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Research article

Machine learning-based model to predict severe acute kidney injury after total aortic arch replacement for acute type A aortic dissection

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ABSTRACT

Background: Severe acute kidney injury (AKI) after total aortic arch replacement (TAAR) is related to adverse outcomes in patients with acute type A aortic dissection (ATAAD). However, the early prediction of severe AKI remains a challenge. This study aimed to develop a novel model to predict severe AKI after TAAR in ATAAD patients using machine learning algorithms.
Methods: A total of 572 ATAAD patients undergoing TAAR were enrolled in this retrospective study, and randomly divided into a training set (70 %) and a validation set (30 %). Lasso regression, support vector machine-recursive feature elimination and random forest algorithms were used to screen indicators for severe AKI (defined as AKI stage III) in the training set, respectively. Then the intersection indicators were selected to construct models through artificial neural network (ANN) and logistic regression. The AUC-ROC curve was employed to ascertain the prediction efficacy of the ANN and logistic regression models.
Results: The incidence of severe AKI after TAAR was 22.9 % among ATAAD patients. The intersection predictors identified by different machine learning algorithms were baseline serum creatinine and ICU admission variables, including serum cystatin C, procalcitonin, aspartate transaminase, platelet, lactic dehydrogenase, urine N-acetyl-β-D-glucosidase and Acute Physiology and Chronic Health Evaluation II score. The ANN model showed a higher AUC-ROC than logistic regression (0.938 vs 0.908, $p < 0.05$). Furthermore, the ANN model could predict 89.1 % of severe AKI cases beforehand. In the validation set, the superior performance of the ANN model

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was further confirmed in terms of discrimination ability (AUC = 0.916), calibration curve analysis and decision curve analysis.

Conclusion: This study developed a novel and reliable clinical prediction model for severe AKI after TAAR in ATAAD patients using machine learning algorithms. Importantly, the ANN model showed a higher predictive ability for severe AKI than logistic regression.

1. Introduction

Acute type A aortic dissection (ATAAD) is an emergency and critical cardiovascular condition with a high risk of complications, and the mortality rate can reach 25 % after surgery [1]. Based on Stanford classification, ATAAD opens in the ascending aorta and is usually torn at the proximal or distal end, requiring emergency surgical repair. When ATAAD involves the aortic arch, patients need a more stringent surgical procedure and perioperative nursing. Recent studies have reported that total aortic arch replacement (TAAR) with frozen elephant trunk is widely used in complex aortic arch diseases and can decrease organ dysfunction after surgery [2,3]. Hence, TAAR has become a routine surgical procedure for ATAAD patients.

Acute kidney injury (AKI) is a common complication after surgery among ATAAD patients. Past studies reported that the incidence of AKI after thoracic aortic surgery ranged from 26.0 % to 77.6 % [4–8]. Postoperative AKI is closely correlated with major adverse outcomes [9,10]. Importantly, severe AKI (defined as AKI stage III) is associated with a higher renal replacement therapy (RRT) rate, longer ICU stay and increased mortality than nonsevere AKI [11–13]. Studies have recently been performed on renal outcomes after the TAAR procedure among ATAAD patients [14–16]. However, few studies have predicted severe AKI after TAAR in ATAAD patients, and some classic renal biomarkers have also not been included [17]. A previous study demonstrated that combining classic renal

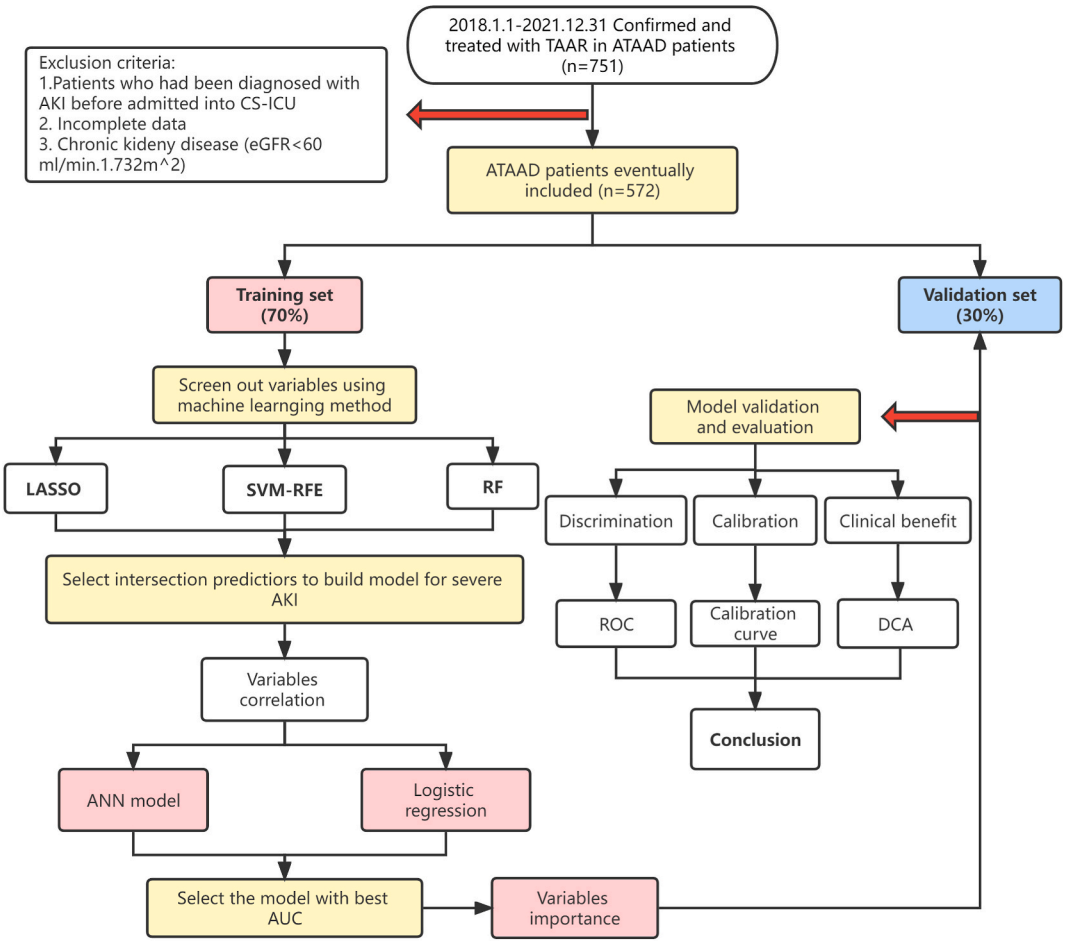

Fig. 1. Flowchart of this study. TAAR, total aortic arch replacement; ATAAD, acute type A aortic dissection; CS-ICU, cardiac surgery intensive care unit; eGFR, estimated glomerular filtration rate; LASSO, least absolute shrinkage and selection operator; SVM-RFE, support vector machine-recursive feature elimination; RF, random forest; AKI, acute kidney injury; ANN, artificial neural network; AUC, area under the curve; ROC, receiver operating characteristic; DCA, decision curve analysis.

biomarkers of different properties might improve the prediction performance for AKI [18]. In addition, the International Society of Nephrology proposed an initiative to achieve zero preventable AKI deaths by 2025 [19]. Therefore, it is essential to develop a novel and effective model to identify ATAAD patients at a high risk of severe AKI after TAAR.

Machine learning (ML) is a subfield of artificial intelligence that may have better prediction performance and higher interpretability than traditional statistical methods for prediction. Studies showed that ML algorithms have been frequently employed to improve prediction ability for clinical outcomes [20–22]. For example, some studies on heart diseases demonstrated that ML algorithms were superior to traditional regression methods in predicting outcomes [23,24]. Furthermore, a systematic review indicated that the ANN algorithm showed the best prediction performance among different ML methods for cardiovascular complications in diabetic patients [25]. However, there is a lack of studies on predicting severe AKI after TAAR in ATAAD patients using ML algorithms, especially in combination with classic biomarkers of AKI. Therefore, this study aimed at building a novel clinical prediction model for severe AKI after TAAR in ATAAD patients based on ML algorithms to help improve risk stratification for severe AKI in clinical practice.

2. Methods

2.1. Study design

Clinical data of a total of 751 ATAAD patients who undergoing TAAR procedure were retrospectively collected from the intensive care unit of cardiac surgery (CS-ICU) at Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University. Patients were consecutively enrolled from January 2018 to December 2021. All patients signed written informed consent forms before TAAR. The exclusion criteria included age under 18 years; incomplete clinical data; preexisting AKI or RRT before CS-ICU admission; chronic kidney disease (eGFR <60 ml/(min·1.732 m^2)); previous renal transplantation or nephrectomy; and pregnancy. Fig. 1 shows the flowchart of this study. Finally, a total of 572 patients were included in this study, and randomly split 7:3 into a training set ($n = 394$) and a validation set ($n = 178$). Patients were randomized through SPSS version 26.0 software (IBM, Armonk, USA). The training set was used to screen out predictors and optimize models using three ML algorithms, and the validation set was used to test the prediction performance of models. This study was approved by the Ethics Committee of Guangdong Provincial People's Hospital (approval ID: KY2023-702) and was conducted in accordance with the Declaration of Helsinki of 1975 (as revised in 1983).

2.2. Data collection

All patient data were retrospectively collected from Electronic Medical Record, and all personal information was de-identified to protect patient privacy. The following clinical data were recorded: demographics (age, sex, weight), underlying diseases (coronary heart disease, diabetes, hyperlipidaemia, hypertension and chronic kidney disease), American Society of Anesthesiologists (ASA) classification, preoperative medication (nephrotoxic drugs, radiographic contrast and mannitol), preoperative systolic blood pressure and diastolic blood pressure. Laboratory indicators included baseline serum creatinine (sCr), preoperative haemoglobin, postoperative sCr and haemoglobin, preoperative echocardiographic features (left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVDd), ascending aorta (AA) diameter and aortic regurgitation area), the state of renal artery involvement, and preoperative D-dimer and serum albumin. The level of sCr was also measured after the operation at ICU admission and thereafter at least once per day as the routine clinical test during the CS-ICU stay. Some routine indicators were immediately recorded at CS-ICU admission, including alanine aminotransferase, aspartate aminotransferase, total bilirubin, conjugated bilirubin, lactic dehydrogenase, uric acid, platelets, white blood cells, lactic acid, procalcitonin, serum cystatin C (sCysC), urine N-acetyl-β-D-glucosaminidase (uNAG), urine albumin creatinine ratio (uACR), systolic blood pressure, diastolic blood pressure and Acute Physiology and Chronic Health Evaluation (APACHE) II score [26].

Surgical data were recorded, including emergency operation, surgical procedures, operation time, cardiopulmonary bypass (CPB) time, aortic occlusion time, deep hypothermic circulatory arrest time, amount of intraoperative blood loss, intraoperative use of mannitol and transfusions (red blood cells, plasma and platelets). The primary outcome was the development of severe AKI (defined as AKI stage III). The secondary outcomes were RRT, mechanical ventilation, length of ICU stay, in-hospital mortality and total hospitalization expenses.

2.3. Surgical procedure

The detailed surgical procedure for TAAR was performed as described previously [27,28]. In short, right axillary artery cannulation was employed for CPB, with routine moderate hypothermic circulatory arrest (MHCA, 25–28 °C) and selective cerebral perfusion (ACP, 5–15 mL/kg/min) during the operation. The operative procedure involves deployment of a stent graft in the true lumen of the descending aorta, followed by TAAR with a 4-branched vascular graft. This surgical procedure may also include valvular repair or replacement and proximal aortic operation.

2.4. AKI definition

AKI stage III after TAAR in ATAAD patients was diagnosed based on the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) criteria [29]: an increase $\geq$ 3-fold in baseline sCr, an increase in sCr to $\geq$4.0 mg/dL (353.6 μmol/L), or the initiation of RRT within a

Table 1
ATAAD patient characteristics and perioperative variables.

Characteristics	All (n = 572)	Training set (n = 394)	Validation set (n = 178)	p value
Demographic features				
Male, n (%)	572 (77.6)	302 (76.6)	142 (79.8)	0.406
Age, years	530 (46.0, 61.0)	53.0 (46.0, 62.0)	53.0 (45.2, 61.0)	0.668
Weight, kg	68.0 (60.0, 75.0)	68.0 (60.0, 75.0)	67.8 (60.0, 76.0)	0.771
Underlying diseases				
Hypertension, n (%)	313 (54.7)	221 (56.1)	92 (51.7)	0.327
Diabetes mellitus, n (%)	21 (3.7)	14 (3.6)	7 (3.9)	0.823
Hyperlipidaemia, n (%)	6 (1.1)	2 (0.5)	4 (2.2)	0.148
Coronary artery disease, n (%)	21 (3.7)	14 (3.6)	7 (3.9)	0.823
Preoperative medication				
Nephrotoxic drugs, n (%)	157 (27.4)	104 (26.4)	53 (29.8)	0.402
Angiography, n (%)	77 (13.5)	49 (12.5)	28 (15.7)	0.509
Preoperative variables				
Smoking, n (%)	213 (37.2)	143 (36.3)	70 (39.3)	0.487
Emergency operation, n (%)	384 (67.1)	266 (67.5)	118 (66.3)	0.774
SBP, mmHg	126 (116,138)	127 (117, 139)	123 (115, 137)	0.218
DBP, mmHg	75 (65, 82)	75 (65, 82)	75 (66, 80)	0.471
Haemoglobin, g/L	126.0 (110.0,139.0)	126.0 (109.0, 138.0)	127.0 (112.2, 141.8)	0.152
D-dimer, ng/mL	3780 (1322,12712)	4250 (1412, 13970)	2935 (1145, 9820)	0.096
Albumin, g/L	38.1 (35.3, 40.6)	38.2 (35.3, 40.5)	37.9 (35.3, 40.6)	0.973
Baseline serum creatinine, μmol/L	75.6 (65.4,89.4)	75.5 (65.4, 90.8)	75.8 (65.8, 87.0)	0.599
Ascending aorta diameter, mm	42.0 (37.0,48.0)	42.0 (37.0, 47.0)	42.0 (37.0, 49.0)	0.922
LVDd, mm	48.0 (44.0, 53.0)	48.0 (44.0, 54.0)	47.0 (44.0, 52.0)	0.667
LVEF, %	64.0 (60.0,67.0)	64.0 (61.0, 68.0)	64.0 (60.0, 66.0)	0.402
Aortic regurgitation, cm^2	1.8 (0, 5.4)	1.7 (0, 5.2)	2.0 (0, 5.5)	0.414
Renal artery involvement, n (%)				0.432
Unilateral	221 (38.6)	159 (40.4)	62 (34.8)	
Bilateral	28 (4.9)	18 (4.6)	10 (5.6)	
ASA classification, n (%)				0.197
2	44 (7.7)	31 (7.9)	13 (7.3)	
3	325 (56.8)	229 (58.1)	96 (53.9)	
4	202 (35.3)	134 (34.0)	68 (38.2)	
5	1 (0.2)	0 (0)	1 (0.6)	
Primary outcomes				
Severe AKI, n (%)	131 (22.9)	93 (23.6)	38 (21.3)	0.552
Secondary outcomes				
Mechanical ventilation, hours	86.0 (40.0,153.0)	88.0 (41.0, 157.0)	66.0 (39.0, 140.0)	0.197
ICU stay, hours	160.0 (89.0, 250.8)	160.5 (89.0, 260.0)	160.0 (89.0, 234.5)	0.822
Renal replacement therapy, n (%)	77 (13.5)	55 (14.0)	22 (12.4)	0.604
Mortality, n (%)	31 (5.4)	22 (5.6)	9 (5.1)	0.796
Hospitalization expenses, CNY	2.5×10^5 (2.1×10^5, 3.2×10^5)	2.5×10^5 (2.2×10^5, 3.2×10^5)	2.4×10^5 (2.0×10^5, 3.1×10^5)	0.134
Surgical procedures				
Wheat procedure, n (%)	51 (8.9)	35 (9.4)	16 (9.0)	0.812
David procedure, n (%)	14 (2.4)	11 (2.8)	3 (1.7)	0.617
Bentall procedure, n (%)	158 (27.6)	106 (26.9)	52 (29.2)	0.567
Cabrol procedure, n (%)	7 (1.2)	6 (1.5)	1 (0.6)	0.577
Sun's procedure, n (%)	478 (83.6)	331 (84.0)	147 (82.6)	0.670
CABG, n (%)	30 (5.2)	18 (4.6)	12 (6.7)	0.280
AVP, n (%)	151 (26.4)	100 (25.4)	51 (28.7)	0.411
Intraoperative CPB parameters				
Operation time, mins	435.0 (375.0, 489.0)	435.0 (375.0, 485.0)	437.5 (375.0, 498.8)	0.826
CPB time, mins	235.0 (202.0, 275.0)	235.5 (203.0, 274.8)	234.0 (198.5, 274.0)	0.658
ACC time, mins	123.0 (98.0, 155.0)	123.0 (98.0, 154.8)	124.0 (97.2, 154.0)	0.904
DHCA time, mins	19.0 (14.0, 23.0)	19.0 (14.0, 23.0)	18.0 (14.0, 22.8)	0.347
Intraoperative transfusion				
Red blood cells, units	4.0 (0, 6.0)	4.0 (0, 6.0)	4.0 (0, 6.0)	0.650
Platelets, units	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	0.222
Plasma, mL	0 (0,400.0)	0 (0, 400.0)	150.0 (0, 400.0)	0.290
Mannitol, n (%)	457 (79.9)	320 (81.2)	137 (77.0)	0.240
Other intraoperative variables				
Blood loss, mL	400.0 (300.0, 500.0)	400.0 (300.0, 500.0)	400.0 (312.5, 500.0)	0.767
Urine output, mL	1000 (600,1600)	1000 (600, 1600)	1000 (600, 1700)	0.165
Variables at ICU admission				
SBP, mmHg	110 (100,119)	110 (100, 120)	108 (100, 118)	0.303
DBP, mmHg	60 (52, 65)	60 (52, 66)	60 (52, 65)	0.777
Neutrophils, × 109/L	10.9 (8.6, 13.5)	10.9 (8.6, 13.6)	10.7 (8.7, 13.2)	0.541
Platelets, × 109/L	138.0 (109.0, 183.0)	141.0 (110.0, 182.8)	135.5 (103.2, 179.8)	0.500

(*continued on next page*)

Table 1 (*continued*)

Haemoglobin, g/L	107.0 (98.0,115.0)	107.0 (98.0, 115.0)	106.0 (98.0, 115.0)	0.691
ALT, U/L	25.0 (17.0, 39.0)	24.0 (17.0, 38.0)	25.0 (17.0, 41.0)	0.600
AST, U/L	62.0 (46.0, 81.0)	62.0 (47.0, 79.0)	62.5 (45.2, 81.0)	0.868
LDH, U/L	539.0 (426.0, 645.0)	539.0 (433.2, 649.5)	540.0 (416.0, 636.0)	0.800
Total bilirubin, μmol/L	37.6 (24.7, 57.3)	38.0 (25.3, 55.4)	36.5 (23.8, 59.1)	0.785
Conjugated bilirubin, μmol/L	14.5 (8.1, 26.6)	14.6 (8.2, 26.4)	13.9 (7.9, 27.2)	0.937
Albumin, g/L	37.8 (34.6, 41.0)	38.2 (34.6, 41.1)	37.4 (34.8, 40.8)	0.463
Uric acid, μmol/L	367.2 (271.7, 477.2)	365.1 (274.4, 466.1)	382.6 (270.2, 493.5)	0.324
Procalcitonin, ng/mL	7.5 (2.9, 20.9)	7.4 (3.1, 18.9)	7.6 (2.5, 26.5)	0.610
sCysC, mg/L	1.1 (0.9, 1.4)	1.2 (0.9, 1.4)	1.1 (0.9, 1.4)	0.446
uNAG, U/g Cr	18.4 (10.6, 37.2)	18.0 (10.2, 37.9)	22.0 (12.0, 36.9)	0.141
uACR, mg/g Cr	141.9 (57.7, 417.3)	141.0 (59.8, 419.7)	145.0 (54.3, 371.8)	0.565
Lactic acid, mmol/L	4.3 (2.8, 6.5)	4.2 (2.9, 6.5)	4.4 (2.6, 6.4)	0.873
APACHE II score	11.0 (9.0, 14.0)	11.0 (9.0, 14.0)	11.0 (9.0, 13.0)	0.058

Note: ATAAD, acute type A aortic dissection; P value represents the difference between the training set and validation set. SBP, systolic blood pressure; DBP, diastolic blood pressure; LVDd, left ventricular diastolic diameter; LVEF, left ventricular ejection fraction; ASA, American Society of Anesthesiologists; AKI, acute kidney injury; ICU, intensive care unit; CABG, coronary artery bypass grafting; AVP, aortic valvuloplasty; CPB, cardiopulmonary bypass; ACC, aortic clamp closure; DHCA, deep hypothermic circulatory arrest; ALT, glutamic pyruvic transaminase; AST, glutamic oxaloacetic transaminase; LDH, lactic dehydrogenase; sCysC, serum cystatin C; uNAG, urine N-acetyl-β-D-glucosidase; uACR, urinary albumin creatinine ratio; APACHE II, Acute Physiology and Chronic Health Evaluation II scoring system.

week after surgery. In this study, the primary outcome was severe AKI, which was defined as AKI stage III. We adopted sCr rather than urinary output to define AKI since the urinary output was influenced by the body fluid volume of the patient and the use of diuretics [30]. Baseline sCr was determined by using the rules as previously described [31]. The duration of mechanical ventilation referred to the total time of ventilation using endotracheal intubation. Total hospitalization expenses were calculated by the Electronic Medical Record System. The diagnosis of ATAAD was confirmed by a contrast-enhanced CT scan, with the onset of symptoms within 48 h.

2.5. Statistical analysis

All participants were divided in severe AKI or nonsevere AKI groups based on KDIGO criteria [29]. Categorical variables are expressed with numbers (n) and percentages (%), and the chi-square test was used to analyse the differences between groups. Continuous variables are described as the means ± standard deviations (X ± SDs) or interquartile ranges. The Kolmogorov-Smirnov test was utilized to assess the normal distribution of variables. If the variables followed a normal distribution, the *t*-test was utilized to make comparisons between groups. If the variables did not follow a normal distribution, the Wilcoxon rank-sum test was used to test for two independent samples. The DeLong test was used to compare the areas under the receiver operating characteristic curves (AUCs) among models. A p value < 0.05 was considered statistically significant. R programming language version 4.2.3 (https://www.r-project.org) was used for statistical computing and analysis, for example, random forest (RF), support vector machine-recursive feature elimination (SVM-RFE), least absolute shrinkage and selection operator (Lasso) regression and artificial neural network (ANN) algorithms. Xiantao Project software (https://www.xiantaozi.com) and SPSS 26.0 (IBM, Armonk, USA) were utilized for data analysis and research mapping.

2.6. Selection of predictors

Firstly, we screened out predictors for severe AKI using three ML methods in the training set, including RF, SVM-RFE and Lasso regression. For the RF algorithm, we selected predictors by the combination of bootstrapping and decision trees. For the SVM-RFE algorithm, we screened the predictors by combining RFE and ten-fold cross-validation methods to avoid overfitting and increase clinical controllability, and a stable model was output when the root mean square error was minimal. The Lasso regression algorithm can impose penalties on indicators with high square differences to eliminate the number of indicators and was used to reduce high-dimensional indicators and enhance the predictive ability. In short, bootstrapping resampling (1000 times) was conducted to randomly select some samples from the training set for primary modelling, and a tenfold cross-validation method was used for unsampled data to output stable and reliable models. These methods have advantages and disadvantages in different conditions. Therefore, we selected the intersection predictors identified by three ML methods to construct a more stable model and avoid overfitting. Then, we performed Pearson correlation analysis on the prescreened intersection predictors to exclude variables with serious collinearity.

2.7. Establishment of models

To assess the discrimination ability two different algorithms (ANN and logistic regression) of the models, we determined some clinical-friendly measures, including AUC, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). We selected the model with the maximum AUC for further analysis, including calibration curve analysis and clinical benefit analysis. The calibration curve was used to represent the difference between the predicted results and true results, where the x-axis indicated the

probability of the predicted results, and the y-axis showed the actual probability of true results. Decision curve analysis (DCA) was conducted to evaluate the clinical utility of the models, where the x-axis of the curve was the threshold probability, and the y-axis represented the net benefit value.

3. Results

3.1. Baseline characteristics

A total of 572 patients with ATAAD after TAAR were included in this retrospective study and were randomly divided into a training set (394 individuals) and a validation set (178 individuals). Table 1 shows the baseline characteristics and clinical outcomes of the patients. Overall, the median age of the 572 patients was 53.0 [46.0, 61.0] years. The percentage of males was 77.6 % (444/572), and approximately 54.7 % (313/572) of patients had been diagnosed with hypertension before hospitalization. Additionally, approximately 3.7 % (21/572) of patients had a history of diabetes mellitus and coronary artery disease.

The incidence of severe AKI was 22.9 % (131/572) among all patients within 1 week after TAAR, and 13.5 % (77/572) of patients needed RRT. The total in-hospital mortality rate was 5.4 % (31/572). The mortality rates of patients with severe AKI and nonsevere AKI were 15.3 % (20/131) and 2.5 % (11/441), respectively. All variables and outcomes between the training set and the validation set showed no significant difference (Table 1**)**. Hence, the two datasets were homogeneous and comparable for further analysis.

3.2. Screening out model predictors through ML methods

The key parameters of RF, SVM-RFE and Lasso regression in R program could be found in Table 2. The track diagrams of different ML algorithms were showed in Fig. 2. The predictors screened by the SVM-RFE algorithm were baseline sCr and variables at CS-ICU admission, including sCysC, uNAG, APACHE II score, procalcitonin (PCT), platelets, aspartate transaminase and lactate dehydrogenase (Fig. 2A). The RF algorithm selected predictors and showed the importance of variables in terms of the mean decrease in the Gini value (Fig. 2B-C). Lasso regression revealed that preoperative LVEF, haemoglobin and postoperative platelet levels were protective factors, while baseline sCr and CS-ICU admission variables (CysC, uNAG, APACHE II score, PCT, aspartate transaminase, lactate dehydrogenase, lactic acid and serum albumin) were risk factors (Fig. 2D-E). The intersection predictors from the SVM-RFE, RF and Lasso algorithms were baseline sCr, sCysC, uNAG, APACHE II score, PCT, platelets, aspartate transaminase and lactate dehydrogenase (Fig. 2F).

3.3. Development and validation of models through the ANN algorithm

There was no significant correlation between the prescreened intersection predictors (Fig. 3A). Fig. 3B indicated the network relationships of the ANN for predicting severe AKI using intersection predictors. The ANN algorithm defined an AUC of 0.938 (95 % CI: 0.910–0.963) in the training set (Fig. 3C), and the variables importance to the ANN model was shown in Fig. 3D. Importantly, the ANN model could predict 89.1 % of severe AKI cases in advance. However, the AUC-ROC of logistic-regression model was 0.908 (95 % CI: 0.876–0.939) (Fig. 3E), which was significantly lower than the ANN model ($p < 0.05$). Besides, the ANN model was superior to logistic-regression model in terms of sensitivity, specificity, PPV and NPV (Table 3). Therefore, we selected the ANN model for further evaluation and validation. The calibration curve of the model fit the ideal curve (Fig. 3F), and DCA showed good clinical benefit in the training set (Fig. 3G). Encouragingly, the ANN model also presented favourable predictive performance with an AUC of 0.916 (95 % CI: 0.863–0.962) in the validation set (Fig. 4A). The calibration curve analysis and DCA validated the ANN model with good prediction accuracy (Fig. 4B-C).

4. Discussion

AKI is a common clinical syndrome after TAAR in ATAAD patients, and is closely associated with adverse outcomes [32,33]. In this

Table 2
Key parameters of techniques (R-project).

Machine learning methods	R packages	Parameter settings
Support vector machine-recursive feature elimination (SVM-RFE)	Packages ("e1071") Packages ("kernlab") Packages ("caret")	Functions = caretFuncs, method = cv, methods = svmRadial
Random Forest (RF)	Packages ("randomForest")	Seed = 123456, ntrees = 500
Least absolute shrinkage and selection operator regression (Lasso)	Packages ("glmnet")	Seed = 123, Family = binomial, alpha = 1, nfolds = 10 (cross-validation)
Artificial neural network (ANN)	Packages ("neuralnet") Packages ("NeuralNetTools")	Seed = 12345678, Hidden layer = 5, Stepmax = 10^7

Note: cv, coefficient of variation.

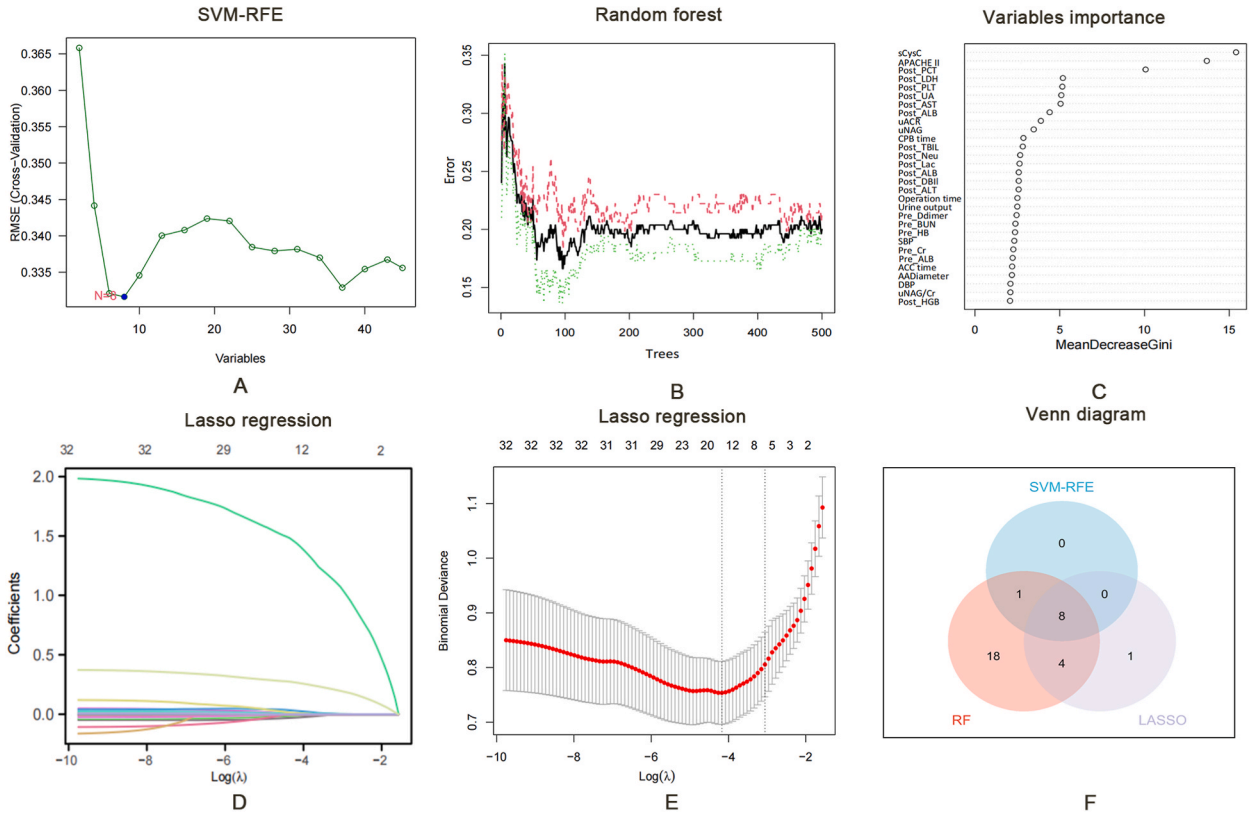

Fig. 2. Identification of feature variables for the model using three machine learning methods. A, Predictors for the model were screened out with the SVM-RFE method, and the model with the minimal root mean square error (RMSE) was selected. B, The predictors for the model were selected using random forest. D shows the importance of the variables in the model. D and E, Screening out the predictors and variable coefficients for the model using the Lasso regression method after 10-fold cross-validation. F, The intersection variables screened by three machine learning methods were selected, including sCysC, APACHE II, Post_PCT, Post_AST, Post_LDH, uNAG, Pre_Cr and Post_PLT. sCysC, serum cystatin C; APACHE II, Acute Physiology and Chronic Health Evaluation II; Pre_, preoperative; Post_, postoperative; PCT, procalcitonin; LDH, lactic dehydrogenase; PLT, platelet; ALB, albumin; uACR, urine albumin creatinine ratio; CPB, cardiopulmonary bypass; Neu, neutrophils; Lac, lactic acid; Bun, blood urea nitrogen; HGB, haemoglobin; Cr, creatinine; AA, ascending aorta; ACC, aortic clamp closure; uNAG, urine N-acetyl-β-D-glucosaminidase; Lasso, least absolute shrinkage and selection operator; SVM-RFE, support vector machine-recursive feature elimination; RF, random forest.

study, the incidence rates of AKI and severe AKI among postoperative ATAAD patients were 51.6 % and 22.9 % based on the KDIGO criteria, respectively. Correlation analysis showed that severe AKI was closely associated with a higher RRT rate, longer duration of mechanical ventilation, higher in-hospital mortality and increased hospitalization costs, which was consistent with previous studies [4,5,12,34]. Importantly, this study is the first to report a novel and effective predictive model based on ML algorithms for severe AKI after TAAR in ATAAD patients. Besides, this study included as many comprehensive clinical features and laboratory indicators as possible and confirmed that classic biomarkers (including sCysC and uNAG) could improve the discrimination ability for severe AKI after TAAR.

Previous studies have reported some risk factors for AKI after surgery in ATAAD patients, including advanced age, hypertension, preoperative elevated sCr, and CPB time [4,35,36]. However, there are few researches on the risk factors and predictive models for severe AKI, especially in patients who undergo TAAR patients [11,12]. In this study, we mainly focused on severe AKI after TAAR in ATAAD patients. First, correlation analysis revealed that severe AKI was likely associated with adverse outcomes, such as long mechanical ventilation time, frequent RRT and high in-hospital mortality. Second, the TAAR procedure was relatively complex and challenging, and thus causing more frequent postoperative complication. Third, several existing studies lacked an effective predictive performance for severe AKI [17,37,38]. In recent years, ML has presented a better performance in clinical prediction than traditional logistic regression methods [20,39]. Therefore, it is important to develop a risk prediction model for severe AKI after TAAR in ATAAD patients using ML algorithms.

To develop a high-efficiency assessment tool, this study employed ML algorithms to screen out predictors and construct models for severe AKI after TAAR in ATAAD patients. ML is a subfield of artificial intelligence that may have better prediction performance and higher interpretability than traditional statistical methods for prediction [20,39]. It is probably because ML algorithms makes decisions in a yes or no manner regardless of whether the variables are linear or not and helps explore the nonlinear and high-order relationships between variables, and thus improving clinical decision-making abilities [40,41]. In recent years, Li et al. [42]

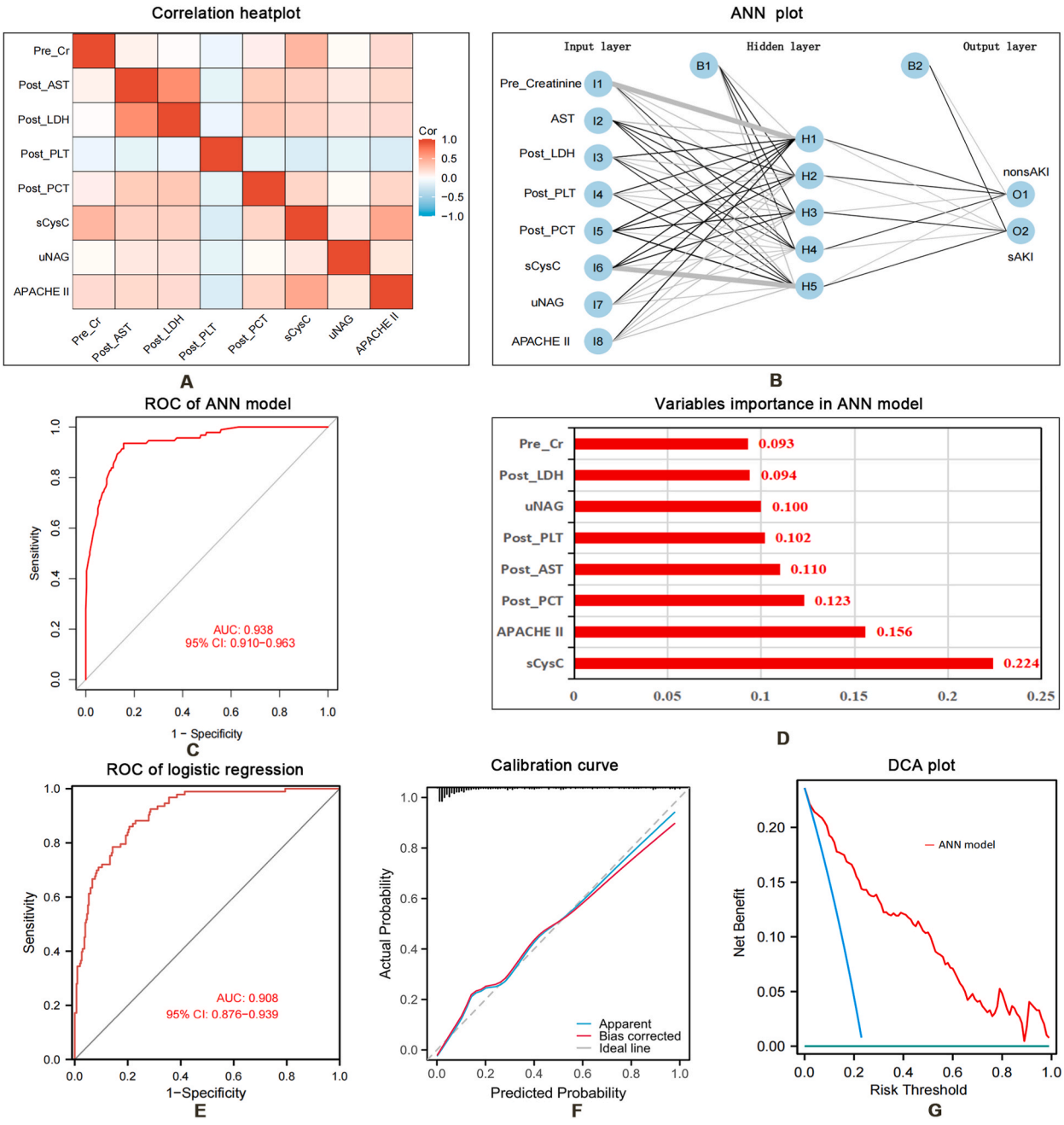

Fig. 3. Comparison between artificial neural network (ANN) and logistic regression analysis in the training set. A shows the correlation heatmap of intersection variables. B indicates the network relationships of the ANN for predicting severe AKI. C shows the area under the curve (AUC) of the receiver operating characteristic (ROC) curve using the ANN algorithm, AUC = 0.938 (95 % CI: 0.910–0.963). D shows the variable importance in the ANN algorithm. E shows the AUC of the ROC using the logistic regression method, AUC = 0.908 (95 % CI: 0.876–0.939). F shows the calibration curve of the model. G shows the decision curve analysis of the model. Pre_, preoperative; Post_, postoperative; LDH, lactic dehydrogenase; PLT, platelet; PCT, procalcitonin; sCysC, serum cystatin C; uNAG, urine N-acetyl-β-D-glucosaminidase; APACHE II, Acute Physiology and Chronic Health Evaluation II; nonsAKI, nonsevere acute kidney injury; sAKI, severe acute kidney injury; DCA, decision curve analysis.

reported that the AUC of the model for severe AKI after surgery in ATAAD patients was only 0.734, because this study might lacked efficient algorithms and some classic biomarkers of AKI (e.g., sCysC and uNAG). Hence, sCysC and uNAG were included in this study, and the ANN algorithm was used for modelling.

We compared the discrimination ability of the ANN model with the reference logistic regression-based model. Discrimination ability refers to the ability to distinguish patients who have experienced an event from patients who have not experienced an event,

Table 3
Comparison of ANN algorithm and logistic regression in terms of AUC, sensitivity, specificity, PPV and NPV.

Mathematical algorithms	AUC-ROC (95%CI)	Sensitivity	Specificity	PPV	NPV	p-value*
ANN	0.938 (0.910–0.963)	94.0 %	81.0 %	79.8 %	94.0 %	0.045
Logistic regression	0.908 (0.876–0.939)	86.0 %	79.7 %	56.3 %	94.8 %	

Note:AUC-ROC, area under the receiver operating characteristic curve; CI, confidence interval; ANN, artificial neural network; *ANN versus logistic regression.

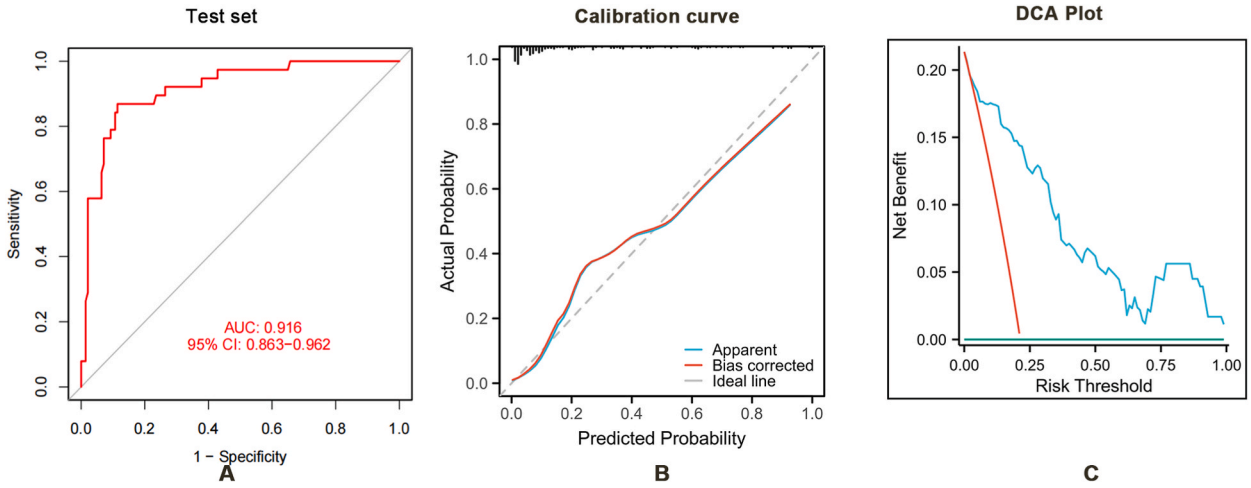

Fig. 4. The predictive ability of the ANN model in the validation set. A shows the area under the curve (AUC) of the receiver operating characteristic (ROC) curve in the validation set, AUC = 0.916 (95 % CI: 0.863–0.962). B shows the calibration curve of the model in the validation set. C shows the decision curve analysis of the model in the validation set. DCA, decision curve analysis.

which is evaluated with the AUC [43]. The ANN algorithm defined an AUC of 0.938, which was significantly higher than the traditional logistic regression-based model (AUC = 0.908). Encouragingly, the discrimination ability of our model was significantly better than logistic regression-based model (AUC = 0.739) in previous study [37]. The reliability of the ANN model was evaluated in terms of discrimination ability, calibration curve analysis and DCA in the validation set. First, we used the parameters of the ANN model in the training set to predict severe AKI. The AUC of the ANN model for severe AKI in the validation set was 0.916, which was within the 95 % confidence interval of the AUC in the training set. Second, there was good correlation between the calibration curve analysis and the DCA with the training set. To elaborate, these findings revealed that a ML-based clinical prediction model was successfully established for severe AKI after TAAR in ATAAD patients.

In this study, we screened out some important predictors through SVM-RFE, Lasso regression and RF, including baseline sCr and CS-ICU admission variables (sCysC, uNAG, PCT, APACHE II score, platelets, aspartate transaminase and lactate dehydrogenase). This study showed elevated baseline sCr was a key risk factor postoperative AKI, which was consistent with previous studies [44,45]. Low-level platelet is correlated with the occurrence of AKI and a severe stage of the disease, this might contribute to platelet depletion after the activation of platelets and coagulation systems [46]. Similarly, this study also found that the level of platelets significantly decreased in postoperative patients with severe AKI, which might be related to the activation of the platelet coagulation pathway and renal glomerular artery microthrombosis induced by the TAAR procedure. In short, both elevated sCr and decreased platelet levels are related to the dominant mechanisms of AKI after surgery in patients with ATAAD, including ischaemia-reperfusion injury, inflammatory responses and oxidative stress [47,48].

Other clinical laboratory indicators have also been discussed in some studies. Some studies found that PCT could be an independent risk factor for AKI and was not affected by infectious factors [49–52]. This study indicated that PCT was positively associated with severe AKI, and this attributed to the sterile inflammatory response induced by surgery (called systemic inflammatory response syndrome) and the decrease of renal excretion [53–55]. This evidence indicates that PCT may facilitate the early diagnosis of severe AKI after TAAR in ATAAD patients. Both of aspartate transaminase and lactate dehydrogenase are the biomarkers of cardiac injury. Our study revealed that lactate dehydrogenase was a good biomarker for predicting AKI in critically ill patients, which is consistent with in previous study [18]. Besides, APACHE II scoring system is a useful predictor of model for severe AKI in this study, which is widely used to assess the prognosis of critically ill patients [26]. A previous study indicated that the sCysC level plus APACHE II score could significantly improve the predictive performance for AKI or severe AKI in critically ill patients [18]. This study further confirmed that the APACHE II score could improve the prediction efficacy of model for severe AKI.

Some classic renal biomarkers were useful to identify AKI in advance in previous clinical studies, e.g., sCysC and uNAG [56]. Therefore, we focused on prediction of these biomarkers for severe AKI after TAAR in ATAAD patients. AKI is a heterogeneous

syndrome, and a single biomarker cannot fully reflect multiple pathophysiological mechanisms. The Acute Dialysis Quality Initiative (ADQI) advises clinicians to combine biomarkers of renal glomerular injury and tubular injury to improve the predictive efficacy of AKI [57]. sCysC is considered as a biomarker of renal glomerular injury, while uNAG represents renal tubular injury [58]. sCysC and uNAG represent two different pathophysiological conditions of AKI. In our previous studies, sCysC plus uNAG achieved satisfactory predictive efficacy for AKI in critically ill patients [56,59,60]. In this study, the combination of sCysC and uNAG presents better diagnostic performance for severe AKI after TAAR in ATAAD patients, which is more conducive to early disease diagnosis and clinical decision-making.

4.1. Limitations

We should acknowledge several potential limitations in this study. First, this was a retrospective observational study with a relatively small sample size, and the data distribution of this study might differ from those of studies with large sample sizes. Second, we used KDIGO as the diagnostic criteria for AKI, while some previous studies were based on the RIFLE or AKIN classifications [4,61]. It may be difficult to compare this study with some previous studies. Finally, this model was validated from single-centre data not including data from other centers. Therefore, these findings need external validation in a multicenter prospective study in the future.

5. Conclusion

In this study, we successfully constructed and validated a novel clinical prediction model for severe AKI after TAAR in ATAAD patients using different ML algorithms. The ANN algorithm presented a higher discrimination ability for severe AKI than logistic regression, which may help improve risk stratification for severe AKI after TAAR.

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Additional information

No additional information is available for this paper.

Statement of informed consent and ethical approval

This study was reviewed and approved by Research Ethics Committee Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, with the approval number: KY2023-702. All participants signed written informed consent to participate in the study.

Data availability statement

All data generated or analyzed during this study are including in this published article, and raw data are available on reasonable request.

CRediT authorship contribution statement

Xiaolong Liu: Writing – original draft, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Miaoxian Fang:** Writing – review & editing, Resources, Formal analysis, Conceptualization. **Kai Wang:** Validation, Resources, Investigation. **Junjiang Zhu:** Validation, Resources, Investigation. **Zeling Chen:** Validation, Resources, Formal analysis. **Linling He:** Software, Methodology. **Silin Liang:** Validation, Resources, Investigation. **Yiyu Deng:** Writing – review & editing, Supervision, Project administration, Methodology, Conceptualization. **Chunbo Chen:** Supervision, Project administration, Funding acquisition, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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