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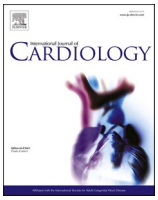

Predictive nomogram for 28-day mortality risk in mitral valve disorder patients in the intensive care unit: A comprehensive assessment from the MIMIC-III database

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ABSTRACT

Background: Mitral valve disorder (MVD) stands as the most prevalent valvular heart disease. Presently, a comprehensive clinical index to predict mortality in MVD remains elusive. The aim of our study is to construct and assess a nomogram for predicting the 28-day mortality risk of MVD patients.

Methods: Patients diagnosed with MVD were identified via ICD-9 code from the MIMIC-III database. Independent risk factors were identified utilizing the LASSO method and multivariate logistic regression to construct a nomogram model aimed at predicting the 28-day mortality risk. The nomogram's performance was assessed through various metrics including the area under the curve (AUC), calibration curves, Hosmer-Lemeshow test, integrated discriminant improvement (IDI), net reclassification improvement (NRI), and decision curve analysis (DCA).

Results: The study encompassed a total of 2771 patients diagnosed with MVD. Logistic regression analysis identified several independent risk factors: age, anion gap, creatinine, glucose, blood urea nitrogen level (BUN), urine output, systolic blood pressure (SBP), respiratory rate, saturation of peripheral oxygen (SpO_2), Glasgow Coma Scale score (GCS), and metastatic cancer. These factors were found to independently influence the 28-day mortality risk among patients with MVD. The calibration curve demonstrated adequate calibration of the nomogram. Furthermore, the nomogram exhibited favorable discrimination in both the training and validation cohorts. The calculations of IDI, NRI, and DCA analyses demonstrate that the nomogram model provides a greater net benefit compared to the Simplified Acute Physiology Score II (SAPSII), Acute Physiology Score III (APSIII), and Sequential Organ Failure Assessment (SOFA) scoring systems.

Conclusion: This study successfully identified independent risk factors for 28-day mortality in patients with MVD. Additionally, a nomogram model was developed to predict mortality, offering potential assistance in enhancing the prognosis for MVD patients. It's helpful in persuading patients to receive early interventional catheterization treatment, for example, transcatheter mitral valve replacement (TMVR), transcatheter mitral valve implantation (TMVI).

1. Introduction

Mitral valve disorder (MVD) is the most common heart valve disease, affecting >24 million people worldwide [1]. It is particularly prevalent in the elderly population, with a prevalence of over 10% in individuals aged 75 and above [2]. Pathological changes at any level of the mitral

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valve apparatus can lead to its dysfunction [3].There are two main types of dysfunction associated with MVD: mitral stenosis and mitral regurgitation, which may occur simultaneously [3,4]. Mitral stenosis has fewer causes, with post-inflammatory/rheumatic diseases and congenital malformations being the most common [3]. Mitral regurgitation, however, is the primary cause of most MVDs in the developed world and its prevalence is increasing with age [5]. The disease usually progresses unnoticed as the heart compensates for the increased regurgitant flow by left atrial enlargement, resulting in left ventricular overload and dysfunction. Severe cases of MVD have a poor prognosis [6].

MVD can result in left ventricular dysfunction, congestive heart failure, and death [2]. Therefore, appropriate management of MVD, often necessitating surgical repair or valve replacement, is critical. Surgical options include conotruncation, mitral valve replacement, and cusp valve repair [4], with many new techniques currently under development. The field of diagnosing and managing MVD is rapidly evolving, although fewer studies have explored risk factors for prognosis beyond therapeutic treatments. Therefore, early and accurate prediction

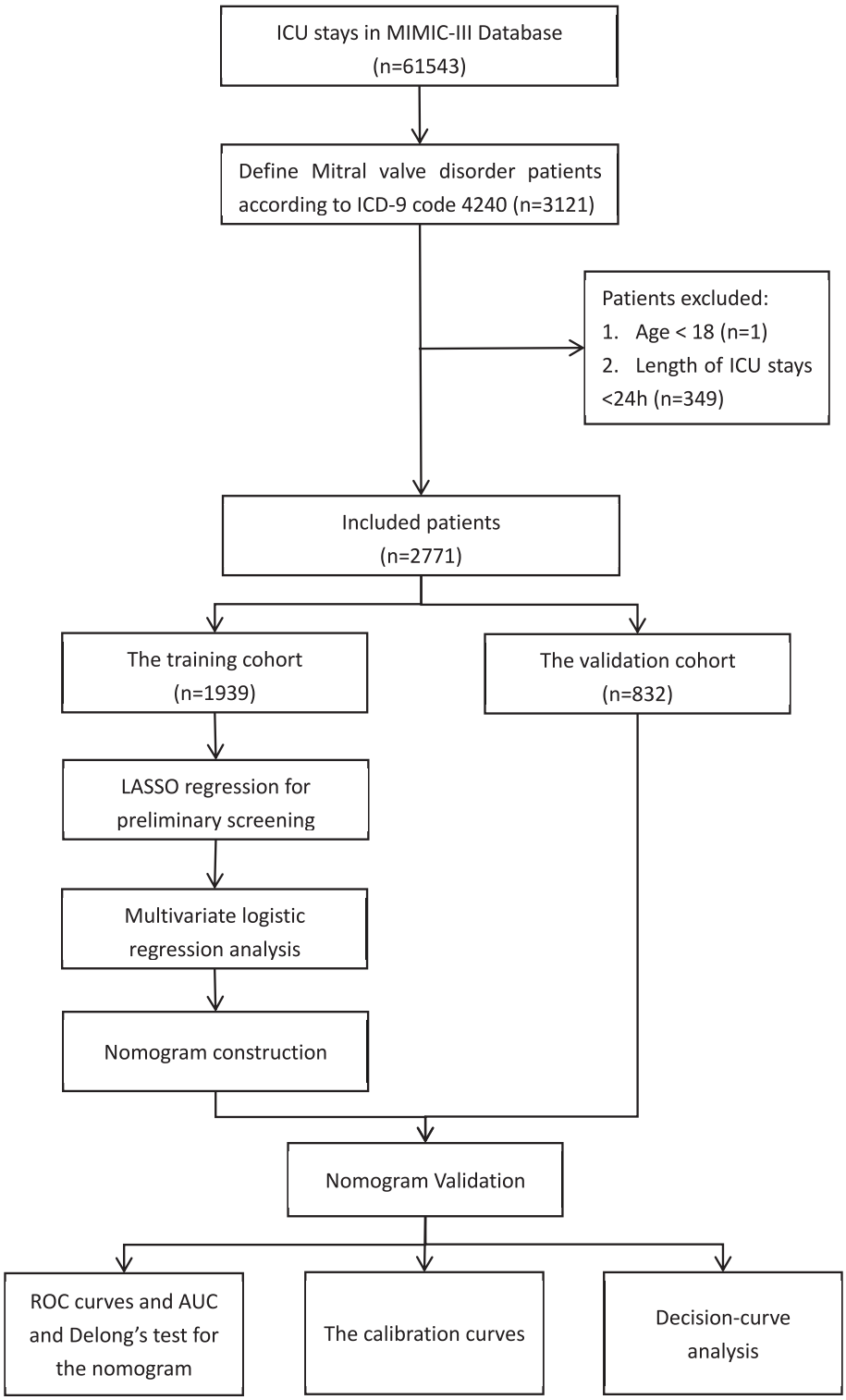

Fig. 1. Flow diagram of the study.

of clinical prognosis is important for guiding treatment planning and assessing treatment outcomes.

Previous studies have identified age [7], hypertension, body mass index [8], and serum creatinine [9] as risk factors for poor prognosis in patients with MVD. A nomogram, a continuous scoring system developed using several key parameters, serves as a visual statistical tool to calculate precise risk probabilities for specific endpoints such as disease progression or death in individual patients [10]. Despite many physicians and academics researching risk factors for poor prognosis in patients with MVD, few studies have focused on implementing the nomogram, especially during short period. In this study, we constructed a nomogram capable of predicting the 28-day risk of death in patients with MVD based on a large sample retrieved from the MIMIC-III database.

2. Materials and methods

2.1. Data source

All data in this experiment were sourced from the Medical Information Mart for Intensive Care III (MIMIC-III) database. MIMIC-III contains comprehensive clinical data (Johnson AE, Pollard TJ, Shen L, Le) of 53,423 adult patients (aged 16 and over) admitted to the intensive care unit of Beth Israel Deaconess Medical Center in Boston, Massachusetts, from 2001 to 2012 [11]. Informed consent was not required for this study because details about patients' clinical care in the database were anonymized. Access to the MIMIC-III database (certificate number 40269495) was granted to researchers after completing a series of courses provided by the National Institutes of Health, as well as the required relevant assessments.

2.2. Patients and variables

The necessary data were extracted using structured query language in DBeaver (version 23.3.4). Patients diagnosed with MVD were extracted using ICD-9 code "4240" in the MIMIC-III database. The exclusion criteria were as follows: (1) age <18 years and (2) those who had been treated in the ICU for <24 h. The flowchart of the study is shown in Fig. 1.

Data were extracted from the corresponding tables using the "icustay_id" parameter, such as age, gender, marital status, race, laboratory parameters, severity score, vital signs, urine output, and comorbidities. Vital sign values used included heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), respiratory rate, temperature, and saturation of peripheral oxygen (SpO_2), which were averaged over the first 24 h. Laboratory results included anion gap (AG), bicarbonate, creatinine (Cr), chloride, glucose, hematocrit, hemoglobin, platelet count (PLC), potassium levels (K^+), partial thromboplastin time (PTT), international normalized ratio (INR), prothrombin time (PT), sodium levels (Na^+), blood urea nitrogen level (BUN), and white blood cell (WBC) count. The selected comorbidities included congestive heart failure, valvular disease, pulmonary circulation, peripheral vascular, hypertension, chronic pulmonary, diabetes complicated, renal failure, liver disease, aids, metastatic cancer, solid tumor, fluid electrolyte, derium. Glasgow Coma Scale (GCS) [12,13], Simplified Acute Physiology Score II (SAPSII) [14–16], Sequential Organ Failure Assessment (SOFA) [17–19] and Acute Physiology Score III (APSIII) [20,21] were used as the severity scoring system.

The 28-day mortality for patients with MVD admitted to the ICU was the outcome, and those who were alive at the time of discharge were designated as survivors.

2.3. Statistical analysis

After exporting the data from the MIMIC-III database, these data need to be pre-processed to filter out the required patient data according to the exclusion criteria firstly. Multiple interpolation of missing data was then also required, where indicators with >20% missing values were excluded. All screened patients with MVD were randomly divided into a training group (70%) and a validation group (30%). The training group was used for screening variables, constructing nomograms, and performing internal validation, whereas the validation group was used for external validation of the results obtained in the training group. The Shapiro-Wilk test was used to determine whether the continuous variables had a normal distribution. Continuous variables that conformed to normal distribution were described as mean and standard deviation and compared using *t*-test or Mann-Whitney *U* test. If continuous variables did not conform to normal distribution, they were described as median and interquartile range. In contrast, categorical variables expressed as frequencies and proportions were compared across groups using chi-square or Fisher exact probability tests.

Independent risk factors for death within 28 days in patients with MVD were determined by logistic regression. Risk factors were first identified by performing least absolute shrinkage and selection operator (LASSO) regression analyses, integrating various characteristics and different clinical outcomes in the training cohort to screen for potential factors contributing to adverse outcomes in MVD. In LASSO, data values are contracted towards the centroid and the algorithm aids in variable selection and parameter elimination [22]. Then, different AUC values in the lambda range are estimated using cross-validation technique. The maximum value of lambda was selected within the lambda range where the cross-validation error was within double the standard error of the minimum value. Subsequently, the selected variables were subjected to multivariate logistic regression analyses to identify meaningful independent prognostic factors, and the results were expressed in terms of odds ratios (ORs) and 95% confidence intervals (CIs). Finally, a nomogram was constructed based on independent risk prognostic factors and used to predict 28-day mortality in patients with MVD.

For the discriminative power of the model, several metrics were used to internally and externally validate the nomogram. The Harrell's concordance index (C-index) was chosen to assess its predictive accuracy, and the area under the curve (AUC) of our model was compared with existing SAPSII, APSIII, and SOFA scoring systems. Larger AUC values indicate more accurate prognostic stratification [10,23]. Receiver operating characteristic (ROC) curves were used to determine the optimal cut-off point and its sensitivity and specificity according to the Youden index. In addition, integrated discriminant improvement (IDI) and net reclassification improvement (NRI) were applied to calculate the difference in predicting 28-day mortality in patients with MVD between the constructed model and the SAPSII, APSIII and SOFA scoring systems. In addition, agreement between model-predicted survival probabilities and observed unfavorable outcomes was assessed by calibration curves, and the calibration of the column-line plots was evaluated using the Hosmer-Lemeshow test. Finally, the clinical validity of the model was validated by calculating the net profit of a series of threshold probabilities based on decision curve analysis (DCA), comparing the nomograms with the SAPSII, APSIII and SOFA scoring systems.

Statistical analyses were performed using R (version 4.0.3) and SPSS (version 24.0) software. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Baseline characteristics

After applying the selection and exclusion criteria, 2771 patients with MVD were identified from the MIMIC-III database, divided into 1939 patients in the training group and 832 patients in the validation group. The lengths of ICU stay (2.82 [1.70, 4.93] days for the training group vs. 2.78 [1.66, 5.04] days for the validation group, $P = 0.744$) and hospital admission times (8.11 [5.25, 13.21] days for the training group vs. 8.47 [5.28, 12.97] days for the validation group, $P = 0.744$) were not significantly different between the two groups. In both the training and

validation cohorts, males constituted 52.3% and 53.6% of the MVD patients, respectively. The median ages were 71.47 years [60.32, 80.13] for the training group and 71.03 years [60.58, 79.89] for the validation group. The prevalence of congestive heart failure was 0.6% in both cohorts. Peripheral vascular disease was found in 1.4% of the training group and 1.3% of the validation group, while metastatic cancer was present in 0.3% of the training group and 0.4% of the validation group, respectively. The median SAPSII scores were 35.00 [28.00, 44.00] for the training group and 36.00 [28.00, 44.00] for the validation group. Average levels of Cr (mg/dL) were 1.03 [0.80, 1.55] for the training group and 1.00 [0.77, 1.50] for the validation group, while the BUN levels (mmol/L) were 21.00 [14.50, 34.50] for the training group and 20.00 [14.00, 34.00] for the validation group. Additional baseline characteristics are presented in Table 1.

3.2. Nomogram construction

LASSO regression was employed to identify independent risk factors influencing the mortality of patients with MVD in the ICU within 28 days. Fig. 2 illustrates the various mean square errors across the logarithmic lambda range. The maximum lambda value is chosen when the cross-validation error is less than the standard error of the minimum value [24]. Multiple logistic regression identified age, AG, Cr, glucose, BUN, urine output, SBP, respiratory rate, SpO_2, GCS score, and metastatic cancer as independent risk factors for death during hospitalization in patients with MVD. The risk of death within 28 days in elderly patients was 1.042 times higher than in younger patients (95% CI = 1.0257–1.0590).

In the initial laboratory examination, the mortality risk of patients with a high AG was 1.135 times higher than that of patients with normal results (95% CI = 1.0691–1.2056). Patients with a higher respiratory rate upon ICU admission had a 1.069 times higher risk of death than patients with normal results (95% CI = 1.0224–1.1177). Upon entering the ICU, the mortality risk of patients with metastatic cancer was 16.304 times higher than that of normal patients (95% CI = 2.0257–98.6225). Additionally, glucose (OR = 1.003, 95% CI = 1.0001–1.0067) and BUN level (OR = 1.023, 95% CI = 1.0136–1.0318) were also identified as risk factors for 28-day mortality in patients with MVD. Conversely, Cr (OR = 0.818, 95% CI = 0.6912–0.9533), urine output (OR = 0.999, 95% CI = 0.9993–0.9997), SBP (OR = 0.978, 95% CI = 0.9642–0.9906), SpO_2 (OR = 0.927, 95% CI = 0.8628–0.9912), and GCS (OR = 0.917, 95% CI = 0.8648–0.9751) were identified as protective factors (Table 2). These factors were used to develop a nomogram for estimating the risk of death in patients with MVD within 28 days (Fig. 3).

3.3. Nomogram validation

In the training group, the C-index was 0.836 (95% CI = 0.870–0.810), while in the validation group, it was 0.821 (95% CI = 0.870–0.770). The ROC curves confirmed the overall predictive performance (Fig. 4). The area under the curve (AUC) of the nomogram in the training and validation groups was 0.826 (95% CI = 0.796–0.856) and 0.821 (95% CI = 0.771–0.872), respectively.

Comparing our nomogram's AUC values with those of SAPSII, APSIII, and SOFA in both training and validation groups revealed superior performance. In the training group, the nomogram's best cutoff value was 0.111, with a specificity of 0.785 and sensitivity of 0.720. In the validation group, the best cutoff value was 0.137, and the specificity and sensitivity were 0.825 and 0.738, respectively.

Compared to traditional SAPSII, APSIII, and SOFA scoring systems, the NRI values for the nomogram were 0.227 (95% CI = 0.133–0.419), 0.293 (95% CI = 0.1845–0.442), and 0.449 (95% CI = 0.311–0.601) in the training group. In the validation group, the NRI values were 0.351 (95% CI = 0.163–0.604), 0.134 (95% CI = −0.041-0.467), and 0.428 (95% CI = 0.216–0.671). The IDI values for the training group were 0.077 (95% CI = 0.0491–0.105), 0.079 (95% CI = 0.0541–0.1041), and 0.121 (95% CI = 0.0909–0.1502), respectively. In the validation group, the IDI values were 0.072 (95% CI = 0.0387–0.1052), 0.032 (95% CI = 0.0012–0.0621), and 0.095 (95% CI = 0.0586–0.1317). These values collectively indicate that our nomogram exhibits excellent discriminative ability, comparable to widely used scoring systems, such as SAPSII, APSIII, and SOFA.

The calibration curve of the nomogram is depicted in Fig. 5. As evident from the figure, the calibration curves for both the training and validation groups closely align with the diagonal. Notably, no significant differences were observed in the Hosmer-Lemeshow test (training group: $\chi2 = 7.952$, $p = 0.438$; validation group: $\chi2 = 9.009$, $p = 0.342$). In summary, our nomogram effectively simulates the data.

Fig. 6 illustrates the corresponding DCA curves, comparing the nomogram with the SAPSII, APSIII, and SOFA scoring systems. This highlights the clinical applicability of our nomogram. In both the training and validation groups, the net benefit of clinical interventions guided by our nomogram model surpassed interventions guided by the SAPSII, APSIII, and SOFA scoring systems when the threshold probability ranged from 0.1 to 0.5.

4. Discussion

MVD stands out as the most prevalent heart valve ailment, encompassing mitral stenosis, mitral valve insufficiency [2], or a combination of both [3]. According to international data, contemporary causes of MVD comprise valve degeneration (60%–70%), ischemic mitral regurgitation, endocarditis, and rheumatic diseases [25]. Notably, limited studies have focused on prognostic risk factors for patients with MVD. Therefore, there is a pronounced need for the development of a predictive model to anticipate the risk of mortality in patients with MVD. In this study, we employed LASSO and multivariate logistic regression to identify independent risk factors for death within 28 days of hospitalization in patients with MVD. Subsequently, we constructed a nomogram model for prediction. The aim of our study was to investigate the relationship between these factors and the risk of death among patients with MVD, as well as to develop and validate a corresponding nomogram to predict this risk. The nomogram exhibited strong performance in predicting the risk of in-hospital death among patients with MVD in both the training and validation cohorts.

Our results revealed that age, AG, Cr, glucose, BUN, urine output, SBP, respiratory rate, SpO_2, GCS score, and metastatic cancer were independent risk factors for death within 28 days in patients with MVD. Utilizing these findings, we constructed a nomogram model to assess the risk of 28-day mortality in patients with MVD. The validity of the nomogram was evaluated through various metrics, including the AUC, calibration curves, Hosmer-Lemeshow test, IDI, NRI, and DCA. Additionally, we determined the optimal cut-off value based on the Youden index and calculated the sensitivity and specificity of the corresponding curves. Several metrics from the study indicate that the predictive performance of our constructed nomograms surpasses that of the SAPSII, APSIII, and SOFA scoring systems. Empirical evidence suggests that the model we constructed not only reduces the number of variables, but also demonstrates predictive performance comparable to commonly used scoring systems.

Our findings confirm that age constitutes an independent risk factor for poor prognosis in patients with MVD. Age [7,8,26] is widely acknowledged as a significant risk factor for MVD [7,27]. Valve degeneration stands as the primary cause of MVD [6], with degenerative MVD directly associated with aging [26]. The GCS serves as an objective measure to delineate the extent of impaired consciousness across all categories of acute medical and trauma patients [28]. A lower GCS score correlates with a heightened risk of mortality, aligning with our findings [24,29]. Despite being one of the most robust clinical prognostic indicators, neither the GCS score nor any singular feature should be solely relied upon to prognosticate individual patient outcomes. This stems from the reality that the prognostic significance of the score is

Table 1
Patient characteristic.

Variables	Overall	Training cohort	Validation cohort	p
N	2771	1939	832	
Gender (%)				
Female	1311(47.3)	925(47.7)	386(46.4)	0.554
Male	1460(52.7)	1014(52.3)	446 (53.6)	
Marital (%)				
DSW	739 (26.7)	518 (26.7)	221 (26.6)	0.858
Married	1470 (53.0)	1031 (53.2)	439 (52.8)	
Single	480 (17.3)	330 (17.0)	150 (18.0)	
Unknown	82 (3.0)	60 (3.1)	22 (2.6)	
Race (%)				
Black	199 (7.2)	139 (7.2)	60 (7.2)	0.853
Other	588 (21.2)	417 (21.5)	171 (20.6)	
White	1984 (71.6)	1383 (71.3)	601 (72.2)	
Age (year)	71.30 [60.40,80.02]	71.47 [60.32,80.13]	71.03 [60.58,79.89]	0.418
Length of Admission (day)	8.26 [5.26, 13.09]	8.11 [5.25, 13.21]	8.47 [5.28, 12.97]	0.744
Length of ICU stays (day)	2.81 [1.69,4.94]	2.82 [1.70,4.93]	2.78 [1.66,5.04]	0.757
Laboratory test				
Anion gap (mmol/L)	13.33 [11.45,15.67]	13.50 [11.50,15.71]	13.00 [11.00,15.50]	0.28
Bicarbonate (mmol/L)	24.00 [22.00,26.00]	24.00 [22.00,26.00]	24.00 [22.00,26.00]	0.812
Creatinine (mg/dL)	1.02 [0.80,1.55]	1.03 [0.80,1.55]	1.00 [0.77,1.50]	0.466
Chloride (mmol/L)	105.50 [101.50,108.50]	105.33 [101.50,108.50]	105.75 [101.50,108.50]	0.749
Glucose (mg/dL)	131.08 [116.00,153.26]	131.33 [116.35,153.00]	130.35 [115.00,153.34]	0.444
Hematocrit (g/dL)	30.66 [28.00,34.29]	30.70 [28.00,34.42]	30.55 [28.02,33.88]	0.705
Hemoglobin (g/dL)	10.25 [9.30,11.55]	10.28 [9.30,11.60]	10.21 [9.32,11.44]	0.573
Platelet (K/μL)	189.00 [146.00,253.33]	189.00 [146.88,252.38]	189.00 [142.00,255.37]	0.602
Potassium (mmol/L)	4.27 [3.95,4.57]	4.27 [3.93,4.57]	4.28 [4.00,4.58]	0.721
PTT (s)	34.65 [29.30,44.58]	34.63 [29.40,44.64]	34.67 [29.15,44.31]	0.686
INR	1.35 [1.20,1.60]	1.35 [1.20,1.60]	1.33 [1.20,1.60]	0.564
PT (s)	14.70 [13.60,16.35]	14.73 [13.60,16.30]	14.65 [13.60,16.46]	0.983
Sodium (mmol/L)	138.00 [135.83,140.00]	138.00 [135.80,140.00]	137.75 [136.00,139.67]	0.279
BUN (mmol/L)	21.00 [14.33,34.00]	21.00 [14.50,34.50]	20.00 [14.00,34.00]	0.207
WBC (K/μL)	11.40 [8.61,14.84]	11.50 [8.75,14.89]	11.14 [8.47,14.77]	0.303
Urine Output (mL)	1766.00 [1080.00,2670.00]	1760.00 [1078.50,2647.50]	1777.50 [1090.00,2680.25]	0.609
Vital signs				
Heartrate (bpm)	83.48 [74.69,92.40]	83.37 [74.78,92.76]	83.54 [74.51,91.74]	0.725
Systolic BP (mmHg)	110.89 [103.74,120.68]	110.71 [103.63,120.76]	111.37 [104.27,120.46]	0.689
Diastolic BP (mmHg)	56.9 7 [51.69,62.62]	56.89 [51.56,62.49]	57.36 [51.98,62.95]	0.132
Mean BP (mmHg)	73.77 [68.88,79.91]	73.66 [68.93,79.68]	74.17 [68.73,80.35]	0.519
Respiratory rate (rpm)	18.17 [15.96,20.96]	18.17 [15.96,21.00]	18.13 [15.97,20.86]	0.98
Temperature(°C)	36.75 [36.39,37.11]	36.74 [36.38,37.10]	36.78 [36.42,37.12]	0.227
SpO_2 (%)	97.76 [96.39,98.77]	97.77 [96.36,98.74]	97.76 [96.45,98.80]	0.414
Severe Score				
GCS	15.00 [14.00,15.00]	15.00 [14.00,15.00]	15.00 [14.00,15.00]	0.58
SAPSII	35.00 [28.00,44.00]	35.00 [28.00,44.00]	36.00 [28.00,44.00]	0.51
SOFA	4.00 [3.00,6.00]	4.00 [3.00,6.00]	4.00 [3.00,6.00]	0.957
APSIII	40.00 [30.00,53.00]	40.00 [30.00,53.00]	41.00 [30.00,53.00]	0.83
Comorbidities				
Congestive heart failure (%)				
No	2754 (99.4)	1927 (99.4)	827 (99.4)	1
Yes	17 (0.6)	12 (0.6)	5 (0.6)	
Valvular disease (%)				
No	2759 (99.6)	1932 (99.6)	827 (99.4)	0.571
Yes	12 (0.4)	7 (0.4)	5 (0.6)	
Pulmonary circulation (%)				
No	2768 (99.9)	1936 (99.8)	832 (100.0)	0.614
Yes	3 (0.1)	3 (0.2)	0 (0.0)	
Peripheral vascular (%)				
No	2733 (98.6)	1912 (98.6)	821 (98.7)	1
Yes	38 (1.4)	27 (1.4)	11 (1.3)	
Hypertension (%)				
No	2768 (99.9)	1938 (99.9)	830 (99.8)	0.45
Yes	3 (0.1)	1 (0.1)	2 (0.2)	
Chronic pulmonary (%)				
No	2768 (99.9)	1936 (99.8)	832 (100.0)	0.614
Yes	3 (0.1)	3 (0.2)	0 (0.0)	
Diabetes complicated (%)				
No	2766 (99.8)	1934 (99.7)	832 (100.0)	0.328
Yes	5 (0.2)	5 (0.3)	0 (0.0)	
Renal failure (%)				
No	2768 (99.9)	1937 (99.9)	831 (99.9)	1
Yes	3 (0.1)	2 (0.1)	1 (0.1)	
Liver disease (%)				
No	2769 (99.9)	1938 (99.9)	831 (99.9)	1
Yes	2 (0.1)	1 (0.1)	1 (0.1)	

(*continued on next page*)

Table 1 (*continued*)

Variables	Overall	Training cohort	Validation cohort	p
Aids (%)				
No	2770 (100.0)	1939 (100.0)	831 (99.9)	0.663
Yes	1 (0.0)	0 (0.0)	1 (0.1)	
Metastatic cancer (%)				
No	2762 (99.7)	1933 (99.7)	829 (99.6)	1
Yes	9 (0.3)	6 (0.3)	3 (0.4)	
Solid tumor (%)				
No	2747 (99.1)	1919 (99.0)	828 (99.5)	0.226
Yes	24 (0.9)	20 (1.0)	4 (0.5)	
Fluid electrolyte (%)				
No	2768 (99.9)	1937 (99.9)	831 (99.9)	1
Yes	3 (0.1)	2 (0.1)	1 (0.1)	
Derium (%)				
No	2587 (93.4)	1814 (93.6)	773 (92.9)	0.588
Yes	184 (6.6)	125 (6.4)	59 (7.1)	

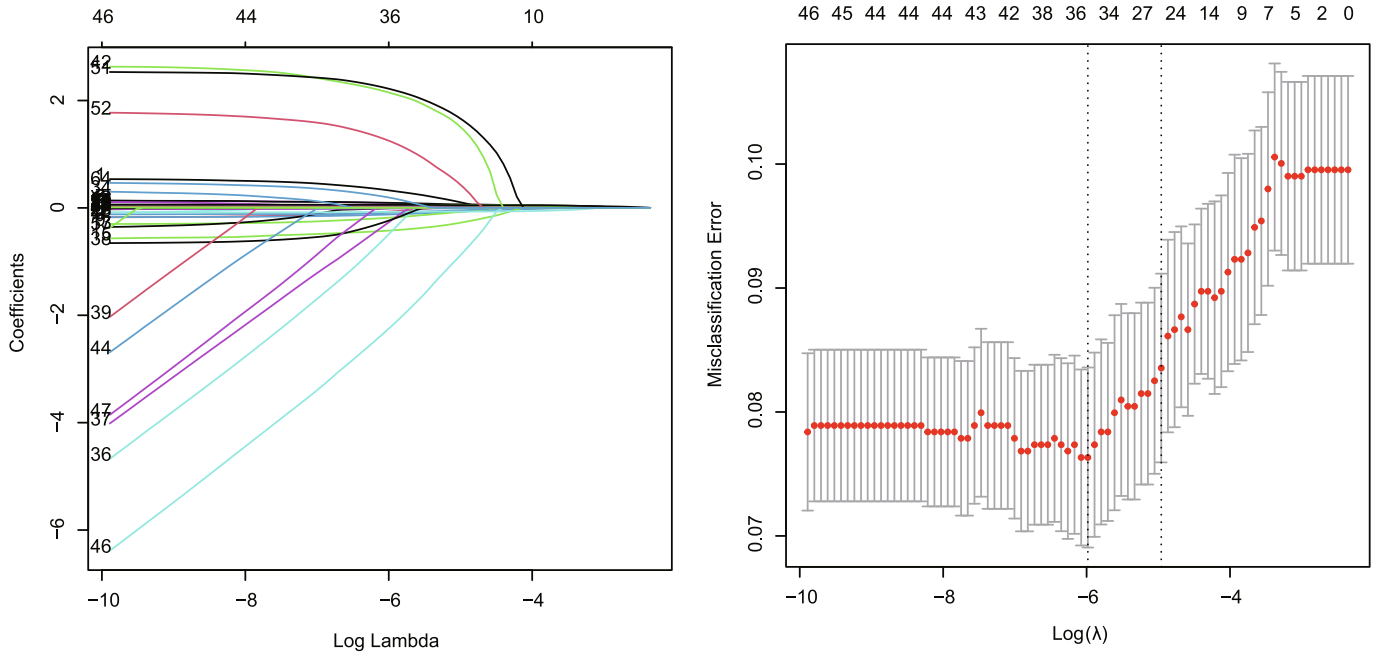

Fig. 2. Least absolute shrinkage and selection operator (LASSO) binary logistic regression model for identifying independent risk factors for mortality in patients with MVD within 28 days. (A) LASSO coefficient profiles of the radiomic features. Each colored line represents the coefficient of each feature. (B) Plot the results of cross-validation, and the red dots in the figure represent the target parameters corresponding to each lambda. The largest lambda value is chosen when the cross-validation error is within one standard error of the minimum. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2
Factors independently associated with 28-day mortality in MVD patients.

Variables	OR	CI	*p*	
Age (year)	1.042	1.0257–1.0590	0	***
Laboratory test				
Anion gap (mmol/L)	1.135	1.0691–1.2056	0	***
Creatinine (mg/dL)	0.818	0.6912–0.9533	0.0141	*
Glucose (mg/dL)	1.003	1.0001–1.0067	0.0382	*
BUN (mmol/L)	1.023	1.0136–1.0318	0	***
Urine Output (mL)	0.999	0.9993–0.9997	0	***
Vital signs				
Systolic BP (mmHg)	0.978	0.9642–0.9906	0.001	**
Respiratory rate (rpm)	1.069	1.0224–1.1177	0.0033	**
SpO2 (%)	0.927	0.8628–0.9912	0.0334	*
Severe Score				
GCS	0.917	0.8648–0.9751	0.0043	**
Metastatic cancer (%)	16.304	2.0257–98.6225	0.0031	**

* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.

influenced by other factors [28].

Research indicates that systemic hypertension serves as the clinical determinant of mitral regurgitation in MVD [8]. The correlation between mitral annulus dysfunction and systemic blood pressure has been established, with systemic blood pressure capable of influencing the severity of valve regurgitation [30]. Nevertheless, the treatment of mitral regurgitation remains contentious. Large-scale randomized trials evaluating the efficacy of vasodilators are lacking, and existing small-scale studies have yielded conflicting results [31]. Evidence suggests that patients with severe mitral annulus separation may derive the most benefit from lowering systolic blood pressure [30]. In parallel investigations, some patients developed mitral regurgitation following short-term vasodilation therapy [32]. This concurs with our findings, suggesting that lower systolic blood pressure may contribute to a poorer prognosis. The reason for this contradiction may be that different patients exhibit diverse etiologies [31], severities, and treatment durations, leading to distinct curative effects. It is certain that blood pressure serves as a crucial risk factor influencing the prognosis of patients with MVD.

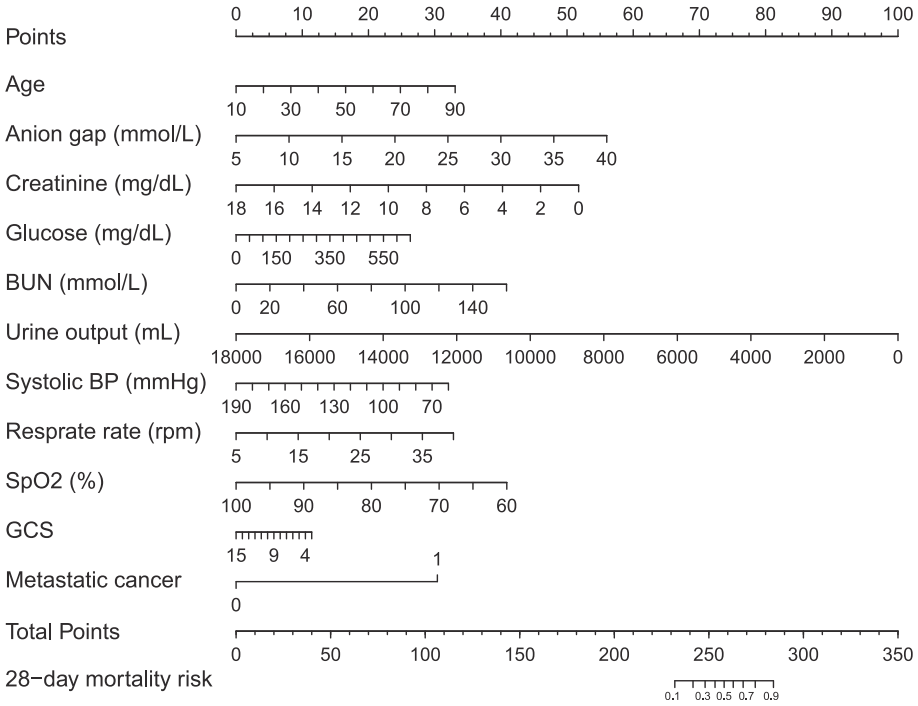

Fig. 3. Nomogram for 28-day mortality of mitral valve disorder patients. Nomogram included age, anion gap, creatinine, glucose, blood urea nitrogen level, urine output, systolic blood pressure, respiratory rate, saturation of peripheral oxygen, GCS, and metastatic cancer for predicting 28-day mortality after a mitral valve disorder. The total point was calculated as the sum of the individual scores for each of the seven variables included in the nomogram. Patients were assessed based on each variable, and the total points were assigned according to the nomogram. Each variable's specific data were used to evaluate the patient, resulting in a total score derived from the nomogram. With this value, the risk of 28-day mortality could be predicted.

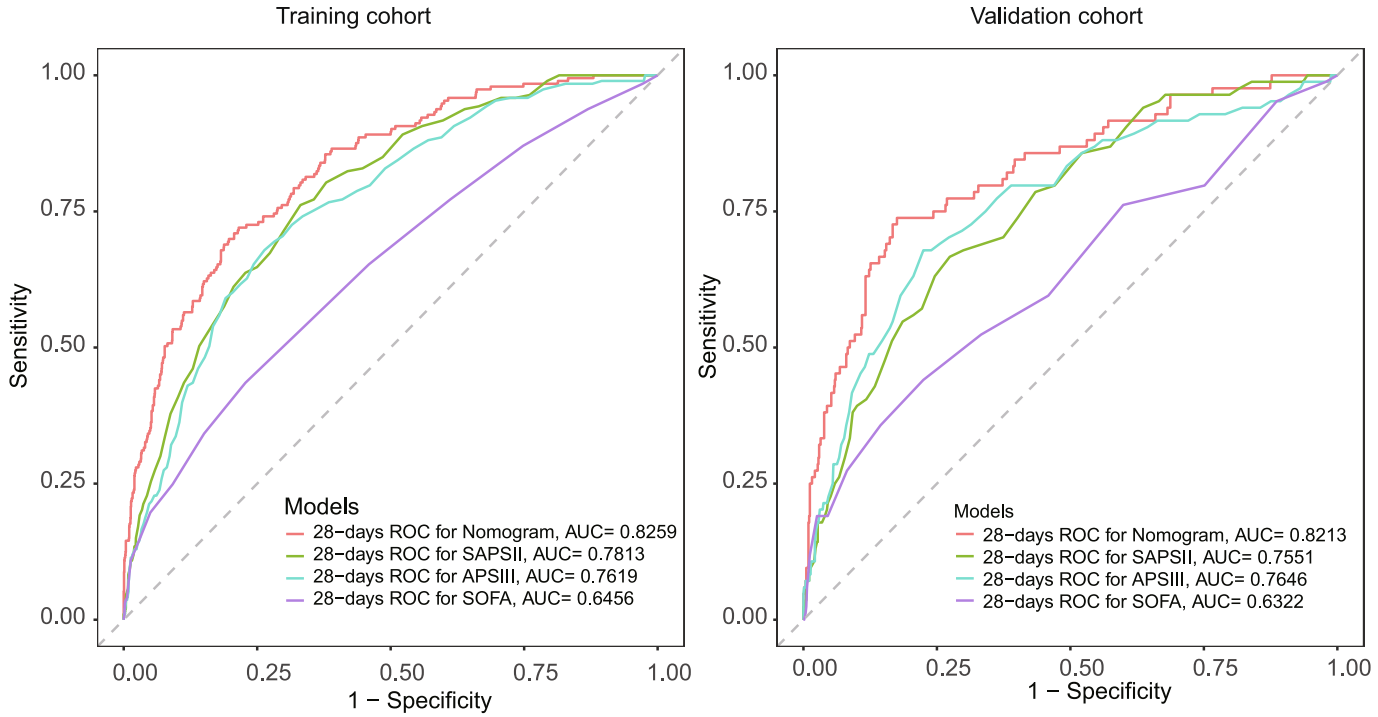

Fig. 4. Receiver operating characteristic (ROC) curves for the SAPSII (Green), APSIII (Blue), SOFA (purple) and the nomogram (Red). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Serum creatinine is not only utilized to assess renal function but also serves as an indicator of muscle mass [33]. Our study has identified that lower serum creatinine levels constitute a risk factor for a poor prognosis in patients with MVD. Research has indicated that ICU patients with low serum creatinine levels experience a higher mortality rate, possibly attributed to diminished muscle mass. Low muscle mass emerges as a robust predictor of an unfavorable prognosis in ICU patients [34]. Moreover, cardiac and aortic surgeries are associated with a relatively

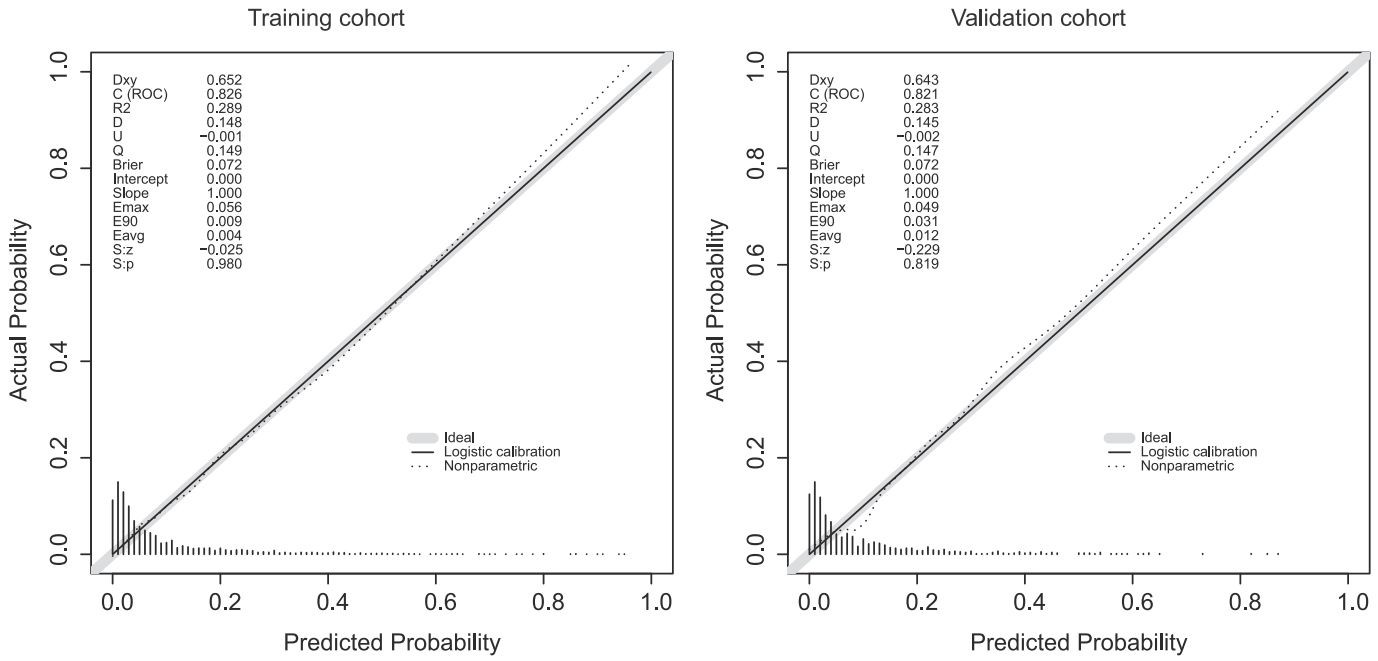

Fig. 5. Calibration curves for the training cohort and the validation cohort.

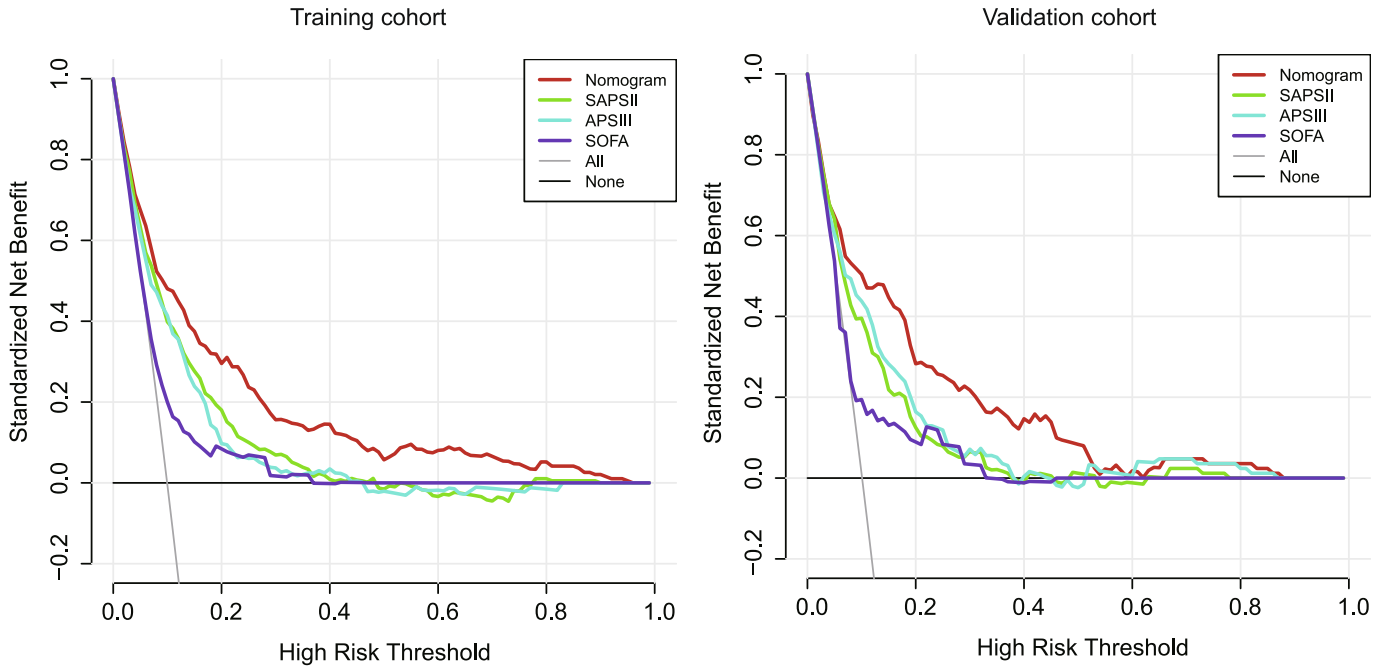

Fig. 6. Decision-curve analysis of the training cohort and the validation cohort. Decision curve analysis depicts the clinical net benefit in pairwise comparisons across the different models. The red line indicates the nomogram, which is the model we built. The green line indicates SAPSII scoring system, the blue line indicates APSIII and the purple line indicates SOFA. Nomogram showed superior net benefit with a wider range of threshold probabilities compared with SAPSII, APSIII and SOFA. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

elevated risk of acute renal failure [35]. The reduced serum creatinine levels may result from a significant increase in the functional creatinine clearance rate and glomerular filtration rate in patients with acute diseases [34]. MVD is independently linked to renal dysfunction [9], and urea nitrogen serves as a crucial index for detecting glomerular filtration function. During the decompensated stage of renal dysfunction, the urea nitrogen levels noticeably increase, and a high blood urea nitrogen level may indicate more severe heart failure [36]. Therefore, in line with our results, an elevated urea nitrogen level represents a risk factor for the prognosis of patients with MVD. Additionally, the severity of acute kidney injury correlates with a reduction in urine volume [37]. The decline in urine output may also predict adverse outcomes in patients with MVD in the ICU, aligning with our findings.

In our nomogram model, we observed that patients with MVD and abnormal blood sugar levels face an increased risk of a poor prognosis. Excessive blood sugar levels may lead to the activation of the coagulation system, inhibition of the fibrinolysis system, and the production of free radicals [24]. Glucose-mediated injury, oxidative stress, and the

formation of advanced glycation end products can result in tissue damage [38]. There is evidence indicating an increased risk of death due to cardiovascular causes in patients with diabetes [39]. In addition, an increase in the anion gap is associated with the severity of the disease [40], consistent with our results. The anion gap is a commonly used calculated value in clinical practice, representing the difference between the concentrations of unmeasured anions and unmeasured cations in serum. An anion gap exceeding 24 mmol/l indicates metabolic acidosis [41].

The most common symptoms associated with MVD include palpitations, exertional dyspnea, and abnormal chest pain [42]. Breathing is closely linked to heart activity [43], and acute respiratory failure is an adverse prognostic event in MVD [44]. Patients with MVD often experience dyspnea, which may be attributed to increased blood resistance pumped by the heart during blood discharge, leading to lung congestion and subsequent dyspnea [45]. Abnormal pulmonary function is significantly correlated with the severity of MVD [46]. In cases where pneumonia induces severe hypoxemia, patients may compensate by increasing breathing frequency and rhythm to enhance oxygen supply. However, the elevated breathing frequency can result in hyperventilation [45]. Concurrently, low SpO_2 levels may exacerbate lung inflammation, potentially having a detrimental effect on MVD [47]. Therefore, a higher respiratory rate and lower SpO_2 levels are indicative of a poor prognosis. Although not identified as a risk factor in our study, the mortality risk for patients with chronic pulmonary conditions upon admission to the ICU was 11.985 times higher than that of normal patients (CI = 0.5275–138.2048), aligning with findings from previous studies [48]. Research has demonstrated a correlation between cardiovascular diseases and chronic obstructive pulmonary disease (COPD) [49]. COPD is prevalent among patients with atrial fibrillation in Europe, predisposing them to heightened risks of various cardiovascular complications and mortality [49,50].

Studies have pointed out that cancer patients are prone to infectious mitral endocarditis [51]. In our research, we discovered that the risk of poor prognosis among patients with metastatic cancer is significantly heightened. This escalation in risk may stem from the metastatic cancer's spread within patients, leading to compromised immunity and cardiopulmonary dysfunction. Furthermore, some scholars posit that right ventricular systolic pressure (RVSP) can enhance the prognostic value of established survival predictors. Resting baseline RVSP emerges as a superior predictor of long-term prognosis compared to peak pressure RVSP. Elevated baseline RVSP is independently linked to long-term mortality in patients with MVD [52].

The strength of our research lies in the establishment of a clinical prediction model with robust predictive performance by leveraging a substantial volume of clinical data sourced from public databases. This model holds potential guiding significance for clinical practice. Numerous studies have validated the accessibility and authenticity of data within the MIMIC-III database. Additionally, our rigorous patient sample selection process helps mitigate potential biases to some extent. The utilization of extensive datasets mitigates randomness, thereby enhancing the reliability of our findings. However, our research also presents certain limitations. Firstly, while this study included a large number of patients, it was conducted solely within a single center. Consequently, there may exist potential biases, warranting further prospective and multi-center studies to validate these findings. Secondly, some patients were excluded from the study due to substantial missing data, which could impact the final results, representing a significant limitation. Additionally, the multivariate logistic regression analysis revealed that the odds ratios of most independent risk factors were close to 1, indicating minimal disparity between the selected and excluded risk factors. Finally, to bolster the credibility of the results, it is imperative to conduct additional external validation using alternative datasets in the future.

5. Conclusion

This study identified the independent risk factors associated with 28-day mortality in patients with MVD and developed a nomogram model for prediction. These findings hold promise in enhancing the prognosis and clinical management of patients afflicted with MVD. It's helpful in persuading patients to receive early interventional catheterization treatment, for example, transcatheter mitral valve replacement (TMVR), transcatheter mitral valve implantation (TMVI).

Ethics statement

The study was an analysis of a third-party anonymized publicly available database with pre-existing institutional review board (IRB) approval. Data extracted from the MIMIC III database do not require individual informed consent because MIMIC III database research data is publicly available, and all patient data are de-identified.

Author contributions

MT and YL conceived the study, YQ, ML and XS created the study protocol, performed the statistical analyses, and wrote the first manuscript draft. ZL assisted with the study design and performed data collection. AM, ZM and ZL assisted with study coordination and helped draft the manuscript. YQ and ML assisted with manuscript revision and data confirmation. MT contributed to data interpretation and manuscript revision. All authors read and approved the final manuscript.

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CRediT authorship contribution statement

Yuxin Qiu: Writing – original draft, Visualization, Software, Investigation. **Menglei Li:** Writing – review & editing, Writing – original draft, Investigation. **Xiubao Song:** Writing – review & editing, Investigation, Funding acquisition, Formal analysis, Data curation. **Zihao Li:** Validation, Software, Data curation. **Ao Ma:** Writing – review & editing, Validation. **Zhichao Meng:** Writing – review & editing, Validation. **Yanfei Li:** Visualization, Validation, Supervision. **Minghui Tan:** Writing – review & editing, Validation, Funding acquisition, Conceptualization.

Data availability

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found below: The data were available on the MIMIC-III website at https://mimic.physionet. org/, https://doi.org/10.13026/C2XW26.

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There is no conflict to declare.

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