OR (95% CI)	*P* value	Multivariate OR (95% CI)	*P* value
Sex (n, %, Female vs Male)	0.91 (0.45–1.85)	0.801	–	–
Age (years, Continuous)	0.99 (0.97–1.02)	0.581	–	–
Diabetes (n, %, Yes vs No)	1.46 (0.41–5.12)	0.558	–	–
Hypertension (n, %, Yes vs No)	0.63 (0.25–1.56)	0.316	–	–
Laterality (n, %, Left vs Right)	1.07 (0.53–2.16)	0.844	–	–
History of eye trauma (n, %, Yes vs No)	2.10 (0.75–5.85)	0.156	–	–
Surgical history (n, %)				
Myopia surgery	1.50 (0.18–12.56)	0.71	–	–
Retinal photocoagulation	0 (0-Inf)	0.99	–	–
Cataract surgery	0.81 (0.18–3.56)	0.776	–	–
No	Ref.	–	–	–
History of the contralateral eye (n, %, RD vs No-RD)	2.76 (0.87–8.72)	0.084	–	–
Duration of central vision loss (days, n, %, >7 vs £7)	0.73 (0.36–1.50)	0.393	–	–
Lens status (n, %)				
Phakic	Ref.	–	–	–
Pseudophakic	1.91 (0.62–5.86)	0.26	–	–
Aphakia	0 (0-Inf)	0.99	–	–
Axial length (mm, n, %, ≥26.00 vs <26.00)	4.43 (2.12–9.28)	<0.0001	4.25 (1.79–10.1)	0.001
Inferior breaks (n, %, Yes vs No)	3.93 (1.92–8.05)	<0.0001	7.19 (2.85–18.18)	<0.0001
Diameter of retinal breaks (PD, n, %, ≥3 vs <3)	2.51 (1.20–5.25)	0.014	3.47 (1.33–9.06)	0.011
Macular status (n, %, Off vs On)	1.79 (0.61–5.23)	0.29	–	–
Surgical methods (n, %)		*P*<0.0001		*P*<0.0001
SB	Ref.	–	Ref.	–
PPV+ gas	3.38 (0.93–12.29)	0.065	9.04 (2.02–40.43)	0.004
PPV+ SO	0.1 (0.02–0.6)	0.012	0.15 (0.02–1.04)	0.055
PPV+SO+SOR	1.87 (0.48–7.29)	0.367	2.60 (0.54–12.54)	0.233

Abbreviations: PPV, pars plana vitrectomy; PPV+ gas, PPV+ vitreous sterile air tamponade; PPV+ SO, PPV+ vitreous silicone oil tamponade; PPV+SO+SOR, PPV+ vitreous silicone oil tamponade + silicone oil removal; SB, scleral buckling.

as models increase in complexity, such models are not only inherently challenging to audit for quality but also limit the user's ability to "debug" or make informed adjustments to the underlying algorithm.[22] Nomogram-based clinical modelling is a reliable statistical and straightforward visual tool. A comprehensive analysis of all related risk factors can accurately calculate and predict disease occurrence, development, prognosis, and survival by nomogram.[23]

This study aimed to investigate the risk factors for re-RD and develop a model for predicting the re-RD. This study analyzed 15 potential variables of re-RD in 403 RRD patients who underwent initial surgical treatment and revealed that axial length, inferior breaks, the diameter of retinal breaks, and surgical methods were independent predictors of re-RD. Using multivariate analyses, we have developed a simple and easy-to-use prediction nomogram for re-RD. Four variables were screened out for the nomogram using backward stepwise regression. This nomogram had excellent diagnostic performance (AUC = 0.892, sensitivity = 79.4%, and specificity = 87.3%) and was validated internally using the bootstrap sampling method. Moreover, according to the results of the decision curve analysis, this prediction model demonstrated superior performance in the clinical setting.

RRD is often repaired with an SB, PPV, PR, or a combination of techniques. Although each method has advantages and disadvantages, its primary purpose is alleviating vitreous traction. The comparative efficacy of PPV, SB, and PR has often been studied.[2] However, there are inconsistencies between the findings of various studies. For example, in 2335 cases, the Primary Retinal Detachment Outcomes Study found that the primary reattachment rates of SB (91.7%) and PPV supplemented with SB (PPV/SB, 91.2%) were higher than PPV (83.1%) in phakic eyes, but the rate of PPV/SB (92.0%) was higher than that of PPV (84.0%) in aphakic eyes.[24,25] At the same time, a recent 2022 meta-analysis found no difference between SB, PPV, and PPV/SB at the final follow-up.[1] Besides, when choosing PPV for treating RRD, it is typically accompanied by a postoperative intraocular tamponade agent.[26] Tamponades have unique benefits and risks,

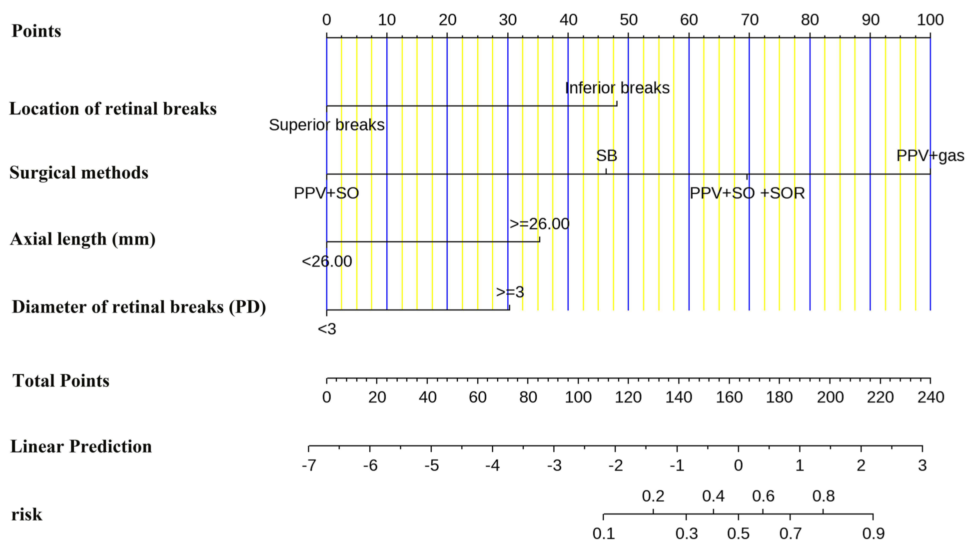

Figure 1 Clinical nomogram predicting the re-RD probability in patients with RRD. Interpretation: The nomogram represents the regression equation visually. It develops scoring criteria based on the magnitude of the regression coefficients of all independent variables in the model. Determine the value of the variable on the corresponding axis, draw a vertical line to the total points axis to determine the points, add the points of each variable, and draw a line from the total point axis to determine the re-RD probabilities at the lower line of the nomogram.

Abbreviation: re-RD, recurrent retinal detachment.

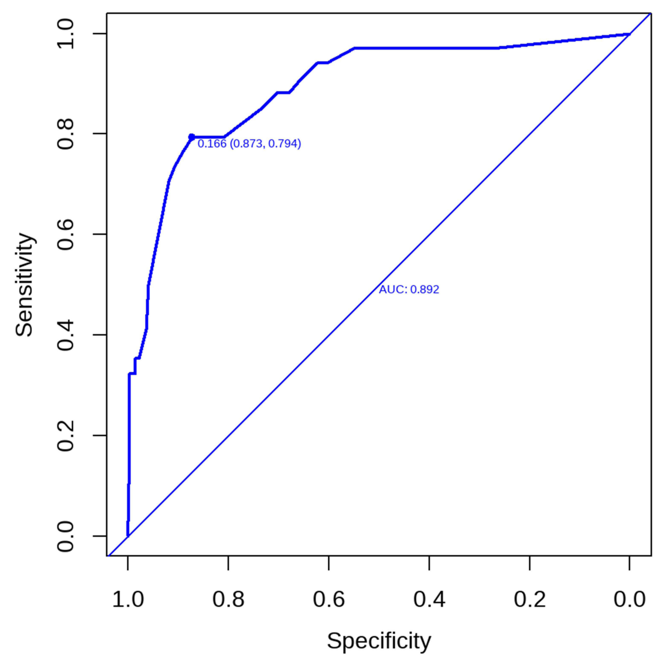

Figure 2 Receiver operating characteristic curve.

Abbreviation: AUC, area under the receiver operating characteristic curve.

and the choice of tamponades should be individualized according to the characteristics of the patient's condition.[27–29] Our study indicated that PPV+ gas is the most at risk for re-RD compared with SB (OR= 9.04, 95% CI:2.02–40.43, P = 0.004). The re-RD rates of PPV+SO+SOR were higher than SB, although the comparison was insignificant (P = 0.233).

Retinal breaks in RRD are usually distributed in more than one quadrant. Previous studies have demonstrated that retinal breaks are most likely to occur in the superotemporal quadrant, and the inferonasal quadrant is the least likely location for a break and the most potential for attached breaks.[30] However, in a series of studies, the primary reattachment rate of RRD with inferior breaks is lower than those with superior breaks when treated by similar

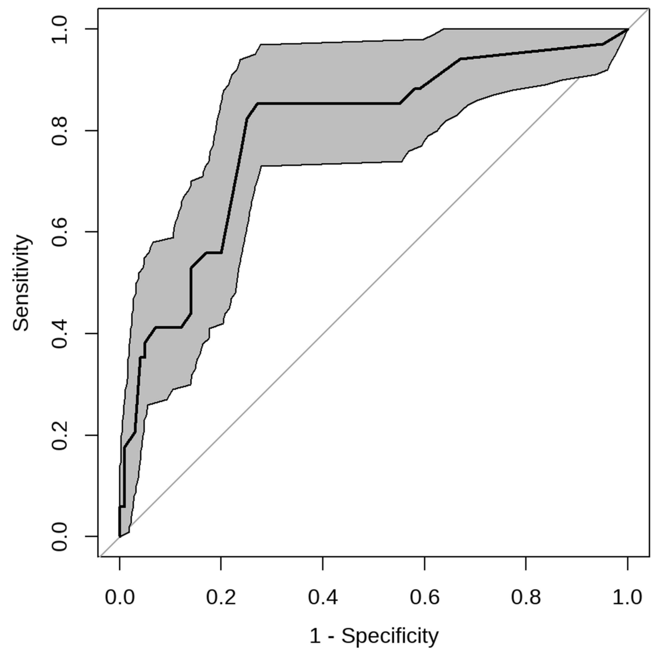

Figure 3 Internal validation of the nomogram using bootstrap sampling. The ROC curve was measured by bootstrapping for 500 repetitions, and the AUC of the bootstrap stepwise model was shown.
Abbreviations: AUC, area under the receiver operating characteristic curve; ROC, receiver operating characteristic.

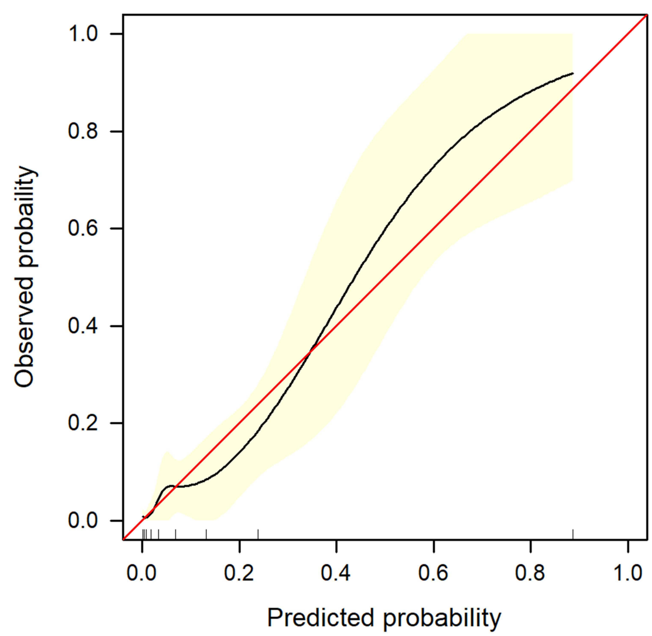

Figure 4 Internal validation of the nomogram using bootstrap sampling. A calibration curve was measured by bootstrapping for 500 repetitions. The X axis is the predicted probability of the nomogram, and the Y axis is the observed probability. The red line shows the ideal calibration line, while the yellow area shows the 95% confidence interval of the prediction model.

techniques.[31–33] Moreover, significant breaks of more prominent than three disk diameters were confirmed as an independent risk for re-RD.[8,34] Our study also found inferior breaks were an independent risk for re-RD (OR= 7.19, 95% CI:2.85–18.18, P <0.0001), consistent with previous studies. Moreover, this study demonstrated that giant retinal breaks (diameter ≥3 PD) are a statistically significant risk factor for re-RD (OR= 3.47, 95% CI:1.33–9.06, P =0.011).

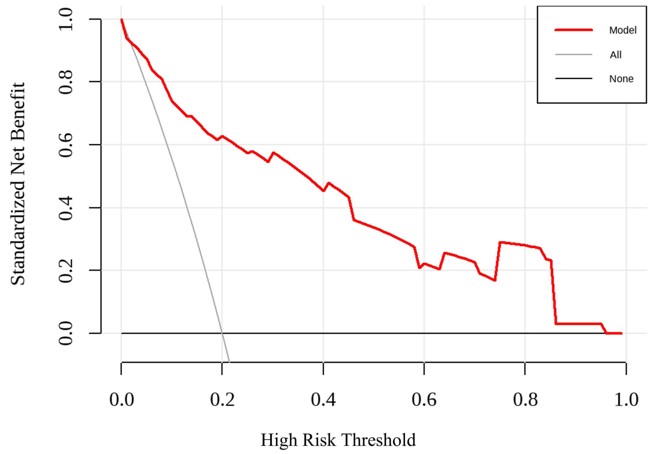

Figure 5 Decision curve analyses depict the prediction nomogram's clinical net benefit. The graph indicates the expected net benefit per patient relative to the nomogram prediction of re-RD. Red solid line: a prediction model. Tin slash line: Assume all patients have re-RD. Solid horizontal line: Assume no patients have re-RD.
Abbreviation: re-RD, recurrent retinal detachment.

Our study's four independent re-RD predictors were axial length (AL). It has been demonstrated that myopic eyes are at a greater risk of developing RRD than emmetropic or hyperopic eyes, and the risk of RD increases with increasing axial length.[35,36] An annual RRD incidence of 15 to 34 per 100,000 for mild myopia, 15 to 73 for moderate myopia, 102 to 128 for high myopia, and 287 in very highly myopic eyes were reported in a 2021 systematic review.[37] In addition, previous studies have reported that AL increases significantly after SB or PPV.[38,39] The change in AL was found to be between 0.1 and 0.6 mm postoperatively.[40] Previous studies focused on the correlation between AL and RRD and AL change after surgical intervention, not only on the relationship between preoperative AL and re-RD in RRD patients who underwent initial surgical intervention. Herein, based on the results of our research, AL ≥ 26.00 mm was a remarkable prognosticator for re-RD compared to AL< 26.00 mm (OR= 4.25, 95% CI:1.79–10.1, *P* = 0.001). Therefore, surgeons should be cautious when choosing surgical techniques for highly myopic patients (AL ≥ 26.00 mm) with RRD.

Although several previous reports on recurrent retinal detachment have been published,[41–43] none of the studies have constructed intuitive nomograms to calculate probability and validated their prediction models (internal or external). This study used a nomogram to calculate the overall likelihood of re-RD for an individual patient. This prediction model is essential for risk estimation, improving communication between patients and physicians, and clinical decision-making. In the present study, four independent variables were screened using stepwise regression, and the nomogram was established to predict the risk of re-RD in RRD patients. Nomograms showed excellent diagnostic performance (AUC= 0.892) and yielded a sensitivity of 79.4% and specificity of 87.3% at the optimal cut-off value. It is the first study to evaluate a nomogram that can be used to predict re-RD in patients with RRD. The nomogram might be a statistical tool to calculate the overall probability of re-RD in patients who underwent initial surgical treatment. This nomogram might serve as an essential early warning sign of re-RD in RRD patients.

Conclusion

Axial length, inferior breaks, retinal break diameter, and surgical methods could be risk factors for re-RD. Based on these four significant risk factors, we developed a practical and reliable nomogram to predict re-RD.

Data Sharing Statement

The original contributions presented in the study are included in the article, and further inquiries can be directed to the corresponding author.

Ethics Approval and Informed Consent

The studies involving human participants were reviewed and approved by the Institutional Ethics Committee of the First Affiliated Hospital of Soochow University (Approval No. 2022346). The patients/participants provided written informed consent to participate in this study.

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Disclosure

The authors report no conflicts of interest in this work.

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