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ARTICLE

A Prediction Nomogram for Early Major Adverse Events after Cardiac Surgery in Infants with Congenital Heart Disease: A Retrospective Study

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ABSTRACT: Background: Early major adverse events (MAEs) after cardiac surgery are associated with substantial postoperative morbidity and mortality in infants with congenital heart disease (CHD). Early identification of patients at increased risk may facilitate timely intervention and optimize postoperative management. This study aimed to identify perioperative predictors of early MAEs and to develop a nomogram for individualized postoperative risk assessment. **Methods:** This single-center retrospective study included 766 infants with CHD who underwent cardiac surgery with cardiopulmonary bypass at Beijing Fuwai Hospital between January 2020 and December 2021. Early MAEs were defined as the occurrence of at least one major adverse event within 48 h after surgery, including unplanned reoperation, acute renal failure, sudden circulatory arrest, emergency chest reopening, extracorporeal membrane oxygenation, low cardiac output syndrome, refractory tachycardia, or all-cause mortality. Patients were randomly assigned to training and testing cohorts in a 7:3 ratio. Least absolute shrinkage and selection operator (LASSO) regression was used for feature selection, followed by multivariable logistic regression to construct the prediction nomogram. Model performance was evaluated by discrimination, calibration, and decision curve analysis. **Results:** Among the 766 infants included in the study, 144 (18.8%) experienced at least one early MAE. Five independent predictors were retained in the final model: body weight, aortic cross clamp time, postoperative 8th hour lactate, off CPB blood glucose and postoperative 4 h urine output. The area under the receiver operating characteristic curve was 0.781 in the training cohort and 0.764 in the testing cohort. Calibration analysis demonstrated good agreement between predicted and observed risks, with calibration-in-the-large values of −0.021 and −0.085 and calibration slopes of 0.958 and 0.931 in the training and testing cohorts, respectively. Decision curve analysis favorable potential clinical utility across a wide range of threshold probabilities. **Conclusions:** A nomogram incorporating five routinely available perioperative variables demonstrated moderate discrimination and satisfactory calibration for predicting early MAEs in infants with CHD after cardiac surgery. External validation is warranted before routine clinical implementation.

KEYWORDS: Major adverse event; congenital heart disease; cardiac surgery; infant; prediction nomogram

1 Introduction

Congenital heart disease (CHD) is the most common birth defect. In China, the prevalence of CHD is estimated at 17.32 cases per 1000 perinatal births [1]. Although advances in surgical techniques, car-

diopulmonary bypass (CPB) management, perioperative monitoring, and intensive care have substantially improved survival, a considerable proportion of infants with severe CHD still require surgical intervention during the first year of life [2]. Despite improvements in perioperative care, early postoperative morbidity remains an important clinical challenge.

Major adverse events (MAEs), including low cardiac output, acute renal failure, circulatory arrest, extracorporeal membrane oxygenation, unplanned reoperation, and death, remain major determinants of postoperative outcomes after pediatric cardiac surgery [3–6]. These complications are associated with prolonged intensive care unit stay, increased healthcare utilization, and higher mortality. Because pediatric cardiac surgery involves complex physiology and limited tolerance for perioperative errors, early identification of patients at increased risk of MAEs is essential for optimizing postoperative monitoring and resource allocation [6,7].

Several perioperative variables, including body weight, cardiopulmonary bypass (CPB) duration, aortic cross clamp time, blood lactate concentration, blood glucose level, vasoactive support, and urine output, have been reported to be associated with adverse postoperative outcomes [3–8]. However, previous studies have primarily focused on identifying individual risk factors rather than developing practical prediction models based on routinely available perioperative variables.

Therefore, the present study aimed to identify independent perioperative predictors of early MAEs occurring within 48 h after cardiac surgery in infants with CHD and to develop and internally validate a clinically applicable nomogram for individualized postoperative risk prediction.

2 Materials and Methods

2.1 Study Design and Population

This single-center retrospective study included infants with CHD who underwent cardiac surgery with CPB at Fuwai Hospital, Beijing, China, between January 2020 and December 2021. The study protocol was approved by the Ethics Committee of Fuwai Hospital (Approval No. IRB2022-1865). Electronic informed consent was obtained from the parents or legal guardians of all participants at the time of hospital admission.

Eligible patients were infants younger than 1 year of age with a confirmed diagnosis of CHD who underwent cardiac surgery requiring CPB and had complete perioperative clinical data available for analysis. Patients were excluded if they had severe preoperative conditions, including multiple organ dysfunction, severe infection, metabolic disorders, or chromosomal abnormalities, or if informed consent was not provided by their parents or legal guardians.

2.2 Definition of Early Major Adverse Events

Early MAEs [3,4,9] were defined as the occurrence of at least one of the following events within 48 h after cardiac surgery, based on previously published studies: unplanned reoperation, acute renal failure, sudden circulatory arrest, emergency chest reopening, requirement for extracorporeal membrane oxygenation (ECMO), low cardiac output syndrome, drug or cardioversion-refractory tachycardia, or all-cause mortality. Diagnosis of acute renal failure was based on the Risk, Injury, Failure, Loss of Kidney Function, and End-stage Kidney Disease (RIFLE) criteria [10]. Diagnosis of low cardiac output syndrome was based on the research in 2022 [11]. Because MAE was defined as a composite endpoint, the occurrence of any of the above events was considered a positive outcome and analyzed as a single binary variable.

2.3 Data Collection

Perioperative clinical variables were extracted from the electronic medical record system. The collected variables included: (1) Demographic characteristics: sex, age, weight, and height. (2) Laboratory variables: alanine aminotransferase, aspartate aminotransferase, albumin, creatinine, urea nitrogen, cystatin C, blood lactate concentration (pre CPB, on CPB, off CPB, Postoperative 0th hour, Postoperative 2nd hour, Postoperative 4th hour, Postoperative 8th hour), and blood glucose concentration (pre CPB, on CPB, off CPB, Postoperative 0th hour, Postoperative 4th hour). (3) Operative and postoperative variables: CPB time, aortic cross clamp (ACC) time, vasoactive inotropic score (Postoperative 2nd hour, Postoperative 4th hour, Postoperative 8th hour), Urine output (Intraoperative, Postoperative 4 h). We confirmed that the dataset was complete for all variables analyzed in this study, with no missing data requiring handling or imputation.

2.4 Model Development and Validation

Patients were randomly assigned to either the training cohort or the testing cohort in a 7:3 ratio using the createDataPartition function in the caret package of R software.

To reduce model overfitting and identify the most informative predictors, least absolute shrinkage and selection operator (LASSO) regression was performed using the glmnet package in R. Variables with non-zero regression coefficients at the optimal penalty parameter (λ) were subsequently entered into a multivariable logistic regression model to identify independent predictors of early MAEs.

Based on the final multivariable logistic regression model, a prediction nomogram was constructed to estimate the individual probability of early postoperative MAEs.

Internal validation was performed using bootstrap resampling with 1000 iterations. Model discrimination was assessed by calculating the area under the receiver operating characteristic (ROC) curve (AUC). Model calibration was evaluated using calibration plots, the Hosmer–Lemeshow goodness-of-fit test, the calibration intercept (calibration-in-the-large), and the calibration slope. Clinical utility was assessed using decision curve analysis (DCA).

2.5 Statistical Analysis

The categorical variables were represented as frequencies and percentages. Continuous variables were represented as median with interquartile range (IQR, 25th–75th percentile) for skewed distribution, mean ± standard deviation for normal distribution. The Mann–Whitney U test and *t*-test were used to compare continuous variables. The χ^2 test and Fisher's exact test were used to compare categorical variables. All statistical tests were two-tailed and a p value < 0.05 was considered statistically significant. All data were analyzed using SPSS 26.0.

To select predictive variables and prevent overfitting, LASSO (least absolute shrinkage and selection operator) regression was employed. The optimal penalty parameter λ was determined by 10-fold cross-validation, using the "1-standard error" rule. In addition to variable selection, the L1 regularization inherent in LASSO shrink regression coefficients, which reduces model variance and enhances stability. The final model was constructed using the non-zero coefficient variables selected at the optimal λ.

3 Results

3.1 Study Population and Early Adverse Events

Clinical data were initially collected from 834 infants who underwent cardiac surgery during the study period. After applying the predefined inclusion and exclusion criteria, 68 patients were excluded, leaving a total of 766 infants with CHD for the final analysis (Fig. 1).

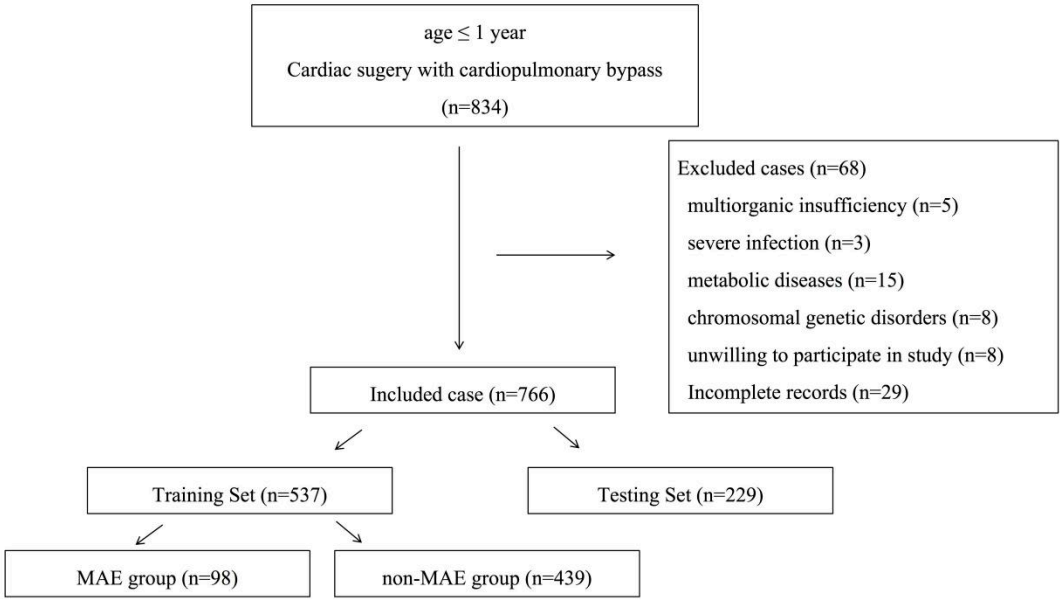

Figure 1: Flow chart for patient selection.

Among the included patients, 176 (23.0%) had simple congenital cardiac defects, including atrial septal defect, ventricular septal defect, patent ductus arteriosus, and pulmonary stenosis, whereas 590 (77.0%) had complex congenital heart disease. Neonatal cardiac surgery was performed in 71 infants (9.3%).

Overall, 144 patients (18.8%) experienced at least one early MAE within 48 h after surgery, whereas 622 patients (81.2%) had an uncomplicated postoperative course.

The most frequently observed MAE was refractory tachycardia (74/766, 9.7%), followed by low cardiac output syndrome (52/766, 6.8%), acute renal failure (25/766, 3.3%), circulatory arrest (10/766, 1.3%), emergency chest reopening (3/766, 0.4%), unplanned reoperation (2/766, 0.3%), extracorporeal membrane oxygenation (ECMO) support (2/766, 0.3%), and all-cause mortality (1/766, 0.1%).

The most common underlying cardiac diagnosis was ventricular septal defect (309/766, 40.3%), followed by tetralogy of Fallot (81/766, 10.6%).

3.2 Baseline Characteristics

The study population was randomly divided into a training cohort (n = 537) and a testing cohort (n = 229) at a ratio of 7:3.

Baseline demographic, laboratory, and perioperative characteristics of the two cohorts are summarized in Table 1. No statistically significant differences were observed between the training and testing cohorts for any baseline variable (all $p > 0.05$), indicating satisfactory comparability between the two datasets.

Within the training cohort, 98 patients (18.2%) developed early MAEs, whereas 439 patients (81.8%) did not.

Compared with patients without MAEs, those who experienced MAEs were significantly younger and had lower body weight, shorter body length, lower serum albumin concentrations, higher cystatin C levels, longer cardiopulmonary bypass duration, and longer aortic cross-clamp time (all $p < 0.05$).

Significant differences were also observed in perioperative biochemical parameters. Patients in the MAE group had significantly higher lactate concentrations during CPB, immediately after CPB, and at 0, 2, 4, and 8 h postoperatively. Similarly, blood glucose concentrations measured before CPB, during CPB, immediately after CPB, and at 0 and 4 h after surgery were significantly higher in the MAE group.

Furthermore, postoperative vasoactive inotropic scores measured at 2, 4, and 8 h were significantly higher in patients who developed MAEs, whereas postoperative urine output during the first 4 h after surgery was significantly lower than that in the non-MAE group.

Detailed comparisons are presented in Table 2.

Table 1: Baseline characteristics in the training set and testing set.

Variable	Training Set (n = 537)	Testing Set (n = 229)	*p*-Value
Sex, n (%)			0.431
Male	302 (56.0%)	121 (53.0%)	
Female	235 (44.0%)	108 (47.0%)	
Age at the surgery (months)	6 (3, 9)	5 (3, 8)	0.168
Weight (kg)	6.6 (5.3, 8)	6.5 (5.1, 7.8)	0.196
Height (cm)	65 (60, 70)	65 (59, 70)	0.379
Alanine aminotransferase (IU/L)	22 (16, 32)	22 (16, 36)	0.365
Aspartate aminotransferase (IU/L)	47 (38, 58)	47 (39, 61)	0.428
Albumin (g/L)	40.7 (38.3, 42.9)	40.5 (37.6, 43.2)	0.762
Creatinine (μmol/L)	28.78 (23.08, 33.63)	28.35 (24.12, 33.22)	0.788
Urea nitrogen (mmol/L)	3.07 (2.14, 4.21)	3.03 (2.33, 4.19)	0.702
Cystatin C (mg/L)	1.05 (0.9, 1.26)	1.04 (0.92, 1.23)	0.871
CPB time (min)	88 (65, 124)	93 (64, 122)	0.586
Aortic crossclamp time (min)	57 (38, 82)	58 (40, 83)	0.440
Lactate (mmol/L)			
pre CPB	0.8 (0.7, 1.0)	0.8 (0.7, 0.9)	0.352
on CPB	1.5 (0.9. 2.1)	1.4 (1.0, 2.0)	0.740
off CPB	1.7 (1.3, 2.5)	1.7 (1.3, 2.3)	0.390
Postoperative 0th hour	1.4 (1.1, 2.0)	1.4 (1.1, 2.0)	0.883
Postoperative 2nd hour	1.4 (1.1, 2.1)	1.6 (1.1, 2.1)	0.127
Postoperative 4th hour	1.1 (0.8, 1.7)	1.2 (0.9, 1.8)	0.276
Postoperative 8th hour	1.2 (0.9, 1.6)	1.2 (0.9, 1.8)	0.276
Blood glucose (mmol/L)			
pre CPB	5.13 (4.51, 5.77)	5.00 (4.38, 5.74)	0.150
on CPB	6.69 (5.66, 7.92)	6.65 (5.62, 8.02)	0.748
off CPB	7.82 (6.67, 9.07)	7.66 (6.57, 8.67)	0.131
Postoperative 0th hour	7.89 (6.70, 9.54)	7.86 (6.77, 9.29)	0.906
Postoperative 4th hour	6.86 (5.87, 8.36)	6.93 (5.90, 8.27)	0.783
Vasoactive inotropic score (VIS)			
Postoperative 2nd hour	10.00 (8.00, 12.00)	10.00 (8.00, 12.00)	0.142
Postoperative 4th hour	9.00 (7.67, 12.00)	8.00 (7.00, 12.00)	0.966
Postoperative 8th hour	8 (6.00, 11.34)	8.00 (7.00, 12.00)	0.624
Urine output (mL)			
Intraoperative	10.0 (4.2, 19.2)	9.7 (4.5, 18.3)	0.983
Postoperative 4 h	6.0 (4.1, 8.0)	6.4 (4.3, 8.5)	0.358

Table 2: Baseline characteristics of the training set in MAE group and non-MAE group.

Variable	MAE Group (n = 98)	Non-MAE Group (n = 439)	*p*-Value
Sex, n (%)			0.716
Male	53 (54.0%)	249 (57.0%)	
Female	45 (46.0%)	190 (43.0%)	
Age at the surgery (months)	4.0 (2.0, 5.0)	6.0 (4.0, 9.0)	<0.001
Weight (kg)	5.48 ± 1.66	6.92 ± 1.88	<0.001
Height (cm)	60 (56, 65)	67 (61, 71)	<0.001
Alanine aminotransferase (IU/L)	22.0 (15.0, 32.0)	22.0 (16.0, 32.0)	0.443
Aspartate aminotransferase (IU/L)	47.5 (38.0, 57.8)	46.0 (38.0, 58.5	0.944
Albumin (g/L)	39.6 (36.92, 41.30)	41.0 (38.6, 43.2)	<0.001
Creatinine (μmol/L)	29.50 (21.78, 34.83)	28.5 (23.1, 33.3)	0.416
Urea nitrogen (mmol/L)	2.94 (2.26, 4.28)	3.09 (2.10, 4.21)	0.665
Cystatin C (mg/L)	1.19 (0.98, 1.37)	1.03 (0.88, 1.22)	<0.001
CPB time (min)	119 (81, 150)	83 (61, 117)	<0.001
Aortic crossclamp time (min)	74 (53, 103)	53 (36, 78)	<0.001
Lactate (mmol/L)			
pre CPB	0.8 (0.7, 1.0)	0.8 (0.7, 1.0)	0.974
on CPB	1.8 (1.1, 2.4)	1.4 (0.9, 2.0)	0.001
off CPB	2.3 (1.7, 3.1)	1.7 (1.2, 2.3)	<0.001
Postoperative 0th hour	2.0 (1.4, 2.7)	1.4 (1.0, 1.8)	<0.001
Postoperative 2nd hour	2.1 (1.3, 3.1)	1.3 (1.0, 1.9)	<0.001
Postoperative 4th hour	1.7 (1.1, 2.6)	1.1 (0.8, 1.5)	<0.001
Postoperative 8th hour	1.6 (1, 2.4)	1.1 (0.8, 1.5)	<0.001
Blood glucose (mmol/L)			
pre CPB	5.34 (4.59, 6.07)	5.08 (4.48, 5.68)	0.028
on CPB	7.27 (6.28, 8.04)	6.56 (5.56, 7.91)	0.005
off CPB	8.30 (6.83, 9.97)	7.72 (6.64, 8.95)	0.016
Postoperative 0th hour	8.84 (7.41, 10.96)	7.72 (6.66, 9.27)	<0.001
Postoperative 4th hour	7.42 (6.14, 9.76)	6.74 (5.75, 8.05)	<0.001
Vasoactive inotropic score (VIS)			
Postoperative 2nd hour	10.00 (8.00, 13.50)	10.00 (8.00, 12.00)	0.014
Postoperative 4th hour	10.00 (8.00, 13.5)	8.00 (7.00, 11.00)	0.002
Postoperative 8th hour	10.00 (8.00, 12.37)	8.00 (6.00, 11.00)	0.002
Urine output (mL)			
Intraoperative	14.1 (6.8, 24.3)	9.0 (3.8, 18.5)	<0.001
Postoperative 4 h	5.6 (3.6, 7.5)	6.2 (4.3, 8.1)	0.039

3.3 Variable Selection and Identification of Independent Predictors

Least absolute shrinkage and selection operator (LASSO) regression analysis was performed to reduce multicollinearity and identify the most informative candidate predictors before multivariable analysis. Using the optimal penalty parameter determined by 10-fold cross-validation, nine variables with non-zero regression coefficients were retained. These variables included age at surgery, body weight, aortic cross-clamp time, postoperative 0 h lactate, postoperative 8-h lactate, blood glucose levels during CPB and immediately after CPB, postoperative 4 h blood glucose, and postoperative 4 h urine output (Fig. 2).

These candidate variables were subsequently entered into a multivariable logistic regression model. Five variables remained independently associated with the occurrence of early MAEs. Lower body weight was associated with an increased risk of MAEs (OR = 0.651, 95% CI: 0.555–0.756, $p < 0.001$). Longer aortic cross-clamp time independently increased the risk of postoperative MAEs (OR = 1.009, 95% CI: 1.001–1.016, $p = 0.020$). Higher postoperative 8-h lactate levels (OR = 1.393, 95% CI: 1.069–1.814, $p = 0.014$) and higher blood glucose levels immediately after CPB (OR = 1.147, 95% CI: 1.012–1.298, $p = 0.030$) were also identified as independent risk factors. In contrast, greater urine output during the first 4 postoperative hours was

associated with a lower risk of early MAEs (OR = 0.908, 95% CI: 0.835–0.982, p = 0.020). Detailed results of the multivariable logistic regression analysis are presented in Table 3.

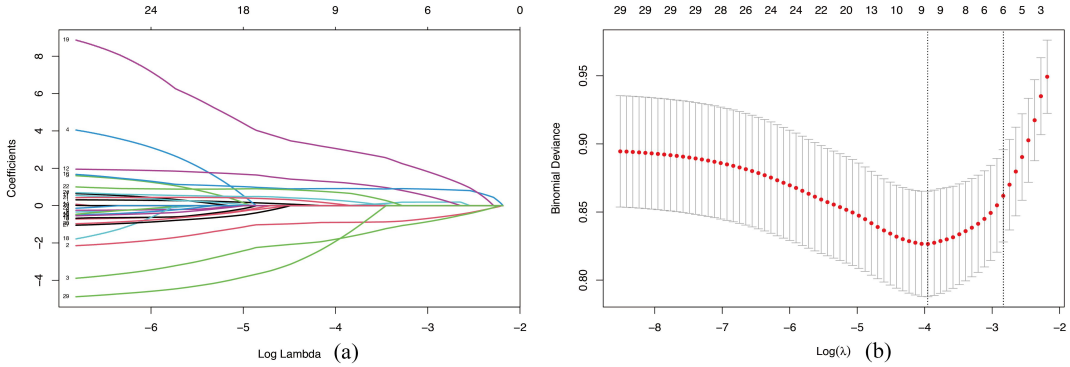

Figure 2: LASSO regression analysis. (**a**) Employing 10-fold cross-validation to draw vertical lines, and showing the variable coefficients. (**b**) minimum mean square error (λ = 0.019) and the standard error of the minimum diatance (λ = 0.064).

Table 3: Multivariate logistic regression analysis.

Variable	*B*	*SE*	*Wald*	*p*	OR (95% CI)
(Intercrept)	−0.502	0.822	0.373	0.541	0.606 (0.121, 3.050)
Weight (kg)	−0.430	0.079	29.605	<0.001	0.651 (0.555, 0.756)
Aortic crossclamp time (min)	0.009	0.004	5.395	0.020	1.009 (1.001, 1.016)
Postoperative 8th hour lactate	0.331	0.135	6.053	0.014	1.393 (1.069, 1.814)
off CPB blood glucose	0.137	0.063	4.694	0.030	1.147 (1.012, 1.298)
Postoperative 4 h urine output	−0.096	0.041	5.433	0.020	0.908 (0.835, 0.982)

3.4 Development and Validation of the Prediction Nomogram

A prediction nomogram was constructed based on the five independent predictors identified in the multivariable logistic regression model (Fig. 3). The total score generated by the nomogram corresponded to the estimated probability of developing an early MAE, with higher scores indicating a greater postoperative risk.

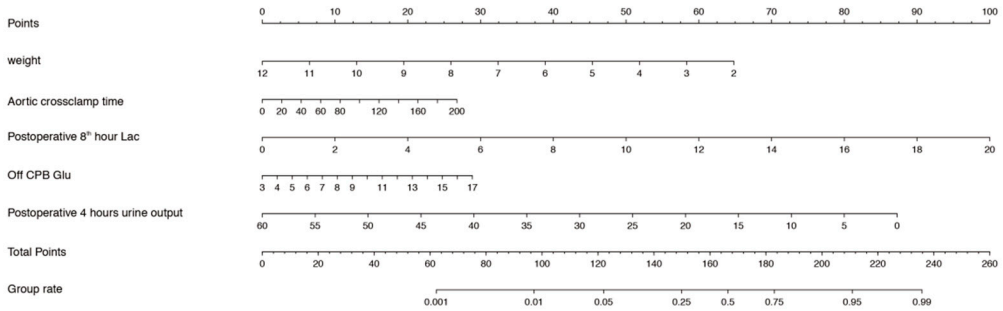

Figure 3: Nomogram for the perioperative prediction of MAE. MAE: Major adverse event.

The nomogram demonstrated good discriminative performance. In the training cohort, the area under the receiver operating characteristic (ROC) curve (AUC) was 0.781, whereas the AUC in the testing cohort was 0.764 (Fig. 4), indicating satisfactory predictive accuracy in both datasets.

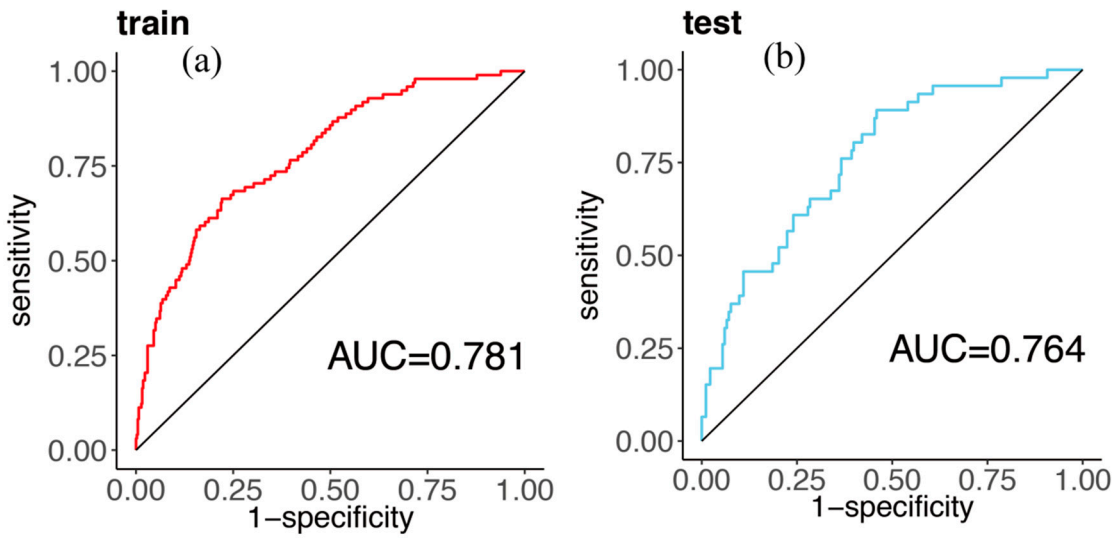

Figure 4: (**a**) Training set ROC and AUC. (**b**) testing set ROC and AUC.

Calibration analysis showed good agreement between predicted and observed event probabilities. In the training cohort, the calibration curve closely approximated the ideal reference line, and the Hosmer–Lemeshow goodness-of-fit test indicated adequate model fit (χ^2 = 6.105, p = 0.636). The calibration intercept (calibration-in-the-large) was −0.021, and the calibration slope was 0.958.

Similarly, in the testing cohort, the calibration intercept and calibration slope were −0.085 and 0.931, respectively, demonstrating acceptable calibration and consistent predictive performance (Fig. 5).

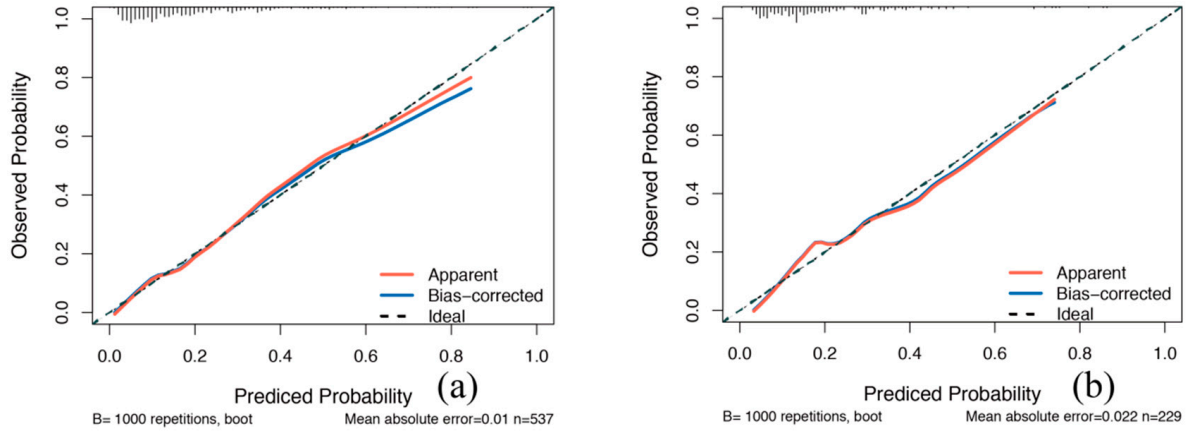

Figure 5: Calibration curve for predicting probability of MAE. (**a**) Training cohort. (**b**) Validation cohort.

Decision curve analysis (DCA) further demonstrated that the nomogram provided a greater net clinical benefit than the treat-all or treat-none strategies across a broad range of threshold probabilities in both the training and testing cohorts (Fig. 6), supporting its potential clinical applicability.

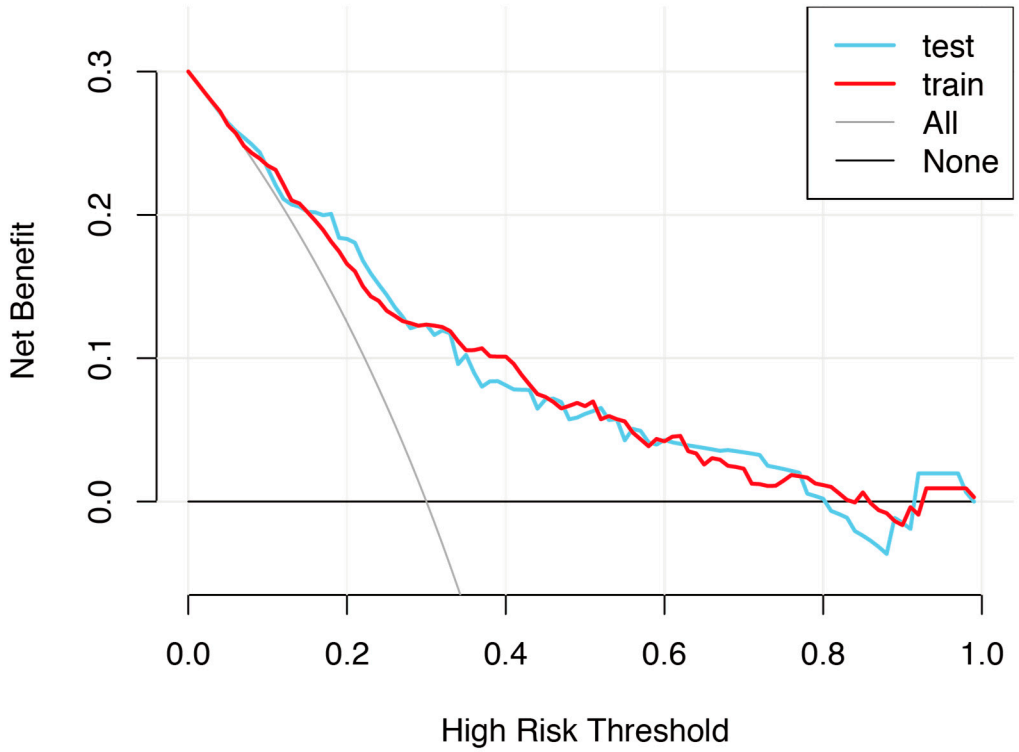

Figure 6: Clinical decision curve analysis.

4 Discussion

Major adverse events (MAEs) remain one of the important determinant of postoperative outcomes in infants undergoing cardiac surgery [3–9]. Despite substantial advances in surgical techniques, cardiopulmonary bypass management, and perioperative intensive care, early postoperative complications continue to contribute significantly to morbidity, prolonged intensive care unit (ICU) stay, increased healthcare resource utilization, and mortality. Therefore, early identification of patients at high risk of postoperative MAEs is essential for optimizing perioperative management and improving clinical outcomes.

In this single-center retrospective study, we developed and internally validated a nomogram for predicting the risk of early MAEs in infants with CHD undergoing cardiac surgery with cardiopulmonary bypass. By combining LASSO regression with univariate logistic regression, we identified five routinely available perioperative variables, including weight, aortic clamp time, postoperative 8th hour lactate, off CPB blood glucose and postoperative 4 h urine output, as independent predictors of early MAEs. The resulting nomogram demonstrated satisfactory discrimination and calibration, suggesting its potential value as an individualized risk assessment tool during the early postoperative period. We finally made a risk stratification based on total points calculated using the nomogram. Patients with CHD surgery were divided into three risk groups [5–8]: low risk (total points < 150), middle risk (150 ≤ total points < 185, and high risk (total points ≥ 185). The present prediction model was designed to identify infants at increased risk of overall early postoperative complications rather than to predict any individual subtype of severe adverse event. Because MAE was defined as a composite endpoint, the predicted probability represents the overall risk of experiencing at least one clinically significant postoperative complication within 48 h after surgery. In the present cohort, resistant tachycardia was the most frequent event (74/766, 9.7%), followed by low cardiac output (52/766, 6.8%), acute renal failure (25/766, 3.3%), circulatory arrest (10/766,

1.3%), emergency chest opening (3/766, 0.4%), unplanned reoperation (2/766, 0.3%), ECMO (2/766, 0.3%), and all-cause mortality (1/766, 0.1%). Therefore, the model should be interpreted as a tool for identifying patients at elevated risk of overall postoperative complications rather than for predicting any specific adverse event subtype.

Most previous studies on MAE focused on analyzing the risk factors, while only a few of them evaluated the predictive factors or developed a prediction model. A study of 240 full-term neonates with cardiac surgery showed that cerebral near-infrared spectroscopy changes > 30%, high blood lactate levels, and VIS score within the 48 h were strongly predicted MAE [3]. The VIS score, Risk Adjustment in Congenital Heart Surgery score, age, Pediatric Index of Mortality, cardiopulmonary bypass and aortic clamping duration were significantly associated with adverse events in a study with a cohort of 238 pediatric cardiac surgery samples [5]. However, all these study only included limited samples and did not develop the model, which could limit their clinical application. Our study had a large sample size, and inclusion clinical routine indicators, are readily available in routine clinical practice in PICU. The clinical benefits of the nomogram were compared with those of the RACHS-1, VIS score, our nomogram included multidimensional indicators, rather than simply including disease type or vasoactive drug dose.

Weight was identified as one of the strongest predictors in the present model [12,13]. Low weight has consistently been associated with unfavorable perioperative outcomes in infants with CHD [12]. Several mechanisms may explain this association. Infants with severe CHD frequently experience chronic cyanosis, congestive heart failure, pulmonary hypertension, and increased metabolic demands, all of which contribute to impaired nutritional status and growth restriction [13,14]. Besides, postoperative fluid restriction and gastrointestinal dysfunction may further aggravate malnutrition [14,15]. Previous studies have demonstrated that low body weight is associated with increased postoperative morbidity, prolonged mechanical ventilation, extended ICU stay, and higher mortality [14–16]. Consistent with these findings, lower body weight independently predicted a higher risk of early MAEs in our study, highlighting the importance of preoperative nutritional assessment and optimization.

Aortic cross clamp time was another independent predictor identified in our model. Longer cross-clamp duration generally reflects greater surgical complexity and prolonged myocardial ischemia [17]. Extended myocardial ischemia has been associated with increased myocardial injury, systemic inflammatory activation, and postoperative organ dysfunction [18–22]. Previous studies have reported significant associations between prolonged aortic cross-clamp time and adverse postoperative outcomes, including prolonged ICU stay and increased morbidity. Our findings further support the importance of minimizing cross-clamp duration whenever technically feasible.

Blood lactate concentration is widely recognized as a marker of tissue hypoperfusion and impaired oxygen delivery Elevated perioperative lactate levels have repeatedly been associated with low cardiac output syndrome, inadequate systemic perfusion, and poor postoperative outcomes following pediatric cardiac surgery [23–25]. In our cohort, lactate concentrations increased during CPB, peaked immediately after CPB, and gradually declined during the postoperative period. However, postoperative lactate measured at 8 h remained an independent predictor of MAEs. This observation suggests that persistent hyperlactatemia after surgery may reflect ongoing circulatory insufficiency or impaired lactate clearance rather than transient metabolic alterations related to CPB itself [26,27]. Therefore, postoperative lactate monitoring may provide valuable prognostic information during early postoperative management.

Cardiopulmonary bypass glucose level was associated with systemic inflammatory response syndrome and endocrine metabolic imbalance [28]. Intraoperative hyperglycemia was common in children undergoing cardiac surgery, and often lead to a poor prognosis [29,30]. In our study, off CPB glucose was an independent

risk factor for early MAE. The higher sugar level, the higher the risk of postoperative complications, similar to Naghipour et al.'s, Yates et al.'s, Matsumoto et al.'s and Zhi-Hua et al.'s study [29–32]. Glycemic control at CPB period was necessary to reduce postoperative complications [29,30,33]. Patients with CPB glucose no more than 8.1 mmol/L had the lower risk probability [32]. Considering Asian origin have a higher insulin resistance [34], timely targeting age-adjusted glycaemia with insulin infusion could improve short outcome [35].

Early postoperative urine output, a common parameter that reflects organ tissue perfusion and body fluid balance, is an important indicator to evaluate cardiac function, and renal function [36]. Urine output assessment in the early postoperative period is still a challenge [37]. Most children can regain normal urine output by volume replenishment, appropriate blood pressure elevation, and diuretics use [36,37]. The patient with persistent oliguria after surgery would had bad outcomes for renal injury or renal failure [38]. In our study, postoperative 4 h urine output was an independent risk factor. The lower the urine output, the higher the postoperative risk. Use of peritoneal dialysis might allow for superior fluid management with improved clinical outcomes [39].

The study constructed and validated a prediction model that enables physicians to distinguish patients at high risk for MAE who underwent cardiac surgery. To apply the model in daily clinical treatment and increase the understanding of risk factors in the model, we transformed the prediction model into a simple risk score. Lower weight, prolonged aortic cross-clamp time, higher postoperative 8th hour lactate, higher off CPB blood glucose level and reducing postoperative 4 h urine output meant to higher risk of MAE. Based on the MAE prediction model, PICU physicians could identify and stratify the patients with high risk of MAE, and take appropriate measures simultaneously.

5 Limitations

There are several limitations to our study. First, there was no gold standard inclusion or exclusion criteria for early MAE. The definition of early MAE was derived from several previous studies and consensus. Second, it is a retrospective single-center study, not a multi-center study. Internal bias and selection bias are inevitable due to retrospective analysis. Third, external validity has not been verified. Although internal validation using bootstrapping was conducted to support the reliability of the model, the absence of external validation limits the generalizability of the nomogram. To address this, we have developed a concrete action plan, and we will initiate external validation by collaborating with two other pediatric cardiac centers (Center A and Center B) within the next 6–9 months. The validation cohort will include infants meeting the same inclusion criteria (age < 1 year, undergoing cardiac surgery for congenital heart disease) and a target sample size of at least 150 patients. We plan to complete data collection and analysis within 12 months. This step is essential before the model can be considered for widespread clinical application. Fourth, some potentially meaningful predictors, such as blood pressure, heart rate, body temperature, and ventilator conditions were not be assessed. Preoperative nutritional status, surgical classification, duration of mechanical ventilation, and ICU length of stay were not available in the present dataset and therefore could not be incorporated into the analysis. These context-dependent variables may limit the model's performance in specific subgroups and subgroup-specific validation could be developed in future studies. Evidence-based methods to screen predictors should be used in the future. Fifth, more prospective cases controlled studies are needed to further explain the association between risk factors and early MAE in infants. By providing these specific plans, we aim to strengthen our commitment to improving the generalizability of the model.

6 Conclusion

This study constructed a prediction nomogram for early major adverse events in congenital heart disease infants after cardiac surgery and revealed that weight, aortic clamp time, postoperative 8th-hour lactate, off-CPB blood glucose, and postoperative 4-h urine output were predictors of early MAE. It provided physicians with a tool for early prediction and enabled the implementation of timely preventive measures.

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Availability of Data and Materials: The authors confirm that the data supporting the findings of this study are available within the article.

Ethics Approval: The review of clinical records was approved by the Institutional Review Board of Fuwai Hospital (Approval No. IRB2022-1865), and was conducted in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Electronic informed consent was obtained from the parents or legal guardians of all participants at the time of hospital admission.

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