

Predicting the Risk of Unplanned Readmission at 30 Days After PCI: Development and Validation of a New Predictive Nomogram

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Objective: This study aimed to develop and validate a risk prediction model that can be used to identify percutaneous coronary intervention (PCI) patients at high risk for 30-day unplanned readmission.

Patients and Methods: We developed a prediction model based on a training dataset of 1348 patients after PCI. The data were collected from January 2020 to December 2020. Clinical characteristics, laboratory data and risk factors were collected using the hospital database. The LASSO regression method was applied to filter variables and select predictors, and feature selection for a 30-day readmission risk model was optimized using least absolute shrinkage. Multivariate logistic regression was used to construct a nomogram. The performance and clinical utility of the nomogram were evaluated with a receiver operating characteristic (ROC) curve, a calibration curve, and decision curve analysis (DCA). Internal validation of the predictive accuracy was performed using bootstrapping validation.

Results: The predictors included in the prediction nomogram were medical insurance, length of stay, left ventricular ejection fraction on admission, history of hypertension, the presence of chronic lung disease, the presence of anemia, and serum creatinine level on admission. The area under the receiver operating characteristic curve for the predictive model was 0.735 (95% CI: 0.711–0.759). The P value of the Hosmer–Lemeshow goodness of fit test was 0.326, indicating good calibration, and the calibration curves showed good agreement between the classifications and actual observations. DCA also demonstrated that the nomogram was clinically useful. A high c-index value of 0.723 was obtained during the internal validation.

Conclusion: We developed an easy-to-use nomogram model to predict the risk of readmission 30 days after discharge for PCI patients. This risk prediction model may serve as a guide for screening high-risk patients and allocating resources for PCI patients at the time of hospital discharge and may provide a reference for preventive care interventions.

Keywords: percutaneous coronary intervention, 30-day readmission, nomogram, prediction model

Background

The American Heart Association (AHA) estimated that 130 million people will suffer from cardiovascular diseases by 2035. Among these diseases, coronary artery disease (CAD) is one of the main causes of mortality. According to the 2020 China Cardiovascular Disease Report, the CAD population in China has reached 11.39 million.^{1,2}

At present, percutaneous coronary interventions (PCIs), including balloon dilatation and stenting, constitute the most widely used forms of revascularization among patients with CAD.^{3,4} After a long history of development, PCI has been widely used in clinical practice with good efficacy and safety profiles. However, in-stent restenosis, bleeding and swelling at the puncture site, cardiac rupture (CR), recurrent angina pectoris, acute myocardial infarction (AMI), and chest pain may all be responsible for the multiple, repeated hospital admissions among PCI patients. Unplanned readmissions after hospital discharge are common and costly and serve as an indication of poor health care quality delivery; they undoubtedly increase the burden on the health care system and result in the unnecessary waste of medical

resources.⁵ In the United States, more than one in every five patients will be readmitted each year. The cost of readmission after PCI accounts for 33% of the total PCI cost, which is as high as 26 billion US dollars, resulting in a low quality of life and substantial social burden for patients. Notably, 75% of hospital readmissions in the Medicare cohort are considered potentially preventable.^{6–8} Furthermore, studies have shown that the 30-day readmission rate of patients after PCI ranges from 4.7% to 22.0%.^{9,10} However, the 30-day readmission rate may be underestimated because readmissions can also occur at a hospital other than that of the index admission.

Research on readmissions focuses on two main areas, namely, the prediction of readmission risk factors and assessment of the ability to prevent readmission. To date, there is a lack of risk-stratification tools. Therefore, we sought to use the hospital database to collect variables related to 30-day PCI readmission. Since there are no population-based studies on 30-day PCI readmission risk prediction models specific to the Chinese primary care population, the purpose of this study was to develop a valid but simple risk prediction model to provide a reference for the timely screening of patients with a high risk of readmission and for early clinical interventions.

Materials and Methods

Study Population and Design

For this study, it was assumed that a minimum of 10 variables would be entered into the final model. According to sample size calculation requirements, a minimum of 10 events per variable were necessary for the multivariate analysis.^{11,12} A total of 1348 patients were eventually included. This retrospective study used the hospital database to obtain data on patients admitted to the Department of Cardiology at the Second Affiliated Hospital of Nanchang University. In the study, 1760 PCI patients were included from January 2020 to December 2020, of whom 412 patients were excluded because of incomplete clinical information or because they met the exclusion criteria, bringing the final total to 1348 PCI patients who were eligible for participation.

The following inclusion criteria were applied: (i) Patients who met the WHO diagnostic criteria for coronary heart disease; (ii) those who underwent diagnostic investigations, including electrocardiography, electrocardiogram (ECG), and coronary angiography; and (iii) those who underwent a PCI procedure with complete revascularization (age ≥ 18 years).

The exclusion criteria were as follows: (i) Patients with end-stage liver disease, end-stage renal disease, or a diagnosis of malignancy; (ii) patients with known severe mental illness or cognitive dysfunction; and (iii) patients with incomplete clinical or laboratory data. The study was reviewed and approved by the ethics committee of the Second Affiliated Hospital of Nanchang University (approval number: [2020](085)).

Data Collection

The variables were selected according to expert opinion and a comprehensive review of the literature. The risk factors for 30-day readmission after PCI were identified, obtaining a total of 33 variables. Clinical data were collected using a custom-designed survey and included the following: (i) general clinical data, such as patient ID, sex, age, time of admission, method of admission (emergency department, outpatient clinic, or transfer from another hospital), types of medical insurance, length of stay, history of smoking and history of alcohol consumption; (ii) admission clinical data related to cardiovascular disease, namely, left ventricular ejection fraction (LVEF), number of diseased vessels, and New York Heart Association (NYHA) heart function classification; (iii) medical history data, including comorbidities (hypertension, diabetes, atrial fibrillation, chronic lung disease, renal insufficiency, heart failure, hyperlipidemia, peripheral vascular disease, stroke, anemia) and medical history (history of coronary artery bypass grafting (CABG), history of PCI, history of gastrointestinal bleeding); (iv) related laboratory indicators obtained at the time of hospital admission, including B-type (brain) natriuretic peptide levels (BNP), estimated glomerular filtration rate (eGFR), creatinine, D-dimer, triglycerides (TG), serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c); and (v) scores on rating scales, namely, the activities of daily living (ADL) scale and the (Morse) fall score. Our primary outcome was whether an index hospitalization was followed by an unplanned readmission within 30 days. Data were extracted from the hospital database by one researcher and checked by another; both researchers previously received unified training.

Statistical Analysis

Normally distributed variables are described as means and standard deviations, and skewed distributional data are expressed as medians and interquartile ranges. Count data are expressed as rates, percentages or constituent ratios. Comparisons among the different groups were performed with Fisher's exact test or the chi-squared test. For dimensionality reduction of the data and variable selection, feature selection was performed with the least absolute shrinkage and selection operator (LASSO) method to identify the optimal predictive features. The optimal parameter lambda (λ) was selected by ten fold cross-validation, the lambda value with the smallest cross-validation error was used as the optimal value of the model, and the number of variables corresponding to the nonzero regression coefficients at this time was counted. Subsequently, multiple logistic regression analyses were used to identify the independent risk factors and establish a nomogram model. Receiver operating characteristic (ROC) curves were generated to assess sensitivity and specificity. The Hosmer–Lemeshow goodness of fit test was used to assess the model fit and efficacy of the risk model. Decision curve analysis (DCA) was used to estimate the clinical utility of the proposed nomogram by calculating the net benefit at different threshold probabilities, which was calculated as follows: net benefit = true-positive rate - false-positive rate * Pt(1-Pt).^{13,14} Internal validation was performed by the bootstrap resampling technique (1000 bootstrap samples). All statistical tests were 2-sided at a significance level of 0.05. SPSS version 24.0 (SPSS Inc., Chicago, IL, USA) and R software (Version R-4.1.1; <https://www.R-project.org/>) were used for all statistical analyses.

Results

Patient Characteristics

This study included 1348 patients. Overall, 107 unplanned readmissions occurred over the 30 days following discharge, and the readmission rate was 7.94%. The patients (988 males and 360 females) had a mean (SD) age of 66.39±11.12 years (range, 28–97 years). There were three methods of admission: 400 patients via the emergency department, 907 via outpatient readmission and 41 via transfer from another health care facility. All patient data, including general clinical characteristics, disease, and laboratory examination data, are given in Table 1.

LASSO Regression Analysis Results

The model was considered optimal when the lambda was 0.012, and 33 features were reduced to 8 predictive variables. These predictors were length of stay, LVEF, number of diseased vessels, hypertension, chronic pulmonary disease, anemia, BNP level, and creatinine level. The results of LASSO regression are displayed in Figure 1.

Predictive Nomogram Development

For further analysis, the 8 features obtained by LASSO regression were included in multivariable logistic regression models for adjustment. The logistic regression analysis results, including length of stay, number of diseased vessels, hypertension, chronic pulmonary disease, anemia and creatinine, are shown in Table 2. Based on previous studies and its clinical importance, LVEF was also put into the final model. A nomogram was developed and presented based on incorporation of the above independent predictors of 30-day unplanned readmissions after PCI (Figure 2). The values for a patient were marked on each axis, and a line was drawn perpendicular to the point axis; then, the number of points for all variables were summed. Next, the sum was marked on the total point axis, and a line was drawn perpendicular to the probability axis. The corresponding value on the probability axis is the probability of a 30-day readmission for that patient.

Apparent Performance of the Risk Nomogram

The area under the ROC curve (AUC) of the nomogram was 0.735 (95% CI: 0.711–0.759) (Figure 3). At this level, the maximal Youden Index value was 0.346, the sensitivity was 66.4%, and the specificity was 68.3%. The results indicated that the nomogram had acceptable and favorable discriminatory ability. Additionally, good calibration was found, and the Hosmer–Lemeshow test indicated no statistically significant difference (chi-square=9.191, df=8, P=0.326). There was good agreement between the observed and predicted risks. In addition, internal validation was performed using the

Table I Baseline Patient Characteristics

Characteristics	Not Readmitted (1241)	Readmitted (107)	P value
Age, years, (mean±SD)	67.74 ±11.36	66.27±11.09	0.191
Sex, %			0.581
Male	912(73.49)	76(71.03)	
Female	329(26.51)	31(28.97)	
Admission status, %			0.229
Emergency department	361(29.09)	39(36.45)	
Outpatient department	843(67.93)	64(59.81)	
Transfer from other medical institutions	37(2.98)	4(3.74)	
Type of medical insurance, %			<0.001
None	38(3.06)	13(12.15)	
Urban workers insurance	448(36.10)	55(51.40)	
Urban and rural residents insurance	755(60.84)	39(36.45)	
Length of stay, days, M(Q1, Q3)	6(4,8)	7(6,9)	<0.001
LVEF, %, M (Q1, Q3)	67(58,74)	56(44,63)	<0.001
Number of diseased vessels, %			<0.001
1	550(44.32)	21(19.63)	
≥2	691(55.68)	86(80.37)	
NYHA functional class, %			0.480
Class 1	73(5.88)	7(6.54)	
Class 2	584(47.06)	42(39.25)	
Class 3	518(41.74)	52(48.60)	
Class 4	66(5.32)	6(5.61)	
Hypertension, %			<0.001
No	494(39.81)	21(19.63)	
Yes	747(60.19)	86(80.37)	
AF, %			0.083
No	1175(94.68)	97(90.65)	
Yes	66(5.32)	10(9.35)	
DM, %			0.097
No	818(65.91)	62(57.94)	
Yes	423(34.09)	45(42.06)	
Chronic lung disease, %			<0.001
No	1186(95.57)	93(86.92)	
Yes	55(4.43)	14(13.08)	
Renal insufficiency, %			0.001
No	902(72.68)	62(57.94)	
Yes	339(27.32)	45(42.06)	
HF history, %			0.002
No	1179(95.00)	94(87.85)	
Yes	62(5.00)	13(12.15)	
Hyperlipidemia, %			0.771
No	853(68.73)	75(70.09)	
Yes	388(31.27)	32(29.91)	
Peripheral vascular disease, %			0.248
No	589(47.46)	57(53.27)	
Yes	652(52.54)	50(46.73)	
Stroke, %			0.043
No	1156(93.15)	94(87.85)	
Yes	85(6.85)	13(12.15)	

(Continued)

Table I (Continued).

Characteristics	Not Readmitted (1241)	Readmitted (107)	P value
Anemia, %			<0.001
No	1213(97.74)	96(89.72)	
Yes	28(2.26)	11(10.28)	
Prior CABG, %			0.220
No	1239(99.84)	106(99.07)	
Yes	2(0.16)	1(0.93)	
Prior PCI, %			0.100
No	1066(85.90)	98(91.59)	
Yes	175(14.10)	9(8.41)	
Gastrointestinal bleeding, %			0.699
No	1229(99.03)	105(98.13)	
Yes	12(0.97)	2(1.87)	
Smoking, %			0.868
No	872(70.27)	76(71.03)	
Yes	369(29.73)	31(28.97)	
Alcohol consumption, %			0.185
No	984(79.29)	79(73.83)	
Yes	257(20.71)	28(26.17)	
Activities of daily living, points, M (Q1, Q3)	60(50,65)	60(50,70)	0.997
Morse fall scale, points, M (Q1, Q3)	35(20,45)	35(22.5,45)	0.746
BNP, pg/mL, M (Q1, Q3)	109.12(40.69,347.68)	236.67(73.765,1026.22)	<0.001
eGFR, mL/min, (Q1, Q3)	83.94(67.47,100.85)	75.02(57.925,94.565)	0.003
Cre, μ mol/L, M (Q1, Q3)	80.11(67.75,97.07)	83.6(71.61,108.01)	0.017
D dimer, mg/IFEU, M (Q1, Q3)	0.4(0.25,0.75)	0.57(0.345,1.615)	<0.001
TG, mmol/L, M (Q1, Q3)	4.4(3.64,5.21)	4.19(3.375,4.98)	0.089
TC, mmol/L, M (Q1, Q3)	1.38(0.97,2.05)	1.31(1.1,1.835)	0.410
HDL-C, mmol/L, M (Q1, Q3)	1.09(0.89,1.28)	1.02(0.83,1.255)	0.062
LDL-C, mmol/L, M (Q1, Q3)	2.6(2.3,2.6)	2.52(1.785,3.09)	0.127

Abbreviations: LVEF, left ventricular ejection fraction; AF, atrial fibrillation; DM, diabetes mellitus; HF, heart failure; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration rate; Cre, creatinine; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein; LDL-C, low-density lipoprotein; LOS, length of stay.

bootstrap resampling method and was found to be 0.723. The apparent performance of the nomogram to predict the risk of 30-day unplanned readmission after PCI indicated a good predictive capability.

Clinical Utility

Moreover, considering the clinical utility of the risk model, we drew a DCA curve to calculate the clinical net benefit. The DCA curve for the nomogram model predicting the 30-day risk of readmission after PCI is shown in [Figure 4](#). The DCA curves also showed that the nomogram has good clinical utility. This result indicated that the prognostic nomogram model we constructed was accurate. The DCA showed that patients and doctors can benefit from the prediction model when the threshold probability is greater than 2% in predicting the risk of 30-day readmission after PCI.

Discussion

The purpose of a clinical predictive model is to use the fewest easily available and low-cost predictors to predict the risk and prognosis of a disease. Recently, nomograms have been widely used as prognostic devices for a variety of diseases. To date, most studies have primarily focused on independent predictors of poor prognosis of patients after PCI, and only a few clinical studies have proposed a simple risk scoring system to determine the 30-day readmission risk among PCI patients. However, our study established a new simple nomogram. Based on the LASSO regression and logistic multiple

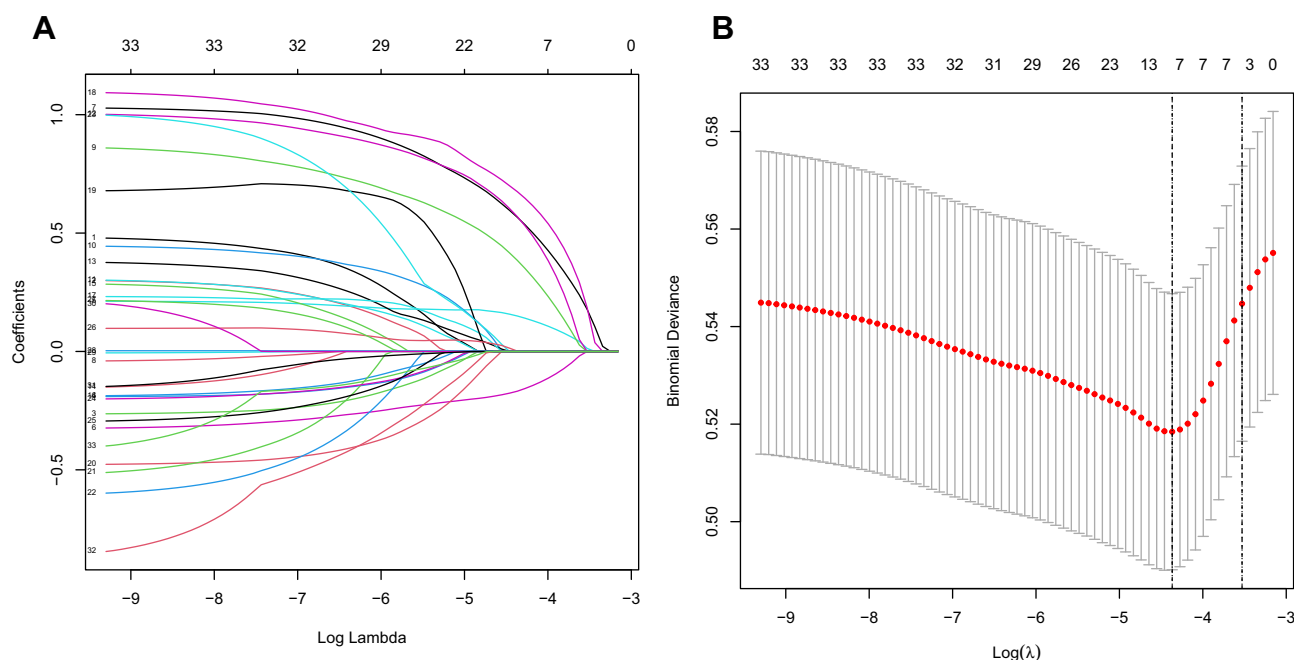


Figure 1 Feature selection using the LASSO binary logistic regression model.

Notes: (A) The figure shows the LASSO coefficient curves for 33 variables based on $\log(\lambda)$. The distribution of the coefficients was generated by the sequence. (B) A vertical line was drawn at the value selected using ten fold cross-validation. The optimal model was acquired when the lambda was 0.01268795, where the optimal lambda resulted in eight features with nonzero coefficients.

regression results, the risk factors for readmission within 30 days after PCI included length of stay, LVEF, number of diseased vessels, hypertension, chronic lung disease, anemia, and creatinine level. Using the clinical results to develop predictive models for screening high-risk populations, we presented an interpretable model based on past medical history and preoperative variables. The apparent and internal validation of the model's performance demonstrated good discrimination and calibration power.

Table 2 Multivariate Logistic Regression Analysis

Intercept and Variable	Prediction Model		
	β	OR (95% CI)	P value
Intercept	-3.990	0.018(0.005–0.540)	<0.001
LOS, day			
6–10	0.510	1.666(1.019–2.794)	0.046
11–15	0.234	1.264(0.545–2.756)	0.567
>15	0.943	2.567(0.909–6.764)	0.063
LVEF, %			
35–44%	0.191	1.211(0.462–3.484)	0.707
45–49%	-0.147	0.350(0.823–1.352)	0.130
≥50%	-0.528	0.589(0.243–1.611)	0.267
Multivessel disease, yes vs no	0.953	2.594(1.59–4.402)	<0.001
Hypertension, yes vs no	0.733	2.082(1.272–3.548)	0.005
Chronic lung disease, yes vs no	0.961	2.616(1.273–5.082)	0.006
Anemia, yes vs no	1.051	2.862(0.179–6.467)	0.014
Cre, yes vs no	0.003	1.002(1.000–1.005)	0.019

Note: β is the regression coefficient.

Abbreviations: LOS, length of stay; Cre, creatinine.

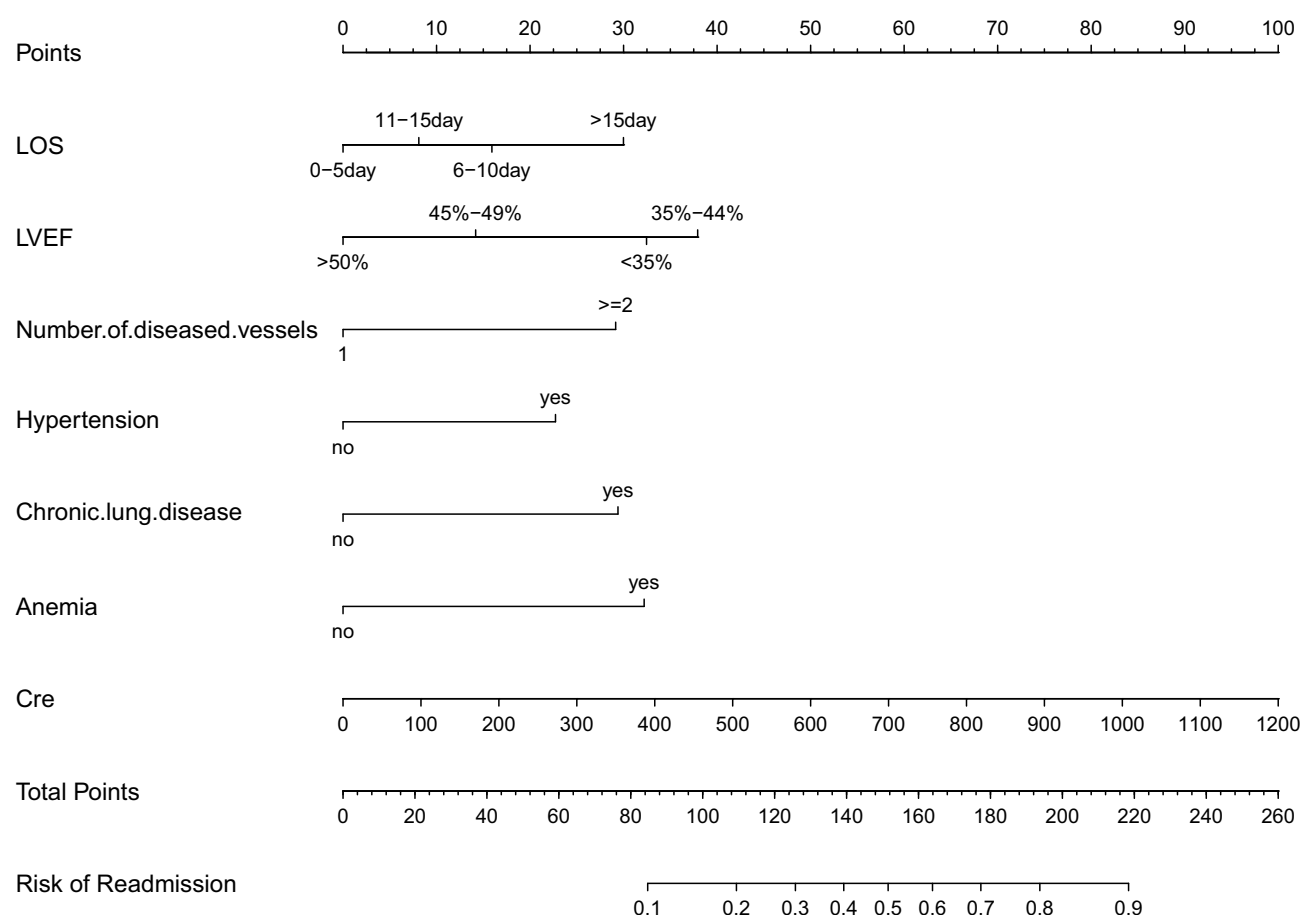


Figure 2 Development of a nomogram to predict 30-day unplanned readmission.

Abbreviations: LOS, length of stay; Cre, creatinine.

The study showed that patients at high risk for 30-day unplanned readmission tended to spend more days in the hospital. To the best of our knowledge, patients with shorter lengths of stay had relatively mild disease, and the majority of those patients were low-risk patients.¹⁵ This is probably because patients with longer lengths of stay often had severe disease and a high burden of comorbidities. Additionally, such patients were more frequently prescribed antithrombotic and antidiabetic treatments and were more likely to have vascular, bleeding or cardiac complications.^{16,17} Identifying these patients and paying close attention to their health may play a potential role in preventing early readmission of patients after PCI.

LVEF is a critical indicator of cardiac function.¹⁸ Studies have shown that the lower the LVEF is at admission, the higher the probability of adverse cardiovascular endpoint events is; patients with a low LVEF tend to have more severe myocardial injury and are prone to complications of pulmonary infection and renal impairment due to a prolonged decline in cardiac output. In particular, patients with an LVEF $\leq 35\%$, reversal of myocardial remodeling and poorer recovery of cardiac function are more likely to undergo repeat revascularization, leading to readmission.^{19,20}

In the present study, the results showed that compared with patients with single-vessel disease, those with multivessel disease had a higher risk of 30-day readmission. This is consistent with the study by Yudi et al²¹ who revealed that patients with multivessel disease were more likely to be older, have more severe atherosclerosis, have suboptimal controlled comorbidities and have impaired cardiac function and poor prognosis.²²

In recent years, additional studies have reached conclusions similar to those of our study: hypertension, chronic lung disease, and anemia were high-risk factors for 30-day readmission after PCI for patients. Hypertension negatively influences microcirculatory hemodynamics, which increases the incidence of major adverse cardiovascular events.^{23,24} Moreover, chronic lung disease leads to an imbalance in oxygen supply, deterioration of pulmonary

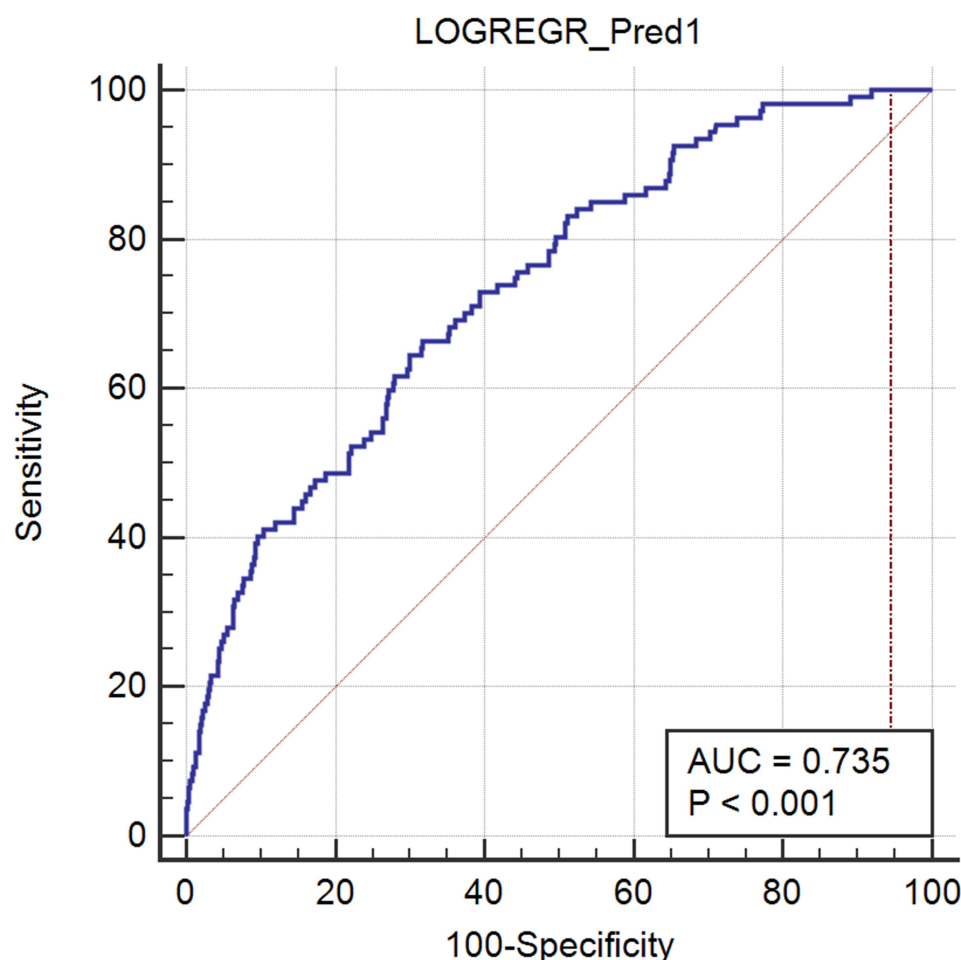


Figure 3 ROC curves of the nomogram for predicting 30-day readmission risk after PCI.

function, and increased cardiac workload, which also increases the readmission risk within 30 days after PCI.²⁵ In addition, there are data suggesting that PCI patients with chronic obstructive pulmonary disease have a nearly fourfold increase in the risk of readmission within 30 days.²⁶ Hence, emphasizing the positive and substantial effect of simultaneous pulmonary rehabilitation is important for PCI patients with pulmonary diseases. Additionally, evidence has confirmed a correlation between anemia and cardiovascular diseases. The number of endothelial cells in the peripheral circulation is decreased in patients with anemia compared to those who do not have any kind of anemia, and an inflammatory response caused by myocardial necrosis results in reduced erythroid function, which impairs vascular healing capacity and leads to poor patient prognosis. Finally, anemia contributes to unfavorable prognosis and early readmission.^{27,28} To ameliorate the effect of anemia on readmission of patients after PCI, a previous study suggests that anemia should be treated in a timely manner for patients whose hemoglobin level is <8 g/dL.²⁹ In summary, interventions such as transitional care management and regular follow-up strategies for PCI patients with comorbidities must be tailored to the particular disease to reduce the incidence of 30-day readmission and alleviate the burden on the patient.

There is also a relationship between creatinine and readmission within 30 days after PCI. Creatinine was shown to be significantly associated with cardiovascular disease prevalence [OR=1.79 (1.47–2.20), $P<0.001$].³⁰ Serum creatinine levels can be assessed as a marker of renal function, and creatinine is normally cleared by healthy kidneys. Deteriorating kidney function can lead to an increased serum creatinine concentration, which has predictive value for both short-term and long-term prognosis after discharge. Therefore, careful consideration is recommended concerning the use of contrast agents for PCI patients with high creatinine levels. In addition, adequate hydration should be given to minimize renal

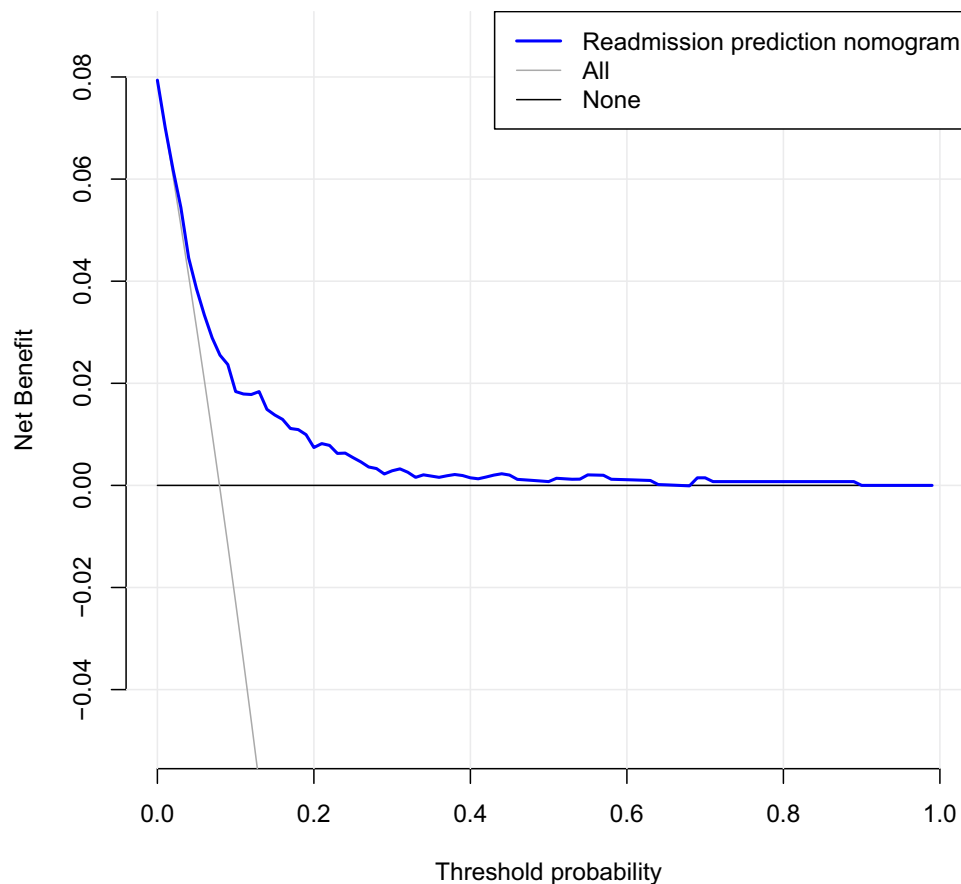


Figure 4 Decision curve analysis of the nomogram for 30-day readmission risk prediction after PCI.

Notes: The x-axis shows the threshold probability, and the y-axis measures the net benefit. Blue curves denote the actual 30-day readmission risk after PCI. Through the decision curve, we can see that when the probability threshold was greater than 2%, the nomogram was better than “all 30-day readmission” or “no 30-day readmission”.

damage. Patients who are identified as having a greater risk should be further treated with other mechanical circulatory support devices.^{31,32} However, whether creatinine can be used as a prognostic biomarker for patients after PCI remains unclear pending further validation.

Moreover, our nomogram is an important priority for programs designed to reduce unplanned hospital readmissions. As a quantitative tool for evaluating risks and benefits, nomograms can provide more objective and accurate information to medical staff and patients to facilitate the early identification of high-risk individuals, assisting clinicians in making a decision on the choice of postdischarge management strategy. This will also reduce the financial burden on patients. The results of various studies show that early interventions such as medication reminders, discharge plans, motivational telephone follow-up, multimodal strategies, real-time follow-up and monitoring of disease progression are beneficial to prevent 30-day readmission after PCI.^{33–35} By evaluating patients with accurate readmission risk prediction models and identifying high-risk patients, the subsequent interventional strategies can reduce the rate of early readmission and improve the quality of medical care.³⁶ This nomogram is helpful for providing new ideas for the rehabilitation protocols of patients in the transitional period after PCI and is beneficial for focusing more effort and resources on patients with a higher risk of readmission to avoid wasting health care resources to the greatest extent. Timely evaluation may not be the final answer. The most critical question is whether to explore more effective intervention schemes.

Limitations

This study has some limitations that need to be taken into account. First, since this is a retrospective study, it has inherent biases and many unmeasured confounders in the collection of patients' medical histories. Some potential variables, such

as the experience of surgeons or the psychosocial burden on patients, were not investigated in the study. Second, there may be a bias issue in the readmission rate. The readmission rate is probably underestimated because patients are more likely to visit other hospitals. Finally, our nomogram was verified internally by bootstrap resampling, which affects the external general applicability of the model to some extent. To this end, external validation is warranted. The next step is to collect prospective data from multiple centers for external verification to increase the generalizability of the model.

Conclusion

The 30-day readmission rate is an important indicator of the quality of medical care. Readmission to the hospital within 30 days is not rare among patients after PCI. In this study, a screening tool with relatively good accuracy was developed for medical staff to screen high-risk patients for readmission within 30 days after PCI. Further research is needed in the future.

Data Sharing Statement

The raw data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation.

Ethical Considerations

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee for medical research at the Affiliated Hospital of the Second Affiliated Hospital of Nanchang University. Due to the retrospective nature of the study and the fact that no confidential patient information was involved, the requirement of written informed consent was waived by the review board.

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Disclosure

The authors declare that they have no conflicts of interest related to this work.

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