Research Square

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Development and External Validation of a Machine Learning Model for Postoperative Infection After Cardiopulmonary Bypass Surgery

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Abstract

Background

Postoperative infection after cardiopulmonary bypass (CPB) surgery is associated with adverse outcomes, but early prediction tools remain limited. In an effort to address this gap, we set out to develop and validate an interpretable machine learning model aimed at predicting postoperative infections within 30 days of CPB surgery.

Methods

To construct prediction model, we utilized data from the MIMIC-IV database, with 70% of the data allocated for model development and the remaining 30% for internal validation. We tested five different prediction models - LR, XGBoost, GBM, SVM, and Neural Network - using cross-validation tuning. Following this, the best-performing model was validated externally in a separate prospective cohort study conducted at the Affiliated Hospital of Qingdao University. Model performance was assessed using discrimination (AUC), calibration, and decision curve analysis (DCA). Shapley additive explanations (SHAP) were used for interpretability.

Results

Among 2,166 MIMIC-IV participants, 268 (12.4%) developed postoperative infection; external cohort recruited 96 participants, of whom 19 (19.8%) developed postoperative infection. The GBM model demonstrated the best overall performance, with AUCs of 0.861, 0.791, and 0.742 in the development, internal validation, and external validation cohorts, respectively. Calibration curves and DCA also showed good agreement and net clinical benefit. The final GBM model incorporated eight variables within 48 hours after surgery, including admission type, neutrophil count, creatinine, respiratory rate, heart rate, body temperature, oxygen saturation, and albumin. SHAP analysis identified temperature and creatinine as top contributors.

Conclusions

With solid discrimination and calibration across internal and external validation, the GBM model holds promise for early postoperative infection risk assessment in CPB patients.

Trail Registration

: Chinese Clinical Trial Registry identifier, ChiCTR2500110269; registered October 11, 2025. The prospective cohort study was approved by the Medical Ethics Committee of The Affiliated Hospital of

Qingdao University (QYFYEC2025-147). Written informed consent will be obtained from each participant before enrollment.

Introduction

Cardiopulmonary bypass (CPB) has long been widely used in modern cardiothoracic surgery practice(1). However, postoperative infection remains a major complication after cardiac surgery, particularly in patients undergoing CPB, with reported incidences ranging from 3.5% to 26.8%(2). Postoperative infection is a multifactorial complication influenced by patient characteristics, perioperative physiological changes, and surgical factors(2–4). Especially the pathophysiological changes associated with CPB—including extensive surgical trauma, systemic inflammatory response, prolonged mechanical ventilation, hemodynamic instability, impaired organ perfusion, and ischemia–reperfusion injury—further increase the risk of postoperative infection(5–7). Consequently, Patients who develop postoperative infection face a higher risk of prolonged mechanical ventilation, longer hospital stays, elevated medical expenses, and poorer clinical outcomes – ranging from organ failure to death(2). Notwithstanding improvements in perioperative management and CPB techniques, postoperative infection persists as a clinically consequential untoward event after cardiac surgery. Thus, promptly recognizing those at elevated risk for postoperative infection could enable earlier intervention and enhance postoperative care.

Currently, studies on prediction of postoperative infection following cardiac surgery remain predominantly association studies(8). However, with the advancement of critical care medicine and the improvement of perioperative management standards, it has been recognized that single indicators such as C-reactive protein, neutrophils, and procalcitonin are all unable to accurately identify infection(9, 10). In addition, many conventional scoring tools designed to assess illness severity show only limited ability to predict postoperative infection(11, 12). Therefore, a prediction model integrating multidimensional data may be needed to improve the predictive ability for postoperative infection. According to a recent systematic review, although the number of machine learning studies has increased, model quality remains low – mainly due to a high risk of bias and inadequate reporting of performance measures in most investigations(13). More importantly, only 13% of the models were externally validated(13). Furthermore, differences may exist across medical centers in terms of patient baseline data, perioperative management, and outcome definitions, so the generalizability of existing models still requires further validation. Thus, independent external validation is crucial to facilitate the clinical implementation of machine learning models. In particular, few models have been developed using real-world data and subsequently validated in independent external cohorts. Thus, robust, externally validated predictive tools with strong discriminative performance and clinical utility for postoperative infection after CPB surgery are still needed to provide a reference for early recognition and intervention by anesthesiologists, intensivists, and cardiac surgeons.

This study focused on creating a predictive model using machine learning to anticipate postoperative infections in patients undergoing cardiopulmonary bypass. The model was developed utilizing data from

the Medical Information Mart for Intensive Care (MIMIC) database and later validated with a separate cohort from the Affiliated Hospital of Qingdao University.

Method

Data Source

We obtained the development and internal validation cohort from the Medical Information Mart for Intensive Care IV version 3.1 (MIMIC-IV v3.1) database, a publicly accessible resource that provides de-identified clinical records of patients hospitalized at Beth Israel Deaconess Medical Center (BIDMC, Boston) from 2008 to 2019(14). The database has been approved by the Institutional Review Boards of BIDMC and the Massachusetts Institute of Technology. It contains de-identified demographic information, vital signs, laboratory tests, fluid balance, survival status, International Classification of Diseases, Ninth Revision (ICD-9) codes, nurse-verified hourly vital sign data, and written reports of radiological images, among others. As the data have been de-identified, their use is not considered human subjects research, and thus individual patient informed consent was not required(15). The author of this study (YW Lin) has completed the National Institutes of Health (NIH) training course (certification number: 68757619) and has been granted permission to extract the data.

For external validation, a prospective independent clinical cohort conducted at the Affiliated Hospital of Qingdao University was used. This cohort is not publicly available, as specified in the approved study protocol, due to institutional ethics and patient privacy restrictions (**Supplementary File S1**). The study was approved by the Medical Ethics Committee of the Affiliated Hospital of Qingdao University (approval number: QYFYEC2025-147). This trial strictly adhered to the principles outlined in the Declaration of Helsinki and has been registered with the Chinese Clinical Trial Registry (https://www.chictr.org.cn, ChiCTR2500110269) on 1 October 2025. The participants for external validation were enrolled from 1 October 2025 to 28 February 2026, and the end of follow-up date was 28 March 2026. The reporting of this study follows the Strengthening the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis + Artificial Intelligence (TRIPOD + AI) guideline(16). No patients or members of the public were engaged in the planning, execution, reporting, or distribution of this study. Moreover, the study findings have not been directly shared with the participants.

Participants

Data for this study were collected from two centers: the MIMIC-IV database (BIDMC, Boston, USA) and the Affiliated Hospital of Qingdao University (Qingdao, China). The inclusion criteria were as follows: (I) age > 19 years; (II) underwent cardiopulmonary bypass surgery, such as valve replacement or coronary artery bypass graft; (III)first hospital admission and Intensive Care Unit (ICU) stay.

We excluded any patient who had been diagnosed with Human Immunodeficiency Virus disease infection prior to surgery. To guarantee comparability between the two study populations, the external

validation cohort applied the same inclusion and exclusion criteria as the development cohort.

Variable Extraction

We used the pgAdmin PostgreSQL tool (version 1.22.1) and Navicat Premium (version 12.0.28) to obtain the raw data of patients who underwent cardiac surgery with cardiopulmonary bypass assistance in MIMIC-IV. The demographic information we gathered encompassed gender, age, body mass index, marital status, race, type of admission, height, weight, duration of ICU and hospital stays,30-day postoperative mortality, as well as incidents of acute kidney injury. Subsequently, we collected vital signs within the first two days after ICU admission, including temperature, heart rate, respiratory rate, systolic blood pressure, diastolic blood pressure, mean blood pressure and oxygen saturation.

We also collected laboratory indicators within the first two days after surgery, including microbial culture results, blood gas parameters, routine blood tests, liver and kidney function, and electrolytes. All postoperative measurements were taken within the initial 48 hours following surgery. For each variable, we recorded the most extreme value – for example, the lowest red blood cell count, the highest absolute neutrophil count, and the peak lactate level. When a variable could be harmful in both high and low ranges, we captured both extremes – e.g., the maximum and minimum systolic blood pressure. Preoperative comorbidities and medical history included smoker, hypertension, liver disease, diabetes, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease, rheumatic disease, peptic ulcer disease, renal disease, and malignant cancer. Surgical procedures were also classified into six types, including coronary artery bypass grafting (CABG), valve surgery, great vessel surgery, congenital heart disease surgery, combined surgery, and other surgeries. Infection-related indicators, including microbial culture results from the respiratory tract, wound, bloodstream, and venous catheter tip. Furthermore, we integrated two severity scores, the Sequential Organ Failure Assessment (SOFA) and the Acute Physiology Score III, measured on the first postoperative day in the ICU. External validation data were derived from a prospective cohort study conducted at the Affiliated Hospital of Qingdao University, in which postoperative infection outcomes were determined by a dedicated postoperative infection assessment team. Vital signs were diligently recorded every two hours in the ICU, while laboratory indicators were measured immediately post-surgery and then each morning. The definitions of all variables were consistent with those used for the MIMIC database. Definitions, collection time, variable type, and units for all variables are presented in the variable dictionary (**Supplementary table S1**).

Outcome

The outcome measure of our study was postoperative infection, defined as the occurrence of infection within 30 days after surgery based on a combination of postoperative microbial culture results, laboratory indicators, vital signs, and physician diagnosis. For participants from the MIMIC, the definitions of infections were as follows: Sepsis was defined according to the Sepsis-3 international

criteria, identifying patients with evidence of infection and an increase in the SOFA score of 2 points or more(17). Pneumonia: Based on positive respiratory microbial culture results of clinical significance, accompanied by a body temperature higher than 38°C, or a white blood cell count greater than 12×10^9/L or less than 4×10^9/L(18). Catheter-related bloodstream infection (CRBSI): Positive blood culture and positive catheter tip culture, with a central venous catheter indwelling time exceeding 48 hours(19). Surgical site infection: Positive microbial culture of clinical significance from the wound, or diagnosis by a clinician(20). For participants from the prospective cohort, the definitions of infections were described in the trial protocol (**Supplementary File S1**).

Statistical Analysis

All data processing, including statistical analyses and visualizations, relied on R (version 4.4.2) and JD_DCPM (V6.22.3, Jingding Medical Technology Co., Ltd.). Participants in MIMIC with an overall missing rate > 30% were excluded; for the included participants, forest imputation (R package "missForest") was applied to variables with missing rates ≤ 30%. Under the missing-at-random assumption, five imputed datasets were generated, using predictive mean matching for continuous variables and logistic regression for binary variables, with 20 iterations per imputation(21). By contrast, the prospective cohort study had no missing data. For variables following a normal distribution, we reported the mean and standard deviation (SD). Non-normally distributed variables were summarized using the median and interquartile range (IQR). Categorical data are presented as counts (n) and percentages (%). Comparisons of baseline characteristics were conducted using the two-sample t-test, Mann-Whitney U test, or chi-square test, as appropriate based on the data type.

We split the MIMIC cohort randomly, reserving 70% for model training and 30% for internal testing. Predictors were selected using LASSO regression with 10-fold cross-validation to find the optimal penalty parameter (λ.min). The Boruta algorithm was then used for additional variable filtering. Variables with importance consistently above the shadowMax importance were selected.

Using the selected variables, we developed five models: logistic regression (LR), extreme gradient boosting (XGBoost), gradient boosting machine (GBM), support vector machine (SVM), and Neural Network. LR offers good interpretability; XGBoost and GBM support parallel computing and automatic handling of missing values(22–24); and Neural Networks are capable of capturing complex latent patterns and interactions. Hyperparameters were tuned using grid search with 10-fold cross-validation and 5 repeats. Model performance was evaluated based on the area under the receiver operating characteristic curve (AUC) and 95% confidence interval (95% CI), specificity, sensitivity, accuracy, and F1 score, with AUC serving as the primary evaluation metric. Calibration curves gauged the alignment between observed and predicted results, while decision curve analysis (DCA) determined the net clinical benefit. The interpretability of the final predictive model was explored using the shapley additive explanations (SHAP) method. The model with superior predictive capabilities was selected as the main model, validated using an external cohort. A two-sided $P < 0.05$ was considered statistically significant.

Results

Baseline Characteristics

A total of 2,166 patients from the MIMIC database undergoing CPB surgery were included in this study, of whom 268 (12.4%) developed postoperative infection and 1,898 (87.7%) did not (Fig. 1). Baseline characteristics showed that the cohort had a median age of 68 years, was predominantly male, and included multiple surgical subtypes, with CABG being the most common procedure. Compared with the non-infection group, patients with postoperative infection had a higher BMI and were more likely to be admitted emergently. They also exhibited higher postoperative maximum values of temperature, heart rate, respiratory rate, blood pressure, neutrophil count, creatinine, liver enzymes, bilirubin, glucose, and potassium, as well as lower minimum values of blood pressure, oxygen saturation, red blood cell count, albumin, calcium, and hemoglobin during the first 48 postoperative hours (Table 1).

Table 1
Baseline characteristics of the study population stratified by postoperative infection status

Variables	Total	Non-infection	Popinfection	*P*
	N = 2166	N = 1898	N = 268	
Gender (%)				0.377
Male	1517 (70.04%)	1336 (70.39%)	181 (67.54%)	
Female	649 (29.96%)	562 (29.61%)	87 (32.46%)	
Age (years)	68.00 [60.00;77.00]	68.00 [61.00;77.00]	67.00 [58.00;76.25]	0.105
BMI (kg/m²)	28.17 [24.96;31.71]	28.09 [24.87;31.49]	28.96 [25.78;33.18]	0.023
Marital status (%)				0.108
Yes	1424 (65.74%)	1260 (66.39%)	164 (61.19%)	
No	742 (34.26%)	638 (33.61%)	104 (38.81%)	
Race (%)				0.849
White	1558 (71.93%)	1371 (72.23%)	187 (69.78%)	
Black	493 (22.76%)	428 (22.55%)	65 (24.25%)	
Asian	46 (2.12%)	40 (2.11%)	6 (2.24%)	
Other	69 (3.19%)	59 (3.11%)	10 (3.73%)	
Admission type (%)				< 0.001
Elective	1407 (64.96%)	1285 (67.70%)	122 (45.52%)	
Emergency	759 (35.04%)	613 (32.30%)	146 (54.48%)	
Smoking status (%)				0.435
No	1272 (58.73%)	1121 (59.06%)	151 (56.34%)	
Yes	894 (41.27%)	777 (40.94%)	117 (43.66%)	
Surgery type (%)				0.256

BMI, body mass index; SOFA, sequential organ failure assessment; APSIII, Acute Physiology Score III; AKI, acute kidney injury; ICU, intensive care unit; TWA, time-weighted average; CABG, coronary artery bypass grafting; Los, length of stay; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; RBC, red blood cell; So_2, oxygen saturation; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRBSI, catheter-related bloodstream infection; Resp, respiratory; SSI, surgical site infection; Pop, postoperative; min, minimum; max, maximum; abs, absolute count. Lactate_clearance (%) was calculated as (first lactate – last lactate) / first lactate × 100 using the first and last lactate values within the first 48 postoperative hours. Lactate_difference (mmol/L) was defined as the difference between the first and last lactate values over the same 48-hour period.

Variables	Total	Non-infection	Popinfection	*P*
	N = 2166	**N = 1898**	**N = 268**	
CABG	1100 (50.78%)	978 (51.53%)	122 (45.52%)	
Valve	444 (20.50%)	384 (20.23%)	60 (22.39%)	
Aortic	6 (0.28%)	6 (0.32%)	0 (0.00%)	
Congenital heart	35 (1.62%)	32 (1.69%)	3 (1.12%)	
Combined	393 (18.14%)	333 (17.54%)	60 (22.39%)	
Other	188 (8.68%)	165 (8.69%)	23 (8.58%)	
Hypertension (%)				0.002
No	785 (36.24%)	664 (34.98%)	121 (45.15%)	
Yes	1381 (63.76%)	1234 (65.02%)	147 (54.85%)	
Liver disease (%)				< 0.001
No	2072 (95.66%)	1836 (96.73%)	236 (88.06%)	
Yes	94 (4.34%)	62 (3.27%)	32 (11.94%)	
Diabates (%)				0.039
No	1481 (68.37%)	1313 (69.18%)	168 (62.69%)	
Yes	685 (31.63%)	585 (30.82%)	100 (37.31%)	
Myocardial infarction (%)				0.002
No	1601 (73.92%)	1424 (75.03%)	177 (66.04%)	
Yes	565 (26.08%)	474 (24.97%)	91 (33.96%)	
Congestive heart failure (%)				< 0.001
No	1635 (75.48%)	1461 (76.98%)	174 (64.93%)	
Yes	531 (24.52%)	437 (23.02%)	94 (35.07%)	

BMI, body mass index; SOFA, sequential organ failure assessment; APSIII, Acute Physiology Score III; AKI, acute kidney injury; ICU, intensive care unit; TWA, time-weighted average; CABG, coronary artery bypass grafting; Los, length of stay; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; RBC, red blood cell; So_2, oxygen saturation; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRBSI, catheter-related bloodstream infection; Resp, respiratory; SSI, surgical site infection; Pop, postoperative; min, minimum; max, maximum; abs, absolute count. Lactate_clearance (%) was calculated as (first lactate – last lactate) / first lactate × 100 using the first and last lactate values within the first 48 postoperative hours. Lactate_difference (mmol/L) was defined as the difference between the first and last lactate values over the same 48-hour period.

Variables	Total	Non-infection	Popinfection	*P*
	N = 2166	N = 1898	N = 268	
Peripheral vascular disease (%)				0.002
No	1768 (81.63%)	1568 (82.61%)	200 (74.63%)	
Yes	398 (18.37%)	330 (17.39%)	68 (25.37%)	
Cerebro vascular disease (%)				< 0.001
No	1932 (89.20%)	1711 (90.15%)	221 (82.46%)	
Yes	234 (10.80%)	187 (9.85%)	47 (17.54%)	
Chronic pulmonary disease (%)				0.225
No	1652 (76.27%)	1456 (76.71%)	196 (73.13%)	
Yes	514 (23.73%)	442 (23.29%)	72 (26.87%)	
Rheumatic disease (%)				0.784
No	2103 (97.09%)	1844 (97.15%)	259 (96.64%)	
Yes	63 (2.91%)	54 (2.85%)	9 (3.36%)	
Pepticulcer disease (%)				0.023
No	2147 (99.12%)	1885 (99.32%)	262 (97.76%)	
Yes	19 (0.88%)	13 (0.68%)	6 (2.24%)	
Renal disease (%)				< 0.001
No	1893 (87.40%)	1677 (88.36%)	216 (80.60%)	
Yes	273 (12.60%)	221 (11.64%)	52 (19.40%)	
Malignant cancer (%)				0.899

BMI, body mass index; SOFA, sequential organ failure assessment; APSIII, Acute Physiology Score III; AKI, acute kidney injury; ICU, intensive care unit; TWA, time-weighted average; CABG, coronary artery bypass grafting; Los, length of stay; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; RBC, red blood cell; So_2, oxygen saturation; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRBSI, catheter-related bloodstream infection; Resp, respiratory; SSI, surgical site infection; Pop, postoperative; min, minimum; max, maximum; abs, absolute count. Lactate_clearance (%) was calculated as (first lactate – last lactate) / first lactate × 100 using the first and last lactate values within the first 48 postoperative hours. Lactate_difference (mmol/L) was defined as the difference between the first and last lactate values over the same 48-hour period.

Variables	Total	Non-infection	Popinfection	*P*
	N = 2166	N = 1898	N = 268	
No	2111 (97.46%)	1849 (97.42%)	262 (97.76%)	
Yes	55 (2.54%)	49 (2.58%)	6 (2.24%)	
Charlson comorbidity index	5.00 [4.00;7.00]	5.00 [4.00;6.00]	5.00 [4.00;7.00]	< 0.001
Sofa dynamic	6.00 [5.00;8.00]	6.00 [4.00;8.00]	8.00 [5.00;11.00]	< 0.001
APSIII	35.00 [27.00;48.00]	34.00 [27.00;46.00]	45.50 [32.75;73.25]	< 0.001
Pop AKI (%)				< 0.001
No	517 (23.87%)	486 (25.61%)	31 (11.57%)	
Yes	1649 (76.13%)	1412 (74.39%)	237 (88.43%)	
Mortality in 30 days (%)				0.873
No	2127 (98.20%)	1863 (98.16%)	264 (98.51%)	
Yes	39 (1.80%)	35 (1.84%)	4 (1.49%)	
Los in ICU (days)	2.08 [1.25;3.29]	2.01 [1.24;3.18]	3.13 [1.38;8.50]	< 0.001
Los in hospital (days)	7.08 [5.23;10.26]	6.88 [5.16;9.80]	12.00 [7.96;21.62]	< 0.001
Lactate peak (days)	2.70 [2.10;3.60]	2.70 [2.10;3.50]	2.95 [2.18;4.32]	< 0.001
Lactate TWA48 (mmol/L)	1.60 [1.21;2.09]	1.59 [1.20;2.05]	1.69 [1.29;2.31]	0.01
Lactate clear (%)	22.22 [-17.65;47.73]	21.43 [-17.65;47.37]	28.57 [-16.85;50.32]	0.172
Lactate difference (mmol/L)	2.00 [1.60;2.54]	-0.40 [-1.20;0.30]	-0.50 [-1.40;0.30]	0.191
Temperature max (℃)	37.50 [37.11;37.90]	37.44 [37.11;37.89]	37.78 [37.22;38.52]	< 0.001

BMI, body mass index; SOFA, sequential organ failure assessment; APSIII, Acute Physiology Score III; AKI, acute kidney injury; ICU, intensive care unit; TWA, time-weighted average; CABG, coronary artery bypass grafting; Los, length of stay; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; RBC, red blood cell; So_2, oxygen saturation; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRBSI, catheter-related bloodstream infection; Resp, respiratory; SSI, surgical site infection; Pop, postoperative; min, minimum; max, maximum; abs, absolute count. Lactate_clearance (%) was calculated as (first lactate – last lactate) / first lactate × 100 using the first and last lactate values within the first 48 postoperative hours. Lactate_difference (mmol/L) was defined as the difference between the first and last lactate values over the same 48-hour period.

Variables	Total	Non-infection	Popinfection	*P*
	N = 2166	N = 1898	N = 268	
Heartrate max (n/min)	104.00 [93.00;117.00]	102.00 [92.00;115.00]	115.50 [100.00;131.00]	< 0.001
Resprate max (n/min)	29.00 [25.00;33.00]	28.00 [25.00;32.00]	33.00 [28.00;40.00]	< 0.001
SBP max (mmHg)	148.00 [137.00;162.00]	147.00 [137.00;160.00]	156.00 [144.00;171.62]	< 0.001
DBP max (mmHg)	84.00 [74.50;95.00]	83.00 [74.00;94.00]	91.00 [79.00;103.00]	< 0.001
MBP max (mmHg)	102.00 [93.00;116.00]	101.00 [93.00;113.00]	111.50 [97.00;143.25]	< 0.001
Ph max	7.46 [7.43;7.50]	7.46 [7.43;7.50]	7.48 [7.45;7.53]	< 0.001
So_2 max (%)	98.00 [98.00;99.00]	98.00 [98.00;99.00]	98.00 [98.00;99.00]	< 0.001
Lymphocytes abs max (10^9/L)	1.73 [1.31;2.38]	1.73 [1.31;2.37]	1.78 [1.33;2.41]	0.445
Neutrophils abs max (10^9/L)	9.39 [6.55;13.02]	9.12 [6.45;12.44]	11.79 [7.39;16.08]	< 0.001
RBC max (10^9/L)	4.07 [3.70;4.49]	4.06 [3.69;4.48]	4.18 [3.83;4.62]	< 0.001
Creatinine max (mg/dL)	1.10 [0.90;1.40]	1.10 [0.90;1.40]	1.40 [1.00;2.10]	< 0.001
Alt max (U/L)	24.00 [17.00;38.00]	23.00 [17.00;35.00]	35.50 [21.00;86.75]	< 0.001
Ast max (U/L)	33.00 [23.00;59.00]	32.00 [22.00;53.00]	47.50 [28.75;131.25]	< 0.001
Bilirubin total max (mg/dL)	0.60 [0.40;1.00]	0.60 [0.40;0.90]	0.80 [0.50;1.70]	< 0.001
Glucose max (mg/dL)	183.00 [161.00;213.00]	181.00 [160.00;210.00]	202.50 [176.00;232.00]	< 0.001
Potassium max (mmol/L)	5.40 [5.00;5.90]	5.40 [5.00;5.80]	5.60 [5.10;6.00]	< 0.001

BMI, body mass index; SOFA, sequential organ failure assessment; APSIII, Acute Physiology Score III; AKI, acute kidney injury; ICU, intensive care unit; TWA, time-weighted average; CABG, coronary artery bypass grafting; Los, length of stay; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; RBC, red blood cell; So_2, oxygen saturation; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRBSI, catheter-related bloodstream infection; Resp, respiratory; SSI, surgical site infection; Pop, postoperative; min, minimum; max, maximum; abs, absolute count. Lactate_clearance (%) was calculated as (first lactate – last lactate) / first lactate × 100 using the first and last lactate values within the first 48 postoperative hours. Lactate_difference (mmol/L) was defined as the difference between the first and last lactate values over the same 48-hour period.

Variables	Total	Non-infection	Popinfection	*P*
	N = 2166	N = 1898	N = 268	
Heartrate min (n/min)	64.00 [58.00;71.00]	64.00 [58.00;71.00]	63.00 [56.00;70.00]	0.024
Resprate min (n/min)	10.00 [8.00;12.00]	10.00 [8.00;12.00]	9.00 [7.00;11.00]	0.001
SBP min (mmHg)	83.00 [75.00;89.00]	83.00 [76.00;89.00]	77.00 [69.00;86.00]	< 0.001
DBP min (mmHg)	41.00 [35.00;46.00]	41.00 [36.00;46.00]	38.00 [32.00;43.00]	< 0.001
MBP min (mmHg)	54.00 [48.00;59.00]	54.50 [49.00;59.00]	50.00 [42.00;57.00]	< 0.001
Ph min	7.31 [7.27;7.34]	7.31 [7.27;7.34]	7.28 [7.22;7.32]	< 0.001
So_2 min (%)	96.00 [94.00;98.00]	96.00 [94.00;98.00]	95.00 [91.00;97.00]	< 0.001
RBC min (10^9/L)	2.78 [2.53;3.08]	2.80 [2.55;3.11]	2.66 [2.44;2.92]	< 0.001
Albumin min (g/dL)	3.70 [3.10;4.10]	3.70 [3.20;4.10]	3.30 [2.60;3.90]	< 0.001
Creatinine min (mg/dL)	0.80 [0.60;0.90]	0.80 [0.60;0.90]	0.80 [0.60;1.00]	0.402
Calcium total min (mmol/L)	8.10 [7.80;8.40]	8.10 [7.80;8.50]	7.90 [7.60;8.20]	< 0.001
Alt min (U/L)	20.00 [14.00;28.00]	20.00 [14.00;28.00]	20.00 [12.75;30.00]	0.622
Ast min (U/L)	26.00 [20.00;37.00]	26.00 [20.00;36.00]	26.00 [20.75;38.00]	0.517
Bilirubin total min (mg/dL)	0.50 [0.40;0.80]	0.50 [0.40;0.80]	0.50 [0.40;0.70]	0.081
Potassium min (mmol/L)	3.50 [3.30;3.80]	3.60 [3.30;3.80]	3.40 [3.10;3.70]	< 0.001
Hemoglobin min (g/dL)	8.10 [7.10;9.10]	8.10 [7.20;9.10]	7.40 [6.60;8.43]	< 0.001
Pop CRBSI (%)				< 0.001
No	2111 (97.46%)	1898 (100.00%)	264 (98.51%)	

BMI, body mass index; SOFA, sequential organ failure assessment; APSIII, Acute Physiology Score III; AKI, acute kidney injury; ICU, intensive care unit; TWA, time-weighted average; CABG, coronary artery bypass grafting; Los, length of stay; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; RBC, red blood cell; So_2, oxygen saturation; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRBSI, catheter-related bloodstream infection; Resp, respiratory; SSI, surgical site infection; Pop, postoperative; min, minimum; max, maximum; abs, absolute count. Lactate_clearance (%) was calculated as (first lactate – last lactate) / first lactate × 100 using the first and last lactate values within the first 48 postoperative hours. Lactate_difference (mmol/L) was defined as the difference between the first and last lactate values over the same 48-hour period.

Variables	Total	Non-infection	Popinfection	*P*
	N = 2166	**N = 1898**	**N = 268**	
Yes	55 (2.54%)	0 (0.00%)	4 (1.49%)	
Pop SSI (%)				< 0.001
No	2162 (99.82%)	1898 (100.00%)	213 (79.48%)	
Yes	4 (0.18%)	0 (0.00%)	55 (20.52%)	
Pop pneumonia (%)				< 0.001
No	1946 (89.93%)	1898 (100.00%)	50 (18.66%)	
Yes	218 (10.07%)	0 (0.00%)	218 (81.34%)	
Pop sepsis (%)				< 0.001
No	2141 (98.85%)	1898 (100.00%)	243 (90.67%)	
Yes	25 (1.15%)	0 (0.00%)	25 (9.33%)	

BMI, body mass index; SOFA, sequential organ failure assessment; APSIII, Acute Physiology Score III; AKI, acute kidney injury; ICU, intensive care unit; TWA, time-weighted average; CABG, coronary artery bypass grafting; Los, length of stay; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; RBC, red blood cell; So_2, oxygen saturation; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRBSI, catheter-related bloodstream infection; Resp, respiratory; SSI, surgical site infection; Pop, postoperative; min, minimum; max, maximum; abs, absolute count. Lactate_clearance (%) was calculated as (first lactate – last lactate) / first lactate × 100 using the first and last lactate values within the first 48 postoperative hours. Lactate_difference (mmol/L) was defined as the difference between the first and last lactate values over the same 48-hour period.

Model Feature Selection

Nine candidate variables were first identified by LASSO and then further screened by Boruta. Ultimately, eight features were selected for model development: admission type, neutrophil count, creatinine, respiratory rate, heart rate, body temperature, oxygen saturation, and albumin (Fig. 2A and **B**).

Comparison and Analysis of Models

We constructed five models, namely LR, XGBoost, GBM, SVM and Neural Network, to predict postoperative infection. The ROC curves and corresponding AUC values of the models in the development cohort are presented, with AUCs of 0.750 (95% CI: 0.711–0.788) for LR, 0.539 (95% CI: 0.491–0.586) for SVM, 0.861 (95% CI: 0.831–0.890) for GBM, 0.789 (95% CI: 0.754–0.824) for Neural Network, 0.774 (95% CI: 0.735–0.813) for XGBoost (Fig. 3A). Detailed model hyperparameters are provided (**Supplementary Table S2**).

Subsequently, those models were used to assess the generalizability of the models in the internal validation cohort. Consistent with its performance in the development cohort, GBM again showed stable performance in the internal validation cohort, with an AUC of 0.791 (95% CI: 0.737–0.844), accuracy of 0.849, sensitivity of 0.560, specificity of 0.892, precision of 0.439, and F1 score of 0.492 (Fig. 3B and **Supplementary Figure S1**). Calibration curves and decision curve analysis (DCA) were applied to evaluate the calibration and the clinical net benefit across a range of threshold probabilities, indicating that the GBM model has potential clinical utility for postoperative infection prediction (**Supplementary Figure S2 and S3**). Therefore, we selected the GBM model, which demonstrated the best overall performance, for further investigation.

External Validation

Without any further retraining, we applied the final GBM model – originally built from the derivation cohort – to the external validation cohort. In the external validation cohort, a total of 96 patients were enrolled, of whom 19 developed postoperative infection. Among the patients predicted as positive by the model, 15 were true positives and 28 were false positives. Among those predicted as negative, 49 were true negatives and 4 were false negatives. Selected baseline clinical characteristics of the two cohorts are shown (**Supplementary Table S3)**. The AUC of the model in the external validation cohort was 0.742 (95% CI: 0.619–0.866) (Fig. 4), indicating that our model demonstrated reasonable diagnostic performance in both internal and external validation. In terms of discriminative ability, the model achieved an accuracy of 0.667, a sensitivity of 0.789, a specificity of 0.636, a precision of 0.349 and the F1 score was 0.484 (Table 2).

Table 2
Performance of the GBM model in the development, internal validation, and external validation cohorts

Dataset	AUC	AUC 95%CI	Precision	Sensitivity	Specificity	Accuracy	F1 score
Development	0.861	0.831–0.890	0.305	0.842	0.734	0.747	0.448
Internal	0.791	0.737–0.844	0.439	0.560	0.892	0.849	0.492
External	0.742	0.619–0.866	0.349	0.789	0.636	0.667	0.484

GBM, Gradient Boosting Machine; AUC, the area under the receiver operating characteristic curve; PPV, positive predictive value; NPV, negative predictive value.

Model Interpretability

We used the SHAP method to interpret the best-performing GBM model. The feature importance ranking based on the mean absolute SHAP values shown that temperature contributed the most to GBM model, followed by creatinine, respiratory rate, albumin and others (Fig. 5A). The SHAP beeswarm plot further illustrated the direction and distribution of feature effects (Fig. 5B).

The dependence plot further revealed the relationships between key features and the risk of postoperative infection (Fig. 5C). Higher values of temperature, heart rate, respiratory rate, and creatinine within the first 48 hours after surgery, were associated with an increased risk of infection. In contrast, higher minimum oxygen saturation and higher minimum albumin levels were associated with a lower risk of infection. However, for neutrophils, both excessively low and excessively high values increased the risk of infection, while maintaining these features within a certain range significantly reduced the infection risk. Regarding admission type, emergency admission significantly increased the risk of infection.

The SHAP waterfall plot, using a typical patient as an example (Fig. 5D), showed that the baseline predicted log odds (E[f(x)]) was − 2.37, and the actual predicted log odds for this patient was 2.47, corresponding to a predicted probability of postoperative infection significantly above the population average. Respiratory rate (+ 1.51) and temperature (+ 1.21) were the main factors increasing the risk. In addition, creatinine, admission type, albumin, and heart rate also increased the risk of infection. Only oxygen saturation (-0.305) slightly reduced the risk. This example intuitively demonstrates how the model integrates multiple clinical variables to derive an individualized risk prediction, which may help clinicians understand the decision-making logic of the model.

Convenient Application for Clinical Utility

For the convenience of clinical application, the final GBM prediction model was implemented as an app (**Supplementary File S2**). After opening R (version > 4.2.0) and launching the app, the user enters the eight required feature values, and the application then returns the predicted probability of postoperative infection.

Discussion

In this study, we developed a machine learning model for predicting postoperative infection after cardiac surgery requiring CPB based on the MIMIC database and validated it in an independent prospective external validation cohort. The GBM model outperformed all other tested algorithms in internal validation and maintained strong discriminative ability during external validation. SHAP analysis further improved interpretability by identifying key contributors to infection risk.

Machine learning models may capture the complex interactions among perioperative physiological variables more effectively than conventional regression-based approaches or single biomarkers. Previous studies on the application of machine learning for predicting outcomes in surgical patients have frequently been limited by inadequate external validation and poor interpretability(13). In contrast, our study incorporated an independent prospective external validation cohort and used SHAP analysis to improve model transparency, which may enhance the potential clinical applicability of the proposed model.

In this study, emergency admission was strongly associated with postoperative infection risk. Compared with elective patients, those undergoing emergency surgery often present with greater physiological instability, organ dysfunction, and inadequate preoperative optimization, all of which may increase susceptibility to postoperative infection(25),(26). Previous multicenter cohort study has similarly shown that emergency surgery is associated with worse postoperative outcomes(27). Several important predictors identified by the model reflected postoperative inflammatory and immune responses. Neutrophils not only reflect the current intensity of inflammation in the body but also indicate the body's immune response capacity(28). In this study, postoperative neutrophil levels were significantly elevated in nearly all patients. However, neutrophil levels within the moderate range during the first 48 hours after surgery were associated with a lower risk of infection, demonstrating a clear nonlinear relationship with infection risk. First, the elevation of neutrophil levels soon after cardiopulmonary bypass is a normal occurrence, resulting from the considerable surgical stress and inflammatory response(29). In a subset of patients with only modest postoperative neutrophil elevation, CPB may induce immunosuppression or "immune paralysis," characterized by inadequate neutrophil response or dysfunction, thereby increasing infection susceptibility(29, 30). However, as neutrophil levels rise further, their contribution to infection risk becomes positive, suggesting that potentially reflecting hyperactivation, progression of underlying infection, or severe physiological stress is associated with an increased risk of infection(30). Similarly, heart rate, respiratory rate, and body temperature, like neutrophils, are component indicators of the systemic inflammatory response syndrome(31). When these elevations persistently exceed a certain threshold, they may indicate a more severe inflammatory response, a pathological state, and an underlying risk of infection(31). Elevated postoperative creatinine levels were also strongly associated with infection risk, exhibiting a relatively clear threshold effect. As an important indicator of kidney function, creatinine typically reflects AKI or renal insufficiency(32). Previous studies have also shown that AKI a risk factor for infection and adverse prognosis(33, 34). After cardiopulmonary bypass, renal function is susceptible to impairment due to compromised perfusion and ischemia-reperfusion injury(35).This may result in disturbed renal metabolic activities with reduced renin, erythropoietin, and vitamin D production, which adversely affects the immune system(36). Impaired renal function may lead to fluid imbalance, malnutrition, and electrolyte disturbances, all of which may weaken the body's ability to fight infection. Postoperative hypoxemia after CPB often reflects impaired pulmonary function, ventilation–perfusion mismatch, or microcirculatory dysfunction(37). When oxygen delivery is inadequate, immune cell and vital organ functions can be compromised, which reduces the host’s defense against infection(38). In addition, patients with hypoxemia are more likely to experience prolonged mechanical ventilation, which may further increase the risk of respiratory tract infection(39, 40) Finally, patients with lower albumin levels were more susceptible to postoperative infection, and this finding is also biologically plausible. Beyond reflecting nutritional status, albumin helps preserve colloid osmotic pressure and modulate inflammation, both of which are relevant to infection risk(41). Reduced albumin levels may aggravate systemic inflammation, promote interstitial edema, and delay wound healing, ultimately increasing susceptibility to infection(42, 43).

Importantly, SHAP analysis provided insight into the contribution and directionality of individual predictors, thereby improving model interpretability. This may facilitate clinical understanding of model predictions and support postoperative risk stratification in routine practice. Furthermore, the associations observed between several physiological variables and infection risk suggest that postoperative infection after CPB is likely driven by complex interactions among inflammatory, hemodynamic, and organ dysfunction pathways rather than isolated abnormalities. This study used multiple imputation for missing values; the same strategy should be applied in practice. If key variables are missing, predictions should be interpreted with caution, and abnormal values verified before model input. The model uses routine clinical variables and can be implemented with standard software. No advanced programming is required, but basic clinical knowledge is needed for proper data input and interpretation.

Limitations

Variations between the development and external validation cohorts in initial characteristics and postoperative infection definitions could potentially introduce biases, ultimately impacting the model's performance during validation. This, in turn, might reduce the model’s performance during external validation. However, both outcome definitions were based on clinical practice and still have reasonable clinical utility. While the study did undergo external validation with an independent cohort, limitations in sample size and the number of infection cases may have affected the model's reliability. Moreover, our model was built mainly using variables collected from a fixed early postoperative time window. Additionally, the model predominantly utilized variables from a specific early postoperative period, neglecting dynamic changes in vital signs, laboratory results, and clinical interventions .Furthermore, postoperative infections are influenced by a multitude of external factors such as procedural techniques, hospital environment, and patient behaviors, which were not fully considered in the model. Therefore, the model's ability to predict actual clinical infection may be limited. Future studies should focus on large-sample, multicenter validation in diverse populations, and prospective assessment of clinical utility.

Conclusions

The GBM model demonstrated strong performance in the development and internal validation groups, with reliable results also seen in the external validation cohort. This suggests it could be a valuable tool for predicting postoperative infection risk early on.

Abbreviations

AKI
acute kidney injury
ALT
alanine aminotransferase
APSIII

Acute Physiology Score III
AST
aspartate aminotransferase
AUC
area under the curve
BMI
body mass index
CABG
coronary artery bypass grafting
CI
confidence interval
CPB
cardiopulmonary bypass
CRBSI
catheter-related bloodstream infection
DCA
decision curve analysis
GBM
gradient boosting machine
ICU
intensive care unit
IQR
interquartile range
LASSO
least absolute shrinkage and selection operator
LOS
length of stay
LR
logistic regression
MIMIC-IV
Medical Information Mart for Intensive Care IV
NIH
National Institutes of Health
NPV
negative predictive value
PPV
positive predictive value
RBC
red blood cell
ROC

receiver operating characteristic
SD
standard deviation
SHAP
Shapley additive explanations
SOFA
Sequential Organ Failure Assessment
So_2
oxygen saturation
SSI
surgical site infection
SVM
support vector machine
TWA
time-weighted average
XGBoost
extreme gradient boosting

Declarations

Ethics approval and consent to participate

This study used two data sources: the publicly available MIMIC-IV database (approved by the Institutional Review Boards of Beth Israel Deaconess Medical Center and Massachusetts Institute of Technology; informed consent waived due to de-identified data; author Yiwei Lin completed NIH training, certification No. 68757619, and obtained data access permission); and the prospective cohort from The Affiliated Hospital of Qingdao University (approved by the Medical Ethics Committee of the hospital, approval No. QYFYEC2025-147; registered at Chinese Clinical Trial Registry, registration No. ChiCTR2500110269; written informed consent obtained from all participants).

Consent for publication

Not applicable

Conflicts of interest

The authors declare no competing interests and report no financial or non-financial relationships that could have influenced the work.

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Author Contribution

Yiwei Lin extracted data, performed analysis, and wrote the draft. Jingyu Li developed the model. Kaiqiang Fan collected external data. Tianying Qiu verified data. Zhichao Li supervised statistics. Shujie Wang administered the project. Chuan Guo interpreted clinical outcomes. Lei Zhang visualized data. Yang Zhao and Youzhuang Zhu designed the study, supervised the work, and are corresponding authors. All authors approved the final version.

Data Availability

The MIMIC IV database used in this study is a publicly available de identified electronic health record database, accessible at https://physionet.org/content/mimiciv/3.1/. The data from the prospective cohort of The Affiliated Hospital of Qingdao University are not publicly available due to institutional ethics committee and patient privacy restrictions.

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Figures

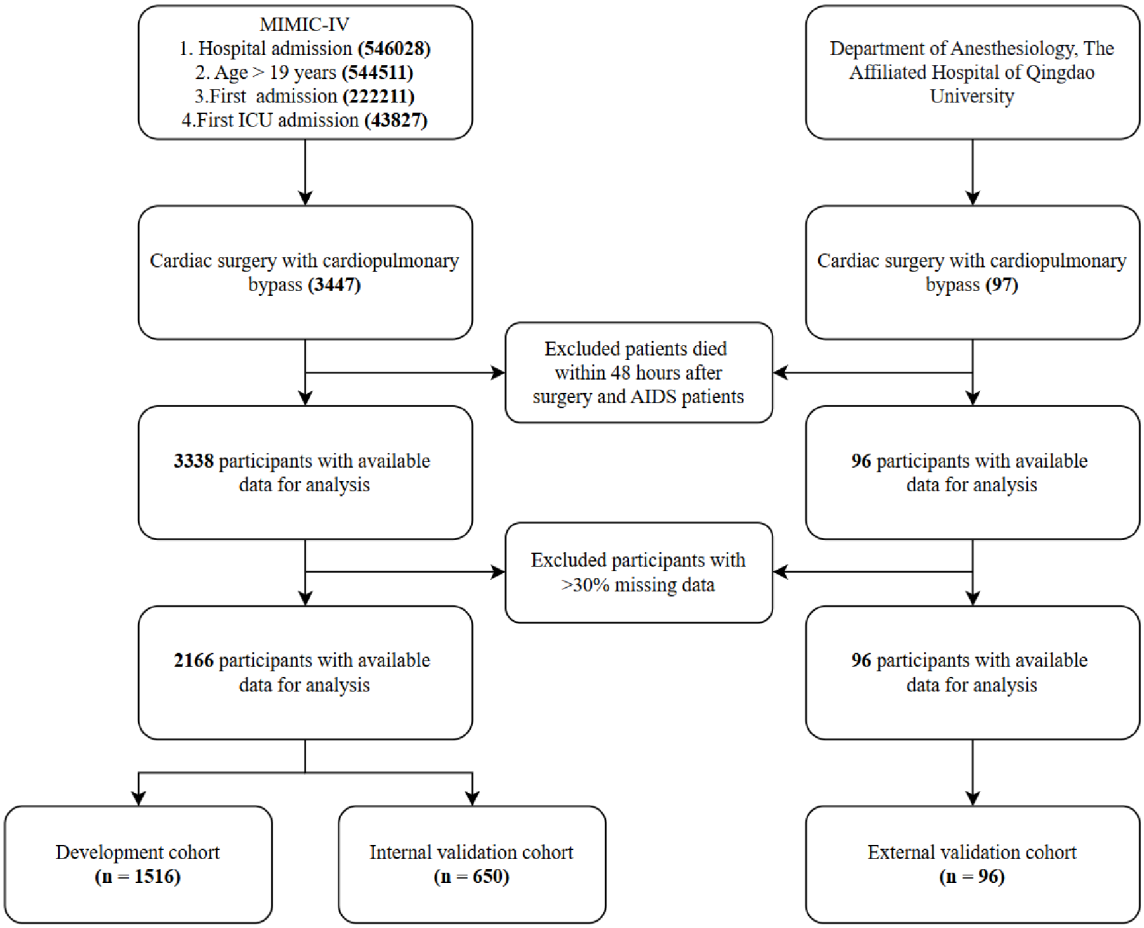


Figure 1

Flowchart of participant enrollment and data extraction.

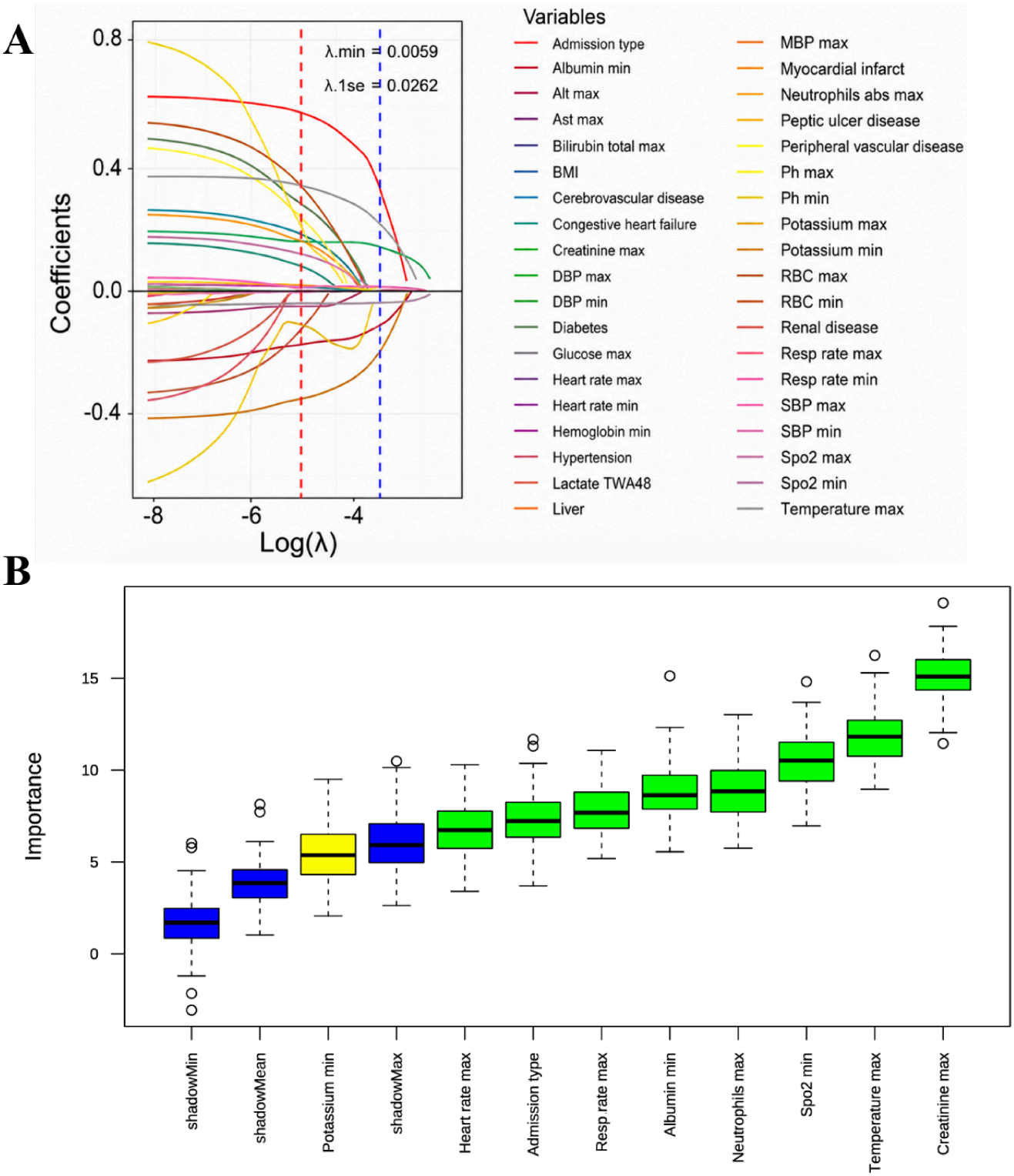


Figure 2

Machine learning model feature selection chart (**A**) LASSO coefficient paths as a function of log(λ). Each colored line represents the trajectory of a coefficient for a candidate variable as the penalty strength (log(λ) increases. (**B**) Feature selection based on the Boruta algorithm. Three shadow variables (shadowMin, shadowMean, and shadowMax) were generated. Variables with importance always above shadowMax were selected.

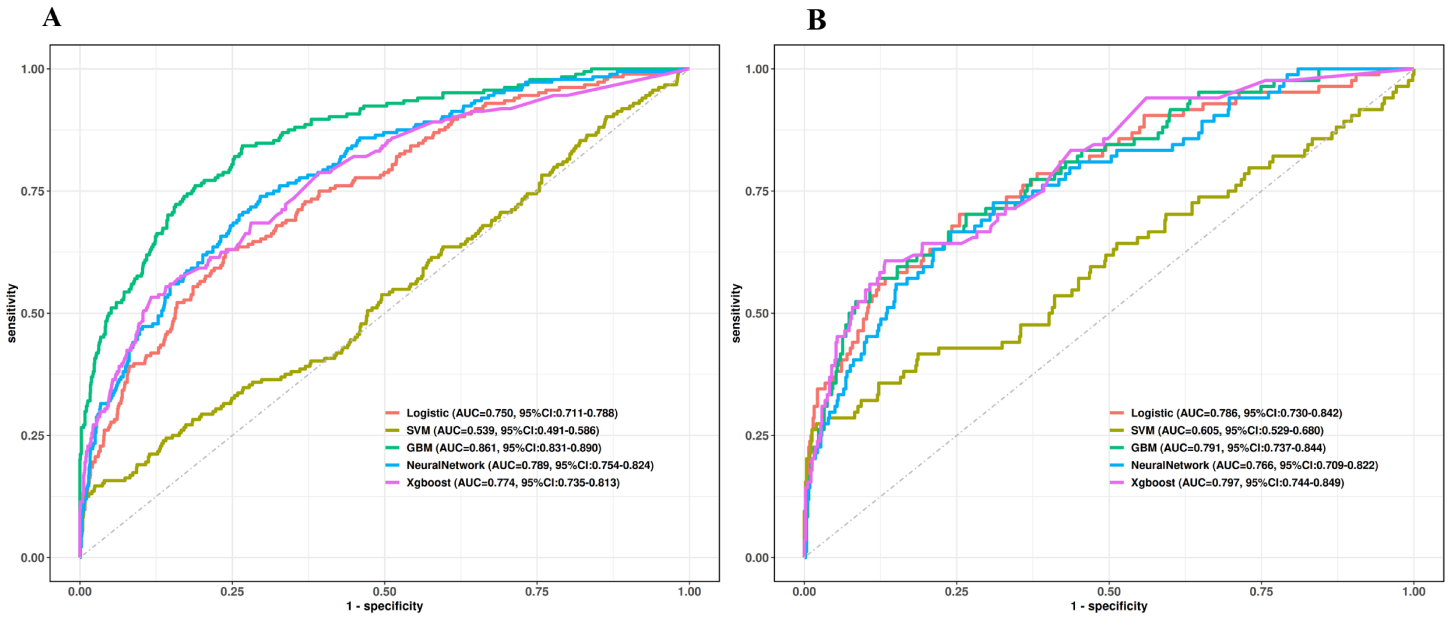


Figure 3

ROC curves for the machine learning models. (**A**) ROC curves of the five prediction models on the development cohort. (**B**) ROC curves of the five prediction models on the internal validation cohort. Logistic, logistic regression; Xgboost, extreme gradient boosting; GBM, gradient boosting machine; SVM, support vector machine; AUC, area under the curve.

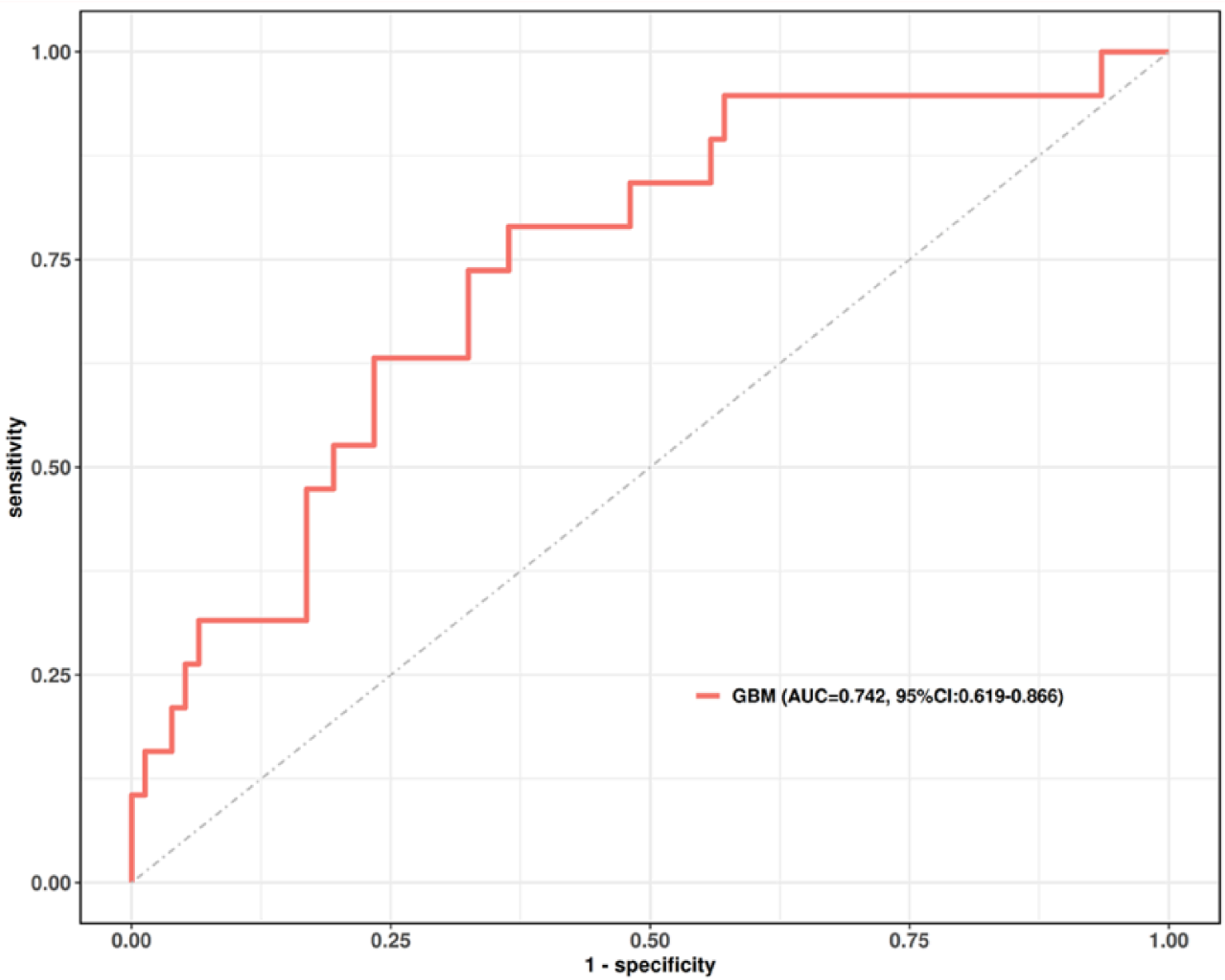


Figure 4

ROC curve of the GBM model on the external validation cohort. GBM, gradient boosting machine; AUC, area under the curve.

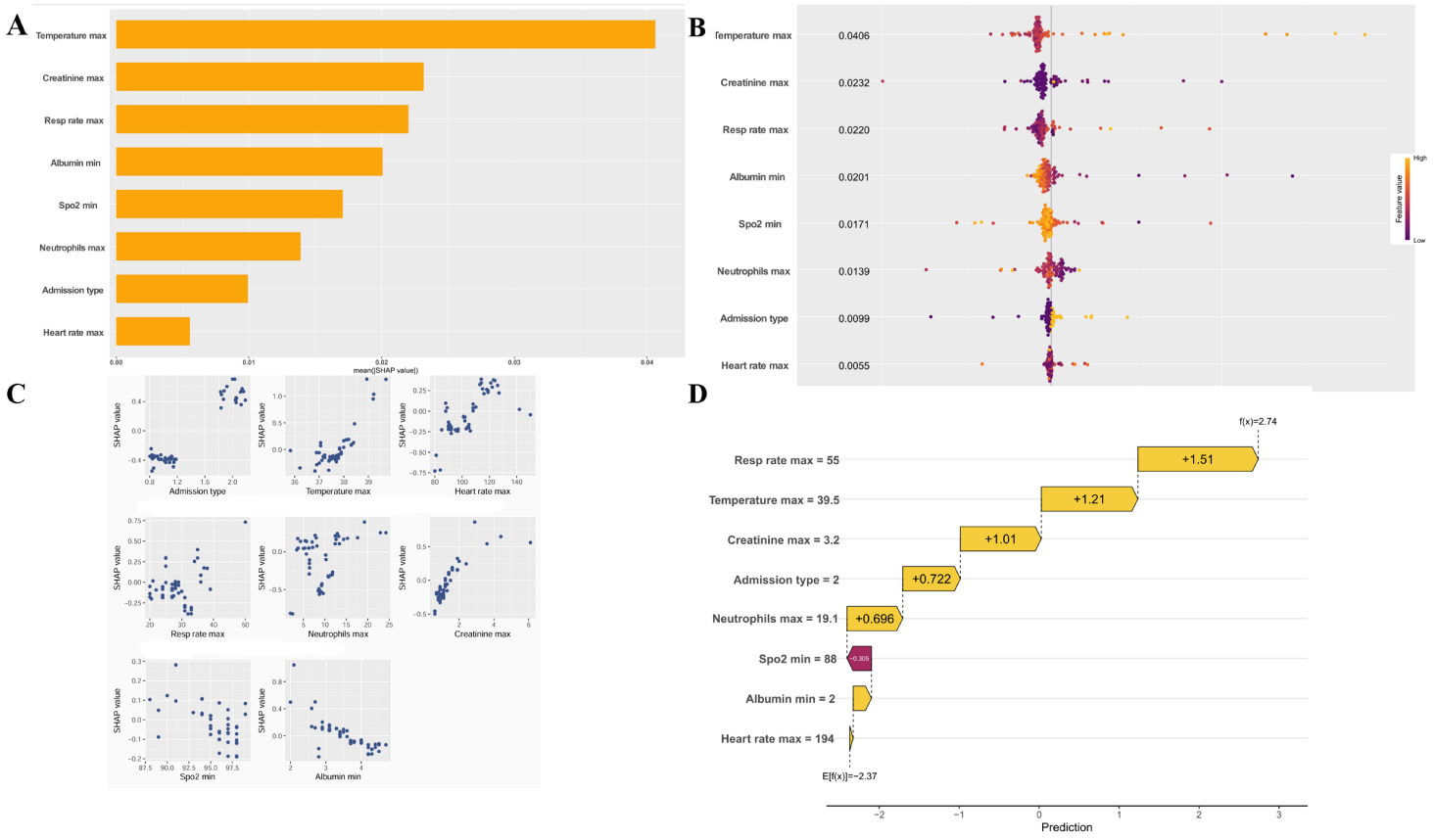


Figure 5

Machine learning model explanation by the SHAP method for the GBM model. (**A**) SHAP feature importance plot. This plot uses the mean SHAP value to evaluate the contribution of each feature to the model and displays them in descending order. (**B**)SHAP beeswarm plot. Each point represents the SHAP value of a patient for a given feature, with the feature value indicated by the color shown on the right side of the figure. Points are stacked vertically to show density. (**C**) SHAP dependence plots. The plots illustrate the direction and magnitude of each feature's impact on the prediction. Each point represents a sample; the y-axis shows the SHAP value (positive indicating increase risk), and the x-axis shows the feature value. (**D**) SHAP waterfall plot. This plot shows the contribution of each feature to the prediction for a particular patient. Yellow bars indicate features that have a positive contribution to the prediction, while red bars indicate features that have a negative contribution.

Supplementary Files

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- SupplementaryTableS1.doc
- SupplementaryTableS2.doc
- SupplementaryFigureS1.pdf
- SupplementaryTableS3.doc

- SupplementaryFigureS2.pdf
- SupplementaryFigureS3.pdf
- SupplementaryFileS1.doc
- SupplementaryFiseS2.zip
- SupplementaryAppendix.doc