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Prediction of Acute Kidney Injury for Acute Type A Aortic Dissection Patients Who Underwent Sun's Procedure by a Perioperative Nomogram

Yuhui Zhang[a, b] Yongrong Lan[c] Tongyun Chen[b] Qingliang Chen[b] Zhigang Guo[b] Nan Jiang[b]

[a]Clinical School of Thoracic, Tianjin Medical University, Tianjin, PR China; [b]Department of Cardiac Surgery, Tianjin Chest Hospital, Tianjin, PR China; [c]Graduate School, Tianjin Medical University, Tianjin, PR China

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Keywords
Acute type A aortic dissection · Sun's procedure · Acute kidney injury · Risk prediction · Nomogram

Abstract
Introduction: Postoperative acute kidney injury (AKI) occurs in 20–40% of acute type A aortic dissection (ATAAD) patients undergoing cardiac surgery. A predictive model could be developed to assess the probability of AKI in patients with ATAAD before and after cardiac surgery in a timely manner. ***Methods:*** This retrospective study enrolled a total of 224 patients with ATAAD. Patients were subjected to total arch replacement using a tetrafurcate graft with stented elephant trunk implantation according to Sun's procedure. Statistical comparison for the collected data was done with Student's *t* test or Mann-Whitney U test (continuous variables) and χ^2 test (categorical variables). The independent predictors were screened by multivariate logistic regression analysis and then incorporated into a nomogram. The reliability of cardiac surgery-associated AKI (CSA-AKI) models was evaluated using the area under the receiver operating characteristic curve (AUC). ***Results:*** This study enrolled 224 ATAAD patients, including 53 patients with AKI and 171 patients without AKI. The incidence of ATAAD-induced AKI in the cohort was 23.66%. The screened predictors for AKI include iliac artery involvement, creatinine, D-dimer, autotransfusion, platelet-rich plasma reinfusion, nasal temperature, red blood cells, fresh frozen plasma, drainage, and mechanical ventilation. The calculated AUC values for model 1, model 2, model 3, and model 4 were 0.710, 0.777, 0.827, and 0.848, respectively. Model 4 was optimum for AKI risk scoring compared with model 1, model 2, and model 3. ***Conclusions:*** AKI prediction models were established for ATAAD patients using preoperative, intraoperative, and postoperative information. Particularly, model 4 shows superiority in risk prediction for CSA-AKI.

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Introduction

Acute kidney injury (AKI) is a common perioperative complication in patients undergoing cardiac surgery. AKI complicates the course of 20–40% of patients admitted to cardiac surgery [1–5]. According to the cardiorenal

Yuhui Zhang and Yongrong Lan contributed equally to this work.

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Correspondence to:
Qingliang Chen, qingliang1971@126.com
Zhigang Guo, zhigangguo@vip.163.com

syndrome (CRS) classification reported in 2019, cardiac surgery-associated AKI (CSA-AKI) is classified as the type 1 form of CRS [6]. CSA-AKI is defined as a bidirectional situation characterized by pathophysiologic disorders occurring in the heart and kidneys [6, 7]. Type 1 CRS reflects a sudden deterioration of cardiac function that leads to AKI [6, 7]. Based on the timing of AKI occurrence, CSA-AKI can be divided into two phases, the early and the late phase [6, 7]. CSA-AKI exhibits as AKI occurring before or after cardiac surgery, as well as presents as acute and chronic CSA-AKI [6, 7]. Normal patients show rapid overall recovery with a transient increase in serum creatinine levels, which can then be quickly reduced to normal levels [8]. For severe CSA-AKI patients, the AKI condition can last for weeks or even months [8]. Severe CSA-AKI correspondingly elevates the cost of care and prolongs the length of stay in the intensive care unit.

Acute type A aortic dissection (ATAAD) is generally defined as a dissection diagnosed within 14 days after the onset of symptoms [9]. ATAAD is the most lethal of dissections involving the ascending aorta [10]. The incidence of ATAAD is 4–6 cases in 100,000 patients per year in emergency departments [11], and its totally in-hospital case-fatality rate was estimated to be 73% [12]. Prompt surgical repair is necessary. Cardiac surgery, especially aortic root replacement, is the first choice for patients with ATAAD [13, 14]. Sun et al. [15] proposed a surgical approach and named it the Sun's procedure that integrates total arch replacement using a tetrafurcated graft with the implantation of a special stented graft in the descending aorta [15, 16]. However, postoperative complications are common following ATAAD repair, like major bleeding, stroke, pneumonia, and AKI, as reported in the Nordic consortium for ATAAD registry [17]. Many reports have shown the incidence of AKI in patients with ATAAD after undergoing aortic root replacement [18–20]. AKI elevates the morbidity of postoperative patients with ATAAD, and the morbidity due to AKI was 70–90% [21, 22]. Postoperative continued renal replacement therapy was required for 27.49% AKI patients with ATAAD [18]. Consequently, it is necessary to evaluate the risk of CSA-AKI for ATAAD patients and the need to continue renal replacement therapy during the perioperative period.

Before cardiac surgery, the diagnosis of AKI is based upon a serum creatinine level that has been obtained within a 3-month period preceding cardiac surgery, according to the Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for AKI [23]. Whereas risk factors for CSA-AKI come from preoperative, intraoperative, and postoperative phases, which affect the outcomes of ATAAD patients after cardiac surgery [18, 20–22, 24]. Analysis of risk factors for CSA-AKI via perioperative hospitalization information enables the early identification of ATAAD patients with a high risk of AKI before or after cardiac surgery [24, 25]. Thereafter, clinicians can develop preventive and therapeutic strategies to manage CSA-AKI patients and minimize the postoperative complications after cardiac surgeries.

Several risk prediction models for AKI have been developed in retrospective cohort studies [26, 27]. Demographic characteristics, clinical condition, preoperative biochemistry results, preoperative medical data, and intraoperative variables were included in the machine learning for construction of the CSA-AKI risk prediction model [26]. The nomogram model using independent predictive factors accurately estimates the risk of AKI for an individual patient receiving cardiac surgery [27]. The Doppler renal resistive index and semiquantitative color Doppler grade have been used to evaluate postoperative persistent AKI after surgery in acute standard type A aortic dissection patients, and its efficiency has been proved [25]. However, there is a lack of comparative studies of predictive models based on preoperative, intraoperative, and postoperative factors for ATAAD patients. Our study aimed to establish a nomogram model based on demographic characteristics, preoperative laboratory data, imaging examination, intraoperative monitoring results, and postoperative records to predict AKI risk for ATAAD patients after cardiac surgeries.

Patients and Methods

Study Population

After obtaining the approval from the Research Ethics Committee of Tianjin Chest Hospital, we performed this retrospective study on ATAAD patients who had undergone cardiac surgery from 1 January 2017 to 1 January 2020. In this study, we enrolled a total of 224 patients with ATAAD demonstrated by computed tomography angiography and color Doppler ultrasound. Patients were subjected to total arch replacement using a tetrafurcate graft with stented elephant trunk implantation according to Sun's procedure [28]. The exclusion criteria were a previous history of traumatic and iatrogenic aortic dissection, aortic aneurysm, Marfan's syndrome, complication of blood system disease, and patients undergoing any of the following conditions: dialysis treatment, brain infarction, emerging cerebral infarction and hemorrhage, acute myocardial infarction with unstable hemodynamics (>6 h), and the time from onset to operation more than 14 days. The flow chart of the inclusion and exclusion in this study is shown in Figure 1. The diagnosis of AKI was based on the 2012 KDIGO AKI definition [29]. According to the 2012 KDIGO AKI definition, AKI is defined as any of the following: an increase in serum creatinine by

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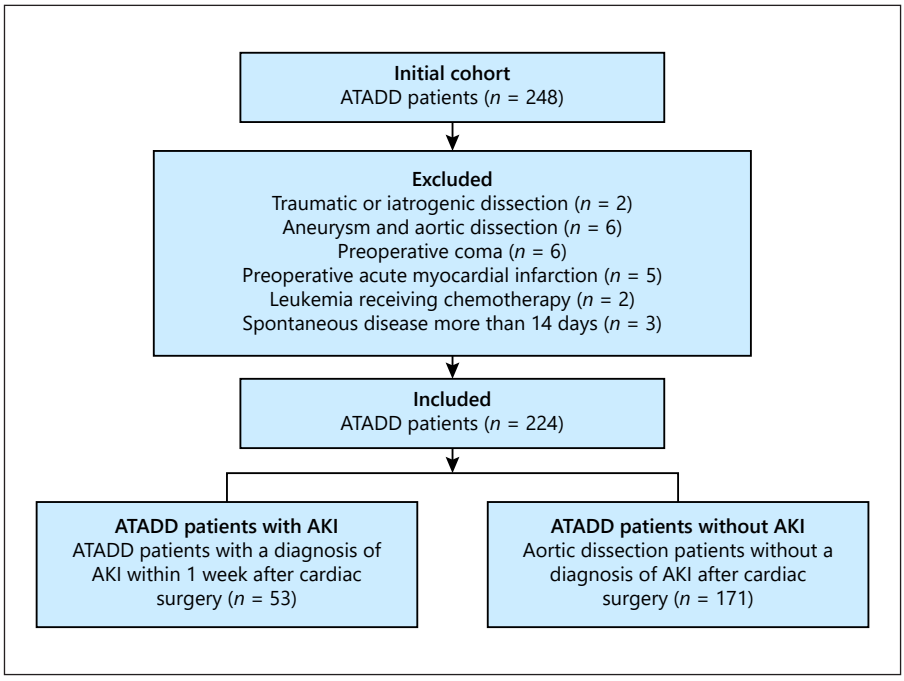


Fig. 1. Flow chart suggesting the inclusion and exclusion criteria in the study cohort. AKI, acute kidney injury; ATAAD, acute type A aortic dissection.

≥0.3 mg/dL (≥26.5 μmol/L) within 48 h; or an increase in serum to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or urine volume <0.5 mL/kg/h for 6 h. In this study, patients with a rise in serum creatinine to more than 3 times the preoperative basal value were diagnosed with AKI. AKI patients were diagnosed within 1 week after cardiac surgery.

Data Collection

The clinical characteristics were extracted and collected from the cardiac surgery database in our hospital. The collected data included demographic characteristics, comorbidities, preoperative laboratory values, preoperative radiologic characteristics, and operative and postoperative outcomes.

Statistical Analysis

All data were processed using IBM SPSS Statistics software (Version 26; IBM SPSS, Chicago, IL, USA) and R software (Version 4.03; https://www.r-project.org). Continuous variables were presented as mean ± standard deviation or median (interquartile range). Student's *t* test or Mann-Whitney U test were done for statistical comparisons of the continuous variables. In terms of categorical variables, the data were suggested as frequency (percentage), and χ^2 test was performed for statistical comparison.

The variables with p values <0.1 were selected as the independent factors and incorporated into a multivariate logistic regression analysis. A forward-elimination model selection procedure was done on the basis of the Wald test to screen the final subset of variables. The Akaike information criterion and Bayesian information criterion were used to demonstrate the favorable model fits statistics. The detected factors including demographic characteristics and comorbidities, preoperative laboratory values, preoperative radiologic characteristics, operative data, and postoperative outcomes were used to establish a risk scoring model. In detail, model 1 was constructed based on preoperative indexes including clinical characteristics, laboratory values, and radiologic features; model 2 on preoperative and operative characteristics; model 3 on preoperative, operative, and postoperative features; and model 4 on operative and postoperative indicators. The area under the receiver operating characteristic curve (AUC) and the receiver operating curve were used to assess the reliability of the risk scoring model of AKI for ATAAD before and after Sun's procedure. The risk scoring model was visualized as nomograms. A calibration curve was plotted to evaluate the reliability of the risk scoring model for AKI associated with ATAAD.

Results

Patients' Characteristics and Risk Factor Analysis for CSA-AKI

In this study, we enrolled 224 patients to construct the risk scoring model for CSA-AKI. The incidence of CSA-AKI in the cohort was 23.66%. The enrolled patients have received total arch replacement using a four-branched graft with the implantation of a stented elephant trunk according to Sun's procedure. Demographical and clinical variables were analyzed to screen predictors for risk prediction model construction.

For demographics, CSA-AKI was associated with advanced age ($t = -1.833$, $p = 0.068$), hypertension ($\chi^2 = 2.776$, $p = 0.096$), and hospital length of stay before surgery ($Z = -3.049$, $p = 0.002$) (Table 1). Several preoperative lab-

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Table 1. Demographic characteristics and comorbidities of ATAAD patients before receiving Sun's procedure

Demographics and comorbidities	AKI (n = 53)	Non-AKI (n = 171)	Significance test
Age, years	55.23±12.25	51.88±11.40	$t = -1.833$, $p = 0.068$
Male, n (%)	38 (71.7)	134 (78.4)	$\chi^2 = 1.008$, $p = 0.315$
BMI	26.98±3.39	26.78±4.19	$t = -0.324$, $p = 0.746$
Smoker, n (%)	29 (54.7)	79 (46.2)	$\chi^2 = 1.176$, $p = 0.278$
Alcohol drinker, n (%)	13 (24.5)	39 (22.8)	$\chi^2 = 0.067$, $p = 0.795$
Hypertension, n (%)	42 (79.2)	115 (67.3)	$\chi^2 = 2.776$, $p = 0.096$
Diabetes mellitus, n (%)	0 (0.0)	5 (2.9)	$p = 0.594$
Stroke, n (%)	4 (7.5)	11 (6.4)	$p = 0.758$
Peripheral tamponade, n (%)	42 (79.2)	116 (67.8)	$\chi^2 = 2.534$, $p = 0.111$
Previous aortic operation, n (%)	1 (1.9)	4 (2.3)	$p = 1.000$
Hypotension, n (%)	40 (75.5)	116 (67.8)	$\chi^2 = 1.116$, $p = 0.291$
Hospital length of stay before surgery	13.0 (8.0, 18.5)	18.0 (10.0, 32.0)	$Z = -3.049$, $p = 0.002$

BMI, body mass index; AKI, acute kidney injury. Values are counts (%), mean ± standard deviation, or time range (day). Statistical analysis was done with T test, χ^2 test, or U test.

Table 2. Preoperative laboratory values of ATAAD patients receiving Sun's procedure

Laboratory values	AKI (n = 53)	Non-AKI (n = 171)	Significance test
WBC, $\times 10^9$/L	12.54±3.83	11.37±3.62	$t = -2.032$, $p = 0.043$
Neutrophil, $\times 10^9$/L	10.84±3.75	10.36±7.93	$t = -0.429$, $p = 0.669$
Lymphocyte, $\times 10^9$/L	0.98±0.66	1.03±0.66	$t = 0.444$, $p = 0.657$
NLR	15.51±11.59	13.14±9.69	$t = -1.482$, $p = 0.140$
RBC, $\times 10^9$/L	4.09±0.50	4.26±0.61	$t = 1.860$, $p = 0.064$
Hb, g/L	119.43±30.49	122.13±37.83	$t = 0.474$, $p = 0.636$
RDW, fL	42.85±3.22	42.47±3.50	$t = -0.705$, $p = 0.482$
PLT, $\times 10^9$/L	165.47±60.43	180.28±68.84	$t = 1.406$, $p = 0.161$
MPV, fL	10.44±0.93	10.46±1.08	$t = 0.303$, $p = 0.923$
hsCRP, mg/L	8.61 (3.61, 12.25)	10.20 (3.54, 22.10)	$Z = -1.018$, $p = 0.309$
CK, n (%)	16 (30.2)	35 (20.5)	$\chi^2 = 2.174$, $p = 0.140$
CK-MB, n (%)	16 (30.2)	28 (16.4)	$\chi^2 = 4.892$, $p = 0.027$
Creatinine, μmol/L	132.57±92.42	92.65±40.54	$t = -3.054$, $p = 0.003$
Uric acid, μmol/L	377.28±118.78	342.56±116.11	$t = -1.892$, $p = 0.060$
GGT, U/L	25.90 (17.75, 37.35)	28.00 (16.60, 47.70)	$Z = -0.646$, $p = 0.528$
D-dimer, μg/L	12.20 (5.55, 20.00)	6.97 (3.30, 12.77)	$Z = -2.858$, $p = 0.004$
NT-proBNP, pg/mL	459.80 (235.25, 826.65)	387.60 (182.10, 768.80)	$Z = -0.803$, $p = 0.422$
Hs-cTnT, n (%)	26 (49.1)	83 (48.5)	$\chi^2 = 0.004$, $p = 0.947$
ALT, U/L	19.60 (11.45, 38.15)	18.60 (11.70, 30.80)	$Z = -0.776$, $p = 0.438$
AST, n (%)	18 (34.0)	28 (16.4)	$\chi^2 = 7.670$, $p = 0.006$
Triglyceride, mmol/L	3.67±0.58	4.00±1.03	$t = 2.963$, $p = 0.004$
Cholesterol, mmol/L	1.32 (1.12, 1.91)	1.26 (1.01, 1.73)	$Z = -1.325$, $p = 0.185$
HDLC2, mmol/L	1.19 (1.04, 1.46)	1.20 (1.09, 1.45)	$Z = -0.382$, $p = 0.702$
LDL2, mmol/L	2.60 (2.20, 2.92)	2.56 (2.15, 3.09)	$Z = -0.289$, $p = 0.773$

WBC, white blood cells; NLR, neutrophil-to-lymphocyte ratio; RBC, red blood cell; Hb, hemoglobin; RDW, red cell distribution width; PLT, platelets; MPV, mean platelet volume; hsCRP, high sensitivity C-reactive protein; CK, creatine kinase; CK-MB, creatine kinase-isoenzyme; GGT, gamma glutamyltransferase; NT-proBNP, N-terminal pro-B-type natriuretic peptide; Hs-cTnT, hypersensitive cardiac troponin T; ALT, alanine aminotransferase; AST, aspartate aminotransferase; HDLC2, high-density lipoprotein cholesterol 2; LDL2, low density lipoprotein 2; AKI, acute kidney injury. Values are counts (%) and mean±standard deviation. Statistical analysis was done with T test, χ^2 test, or U test.

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Table 3. Preoperative radiologic characteristics of ATAAD patients receiving Sun's procedure

	AKI (n = 53)	Non-AKI (n = 171)	Significance test
Coronary involvement, n (%)	18 (34.0)	43 (25.1)	$\chi^2 = 1.587$, $p = 0.208$
Innominate artery involvement, n (%)	26 (49.1)	68 (39.8)	$\chi^2 = 1.434$, $p = 0.231$
Left common carotid artery involvement, n (%)	24 (45.3)	70 (40.9)	$\chi^2 = 0.314$, $p = 0.575$
Left subclavian artery involvement, n (%)	33 (62.3)	90 (52.6)	$\chi^2 = 1.516$, $p = 0.218$
Coeliac trunk involvement, n (%)	13 (24.5)	35 (20.5)	$\chi^2 = 0.396$, $p = 0.529$
Superior mesenteric artery involvement, n (%)	8 (15.1)	31 (18.1)	$\chi^2 = 0.259$, $p = 0.611$
Renal artery involvement, n (%)	25 (47.2)	69 (40.4)	$\chi^2 = 0.782$, $p = 0.379$
Iliac artery involvement, n (%)	27 (50.9)	51 (29.8)	$\chi^2 = 7.951$, $p = 0.005$
AS,[a]n (%)	0 (0.0)	1 (0.6)	$p = 1.000$
AI,[a]n (%)	25 (47.2)	54 (31.6)	$\chi^2 = 4.038$, $p = 0.038$
MI,[a]n (%)	0 (0.0)	4 (2.3)	$p = 0.575$
MS,[a]n (%)	0 (0.0)	1 (0.6)	$p = 1.000$
Ascending aortic diameter,[a] mm	44.74±7.23	45.92±7.25	$t = 1.043$, $p = 0.298$
Aortic sinus diameter,[a] mm	45.11±6.20	44.22±6.23	$t = 0.911$, $p = 0.363$
LAD,[a] mm	36.82±5.00	36.73±5.10	$t = 0.018$, $p = 0.986$
LVEDD,[a] mm	52.58±6.73	51.50±6.13	$t = -1.102$, $p = 0.271$
LVEF,[a] %	54.47±6.52	55.89±5.06	$t = 1.665$, $p = 0.097$

MS, mitral stenosis; MI, mitral insufficiency; AI, aortic insufficiency; AS, aortic stenosis; UCG, ultrasonic cardiogram; LAD, left atrial diameter; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; AKI, acute kidney injury. [a] Analysis by UCG. Values are counts (%), mean ± standard deviation. Statistical analysis was done with T test or χ^2 test.

Table 4. Intraoperative data of ATAAD patients receiving Sun's procedure

	AKI (n = 53)	Non-AKI (n = 171)	Significance test
CPBT, min	177.76±63.37	166.02±34.90	$t = -1.684$, $p = 0.097$
ACCT, min	100.14±25.95	96.04±22.53	$t = -1.145$, $p = 0.254$
DHCAT, min	9.00 (7.00, 12.00)	10.00 (7.00, 21.00)	$Z = -1.278$, $p = 0.201$
Nasal temperature, °C	25.81±1.69	25.34±1.82	$t = -1.774$, $p = 0.077$
Anal temperature, °C	27.39±1.61	27.41±1.88	$t = 0.082$, $p = 0.942$
Amount of hemorrhage, mL	1,240 (945, 1,900)	1,200 (980, 1,400)	$Z = -1.188$, $p = 0.235$
Amount of PRP reinfusion, U	1.60±0.78	1.46±0.82	$t = -1.206$, $p = 0.229$
Amount of autotransfusion, mL	990.0 (767.5, 1,660.3)	900.0 (700.0, 1,100.0)	$Z = -1.533$, $p = 0.025$
Amount of RBC, U	0.0 (0.0, 2.0)	0.0 (0.0, 2.0)	$Z = -2.566$, $p = 0.010$
FFP volume, mL	355.0 (0.0, 700.0)	580.0 (350.0, 752.5)	$Z = -2.920$, $p = 0.003$

CPBT, cardiopulmonary bypass time; ACCT, aortic cross-clamp time; DHCAT, deep hypothermic circulatory arrest time; PRP, platelet-rich plasma; RBC, number of red blood cells transfused during cardiac surgery; FFP, fresh frozen plasma; AKI, acute kidney injury. Values are mean ± standard deviation or number range. Statistical analysis was done with T test or U test.

oratory variables were closely correlated with a higher risk of AKI in patients receiving cardiac surgery, including increased white blood cells ($t = -2.032$, $p = 0.043$), creatinine ($t = -3.054$, $p = 0.003$), uric acid ($t = -1.892$, $p = 0.060$), and D-dimer ($Z = -2.858$, $p = 0.004$), as well as decreased red blood cells ($t = 1.860$, $p = 0.064$) and triglyceride content ($t = 2.963$, $p = 0.004$). The results suggested a high risk of CSA-AKI was associated with the positive detection of aspartate aminotransferase ($\chi^2 = 7.670$, $p = 0.006$) and creatine kinase-isoenzyme ($\chi^2 = 4.892$, $p = 0.027$) (Table 2). According to the preoperative radiologic characteristics, patients with iliac artery involvement ($\chi^2 = 7.951$, $p = 0.005$) and aortic insufficiency ($\chi^2 = 4.038$, $p = 0.038$) have an increased risk of AKI (Table 3).

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Table 5. Postoperative outcomes of ATAAD patients receiving Sun's procedure

	AKI (n = 53)	Non-AKI (n = 171)	Significance test
Ventilator application (>48 h), n (%)	42 (82.4)	46 (27.7)	$\chi^2 = 36.011$, $p < 0.001$
Off the ventilator, n (%)	34 (58.6)	156 (94.0)	$\chi^2 = 41.731$, $p < 0.001$
Time of mechanical ventilation, h	92.5 (39.9, 177.8)	36.0 (14.0, 77.3)	$Z = -4.792$, $p < 0.001$
Cerebral perfusion, mL/kg·min	9.0 (7.00, 12.0)	10.0 (7.0, 21.0)	$Z = -1.292$, $p = 0.196$
24-h postoperative drainage, mL	870.0 (577.5, 1,082.5)	700.0 (450.0, 960.0)	$Z = -3.000$, $p = 0.003$
Hospital length of stay, days	16 (11, 24)	15 (11, 20)	$Z = -0.733$, $p = 0.464$

Values are counts (%) or number range. Statistical analysis was done with χ^2 test or U test. AKI, acute kidney injury.

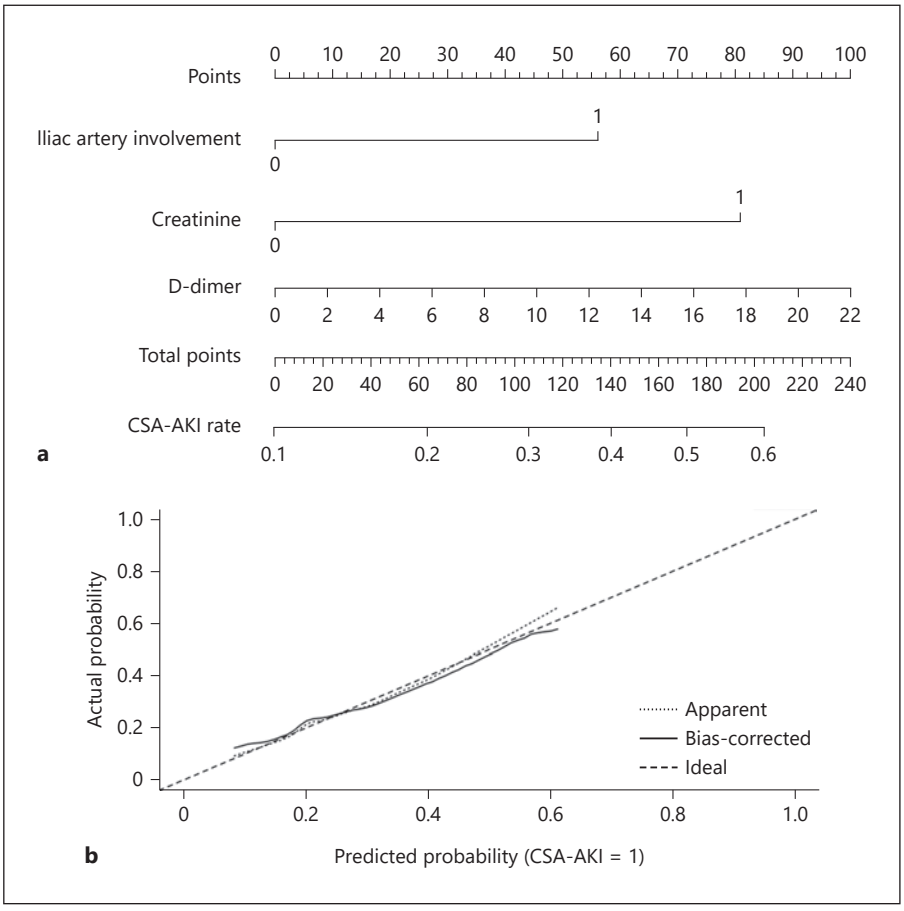


Fig. 2. Nomogram (**a**) and calibration curve (**b**) of risk prediction model 1 for AKI of ATAAD patients. The model was constructed based on preoperative predictors (iliac artery involvement, and serum creatinine, D-dimer). AUC value = 0.710. AUC, area under the receiver operating characteristic curve; AKI, acute kidney injury; ATAAD, acute type A aortic dissection.

Intraoperative data indicated that patients with increased cardiopulmonary bypass time ($t = -1.684$, $p = 0.097$), elevated nasal temperature ($t = -1.774$, $p = 0.077$), increased autotransfusion ($Z = -1.533$, $p = 0.025$), increased number of red blood cells transfused during cardiac surgery ($Z = -2.566$, $p = 0.010$), and decreased fresh frozen plasma transfused during surgery ($Z = -2.920$, $p = 0.003$) showed a potential in CSA-AKI (Table 4). For postoperative outcomes, the extended time of ventilator application ($\chi^2 = 36.011$, $p < 0.001$), mechanical ventilation ($Z = -4.792$, $p < 0.001$), reliance on ventilator ($\chi^2 = 41.731$, $p < 0.001$), increased drainage ($Z = -3.000$, $p = 0.003$), and increased hospitalization time ($Z = -0.733$, $p = 0.464$) indicated an elevated risk of AKI in patients who have undergone Sun's procedure (Table 5).

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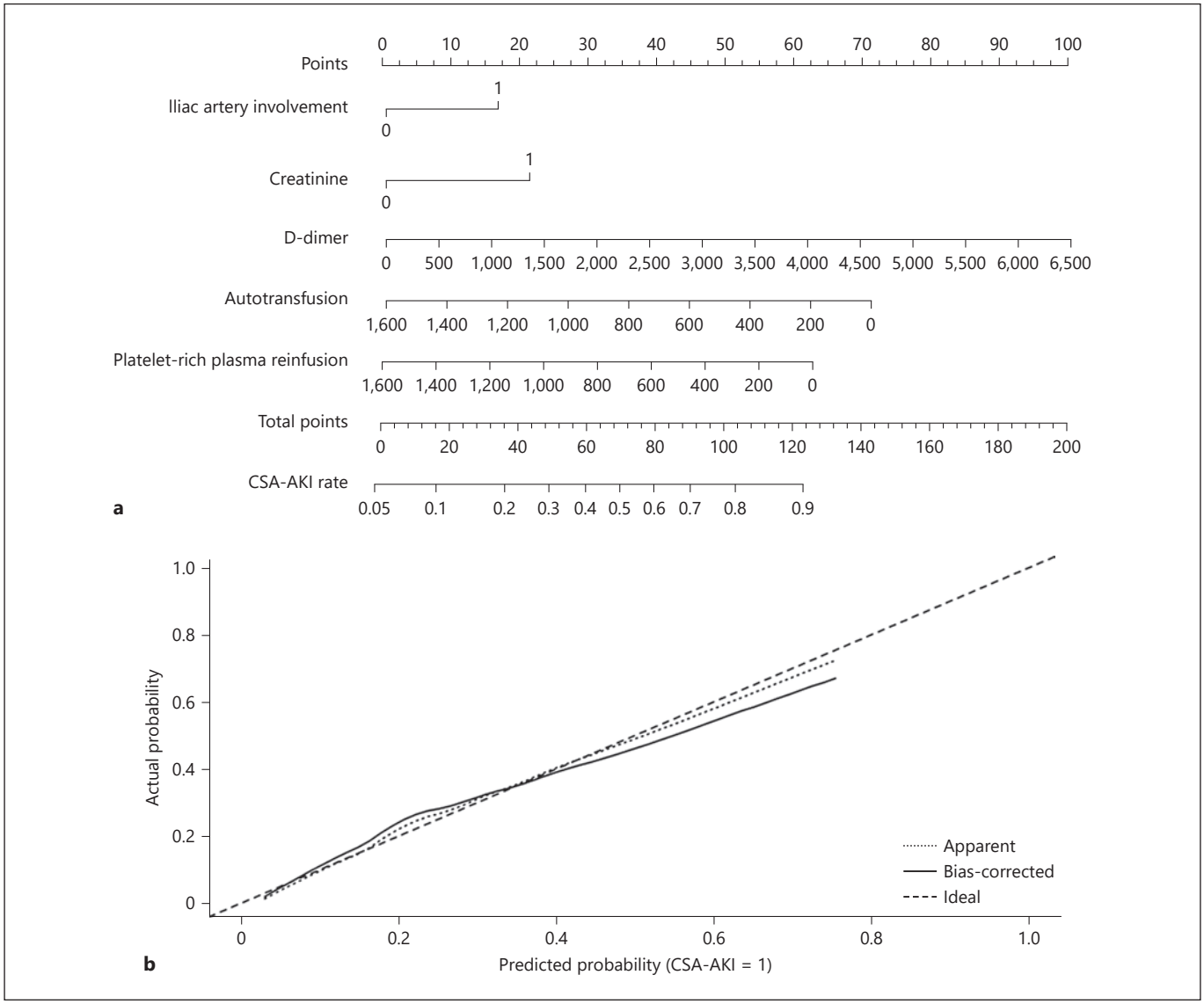


Fig. 3. Nomogram (**a**) and calibration curve (**b**) of risk prediction model 1 for AKI of ATAAD patients. The model was constructed based on preoperative and intraoperative predictors (iliac artery involvement, serum creatinine, D-dimer, autotransfusion, and platelet-rich plasma reinfusion). AUC value = 0.777. AUC, area under the receiver operating characteristic curve; AKI, acute kidney injury; ATAAD, acute type A aortic dissection.

Next, we built risk scoring models according to different classification of detecting indexes. The following characteristics with $p < 0.1$ were accepted as potential risk scoring factors for CSA-AKI: age, hypertension, hospital length of stay before surgery, white blood cells, red blood cells, creatine kinase-isoenzyme, creatinine, uric acid, D-dimer, aspartate aminotransferase, triglyceride, iliac artery, aortic insufficiency, left ventricular ejection fraction, ventilator application, mechanical ventilation, cardiopulmonary bypass time, nose temperature, autotransfusion, number of red blood cells transfused during Sun's procedure, and fresh frozen plasma (Tables 1–5).

Risk Scoring Model Development

Thereafter, a multivariate logistic regression analysis was performed to predict the preoperative (model 1), preoperative and intraoperative (model 2), intraoperative and postoperative (model 3), as well as preoperative, intraoperative, and postoperative (model 4) risks of CSA-AKI occurrence in ATAAD patients. The models incor-

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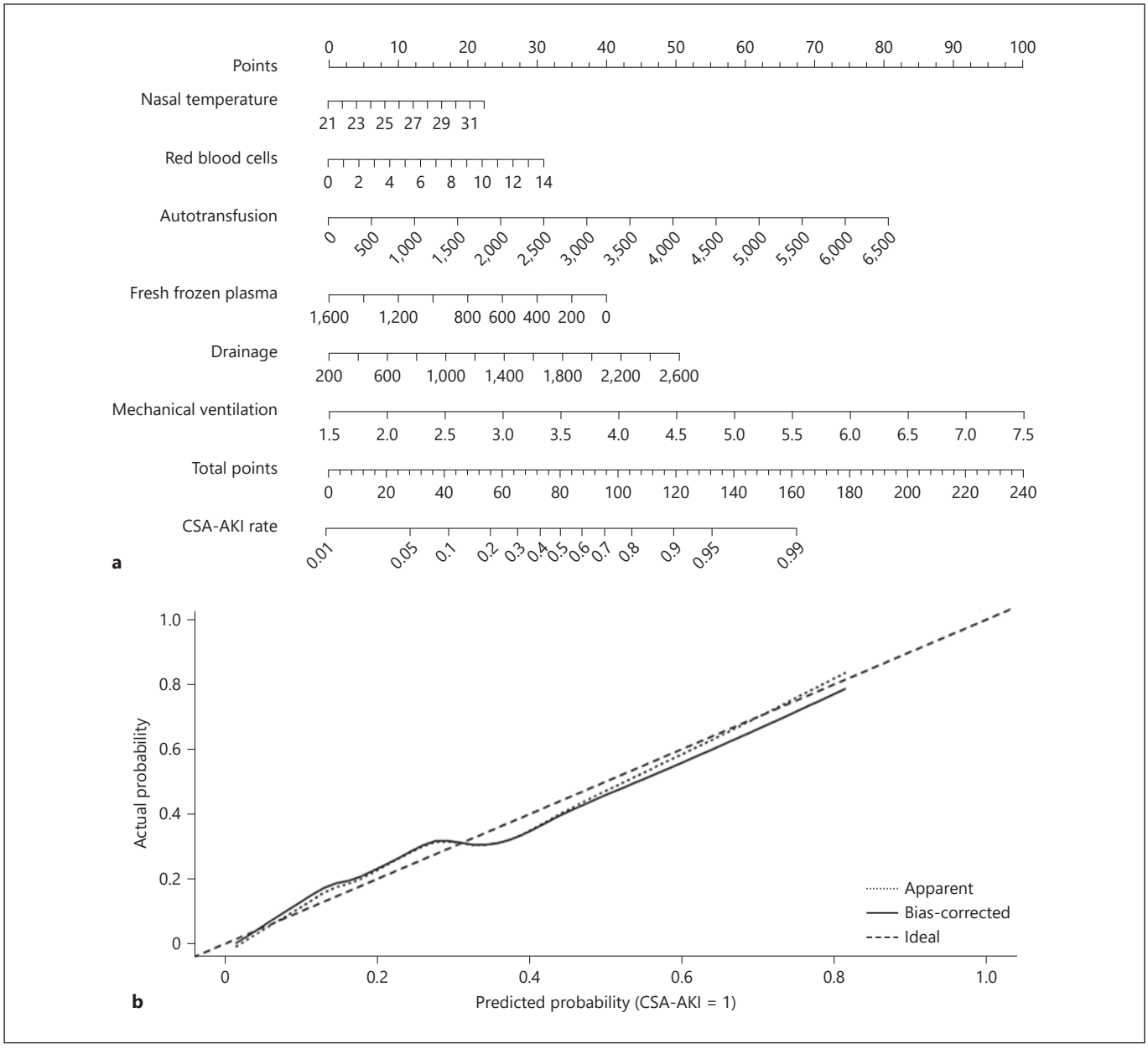


Fig. 4. Nomogram (**a**) and calibration curve (**b**) of risk prediction model 1 for AKI of ATAAD patients. The model was constructed based on intraoperative and postoperative predictors (nasal temperature, red blood cells, autotransfusion, fresh frozen plasma, drainage, and mechanical ventilation). AUC value = 0.827. AUC, area under the receiver operating characteristic curve; AKI, acute kidney injury; ATAAD, acute type A aortic dissection.

porated iliac artery, aortic insufficiency, age, and hospital length of stay before surgery into risk scoring for preoperative CSA-AKI. The detailed variables in the preoperative model 1 included iliac artery involvement, creatinine, and D-dimer. The corresponding nomogram is shown in Figure 2a. The calibration curve for the preoperative model revealed the consistency of the predicted CSA-AKI risk and the actual occurrence of CSA-AKI for ATAAD patients (shown in Fig. 2b).

In terms of model 2, we used preoperative and intraoperative risk factors containing iliac artery involvement, creatinine, D-dimer, autotransfusion, and platelet-rich plasma reinfusion, and a nomogram is shown in Figure 3a. The corresponding calibration curve is shown in Fig-

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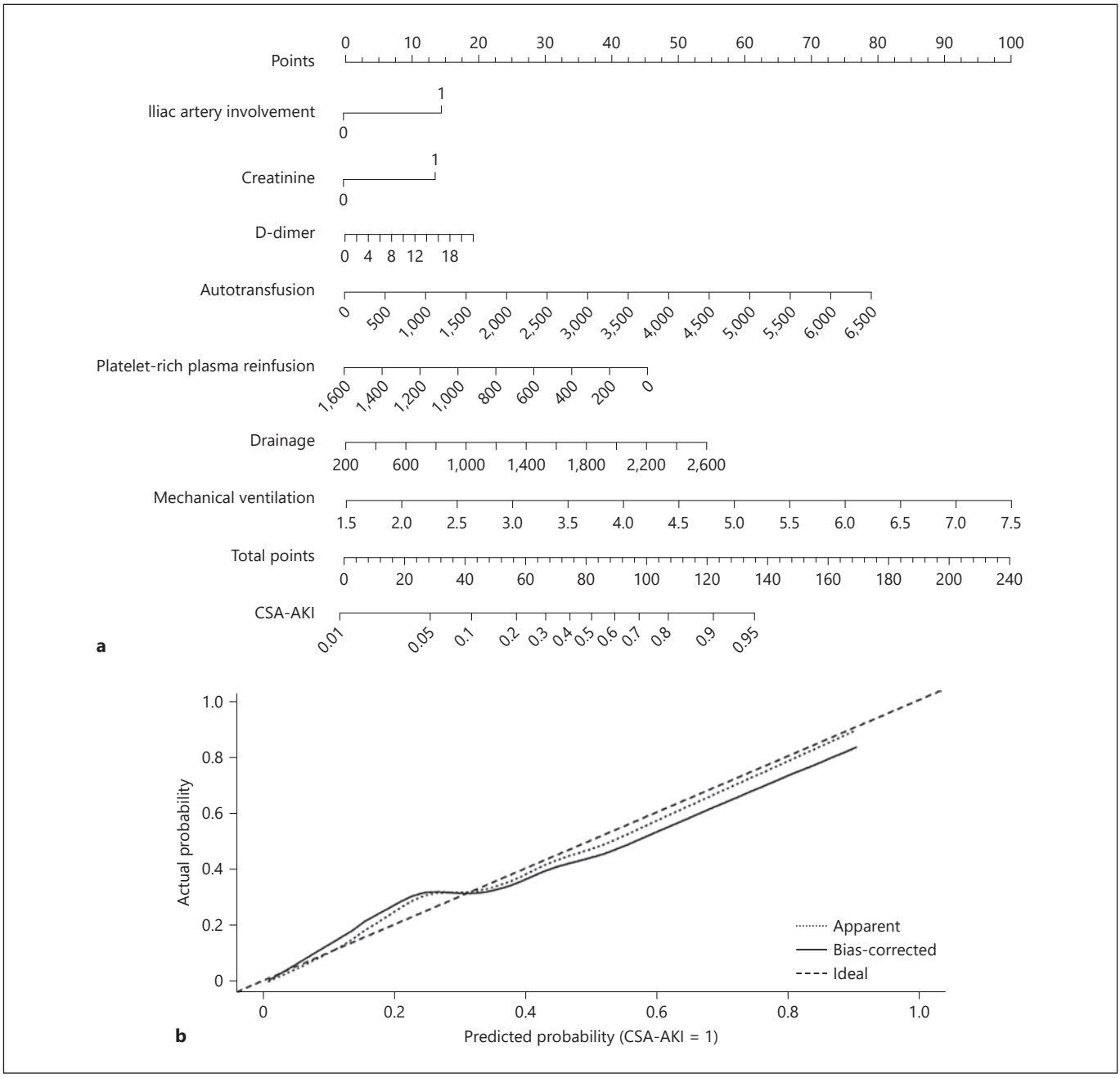


Fig. 5. Nomogram (**a**) and calibration curve (**b**) of risk prediction model 1 for AKI of ATAAD patients. The model was constructed based on intraoperative and postoperative predictors (iliac artery involvement, creatinine, D-dimer, autotransfusion, platelet-rich plasma reinfusion, drainage, and mechanical ventilation). AUC value = 0.848. AUC, area under the receiver operating characteristic curve; AKI, acute kidney injury; ATAAD, acute type A aortic dissection.

ure 3b. Based on the intraoperative and postoperative factors, a risk scoring model 3 was constructed. The relevant parameters were nasal temperature, red blood cells, autotransfusion, fresh frozen plasma, drainage, and mechanical ventilation, which have been shown in the nomogram (shown in Fig. 4a). The consistency of the predicted CSA-AKI risk by model 3 and the actual occurrence of CSA-AKI are shown in Figure 4b. Additionally, we constructed

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Table 6. Comparison of ATAAD-associated AKI risk scoring models based on AUC values

Test result variable, s	AUC	Std. error*	Asymptotic sig**	Asymptotic 95% confidence interval	
				lower bound	upper bound
Model 1	0.710	0.041	0.000	0.629	0.792
Model 2	0.777	0.036	0.000	0.707	0.847
Model 3	0.818	0.032	0.000	0.795	0.888
Model 4	0.848	0.029	0.000	0.792	0.905

AUC, area under the curve. The test result variables (s): predicted probability has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. * Under the nonparametric assumption. ** Null hypothesis, true area = 0.5.

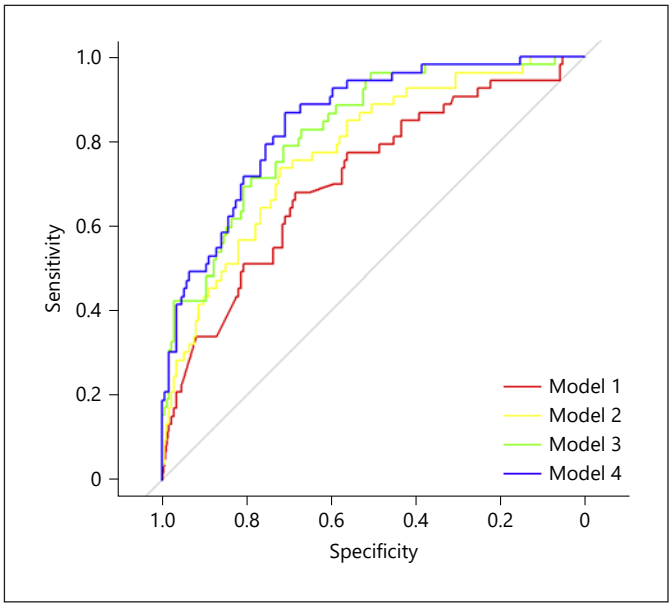


Fig. 6. ROC curves for evaluating the risk scoring of AKI in ATAAD patients. ROC curves were generated based on the data from preoperative (model 1, AUC value = 0.710), preoperative and intraoperative (model 2, AUC value = 0.777), intraoperative and postoperative (model 3, AUC value = 0.818), as well as preoperative, intraoperative, and postoperative (model 4, AUC value = 0.848) examination. AKI, acute kidney injury; ROC, receiver operator characteristic curve; AUC, area under the receiver operating characteristic curve; ATAAD, acute type A aortic dissection; ROC, receiver operating curve.

a risk scoring model 4 for CSA-AKI using the variables from preoperative, intraoperative, and postoperative examination. The parameters were suggested in the nomogram including iliac artery involvement, creatinine, D-dimer, autotransfusion, platelet-rich plasma reinfusion, postoperative suction drainage, and hospital length of stay (shown in Fig. 5a). Figure 5b shows the consistency of actual probability and predicted probability by the risk scoring model 4.

Receiver operating curve curves showed the comparison of AUC among model 1, model 2, model 3, and model 4 for CSA-AKI risk scoring (shown in Fig. 6). The calculated AUC values for the preoperative model 1, preoperative and intraoperative model 2, intraoperative and postoperative model 3, as well as preoperative, intraoperative, and postoperative model 4 were 0.710 (SD = 0.041; 95% CI: 0.629–0.792), 0.777 (SD = 0.036; 95% CI: 0.707–0.847), 0.827 (SD = 0.795; 95% CI: 0.795–0.888), and 0.848 (SD = 0.029; 95% CI: 0.792–0.905), respectively (Table 6), which were all acceptable. Hence, model 4 was optimum for CSA-AKI risk scoring compared with model 1, model 2, and model 3.

Discussion

Epidemiological and observational studies presented a close correlation between AKI and cardiopathic patients after receiving Sun's procedure. Risk assessment for AKI associated with ATAAD allows clinicians to identify perioperative risk levels. However, most constructed risk assessment models fail to synthetically consider preoperative, intraoperative, and postoperative variables [30–33]. In this study, we established four risk assessment models of AKI associated with ATAAD, in which variables include demographic characteristics, preoperative laboratory values and radiologic characteristics, intraoperative data, and postoperative outcomes. The risk prediction model 4, developed with preoperative, intraoperative, and postoperative variables, is optimum for the risk prediction of AKI associated with ATAAD.

For ATAAD patients with a risk of AKI, studies have identified elevated preoperative serum creatinine, preop-

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erative renal malperfusion, and postoperative 72-h drainage volume as the independent risk factors [24, 34]. Body mass index, chronic kidney disease, chronic liver disease, cardiopulmonary bypass duration, red blood cell transfusion, and hypoproteinemia are associated with in-hospital mortality of ATAAD-induced AKI patients [22]. To screen the independent predictors of AKI for ATAAD patients before or after Sun's procedure, we performed multivariable logistic regression analysis and constructed risk prediction models using the screened preoperative demographic and clinical characteristics. These dynamic predictors were successively visualized in a scoring nomogram for the risk prediction of AKI associated with ATAAD from preoperative to early postoperative periods, which have also been reported in other studies [24, 35, 36].

Preoperative risk factors for the development of CSA-AKI contained advanced age, hypertension, and shorter hospital length of stay before surgery. The presence of multiple comorbidities like chronic obstructive pulmonary disease, congestive heart failure, renal disease, and diabetes mellitus has also been considered as preoperative risk factors for CSA-AKI in other studies [37–39]. Our results suggested that an increased white blood cell count was associated with an increased risk of AKI for ATAAD patients. The counts of white blood cells and subtypes (neutrophil, lymphocyte, eosinophil, leucopenia, and leukocytosis) may be attributable to the predictive efficiency in several clinical settings [40]. White blood cells are related to inflammatory processes and involved in the development of AKI [41, 42]. ATAAD patients with AKI exhibited a significant reduction in red blood cell count, which is an additive predictor of all-cause mortality in patients with AKI receiving continuous renal replacement therapy [43]. Creatine kinase-isoenzyme was positively detected in AKI patients with ATAAD after Sun's procedure. Creatine kinase-isoenzyme is an indicator of myocardial injury, and myocardial ischemia/reperfusion-induced injury causes AKI, illustrating the feasibility of creatine kinase-isoenzyme as an indicator [44].

Generally, risk factors for AKI are unmodifiable and common for ATAAD patients, such as local or generalized malperfusion due to the dissection itself [45]. Hypovolemic shock and cardiac malperfusion that are commonly seen in conjunction with ATAAD may induce hypoperfusion to the kidneys, which contributes to kidney function loss [46, 47]. In this study, ATAAD patients with iliac artery involvement, aortic insufficiency, and left ventricular end-diastolic dimension are susceptible to AKI. Patients with distal malperfusion syndromes show an increased incidence of perioperative morbidity, such as hemodialysis [48]. Hemodynamic instability, hypoxia, and inflammation contribute to postoperative AKI [49]. Renal malperfusion is identified as the most important risk factor for AKI [49]. There has been evidence that the dysfunction of the renal microvasculature results in sepsis-associated AKI [50, 51].

Using preoperative parameters, a prediction nomogram was constructed for AKI assessment, with an AUC value of 0.710 (SD = 0.041, 95% CI: 0.629–0.792). Although it is difficult to prevent renal malperfusion, adequate risk evaluation for AKI may improve patient outcomes. In the present study, intraoperative and postoperative risk factors were screened. The study demonstrated that cardiopulmonary bypass time, nasal temperature, autotransfusion volume, the number of red blood cells transfused during Sun's procedure, and decreased fresh frozen plasma have a marked impact on AKI, which indicates that these factors can be used as variables for the construction of a logistic regression model of AKI prediction. A retrospective study revealed that patients with increased postoperative mean platelet volume had an increased odds of generating AKI, while mortality was not significantly affected [1]. Besides, the development of AKI is also affected by the type of cardiac surgical procedure, such as valve replacement [52], valve repair [53], and aortic arch surgery [54], which may affect cardiopulmonary bypass time. Cardiopulmonary bypass time extension causes nonpulsatile flow and activates inflammatory factors, increasing the risk of AKI [55]. Alternatively, AKI results from intraoperative and postoperative insults evidenced by elevations of urinary biomarkers [56], urinary hypoxia [57], and early postoperative serum creatinine [58], as reported by recent research.

According to the risk factors discussed above, predictive nomograms were constructed based on preoperative and intraoperative parameters (AUC value = 0.777, SD = 0.036, 95% CI: 0.707–0.847), intraoperative and postoperative parameters (AUC value = 0.818, SD = 0.032, 95% CI: 0.795–0.888), and preoperative, intraoperative, and postoperative parameters (AUC value = 0.848, SD = 0.029, 95% CI: 0.792–0.905). Predictive nomograms enable early identification of ATAAD patients at high risk of AKI, and prophylactic measurements may subsequently decrease the risk of perioperative AKI. An efficient assessment model 4 facilitates a close monitor process and makes it possible for clinicians to formulate preventive and therapeutic strategies rapidly. Besides clinical risk factors, the integration of circulating cell-free DNA into prediction models promotes the early and efficient iden-

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tification of CSA patients at high risk of AKI [59]. Several risk prediction models for CSA-AKI have been validated using the biomarkers like blood cytokine [60], and renal damage biomarkers [61]. However, the performances of multivariable logistic regression models established with demographic characteristics and clinical features are markedly superior to those constructed with the indicators suggesting AKI had occurred.

Previous literature has reported that most renal functions of patients with unilateral renal artery involvement can be improved with a better prognosis after aortic dissection repair; generally speaking, further specific interventional treatment is unnecessary. In contrast, for cases involving bilateral renal arteries, postoperative renal function is often unsatisfactory; continued renal replacement therapy or even further local renal artery intervention is required to improve renal vascular blood supply and renal function [62]. In this study, aortic dissection involving the renal artery was not included as a risk factor in the final AKI risk prediction model, which may be related to the composition of the type of preoperative renal artery injury in patients. This study did not compare subgroups with respect to the subtypes of aortic dissection involving the renal artery. This study could be followed up with further analysis in this regard.

There are still some limitations like other retrospective studies. An external validation of our models is necessary using independent data, which is required to precisely assess the feasibility of the variables. Besides, our study excluded a majority of ATAAD patients with complication such as blood system disease considering the unfavorable outcomes after Sun's procedure. Additionally, the staging and criteria of AKI should be included in risk evaluation because of the distinct therapies used in different stages of AKI. However, the established model was constructed based on preoperative, intraoperative, and postoperative parameters that are easily collected and analyzed. The regression model was concisely visualized with this predictive nomogram, which shows an advantageous practicality.

Conclusions

Here, we established 4 risk prediction models of AKI for ATAAD patients before or after Sun's procedure. The included variables were demographic characteristics, preoperative laboratory values and radiologic characteristics, intraoperative data, and postoperative outcomes. The risk prediction model 4 is optimum for AKI risk prediction. However, the abovementioned models have not been validated using the independent data. In the future, this model will be used tentatively for risk prediction in electronic medical records.

Statements of Ethics

This study was approved by the Research Ethics Committee of Tianjin Chest Hospital. The data are anonymous, and the requirement for informed consent was therefore waived by the Ethics Committee.

Conflict of Interest Statement

The authors declare that they have no competing interests.

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Author Contributions

Qingliang Chen and Zhigang Guo designed the study. Tongyun Chen and Nan Jiang contributed to clinical information collection and literature search. Yuhui Zhang and Yongrong Lan performed the data analysis and drafted the manuscript. All the authors revised and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this. Further inquiries can be directed to the corresponding author.

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