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Article

Prediction of Acute Kidney Injury after Extracorporeal Cardiac Surgery (CSA-AKI) by Machine Learning Algorithms

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Abstract

Background: Acute renal failure after extracorporeal cardiac surgery under general anesthesia is high and unpredictable, but machine learning algorithms could change this. A feasible approach is to use machine learning models to construct models to predict acute kidney injury after extracorporeal cardiac surgery (CSA-AKI) and screen for the best predictive model. **Method**: From January 2014 to December 2021, 2187 patients undergoing extracorporeal cardiac surgery at the third hospital of Hebei Medical University and the first medical centre of Chinese PLA General Hospital were collected in this study. After excluding 923 patients who did not meet the inclusion criteria, a dataset of 1264 patients with 125 clinical indexes was constructed. After screening the feature variables using Least absolute shrinkage (LASSO) regression, the dataset was randomly divided into a training set (70%), test set (30%), and six machine learning algorithms, including extreme gradient boosting (XGBoost), logistic regression (LRC), light gradient boosting machine (LGBM), random forest classifier (RFC), adaptive boosting (AdaBoost), and K-nearest neighbor (KNN), were used in training set for predicting the CSA-AKI. The machine learning model with the best predictive performance was selected to complete external validation of the test set. The SHapley Additive exPlanations (SHAP) algorithm was used to interpret the model. **Results**: Of all 1264 patients, 372 (29.43%) patients presented with CSA-AKI. The LASSO regression eliminated 22 feature variables out of 125 before model development. Among the six prediction models, the RFC prediction model has the best prediction performance, with an Area Under Curve (AUC) value of 0.778 (95% CI: 0.726–0.830) in the test set and the best net benefit compared to the other tools. SHAP explained the impact of different feature variables on the predicted outcome, where the three most influential feature variables were creatinine clearance (CRC), intraoperative urine output (mL/kg/h) and age. **Conclusion**: We developed an RFC prediction model to predict the CSA-AKI, which has good predictive performance and can explain the factors affecting the prediction results of cases by integrating the SHAP method.

Keywords

acute kidney injury; extracorporeal cardiac surgery; machine learning; prediction models

Introduction

Acute kidney injury (AKI) is a disorder that adversely affects patients' prognoses, increases their economic burden, and is primarily characterized by high serum creatinine and decreased urine output [1]. Post-operative AKI related to extracorporeal cardiac surgery has an incidence of about 20–30%, with a significant proportion of these patients even requiring hemofiltration therapy [2]. Clinically, serum creatinine (SCr) levels are employed as an indicator of AKI and as a basis for grading; however, earlier investigations have demonstrated a lag in SCr levels [3]. Moreover, AKI is a rapidly progressive disease with a high mortality rate, and the early identification and detection of such patients can lead to an early medical intervention to reduce morbidity and medical burden [4–7]. However, there is no efficient clinical prediction model for early AKI detection. Based on a comprehensive analysis of many clinical data variables with complex relationships that may be associated with AKI after extracorporeal cardiac surgery (CSA-AKI) and the selection of an appropriate prediction model algorithm, an effective prediction model can be developed to achieve accurate CSA-AKI prediction [8].

Machine learning is a scientific data learning technique that enables machines to learn patterns from existing complex data to predict future behavioral outcomes and trends [9]. Its robust feature extraction and matching capabilities and capacity to integrate all parts of information regardless of input variable and outcome expectations enable machine learning methods to predict CSA-AKI [10,11]. To estimate the AKI risk occurring at the end of general anesthesia cardiac surgery, Lee *et al*. [12] developed an Internet-based risk estimator that can be used to process patient data in real-time and form predictions. Li *et al*. [13] used a Bayesian networks algorithm to predict AKI after cardiac general anesthesia, with an Area Under

Curve (AUC) value capable of reaching 0.755. Hayward *et al*. [14] developed a machine-learning model that can be used to predict postoperative AKI in pediatric patients undergoing cardiac surgery. Nevertheless, unfortunately, these researchers could not include as many clinical data indicators as possible, while the accuracy of the prediction models could be further improved.

Machine learning models can predict the CSA-AKI, but the training strategy and method directly impact the accuracy of the identification results. This study examined the identification accuracy of six classification models, selected the one with the highest recognition accuracy for analysis, and applied machine learning interpretable algorithms to uncover clinical data variables that can affect CSA-AKI occurrence.

Method

Patient Selection

From January 2014 to December 2021, 2187 patients who underwent extracorporeal cardiac surgery (cardiac bypass surgery) in the third hospital of Hebei Medical University and the first medical centre of Chinese PLA General Hospital were selected as participants in this study. The exclusion criteria were (1) patient age less than 18 years, (2) incomplete medical history data or anesthesia records, and (3) preoperative kidney failure or transplantation. After excluding 923 individuals who did not meet the inclusion criteria, 1264 individuals were included in this study for machine learning model building. This retrospective case-control study followed the Declaration of Helsinki, had minimal risk to all participants, and was exempt from ethical review under local laws.

Surgery and Anesthesia Methods

In this study, all patients underwent cardiac coronary artery bypass surgery under extracorporeal conditions. Target-controlled infusion of Propofol and Remifentanil or inhaled anesthetics under tracheal intubation were used to maintain general anesthesia, while intraoperative hemodynamic conditions, drug usage, and resuscitation were monitored.

Patient Data Collection

Based on previous studies [3,10,15,16], we collected demographic data, medical history, preoperative medication usage, preoperative cardiac ultrasound, preoperative electrocardiogram, baseline laboratory findings, the surgery type and interoperative status, extracorporeal circulation recording, anesthesia records, and AKI in compliance with kidney disease improving global outcomes (KDIGO) standards from the electronic medical record and anesthesia record systems.

Machine Learning Algorithms

The algorithms used in this study are classification model algorithms, which can find the best decision boundary in a specified data set, thus analyzing and predicting the classification of test samples, and their outputs are generally discrete fixed-class terms or fixed-order terms [17]. There are six machine learning methods used in this study for classification, including extreme gradient boosting (XGBoost), logistic regression (LRC), light gradient boosting machine (LGBM), random forest classifier (RFC), adaptive boosting (AdaBoost), and k-nearest neighbor (KNN).

AKI Diagnostic Criteria

Following the latest diagnostic criteria for KDIGO guidelines [18,19], AKI requires one of the following conditions: (1) an SCr increase $\geq$0.3 mg/dL or an SCr $\geq$26.5 µmol/L within 48 h; (2) known or presumed SCr increase $\geq$1.5 times baseline within seven days; (3) urine output $<$0.5 mL/kg/h for 6 h, where baseline SCr value was defined as the last SCr value detected within one week before undergoing extracorporeal cardiac surgery.

Data Analysis and Model Development

This study used Python (ver.2.7, Python Software Foundation, Chicago, USA) software for data analysis and machine learning training. Data of measurements conforming to normal distribution are presented as mean (standard deviation); non-normal distribution is shown as median (bottom quartile and top quartile, i.e., interquartile spacing) and count data are expressed as adoption rate (%) or composition ratio (%). The Python package sklearn (ver.0.22.1) was used to split the data set into a training and a test set, and the statistical analysis of the baseline data was performed using the Python package stats models (ver.0.11.1). The statistical methods were *t*-test, Mann-Whitney-U or chi-square test, depending on the data, with a significance level of α = 0.05. The packages used for the different machine learning algorithms in this study are as follows: the Python package xgboost (ver.1.2.1) was used for XGBoost, the Python package lightgbm (ver.3.2.1) was used for LGBM, and the Python package sklearn (ver.0.22.1) was used for the remaining four.

Additionally, the Python package glmnet (ver.4.1.2) was used in this study to filter the training set for important features like least absolute shrinkage (LASSO), selection operator regression modeling and variable screening. Moreover, the python package shapley additive explanations (SHAP, ver.0.39.0) was used to describe the interpretability of the classification models. For the comparison criteria in this study, Receiver Operating Characteristic (ROC), AUC and Decision Curve Analysis (DCA) were used. All Python packages are available at https://pypi.org/.

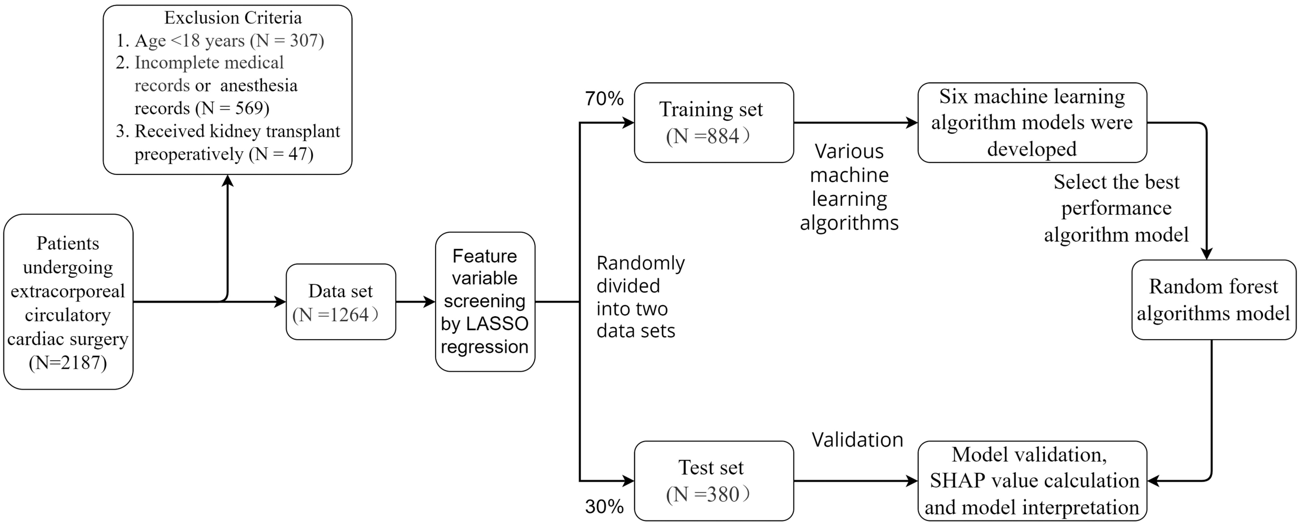

Fig. 1. Flow chart of machine learning model building and validation. A total of 2187 patients' information was collected in this study, and a dataset of 1264 was obtained after excluding 923 individuals who did not meet the criteria. LASSO regression was used to screen out the characteristic variables for subsequent modeling and validation. The dataset was randomly split into a training set (N = 884) and a validation set (N = 380), and the training set was used for machine learning model building. We select the LRC model that has the best prediction performance from the six machine learning models and introduce the validation set data for validation, and finally interpret the model using SHAP analysis of the impact factors. LASSO, least absolute shrinkage; LRC, logistic regression; SHAP, shapley additive explanations.

After screening patients following the exclusion criteria, a dataset of 1264 patients were obtained. Then, the Python package glmnet was used to extract the feature variables in this dataset for subsequent machine-learning model development. Using the randomization algorithm in the Python data package sklearn, the data set is randomly divided into a training set (70%) and a test set (30%). The training set data is imported into Python software and trained by the corresponding machine learning algorithm package described previously. The parameters of the six different machine learning algorithms are as follows. The parameters of the XGBoost algorithm include: (1) objective: binary: logistic, (2) learning_rate: 0.1, (3) max_depth: 8, (4) min_child_weight: 4, (5) reg_lambda (L2 regularization factor): 1. The parameters of the LRC algorithm include: (1) C: 1.0; (2) max_iter: 100; (3) penalty: l2; (4) tol: 0.0001. The parameters of the LGBM algorithm include: (1) boosting_type: gbdt; (2) learning rate: 2; (3) max_depth: 1; (4) n_estimators: 5; (5) num_leaves: 5. The parameters of the RFC algorithm include: (1) criterion: gini; (2) max_depth: 10; (3) min_impurity_decrease: 0; (4) n_estimators: 100. The parameters of the AdaBoost algorithm include: (1) learning_rate: 0.1; (2) n_estimators: 50. The parameters of the KNN algorithm include: (1) n_neighbors: 4; (2) weights: uniform.

The best prediction performance (AUC and DCA as reference criteria) machine learning model algorithm was selected from the above machine learning models, and the test set data was substituted for external validation [20,21]. The flow chart of this study is shown in Fig. 1.

Result

Demographic and Baseline Data

This study included 1264 patients who underwent cardiac surgery with extracorporeal circulation, with a mean age of 57.27 years, including 478 women (mean age 57.54 years) and 786 men (mean age 57.11 years). Of the 1264 patients, 565 (44.70%) had hypertension, 239 (18.91%) had diabetes, 112 (8.86%) were treated with insulin, 456 (36.08%) were smokers, 240 (19.00%) were alcohol drinkers, 187 (14.80%) had heart disease, and 45 (3.60%) had chronic kidney disease. A total of 372 (29.43%) in this study developed CSA-AKI. A randomized grouping was used to randomly divide the 1264 individuals into the training and the test set, and no difference was seen in comparing the baseline data between the two subsets ($p > 0.05$). The baseline data of the two subsets are shown in Table 1.

Feature Variables Screening

The LASSO binary logistic regression model was used for feature variable selection. The LASSO model's tuning parameter (λ) was selected using 10-fold cross-validation through the minimum criterion. The dotted vertical line was drawn at the optimal value using the minimum criteria and the 1-standard error of the minimum criteria (1-s.e. criteria). Based on 1-s.e. criteria, we screened out 22 non-zero

Table 1. Baseline data for the Training set and Test set.

Variants	Training set, (n = 884)	Test set, (n = 380)	*p*
Demographic data			
Age, (median, [IQR])	60.000, [51.000, 67.000]	59.000, [50.000, 65.000]	0.084
Body mass index, (median, [IQR])	25.014, [22.383, 27.365]	24.836, [22.280, 26.927]	0.325
Weight, (median, [IQR])	67.000, [59.000, 76.000]	66.000, [59.000, 75.000]	0.582
Height, (median, [IQR])	165.000, [158.000, 171.000]	166.000, [158.000, 171.000]	0.522
Mean arterial blood pressure, (mean ± SD)	90.785 ± 12.533	91.643 ± 12.403	0.264
Pre diastolic blood pressure, (median, [IQR])	72.000, [64.000, 80.000]	73.000, [64.000, 80.000]	0.603
Pre systolic blood pressure, (median, [IQR])	127.000, [113.000, 141.000]	129.000, [116.000, 143.000]	0.132
Gender, (%)			0.397
Female	341, (38.575)	137, (36.053)	
Male	543, (61.425)	243, (63.947)	
Medical history			
Euroscore II score, (median, [IQR])	1.830, [0.930, 3.410]	1.610, [0.910, 3.080]	0.089
ASA physical status classification, (%)			0.444
1	4, (0.460)	4, (1.070)	
2	137, (15.765)	60, (16.043)	
3	483, (55.581)	195, (52.139)	
4	245, (28.193)	115, (30.749)	
Mallampati airway classification, (%)			0.224
1	362, (41.705)	139, (37.366)	
2	237, (27.304)	106, (28.495)	
3	262, (30.184)	120, (32.258)	
4	7, (0.806)	7, (1.882)	
NYHA functional classification, (%)			0.177
1	224, (25.339)	82, (21.579)	
2	333, (37.670)	152, (40.000)	
3	269, (30.430)	129, (33.947)	
4	58, (6.561)	17, (4.474)	
CCS class 4, (%)			0.943
No	846, (95.701)	364, (95.789)	
Yes	38, (4.299)	16, (4.211)	
Myocardial infarction within 90 days, (%)			0.816
No	849, (96.041)	366, (96.316)	
Yes	35, (3.959)	14, (3.684)	
Dyslipidemia, (%)			0.718
No	804, (90.950)	348, (91.579)	
Yes	80, (9.050)	32, (8.421)	
Diabetes mellitus, (%)			0.166
No	708, (80.090)	317, (83.421)	
Yes	176, (19.910)	63, (16.579)	
Diabetes on insulin, (%)			0.746
No	795, (89.932)	344, (90.526)	
Yes	89, (10.068)	36, (9.474)	
Hypertension, (%)			0.398
No	482, (54.525)	217, (57.105)	
Yes	402, (45.475)	163, (42.895)	
Previous cardiac surgery, (%)			0.893
No	754, (85.294)	323, (85.000)	
Yes	130, (14.706)	57, (15.000)	
Number of previous cardiac operations, (%)			
0	754, (85.294)	323, (85.000)	
1	125, (14.140)	55, (14.474)	
2	4, (0.452)	2, (0.526)	
3	1, (0.113)	0, (0.000)	

Table 1. Continued.

Variants	Training set, (n = 884)	Test set, (n = 380)	p
Chronic kidney disease, (%)			0.403
No	850, (96.154)	369, (97.105)	
Yes	34, (3.846)	11, (2.895)	
Infectious endocarditis, (%)			0.393
No	845, (95.588)	359, (94.474)	
Yes	39, (4.412)	21, (5.526)	
Neurological dysfunction, (%)			0.635
No	832, (94.118)	355, (93.421)	
Yes	52, (5.882)	25, (6.579)	
Pulmonary hypertension, (%)			0.214
0	590, (66.742)	237, (62.368)	
1	172, (19.457)	94, (24.737)	
2	96, (10.860)	38, (10.000)	
3	26, (2.941)	11, (2.895)	
Smoking, (%)			0.347
No	558, (63.194)	250, (65.963)	
Yes	325, (36.806)	129, (34.037)	
Alcohol, (%)			0.585
No	713, (80.747)	311, (82.058)	
Yes	170, (19.253)	68, (17.942)	
Preoperative coronary angiography, (%)			0.672
No	304, (34.389)	126, (33.158)	
Yes	580, (65.611)	254, (66.842)	
Critical preoperative state, (%)			0.161
No	797, (90.158)	352, (92.632)	
Yes	87, (9.842)	28, (7.368)	
Preoperative renal replacement therapy, (%)			0.213
No	876, (99.095)	379, (99.737)	
Yes	8, (0.905)	1, (0.263)	
Preoperative medication usage			
Digoxin, (%)			0.9
No	590, (66.742)	255, (67.105)	
Yes	294, (33.258)	125, (32.895)	
β-Blockers, (%)			0.828
No	406, (45.928)	172, (45.263)	
Yes	478, (54.072)	208, (54.737)	
Angiotensin-converting enzyme inhibitors, (%)			0.481
No	796, (90.045)	347, (91.316)	
Yes	88, (9.955)	33, (8.684)	
Angiotensin receptor inhibitors, (%)			0.366
No	777, (87.896)	327, (86.053)	
Yes	107, (12.104)	53, (13.947)	
Calcium channel blockers, (%)			0.968
No	571, (64.593)	245, (64.474)	
Yes	313, (35.407)	135, (35.526)	
Diuretics, (%)			0.169
No	230, (26.018)	85, (22.368)	
Yes	654, (73.982)	295, (77.632)	
Anticoagulants, (%)			0.982
No	631, (71.380)	271, (71.316)	
Yes	253, (28.620)	109, (28.684)	
Aspirin, (%)			0.992
No	700, (79.186)	301, (79.211)	
Yes	184, (20.814)	79, (20.789)	

Table 1. Continued.

Variants	Training set, (n = 884)	Test set, (n = 380)	*p*
Statins, (%)			0.659
No	636, (71.946)	278, (73.158)	
Yes	248, (28.054)	102, (26.842)	
Insulin, (%)			0.901
No	793, (89.706)	340, (89.474)	
Yes	91, (10.294)	40, (10.526)	
Oral hypoglycemic agents, (%)			0.293
No	745, (84.276)	329, (86.579)	
Yes	139, (15.724)	51, (13.421)	
Preoperative cardiac ultrasound			
Mean pulmonary arterial pressure, (median, [IQR])	22.000, [22.000, 42.000]	22.000, [22.000, 40.000]	0.151
Ejection fraction, (median, [IQR])	61.000, [54.000, 67.000]	61.000, [56.000, 67.000]	0.209
Inner diameter of main pulmonary artery, (median, [IQR])	2.500, [2.300, 2.800]	2.500, [2.200, 2.700]	0.343
Right ventricular diameter, (median, [IQR])	3.000, [2.700, 3.400]	3.100, [2.600, 3.500]	0.494
Right atrial diameter, (median, [IQR])	3.500, [3.200, 4.000]	3.500, [3.200, 4.100]	0.529
Left ventricular posterior wall thickness, (median, [IQR])	1.100, [1.000, 1.200]	1.100, [1.000, 1.200]	0.394
Interventricular septal thickness, (median, [IQR])	1.100, [1.000, 1.200]	1.100, [1.000, 1.200]	0.325
Left ventricular end-diastolic diameter, (median, [IQR])	4.800, [4.200, 5.500]	4.900, [4.300, 5.500]	0.384
Left atrial diameter, (median, [IQR])	4.000, [3.500, 4.800]	3.900, [3.500, 4.900]	0.828
Ascending aorta diameter, (median, [IQR])	3.500, [3.200, 4.000]	3.500, [3.100, 4.000]	0.412
Preoperative electrocardiogram			
Qtc interval, (median, [IQR])	439.000, [419.000, 457.000]	436.000, [415.000, 454.000]	0.113
Qt interval, (median, [IQR])	392.000, [366.000, 420.000]	394.000, [364.000, 422.000]	0.958
Qrs duration, (median, [IQR])	96.000, [86.000, 106.000]	96.000, [84.000, 106.000]	0.912
Pr interval, (median, [IQR])	152.000, [120.000, 172.000]	152.000, [120.000, 174.000]	0.965
Abnormal T wave, (%)			0.904
No	328, (37.273)	143, (37.632)	
Yes	552, (62.727)	237, (62.368)	
Abnormal Q wave, (%)			0.857
No	782, (88.864)	339, (89.211)	
Yes	98, (11.136)	41, (10.789)	
Atrial flutter, (%)			0.724
No	865, (97.851)	373, (98.158)	
Yes	19, (2.149)	7, (1.842)	
Atrial fibrillation, (%)			0.98
No	702, (79.412)	302, (79.474)	
Yes	182, (20.588)	78, (20.526)	
Baseline laboratory findings			
Chloride, (median, [IQR])	102.900, [100.300, 105.100]	102.400, [100.300, 104.900]	0.457
Serum sodium, (median, [IQR])	141.300, [139.550, 143.000]	141.400, [139.400, 142.800]	0.911
Serum potassium, (median, [IQR])	4.040, [3.760, 4.280]	3.990, [3.740, 4.250]	0.199
Urea nitrogen, (median, [IQR])	5.930, [4.778, 7.560]	5.717, [4.550, 7.400]	0.09
Creatinine clearance, (median, [IQR])	79.464, [63.376, 98.350]	82.326, [67.119, 99.972]	0.06
Serum creatinine, (median, [IQR])	78.850, [67.400, 92.700]	78.000, [66.500, 90.900]	0.246
Blood glucose, (median, [IQR])	5.120, [4.640, 6.120]	5.050, [4.580, 5.910]	0.166
Direct bilirubin, (median, [IQR])	4.000, [2.800, 6.000]	4.100, [2.800, 5.900]	0.96
Total bilirubin, (median, [IQR])	12.600, [9.200, 17.750]	12.100, [9.300, 17.500]	0.888
Albumin, (median, [IQR])	40.800, [38.100, 43.300]	40.900, [38.100, 43.450]	0.551
Total protein, (median, [IQR])	67.700, [63.800, 71.900]	67.800, [64.000, 71.600]	0.725
Aspartate aminotransferase, (median, [IQR])	18.200, [14.800, 24.900]	18.200, [15.000, 24.400]	0.978
Alanine aminotransferase, (median, [IQR])	18.300, [12.500, 27.800]	17.900, [12.600, 27.000]	0.989
Plasma fibrinogen, (median, [IQR])	3.090, [2.600, 3.760]	3.050, [2.520, 3.690]	0.308
International normalized ratio, (median, [IQR])	1.060, [1.000, 1.160]	1.060, [1.000, 1.140]	0.791
Activated partial thromboplastin time, (median, [IQR])	36.900, [34.200, 40.100]	37.100, [34.000, 40.500]	0.662

Table 1. Continued.

Variants	Training set, (n = 884)	Test set, (n = 380)	p
Platelet count, (median, [IQR])	191.000, [152.000, 236.000]	188.000, [154.000, 231.000]	0.571
Hematocrit, (median, [IQR])	0.388, [0.352, 0.422]	0.392, [0.350, 0.427]	0.614
Lymphocyte count, (median, [IQR])	0.285, [0.222, 0.355]	0.293, [0.226, 0.349]	0.714
Neutrophil count, (median, [IQR])	0.610, [0.541, 0.680]	0.601, [0.544, 0.674]	0.552
White blood cell count, (median, [IQR])	6.200, [5.070, 7.520]	6.130, [5.050, 7.260]	0.453
Red blood cell count, (median, [IQR])	4.350, [3.960, 4.770]	4.360, [3.950, 4.790]	0.645
Hemoglobin, (median, [IQR])	133.000, [119.000, 146.000]	135.000, [119.500, 147.000]	0.557
Surgery type and interoperative status			
Mean arterial blood pressure (Post), (mean ± SD)	79.155 ± 9.104	79.032 ± 9.857	0.83
Diastolic blood pressure, (mean ± SD)	63.144 ± 9.722	63.226 ± 10.066	0.891
Systolic blood pressure, (median, [IQR])	111.000, [103.000, 120.000]	110.000, [102.000, 120.000]	0.386
Plt transfusion during surgery, (median, [IQR])	0.000, [0.000, 1.000]	0.000, [0.000, 1.000]	0.541
Ffp transfusion during surgery, (median, [IQR])	4.800, [0.000, 5.700]	4.900, [0.000, 5.500]	0.794
Prbc transfusion during surgery, (median, [IQR])	2.500, [0.000, 4.000]	2.500, [0.000, 4.000]	0.984
Operation time, (median, [IQR])	4.667, [3.917, 5.667]	4.583, [3.917, 5.500]	0.726
Anesthesia time, (median, [IQR])	5.500, [4.750, 6.500]	5.500, [4.667, 6.500]	0.688
Cryoprecipitate treatment, (%)			0.182
No	833, (94.231)	365, (96.053)	
Yes	51, (5.769)	15, (3.947)	
Weight of the intervention, (%)			
1	513, (58.032)	230, (60.526)	
2	220, (24.887)	87, (22.895)	
3	126, (14.253)	55, (14.474)	
4	23, (2.602)	8, (2.105)	
5	2, (0.226)	0, (0.000)	
Minimally invasive treatment, (%)			0.979
No	731, (82.692)	314, (82.632)	
Yes	153, (17.308)	66, (17.368)	
Emergency, (%)			0.214
No	837, (94.683)	366, (96.316)	
Yes	47, (5.317)	14, (3.684)	
Anesthesia records			
Neutralizd act, (median, [IQR])	121.000, [112.000, 131.000]	121.000, [112.000, 132.000]	0.402
Heparinized act, (median, [IQR])	575.000, [503.000, 722.000]	566.000, [498.000, 680.000]	0.303
Basic act, (median, [IQR])	118.000, [109.000, 129.000]	119.000, [110.000, 129.000]	0.461
NovoSeven therapy, (%)			0.745
No	848, (95.928)	366, (96.316)	
Yes	36, (4.072)	14, (3.684)	
Intraoperatively used nitroglycerin, (%)			0.849
No	516, (58.371)	224, (58.947)	
Yes	368, (41.629)	156, (41.053)	
Epinephrine administration, (%)			0.201
No	758, (85.747)	336, (88.421)	
Yes	126, (14.253)	44, (11.579)	
Norepinephrine administration, (%)			0.885
No	871, (98.529)	374, (98.421)	
Yes	13, (1.471)	6, (1.579)	
Amiodarone administration, (%)			0.971
No	795, (89.932)	342, (90.000)	
Yes	89, (10.068)	38, (10.000)	
Extracorporeal circulation recording			
Aortic clamp time, (median, [IQR])	91.000, [65.000, 126.000]	85.000, [63.000, 124.000]	0.234
Cardiopulmonary bypass time, (median, [IQR])	122.000, [91.000, 167.000]	118.000, [89.000, 162.000]	0.261
Liquid balance, (median, [IQR])	700.000, [100.000, 1180.000]	750.000, [250.000, 1200.000]	0.185

Table 1. Continued.

Variants	Training set, (n = 884)	Test set, (n = 380)	*p*
Hematocrit after cardiopulmonary bypass, (median, [IQR])	0.310, [0.290, 0.330]	0.310, [0.290, 0.333]	0.467
Hemoglobin after cardiopulmonary bypass, (median, [IQR])	103.000, [96.000, 110.000]	103.000, [96.000, 113.000]	0.53
Urine output (mL/Kg/h), (median, [IQR])	2.653, [1.439, 4.263]	2.570, [1.558, 4.018]	0.704
Urine output (mL/Kg), (median, [IQR])	12.535, [6.818, 20.522]	12.261, [7.031, 19.444]	0.626
Urine output (mL), (median, [IQR])	850.000, [450.000, 1350.000]	800.000, [450.000, 1290.000]	0.565
Body temperature after cardiopulmonary bypass, (median, [IQR])	36.200, [36.000, 36.500]	36.200, [36.000, 36.500]	0.416
Minimum core body temperature, (median, [IQR])	32.200, [31.500, 33.100]	32.400, [31.600, 33.000]	0.308
The total liquid infusion volume, (median, [IQR])	4350.000, [3450.000, 5150.000]	4350.000, [3400.000, 5100.000]	0.912
Htk cardioplegic solution (all), (median, [IQR])	2000.000, [2000.000, 2500.000]	2000.000, [2000.000, 2500.000]	0.169
Htk cardioplegic solution (into body), (median, [IQR])	1900.000, [620.000, 2500.000]	1900.000, [700.000, 2400.000]	0.737
Mannitol injection (25%), (mean ± SD)	180.306 ± 54.967	175.397 ± 51.336	0.139
Sodium bicarbonate injection (5%), (median, [IQR])	300.000, [250.000, 400.000]	300.000, [250.000, 400.000]	0.919
Ringer lactate solution, (median, [IQR])	1400.000, [1300.000, 1400.000]	1400.000, [1300.000, 1400.000]	0.893
Human albumin solution (20%), (median, [IQR])	100.000, [100.000, 100.000]	100.000, [100.000, 100.000]	0.894
Dosage of plasma substitute, (mean ± SD)	119.909 ± 227.694	104.737 ± 202.299	0.262
Perioperative blood loss (mL/Kg/h), (median, [IQR])	1.207, [0.893, 1.579]	1.180, [0.909, 1.490]	0.468
Perioperative blood loss (mL/Kg), (median, [IQR])	5.714, [4.167, 7.500]	5.455, [4.225, 7.143]	0.212
Perioperative blood loss (mL), (median, [IQR])	400.000, [300.000, 500.000]	400.000, [300.000, 500.000]	0.105
Defibrillation treatment, (%)			0.671
No	587, (66.403)	257, (67.632)	
Yes	297, (33.597)	123, (32.368)	
Number of defibrillation, (%)			
	587, (66.403)	257, (67.632)	
1	257, (29.072)	104, (27.368)	
2	29, (3.281)	11, (2.895)	
3	7, (0.792)	7, (1.842)	
4	3, (0.339)	0, (0.000)	
5	1, (0.113)	1, (0.263)	
Temporary pacemaker implantation, (%)			0.654
No	745, (86.931)	319, (85.984)	
Yes	112, (13.069)	52, (14.016)	0.637
AKI in compliance with KDIGO standards			
Acute kidney injury, (%)			0.515
No	619, (70.023)	273, (71.842)	
Yes	265, (29.977)	107, (28.158)	

IQR, Interquartile Range; ASA, American Society of Anesthesiologists; NYHA, New York Heart Association; CCS, Canadian Cardiovascular Society; AKI, Acute kidney injury; KDIGO, Kidney Disease Improving Global Outcomes.

coefficients (Fig. 2). A list of the 22 characteristic variables and their corresponding coefficients are shown in **Supplementary Table 1**.

Machine Learning Model

Machine learning models are evaluated using AUC, the area under the ROC curve enclosed by coordinate axes. AUC ≥0.8 is generally considered a good discriminative power of the machine learning model [22]. In contrast, the horizontal coordinate of the ROC curve is the False Positive Rate (also called False Positive Rate), and the vertical coordinate is the True Positive Rate (True Positive Rat). When comparing the prediction performance of multiple models, only the AUC score needs to be calculated, which enables us to distinguish and compare the prediction performance of different models [23]. This way, a more precise comparison was made between sensitivity and specificity indicators. In the training set, the AUC score of the XGBoost model was 0.959 (95% confidence interval (CI): 0.946–0.972), while the AUC score of the inner validation was 0.763 (95% CI: 0.654–0.871). The LRC model had an AUC score of 0.786 (95% CI: 0.751–0.821), while the inner validation AUC score was 0.772 (95% CI: 0.662–0.881). With the LGBM model, the AUC score was 0.532 (95% CI: 0.505–0.560), while the inner validated AUC score was 0.543 (95% CI: 0.460–0.626). The RFC model had an AUC score of 0.998 (95% CI: 0.996–1.000), compared to 0.781

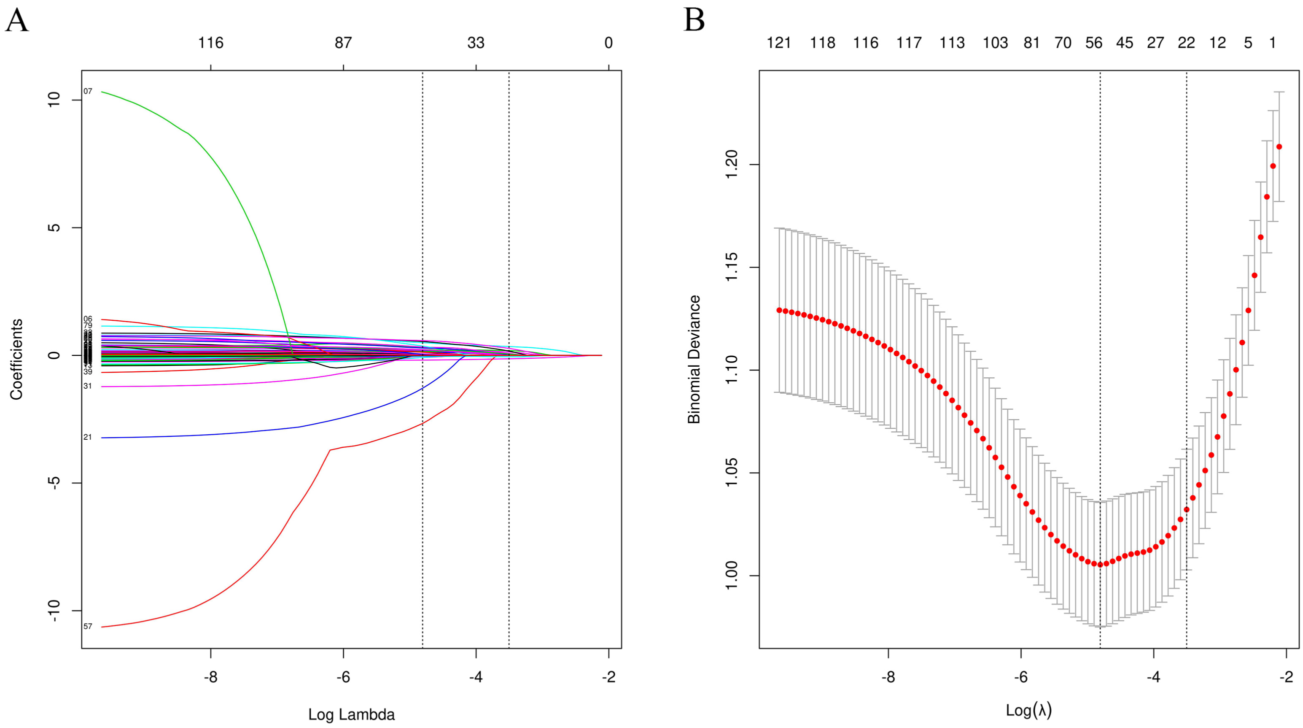

Fig. 2. The result of LASSO regression. (A) LASSO coefficient curves for 125 risk factors. (B) At the best score of the minimum criteria (left) and 1-s.e. criteria (right) we graph two vertical dashed lines. Selected 22 risk factors with the help of LASSO regression analysis (1-s.e. criteria (right)), See **Supplementary Table 1** for detailed information).

(95% CI: 0.677–0.885) for the inner validation. The AdaBoost model had an AUC of 0.831 (95% CI: 0.800–0.861); meanwhile, its inner validated AUC score was 0.744 (95% CI: 0.626–0.862). The KNN model's AUC score was 0.879 (95% CI: 0.857–0.901), whereas the inner validated AUC score was 0.687 (95% CI: 0.569–0.805).

The ROC curves of these six machine learning models are shown in Fig. 3 and , and the values of other metrics are shown in Table 2. K-fold cross-validation can split the training set data into k parts and select one as the new training set for model construction while using the remaining k-1 parts as the inner validation set to avoid overfitting the machine learning model well. Furthermore, taking the DCA curves of the six models together, the RFC model has more robust DCA curves and higher net benefit ratios simultaneously. Therefore, it can be found that the RFC model has the best prediction performance and the best stability among the above six machine learning prediction models.

RFC Model Performance and Interpretation

The RFC machine learning model has the best prediction effect among the above six models. The above RFC model training parameters were used to construct the RFC model with the training set, and then the test set data were used to validate it. Moreover, the Python SHAP package was used to explain the effect of feature variables on the classification prediction results. The AUC scores of the RFC model were 0.997 (95% CI: 0.995–1.000) in the training set, 0.790 (95% CI: 0.685–0.894) in the inner validation set, and 0.778 (95% CI: 0.726–0.830) in the test set, respectively. The ROC and DCA curves of the model are shown in Fig. 4. The values of other metrics are shown in Table 3.

Furthermore, the feature factors in the RFC machine learning model that influence the CSA-AKI are shown in Fig. 5. Among them, the highest impact factor is creatinine clearance (CRC), followed by Age (AGE) and urine output (UOPH (mL/kg/h), under surgery). Fig. 5A depicts the prediction model's SHAP summary plot, comprising 20 feature variables ranked by their impact on the CSA-AKI. The impact of different variables on the prediction results is shown in Fig. 5B. In contrast, red indicates high eigenvalues, purple indicates eigenvalues close to the average total value, and blue indicates low eigenvalues. Moreover, the RFC model's prediction results for a particular individual showed that creatinine clearance and anesthesia time had a higher impact on CSA-AKI (Fig. 5C).

Discussion

The CSA-AKI is driven by various clinical factors, with a fast change in the patient's condition, leading to an increased economic burden [24]. Thus, a prediction model that helps clinicians intervene early to avoid AKI is needed [16]. We used patients' medical records who underwent ex-

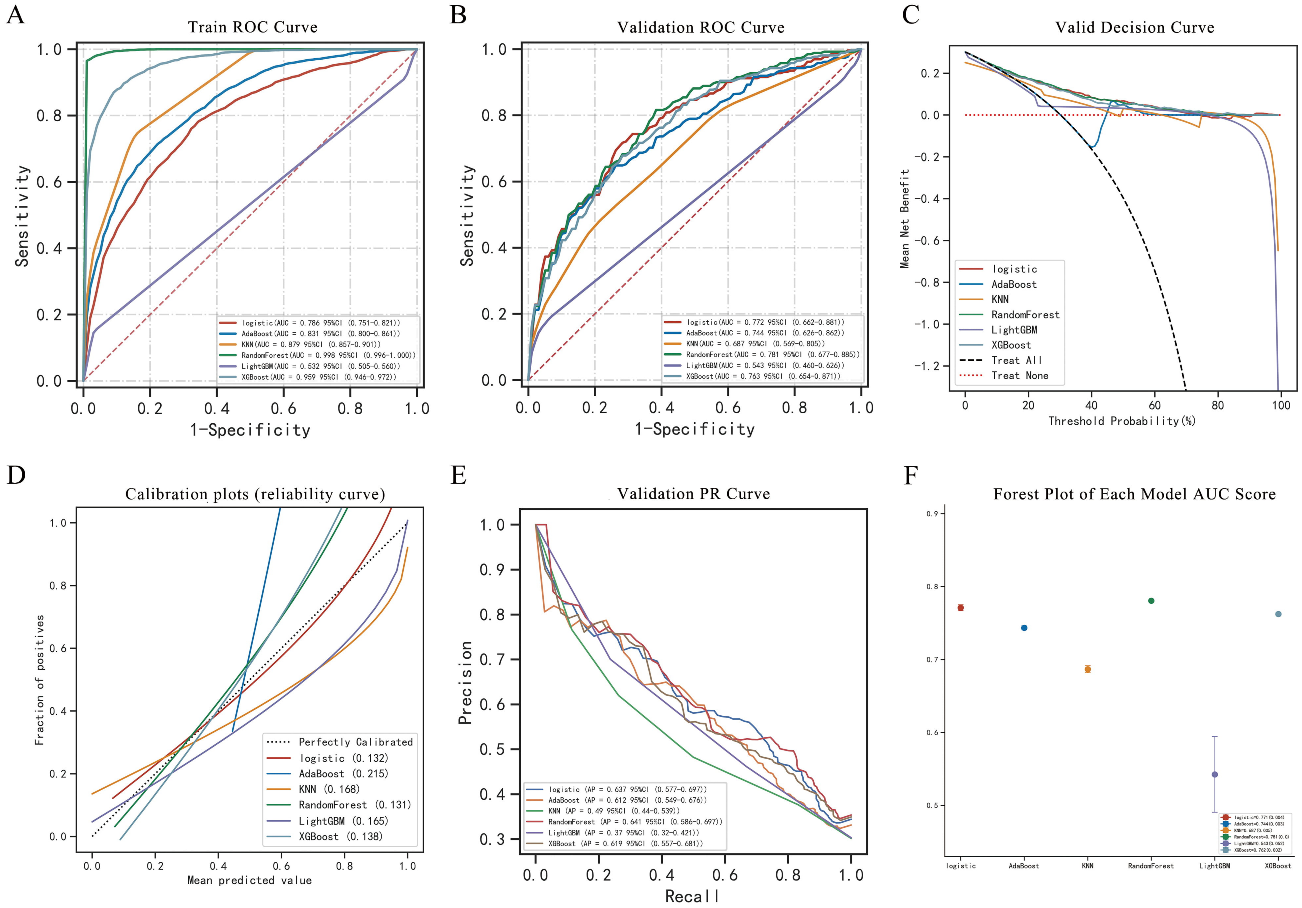

Fig. 3. The ROC curves of different machine learning prediction models. (A) ROC curves and AUC scores of each machine learning model in the training set: XGBoost AUC score is 0.959; LRC AUC score is 0.786; LGBM AUC score is 0.532; RFC AUC score is 0.998; AdaBoost AUC score is 0.831; KNN AUC score is 0.879. (B) ROC curves and AUC scores of each machine learning model in the inner validation set: XGBoost AUC score is 0.763; LRC AUC score is 0.772; LGBM AUC score is 0.543; RFC AUC score is 0.781; AdaBoost AUC score is 0.744; KNN AUC score is 0.687. (C) DCA curves of each machine learning model in the inner validation set. The RFC model (green) has the highest net benefit rate among all machine learning models. (D) Calibration curve. Of all models, the RFC model has a better degree of fit (green). (E) Precision-Recall (PR) curve and Aera under PR curve (AP). RFC model (green) has the largest AP score of 0.641 among all models. (F) Forest Plot of each model AUC score. RFC model (green) has a higher AUC score than other models (AUC score: 0.781). ROC, Receiver Operating Characteristic; AUC, Area Under Curve; LGBM, light gradient boosting machine; RFC, random forest classifier; KNN, k-nearest neighbor; DCA, Decision Curve Analysis.

tracorporeal cardiac surgery, screened for feature variables, and then used multiple machine learning algorithms and built prediction models to predict the occurrence of AKI after cardiac surgery. For this study, the RFC classification prediction model could achieve an AUC value of 0.778 in the test set, while the DCA curve showed a better net benefit than other models. Xue *et al*. [25] have also constructed a CSA-AKI classification prediction model. They found that the random forest model had the best prediction performance and could achieve an AUC value of 0.858 (95% CI: 0.792–0.923). Despite having a stronger predictive performance than our study, the model included only 215 patients, had discrepancies in sample subject selection or the medical record data content, and was not generalizable.

In contrast, this study contains more information on cardiac surgery modalities and medical records than that and maybe more extensive in applicability. Additionally, Petrosyan *et al*. [26] constructed a prediction model using a hybrid machine learning algorithm with 32 medical histories of 6522 patients and an AUC of 0.74. However, the study only used the patient's preoperative history to predict the occurrence of AKI after surgery and failed to include the patient's surgery status and laboratory test data; thus, the model's predictive performance was not satisfied. This study's prediction model outperformed that one. According to previous studies, machine learning algorithms can extract clinical data features and predict clinical outcomes by understanding the link between clinical data features and clinical outcomes. Machine learning models can help physi-

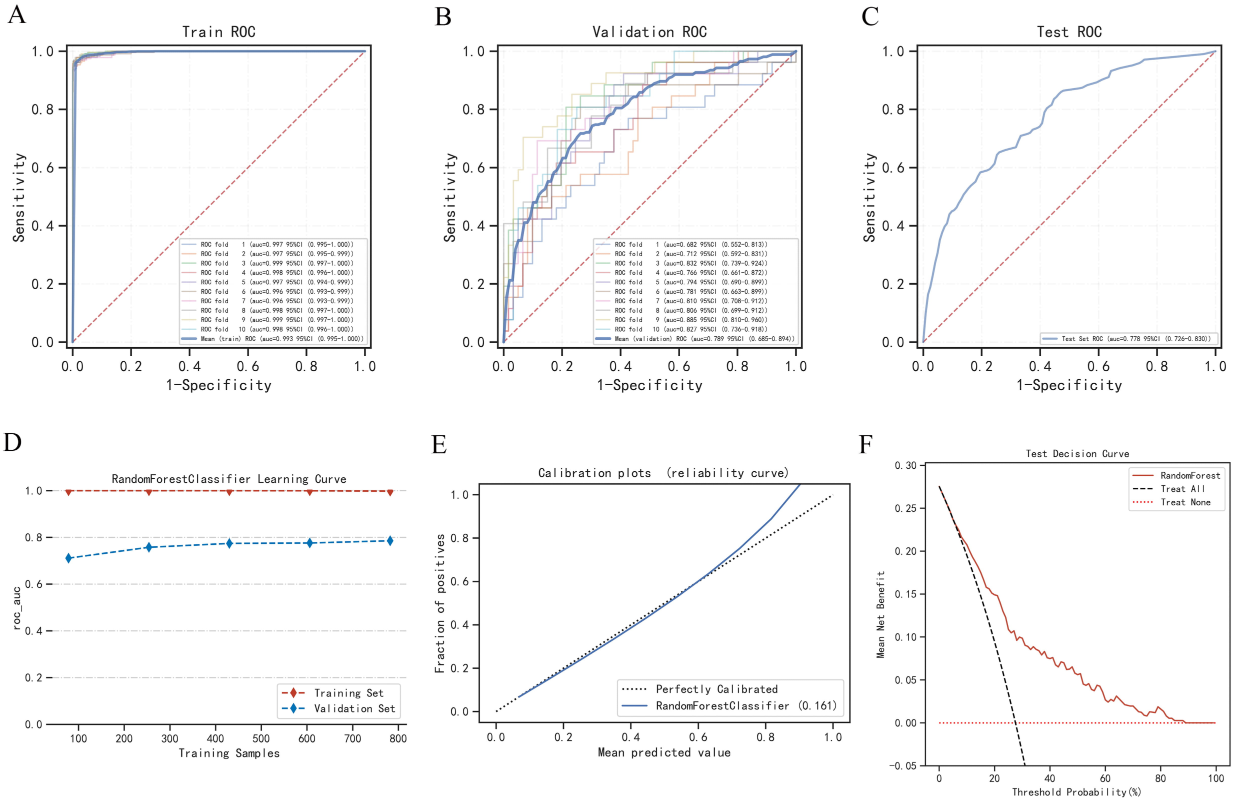

Fig. 4. Diagram of different metrics of RFC model. (A) ROC curve of the RFC model in the training set (10-fold cross-validation) with an AUC value of 0.993. (B) The ROC curve of the RFC model in the inner validation set (10-fold cross-validation) with an AUC value of 0.789. (C) ROC curve of the RFC model in the test set with an AUC value of 0.778. (D) Variation of the AUC values of the RFC model with different training volumes, eventually approaching stability. (E) Calibration curve plot for the RFC model. The dotted line is the calibration curve under ideal conditions, and the dark blue curve is the calibration curve of RFC. (F) DCA curve of RFC model.

cians identify changes in patients and intervene in a timelier manner in the clinical management of such diseases [9,27–30].

Six machine learning algorithms were utilized in our study, chosen for their effectiveness in handling classification tasks on structured data. The selected models included XGBoost, LRC, LGBM, RFC, AdaBoost, and KNN. XGBoost is an ensemble learning technique renowned for its precision and speed, competent for handling high-dimensional data and missing values. LRC is an easily interpretable, uncomplicated linear model that is efficient in performing binary classification tasks. LGBM, akin to XGBoost, is swifter and memory-efficient, making it perfect for large datasets. RFC is another ensemble technique adept at handling high-dimensional data, missing values, and noise. AdaBoost combines weak classifiers for binary classification, renowned for their accuracy and interpretability. KNN is a lazy learning method appropriate for structured data, offering simplicity and interpretability. We opted for these models due to their capability to manage structured data, missing values, noise, and their interpretability, speed, and accuracy. Although other models exist, these six have a validated track record in various applications.

LASSO regression is a penalty-based method for variable selection on sample data, which compresses the coefficients of insignificant variables to filter the feature variables, reduce the model's complexity and improve the model's prediction accuracy [31]. LASSO regression is characterized by variable selection and complexity regularization while fitting a generalized linear model; thus, it can model and predict continuous, binary or multivariate discrete variables [32]. Moreover, the algorithm can control the complexity of the model through a series of parameters to avoid overfitting [33]. This work used LASSO regression to simplify and downscale 125 clinical data, yielding 22 feature variables after removing insignificant variables. Simplifying feature variables enables machine learning models to exclude invalid variables, accurately identify associations between feature variables and clinical outcomes, and improve model prediction performance. Furthermore, the screening feature variables may provide a new perspective on the disease and may help physicians better understand the changes in the patient's condition.

LASSO regression can screen for feature variables but cannot calculate the impact of feature variables on the predicted clinical outcomes [32]. However, SHAP can explain how feature variables affect prediction results and machine

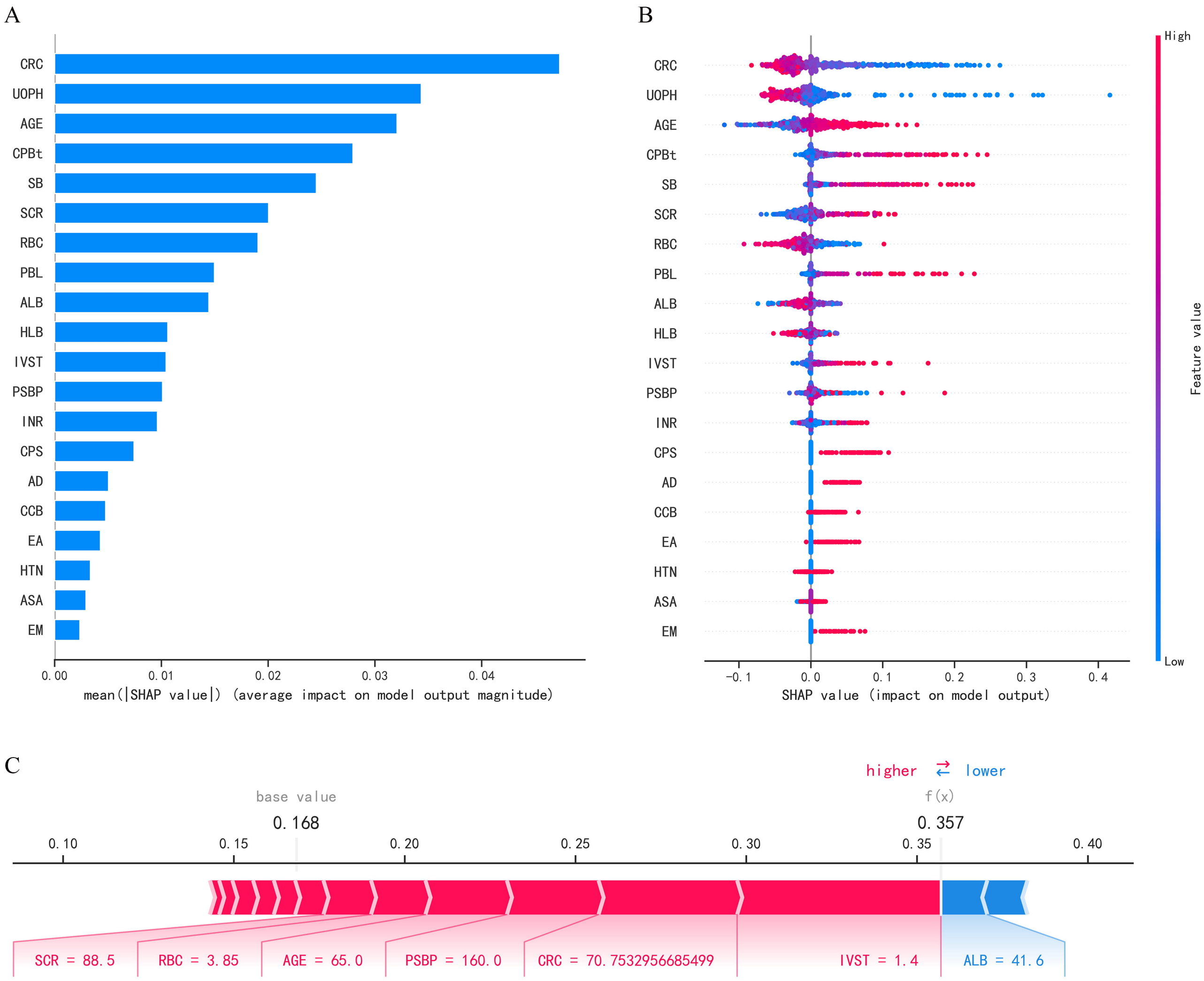

Fig. 5. The SHAP values and interpretation of the model for the RFC model. (A) Top 20 variables ranked in importance by mean (|SHAP value|); (B) Summary of the top 20 risk factors ranked in importance with stability and using the optimal model of interpretation. A higher SHAP value of a feature is associated with a higher risk of death for the patient. Values of features in red represent higher values. (C) Interpretation of the prediction results obtained from the RFC model. AGE, Age; ASA, Asa Physical Status Classification; HTN, Hypertension; CKD, Chronic Kidney Disease; PSBP, Systolic Blood Pressure; CPS, Critical Preoperative State; EA, Epinephrine Administration; AD, Amiodarone Administration; PBL, Perioperative Blood Loss (mL); SB, Sodium Bicarbonate Injection (5%); UOPH, Urine Output (mL/Kg/H); CPBt, Cardiopulmonary Bypass Time; EM, Emergency; IVST, Interventricular Septal Thickness; CCB, Calcium Channel Blockers; HLB, Hemoglobin; RBC, Red Blood Cell Count; INR, International Normalized Ratio; ALB, Albumin; SCR, Serum Creatinine; CRC, Creatinine Clearance; AKI, Acute kidney injury.

learning model prediction factors. It works by calculating each feature variable's contribution value (SHapley Value) in each sample and then summing the SHapley Values of the corresponding feature variables to explain how each feature variable affects the model's predicted value [34].

The SHAP algorithm was used in this study to find the influential factors affecting the RFC prediction model for predicting the CAS-AKI, and the top three variables were creatinine clearance rate (CRC), age and urine output (mL/kg/h), under surgery) in that order (Fig. 4). CRC is an important indicator of kidney function; normal CRC is 80–120 mL/min, and a decrease in CRC indicates diminished kidney filtration function [18]. In the RFC prediction model constructed in this study, a lower CRC value (higher SHAP value) predicted a greater chance of CSA-AKI in that individual (Fig. 5B). However, in this study, the mean CRC value was 82.94 mL/min, whereas AKI patients had a mean value of 72.275 mL/min. Patients without AKI had a mean value of 87.560 mL/min, which was significantly different ($p < 0.001$). This also indicates that preoperative CRC must be closely monitored and followed up to avoid postoperative AKI in patients undergoing cardiac surgery with extracorporeal circulation [35–37]. Second, in the RFC prediction model, post-operative AKI is more common in patien-

Table 2. Machine learning model metric values in the training set and inner validation set.

Machine learning model		Auc (95% CI)	Cutoff (95% CI)	Accuracy (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	F1 score (95% CI)	Kappa (95% CI)
Training set results	AdaBoost	0.831 (0.800–0.861)	0.456 (0.451–0.460)	0.762 (0.748–0.776)	0.729 (0.690–0.768)	0.778 (0.741–0.814)	0.592 (0.562–0.621)	0.869 (0.858–0.880)	0.649 (0.645–0.653)	0.471 (0.457–0.486)
	KNN	0.879 (0.857–0.901)	0.500 (0.500–0.500)	0.795 (0.793–0.798)	0.740 (0.730–0.750)	0.850 (0.843–0.858)	0.852 (0.840–0.864)	0.786 (0.784–0.788)	0.792 (0.783–0.801)	0.425 (0.417–0.434)
	LGBM	0.532 (0.505–0.560)	1.045 (0.986–1.104)	0.698 (0.697–0.699)	0.141 (0.081–0.200)	0.979 (0.971–0.988)	NaN (NaN-NaN)	0.698 (0.698–0.699)	NaN (NaN-NaN)	–0.001 (–0.002–0.001)
	LRC	0.786 (0.751–0.821)	0.273 (0.261–0.285)	0.711 (0.700–0.722)	0.758 (0.737–0.779)	0.693 (0.669–0.717)	0.516 (0.502–0.530)	0.867 (0.862–0.873)	0.613 (0.608–0.617)	0.395 (0.383–0.407)
	RFC	0.998 (0.996–1.000)	0.321 (0.308–0.333)	0.981 (0.978–0.984)	0.971 (0.966–0.976)	0.988 (0.982–0.993)	0.972 (0.960–0.984)	0.986 (0.984–0.988)	0.971 (0.967–0.976)	0.956 (0.949–0.963)
	XGBoost	0.959 (0.946–0.972)	0.376 (0.363–0.390)	0.894 (0.890–0.898)	0.887 (0.872–0.902)	0.899 (0.887–0.911)	0.792 (0.776–0.808)	0.947 (0.941–0.953)	0.836 (0.833–0.840)	0.757 (0.751–0.764)
10-fold cross-validation within the training set	AdaBoost	0.744 (0.626–0.862)	0.456 (0.451–0.460)	0.709 (0.680–0.738)	0.695 (0.610–0.780)	0.753 (0.644–0.862)	0.527 (0.488–0.566)	0.827 (0.804–0.849)	0.592 (0.556–0.628)	0.352 (0.313–0.391)
	KNN	0.687 (0.569–0.805)	0.500 (0.500–0.500)	0.730 (0.709–0.750)	0.554 (0.432–0.676)	0.745 (0.635–0.855)	0.620 (0.537–0.702)	0.746 (0.732–0.760)	0.556 (0.487–0.624)	0.229 (0.161–0.297)
	LGBM	0.543 (0.460–0.626)	1.045 (0.986–1.104)	0.700 (0.696–0.704)	0.252 (0.074–0.429)	0.885 (0.699–1.071)	NaN (NaN-NaN)	0.699 (0.696–0.703)	NaN (NaN-NaN)	0.005 (–0.005–0.016)
	LRC	0.772 (0.662–0.881)	0.273 (0.261–0.285)	0.696 (0.661–0.731)	0.736 (0.647–0.825)	0.761 (0.685–0.837)	0.501 (0.462–0.540)	0.856 (0.825–0.888)	0.593 (0.540–0.647)	0.364 (0.298–0.429)
	RFC	0.781 (0.677–0.885)	0.321 (0.308–0.333)	0.718 (0.685–0.751)	0.778 (0.699–0.857)	0.720 (0.642–0.798)	0.530 (0.483–0.578)	0.839 (0.814–0.863)	0.626 (0.577–0.676)	0.380 (0.312–0.447)
	XGBoost	0.763 (0.654–0.871)	0.376 (0.363–0.390)	0.719 (0.694–0.744)	0.798 (0.740–0.855)	0.656 (0.581–0.731)	0.534 (0.495–0.574)	0.819 (0.800–0.837)	0.636 (0.601–0.672)	0.359 (0.306–0.412)

XGBoost, extreme gradient boosting; AdaBoost, Adaptive Boosting.

Table 3. RFC learning model metric values in the training set, inner validation set and test set.

Metrics	Training set	Inner validation set	Test set
Auc (95% CI)	0.997 (0.995–1.000)	0.790 (0.685–0.894)	0.778 (0.726–0.830)
Cutoff (95% CI)	0.323 (0.310–0.336)	0.323 (0.310–0.336)	0.315
Accuracy (95% CI)	0.982 (0.979–0.984)	0.733 (0.709–0.757)	0.719
Sensitivity (95% CI)	0.969 (0.963–0.975)	0.722 (0.643–0.801)	0.66
Specificity (95% CI)	0.989 (0.984–0.994)	0.789 (0.717–0.862)	0.745
Positive predictive value (95% CI)	0.975 (0.965–0.986)	0.552 (0.518–0.586)	0.492
Negative predictive value (95% CI)	0.985 (0.982–0.987)	0.844 (0.826–0.863)	0.837
F1 score (95% CI)	0.972 (0.968–0.976)	0.621 (0.579–0.662)	0.564

ts with longer anesthetic duration. This may indicate that the longer the general anesthesia, the poorer the kidney blood supply and the greater the probability of impaired function. Zhang *et al*. [38] also found that the AKI risk after liver transplantation increased as the duration of anesthesia increased and intraoperative urine output decreased. This shows that longer anesthesia and higher anesthetic drug use may prolong renal artery constriction, worsening renal injury and leading to AKI. However, the influence of anesthesia duration and intraoperative urine volume on AKI related to other surgeries needs additional study.

The incidence of AKI after extracorporeal and non-extracorporeal cardiac surgery differs, and this study did not address the influence of extracorporeal circulation on AKI [16]. This may be due to more instability in patient hemodynamics under extracorporeal circulation conditions, leading to inadequate renal blood perfusion and acute postoperative renal injury. Furthermore, the surgical trauma and intraoperative anesthesia associated with different surgical procedures are not identical and need to be considered. The RFC machine learning model constructed in this study to predict the CSA-AKI can only be used for patients with extracorporeal circulation conditions. In the next step, we will incorporate all types of cardiac surgery patients, adopt extracorporeal circulation as a feature variable, and analyze surgical trauma from diverse procedures to develop a more comprehensive prediction model.

Conclusion

The LASSO regression and various machine learning algorithms were used in this study to construct a prediction model to predict the occurrence of AKI after cardiac surgery with extracorporeal circulation. The RFC prediction model had the highest AUC value of 0.778 and net benefit according to its DCA curve of the six machine learning models. The SHAP model interpretation algorithm identified the three variables that contributed most to the predicted outcome under the model: CRC, age, and urine output. In summary, a random forest classifier model predicted CSA-AKI with good predictive performance.

Availability of Data and Materials

The original data that were used to support this study can be obtained from the corresponding author.

Author Contributions

YT, XN and FL: Conception of the idea, data collection and analysis, manuscript writing, edition, and critical revision of the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

This study was reviewed by the Ethics Committee of the Third Hospital of Hebei Medical University and the Institutional Review Board of Chinese PLA General Hospital and approved to exclude participants from informed consent (S2022-360-01).

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.59958/hsf.5673.

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