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Development and validation of a clinical prediction model for dialysis-requiring acute kidney injury following heart transplantation: a single-center study from China

Shirui Qian[1†], Bingxin Cao[1†], Ping Li[1*] and Nianguo Dong[1,2*]

Abstract

Objectives This study seeks to construct and internally validate a clinical prediction model for predicting new-onset dialysis-requiring acute kidney injury (AKI) following heart transplantation (HT).

Methods The Kaplan-Meier survival analysis and log-rank test were utilized for conducting the survival analysis. A clinical prediction model was developed to predict postoperative dialysis-requiring AKI, based on a logistic regression model and likelihood ratio test with Akaike Information Criterion. The performance of the prediction model was assessed using C-index, receiver operating characteristic curves, calibration curves, Brier score, and the Spiegelhalter Z-test. Clinical utility was evaluated using decision curve analysis and clinical impact curves.

Results This study included a total of 525 patients who underwent orthotopic HT in the single center located in Wuhan, China between January 2015 and December 2021, with 16.57% developing postoperative dialysis-requiring AKI. Patients who experienced postoperative dialysis-requiring AKI exhibited a lower overall survival rate. All enrolled participants were randomly allocated into derivation ($n=350$) and validation ($n=175$) cohorts at a ratio of 2:1.
The final prediction model comprised six indicators: diabetes, stroke, gout, prognostic nutritional index, estimated glomerular filtration rate, and cardiopulmonary bypass duration. The prediction model demonstrated outstanding discrimination (C-index of 0.792 in the derivation cohort and 0.834 in the validation cohort) as well as calibration performance, indicating strong concordance between observed and nomogram-predicted probabilities. Subgroup analysis based on age, preoperative serum creatine levels, and year of surgery also exhibited robust discrimination and calibration capabilities.

Conclusions Dialysis-requiring AKI following HT is associated with poor clinical prognosis. The prediction model, comprising six indicators, is capable of predicting dialysis-requiring AKI following HT. This prediction model holds

†Shirui Qian and Bingxin Cao contributed equally to this work.

*Correspondence:
Ping Li
LIPINGCPB@126.com
Nianguo Dong
1986xh0694@hust.edu.cn

Full list of author information is available at the end of the article

promise in assisting both patients and clinicians in forecasting postoperative renal failure, thereby improving clinical management.

Clinical trial number Not applicable.

Keywords Prediction model, Acute kidney injury, Heart transplantation, Nomogram, Risk stratification

Introduction

Heart transplantation (HT) is the definitive therapeutic intervention for patients with end-stage heart failure [1], boasting a 1-year survival rate exceeding 85% and a median survival of 14 years [2, 3]. However, while HT aims to improve quality of life and longevity, it also carries an increased risk of comorbidities [4, 5].

Acute kidney injury (AKI) contributes significantly to these comorbidities, with the prevalence of severe cases necessitating dialysis ranging from 4 to 28% [6, 7]. Furthermore, it is correlated with postoperative mortality rates, which ranges from 35 to 50% [8–10]. In addition, to its direct impact on patient prognosis, dialysis-requiring AKI is associated with prolonged mechanical ventilation, extended stays in the intensive care unit, longer hospitalizations, and increased healthcare costs [7, 11, 12].

Despite identified risk factors for dialysis-requiring AKI following HT, there is currently a dearth of a user-friendly predictive scale to evaluate overall risk. Although one study has devised a risk index for forecasting postoperative renal failure [13], it relied on data from 2000 to 2010 which may not accurately represent the present era. Additionally, there is inadequate detailed evaluation of the performance of this risk index.

Therefore, there is a pressing need for the development of a novel prediction model that demonstrates robust discrimination and calibration capabilities. Such a tool would be invaluable in providing guidance for prognostic assessments and clinical care, as well as in stratifying patients for research studies based on their baseline risk. Consequently, the objective of this study is to establish and validate a clinical prediction model specifically designed for identifying dialysis-requiring AKI following HT.

Methods

Ethic statement and study design

This is a retrospective study approved by the Ethics Committee of Tongji College, Huazhong University of Science and Technology (No: IORG0003263). Clinical and research activities comply the 'Declaration of Istanbul on Organ Trafficking and Transplant Tourism' [14]. Written informed consent was obtained from individual or guardian participants.

We retrieved the entire cohort from a single center located in Wuhan, China. All patients who underwent orthotopic HT between January 2015 and December 2021 were encompassed (a total of 665 patients). We excluded those with (1) an age of less than 18 years old; (2) heart re-transplantation or multiple organ transplantation; (3) dialysis prior to HT; (4) insufficient clinical data. After meticulous screening, a total of 525 patients were included in this study and were subsequently randomly divided into the derivation and validation cohorts.

Data collection and outcome measures

Baseline characteristics including recipient, donor and operative variables were conducted within 7 days prior to HT operation. Chronic pulmonary disease encompasses chronic obstructive pulmonary disease, asthma, pulmonary fibrosis, cystic fibrosis, and so on. Chronic kidney disease is defined as abnormalities of kidney structure or function, present for greater than 3 months. This is defined as a GFR less than 60 mL/min/1.73 m^2 or one or more markers of kidney dysfunction including albuminuria (albumin excretion rate ≥ 30 mg/24 h; albumin-to-creatinine ratio ≥ 30 mg/g [≥ 3 mg/mmol]), urine sediment abnormalities, electrolyte and other abnormalities owing to tubular disorders, abnormalities detected by histology, structural abnormalities detected by imaging and history of kidney transplantation. Chronic liver disease is defined as alcoholic liver disease, non-alcoholic fatty liver disease, chronic viral hepatitis and so on.

The baseline serum creatinine level was the most recent measurement before HT. The prognostic nutritional index (PNI) was calculated using the following equation: PNI = 10×Alb, g/L + 5×lymphocyte count, 10^9/L [15]. The estimated glomerular filtration rate (eGFR) was calculated using the following formula [16], where SCr is serum creatinine:

eGFR (men) = 194×SCr-1.094×age-0.287 (mL/min per 1.73m2).
eGFR (women) = eGFR (men)×0.739 (mL/min per 1.73m2).

The primary outcome was the occurrence of dialysis-requiring AKI following HT, defined as the development or exacerbation of AKI necessitating initiation of new renal dialysis during the hospitalization for HT [13, 17, 18]. The institutional criteria for initiating dialysis were as follows: (1) SCr ≥ 400 μmol/L or 2-fold or more increase from the baseline; (2) oliguria, defined as a urine flow ≤ 0.5 ml/kg/hour for ≥ 3 h, despite optimization

of systemic and pulmonary hemodynamic; (3) serum potassium ≥ 6.0 mmol/L and unresponsive to insulin and diuretic therapy; (4) metabolic acidosis; (5) uremia.

Secondary outcomes measured were in-hospital, 30-day, 90-day, and 1-year all-cause mortality. Mortality data were collected from the China Heart Transplant Registration Network until May 26, 2022, as mandated by law that all heart transplant-related deaths must be uploaded to the website database.

Survival analysis

The survival outcome of patients with or without dialysis-requiring AKI was analyzed and compared utilizing the Kaplan–Meier (K-M) survival analysis and log-rank test, respectively.

Derivation and validation cohorts

Participants were allocated into derivation and validation cohorts in a 2:1 ratio using a randomization method. Each participant was assigned a random number generated by the seed 19,950,410, which was then sorted from largest to smallest. The first two-thirds of participants were placed in the derivation cohort, while the remaining participants were assigned to the validation cohort. Baseline characteristics were compared between the derivation and validation cohorts. The Chi-squared test was utilized to compare categorical variables, which were expressed as number (percent). Continuous variables were reported as means ± standard deviation and analyzed using either student's t-test or Mann-Whitney U test (See Fig. 1).

Development of the prediction model in the derivation cohort

The pre- and intra-operative variables, including patients' demographic characteristics, comorbidities, laboratory indexes, and donor characteristics, underwent univariate logistic regression analysis to identify candidate variables for the prediction model. Variables with a P value < 0.1 were included in the multivariate logistic regression analysis. The full logistic regression model was simplified using stepwise backward variable selection in 1000 bootstrapped samples with a significance level of 0.05, employing the likelihood ratio test with Akaike Information Criterion (AIC) as the stopping rule [19]. The analysis was conducted using the R package "rms" [20].

Model evaluation

The discrimination ability of the prediction model was evaluated using the Harrell concordance index (C-index) and receiver operating characteristic (ROC) curves. Calibration accuracy was assessed through calibration curves drawn in 1000 bootstrapped samples, Brier score, and 2-tailed P values of the Spiegelhalter Z-test. The clinical utility of the prediction model was evaluated using decision curve analysis (DCA) and clinical impact curve (CIC) in both derivation and validation cohorts. Subgroup analysis was conducted based on age, preoperative

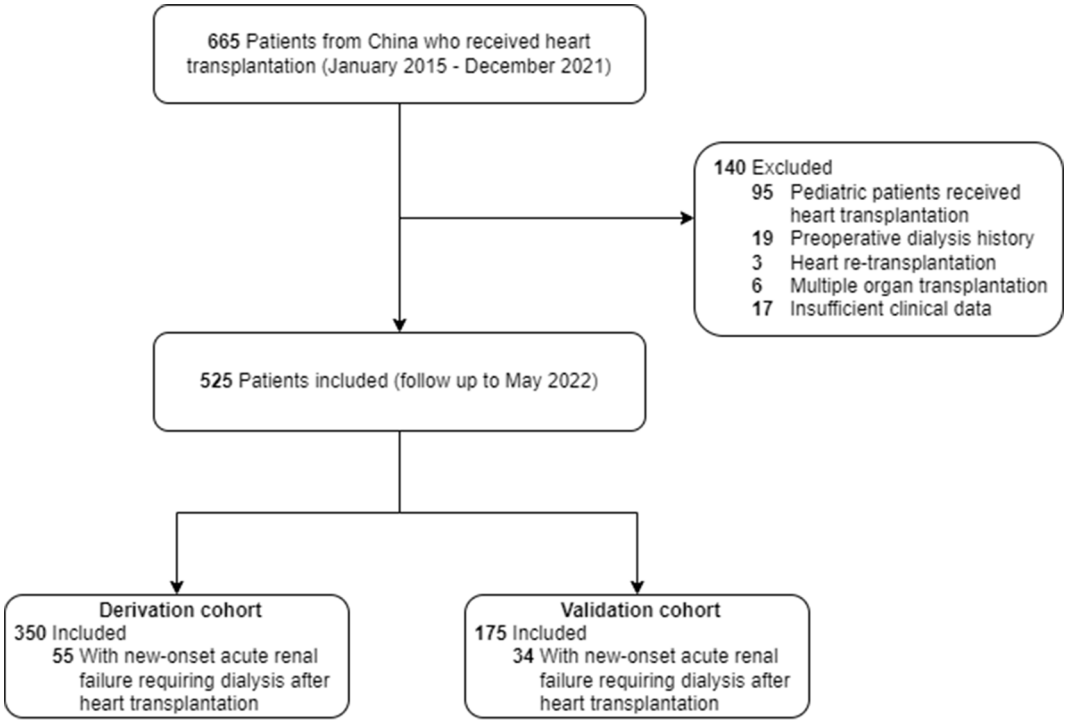

Fig. 1 Flowchart of patients included in the study

SCr, and year of surgical procedure by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

All analysis were performed with SPSS 27.0.1 and R 4.3.0 (The R Foundation for Statistical Computing, Beijing, China). Statistical significance was set at two-sided $P < 0.05$.

Results

Baseline characteristics

A total of 525 eligible patients were included in the final analysis. The average age of recipients was 47.56 ± 12.63, with males accounting for 79.0% (Table 1). The mean preoperative SCr and eGFR were 95.30 ± 41.75 μmol/L and 63.44 ± 21.79 mL/min/1.73m^2, respectively. The mean donor age was 36.18 ± 11.65 years, while the average cold ischemia time was reported to be 333.24 ± 104.41 min.

After conducting an analysis, there were no statistically significant differences in baseline characteristics between the derivation and validation cohorts. Besides, the eTable 1 showed the differences in baseline characteristics between the dialysis-requiring AKI and non-dialysis cohorts.

Incidence and long-term outcomes of acute renal failure patients

The overall incidence of new-onset dialysis-requiring AKI following HT was 16.57% (87 subjects). The rate of in-hospital, 30-day, 90-day and 1-year mortality of the entire cohort were 5.0%, 7.2%, 11.0% and 15.0%. And the rate of in-hospital, 30-day, 90-day and 1-year mortality were all higher in the dialysis-requiring AKI cohort (eTable 1 in the Supplement). The findings from K-M survival analysis demonstrated that patients experiencing postoperative dialysis-requiring AKI had significantly poorer overall survival compared to those not requiring dialysis ($P < 0.001$) (eFigure 1 in the Supplement).

Construction of the prediction model

A total of 350 patients (66.7%) were randomly assigned to the derivation cohort. The findings of the univariate logistic regression analysis are presented in eTable 2 in the Supplement. By utilizing stepwise selection and likelihood ratio test with AIC in the multivariate logistic regression model, a final simplified prediction model retained six predictive variables (diabetes, stroke, gout, PNI, eGFR and cardiopulmonary bypass (CPB) duration). These 6 independent predictors were found to be independently associated with an increased risk of new-onset dialysis-requiring AKI following HT (Table 2). And this model demonstrated the smallest value of AIC which was used to construct the nomogram (Fig. 2).

Assessment of the prediction model in derivation and validation cohorts

The prediction model's performance was evaluated using the area under the receiver operating characteristic curve (AUC) and C-index. The AUC value of the prediction model was 0.792 (95% CI: 0.723–0.861), surpassing that of each individual variable in the model. (Fig. 3A). The C-index of the prediction model was also found to be at a high level of accuracy with a value of 0.792 (95% CI: 0.723–0.861), indicating strong predictive discrimination capabilities. The calibration curve demonstrated a high consistency between predictions and actual observations through 1000 resampling bootstraps with a Brier score of 0.106 and a Spiegelhalter Z-test *P* value 0.948 (Fig. 3B).

Since the prediction model was constructed using the derivation cohort, the validation cohort data was employed to validate it. In the validation cohort, the AUC value of the prediction model was 0.834 (95% CI: 0.762–0.905) (Fig. 3C), with a C-index of 0.834 (95% CI: 0.762–0.905). The calibration curve, based on 1000 resampling bootstraps, demonstrated high consistency between prediction and actual observation. Additionally, the Brier score is 0.117 and the *P* value of Spiegelhalter Z-test was 0.819 (Fig. 3D).

Subgroup validation of the prediction model

The C-index of the prediction model for patients under 50 years old and those 50 years old or older were 0.900 and 0.714, respectively. The *P* values of Spiegelhalter Z-test were 0.913 and 0.956, respectively (Table 3). These findings indicate strong performance of the prediction model. Similar results were observed in the prespecified subgroup analysis based on preoperative SCr and year of surgery.

Clinical utility of the prediction model

The DCA demonstrated that the prediction model exhibited superior net benefits for identifying new-onset dialysis-requiring AKI following HT compared to any single factor in the derivation cohort (Fig. 4A). Similar findings were observed in the validation cohort (Fig. 4C). Furthermore, based on the DCA results, we further plotted CIC to evaluate the clinical utility of the nomograms. The CIC demonstrated a strong alignment between the anticipated probability and the observed probability in the derivation cohort (Fig. 4B). Similar results were found in the validation cohort (Fig. 4D).

The prediction model's clinical application will identify patients at high risk of new-onset postoperative dialysis-requiring AKI based on a range of predicted risk thresholds (Table 4). The result of ROC analysis demonstrated that at a risk threshold of higher than 20%, 24.9% patients in the derivation cohort and 33.7% patients in the validation cohort were categorized as high risk for

Table 1 Baseline characteristics of the derivation and validation cohorts

Variables	Study population ($n=525$)	Derivation cohort ($n=350$)	Validation cohort ($n=175$)	*P* value
Recipients				
Gender (male)	415 (79.0%)	282 (80.6%)	133 (76.0%)	0.225
Age (years)	47.56 ± 12.63	47.94 ± 12.49	46.81 ± 12.91	0.331
BMI (kg/m^2)	23.07 ± 3.93	23.24 ± 4.10	22.73 ± 3.54	0.164
Diagnosis				0.402
Ischemia cardiomyopathy	120 (22.9%)	82 (23.4%)	38 (21.7%)	
Non-ischemia cardiomyopathy	316 (60.2%)	208 (59.4%)	108 (61.7%)	
Congenital heart disease	78 (14.8%)	51 (14.6%)	27 (15.4%)	
Other heart disease	11 (2.1%)	9 (2.6%)	2 (1.1%)	
ABO blood type				0.600
A	176 (33.5%)	120 (34.3%)	56 (32.0%)	
B	142 (27.0%)	99 (28.3%)	43 (24.6%)	
O	170 (32.4%)	108 (30.9%)	62 (35.4%)	
AB	37 (7.0%)	23 (6.6%)	14 (8.0%)	
Hypertension	86 (16.4%)	62 (17.7%)	24 (13.7%)	0.243
Diabetes	110 (21.0%)	77 (22.0%)	33 (18.9%)	0.404
Hyperlipemia	31 (5.9%)	17 (4.9%)	14 (8.0%)	0.150
Stroke	26 (5.0%)	17 (4.9%)	9 (5.1%)	0.887
Chronic pulmonary disease	128 (24.4%)	85 (24.3%)	43 (24.6%)	0.943
Chronic liver disease	31 (5.9%)	20 (5.7%)	11 (6.3%)	0.793
Chronic kidney disease	24 (4.6%)	17 (4.9%)	7 (4.0%)	0.658
Gout	10 (1.9%)	6 (1.7%)	4 (2.3%)	0.652
History of smoking	209 (39.8%)	145 (41.4%)	64 (36.6%)	0.284
History of alcoholism	137 (26.1%)	96 (27.4%)	41 (23.4%)	0.325
Surgery history (yes)	242 (36.1%)	165 (47.1%)	77 (44.0%)	0.496
Cardiac surgery history (yes)	198 (37.7%)	139 (39.7%)	59 (33.7%)	0.181
Preoperative IABP	8 (1.5%)	7 (2.0%)	1 (0.6%)	0.208
Preoperative ECMO	6 (1.1%)	4 (1.1%)	2 (1.1%)	1.000
Donors Characteristics				
Donor gender (male)	453 (86.3%)	302 (86.3%)	151 (86.3%)	1.000
Donor age (years)	36.18 ± 11.65	35.85 ± 11.64	36.84 ± 11.69	0.361
Donor BMI (kg/m^2)	22.54 ± 3.07	22.59 ± 3.11	22.43 ± 2.99	0.552
Donor/recipient BMI	1.03 ± 0.20	1.04 ± 0.21	1.03 ± 0.19	0.412
Donor/recipient age	1.48 ± 0.72	1.51 ± 0.73	1.43 ± 0.70	0.246
Donor/recipient gender				0.596
Male/male	370 (70.5%)	252 (72.0%)	118 (67.4%)	
Male/female	45 (8.6%)	30 (8.6%)	15 (8.6%)	
Female/male	83 (15.8%)	50 (14.3%)	33 (18.9%)	
Female/female	27 (5.1%)	18 (5.1%)	9 (5.1%)	
Recipient/donor blood-type				0.342
Identical	204 (38.9%)	141 (40.3%)	63 (36.0%)	
Different	321 (61.1%)	209 (59.7%)	112 (64.0%)	
Cause of death				0.327
Brain Injury	287 (54.7%)	192 (54.9%)	95 (54.3%)	
Cerebral hemorrhage	187 (35.6%)	120 (34.3%)	67 (38.3%)	
Brain Tumor	16 (3.0%)	10 (2.9%)	6 (3.4%)	
Others	35 (6.7%)	28 (8.0%)	7 (4.0%)	
Cold ischemia time (min)	333.24 ± 104.41	335.74 ± 103.95	328.23 ± 105.45	0.438
Aortic cross clamp time (min)	32.44 ± 10.06	32.49 ± 9.67	32.34 ± 10.82	0.871
Cardiopulmonary bypass duration (min)	119.62 ± 42.29	119.00 ± 42.82	125.99 ± 82.29	0.201
Preoperative Blood Index				
RBC (10^{12}/L)	4.52 ± 1.48	4.57 ± 1.75	4.44 ± 0.67	0.341
HCT (%)	40.50 ± 6.56	40.52 ± 6.39	40.46 ± 6.91	0.923

Table 1 (continued)

Variables	Study population ($n=525$)	Derivation cohort ($n=350$)	Validation cohort ($n=175$)	*P* value
PLT (10^9/L)	184.12 ± 66.44	184.22 ± 66.76	183.93 ± 65.96	0.962
WBC (10^9/L)	6.86 ± 4.92	7.05 ± 5.78	6.50 ± 2.39	0.234
Hb (g/L)	134.37 ± 21.38	134.41 ± 21.30	134.29 ± 21.60	0.948
Bilirubin (μmol/L)	27.16 ± 19.26	27.32 ± 19.26	26.85 ± 19.33	0.792
ALT (U/L)	73.47 ± 289.18	69.82 ± 230.11	80.77 ± 381.51	0.683
AST (U/L)	61.01 ± 245.51	61.97 ± 236.49	59.09 ± 263.31	0.899
SCr (μmol/L)	95.30 ± 41.75	96.19 ± 44.15	93.52 ± 36.54	0.491
eGFR (mL/min/1.73m^2)	63.44 ± 21.79	63.40 ± 22.48	63.51 ± 20.40	0.956
BUN (mmol/L)	8.09 ± 3.64	8.24 ± 3.72	7.78 ± 3.48	0.174
UA (μmol/L)	494.89 ± 171.04	495.81 ± 176.12	493.04 ± 160.86	0.862
TC (mmol/L)	3.98 ± 1.32	4.00 ± 1.34	3.93 ± 1.28	0.544
Alb (g/L)	39.15 ± 4.86	38.88 ± 4.92	39.69 ± 4.72	0.074
LDL-C (mmol/L)	2.09 ± 0.88	2.10 ± 0.88	2.07 ± 0.89	0.700
TG (mmol/L)	1.16 ± 0.63	1.16 ± 0.62	1.16 ± 0.66	0.982
PNI (%)	46.56 ± 8.31	46.27 ± 8.77	47.13 ± 7.29	0.259

BMI, body mass index; IABP, intra-aortic balloon pump; ECMO, extracorporeal membrane oxygenation; RBC, red blood cell; HCT, hematocrit; PLT, platelets; WBC, white blood cell; Hb, hemoglobin; ALT, alanine transaminase; AST, aspartate transaminase; SCr, serum creatine; eGFR, estimated glomerular filtration rate; BUN, blood urea nitrogen; UA, uric acid; TC, total cholesterol; Alb, albumin; LDL-C, low density lipoprotein-cholesterol; TG, triglyceride; PNI, prognostic nutritional index

Table 2 Multivariable β-coefficient an odds ratio for association between predictive variables and new-onset post-transplant renal failure requiring dialysis

Predictive variables	β-Coefficient	Odds ratio (95% CI)	*P* value
Diabetes	1.197	3.311 (1.674–6.548)	< 0.001
Stroke	1.635	5.131 (1.729–15.224)	0.003
Gout	1.754	5.780 (1.082–30.866)	0.040
PNI, per 1% increase	-0.052	0.950 (0.904–0.998)	0.043
eGFR, per 1 mL/min/1.73 m2 increase	-0.022	0.978 (0.962–0.995)	0.010
CPB duration, per 1 min increase	0.015	1.015 (1.008–1.021)	< 0.001

PNI, prognostic nutritional index; eGFR, estimated glomerular filtration rate; CPB, cardiopulmonary bypass

postoperative dialysis-requiring AKI. In both derivation and validation cohorts, the corresponding sensitivity values were 65.5% (95% CI, 52.9-78.0%) and 73.5% (95% CI, 58.7-88.4%), respectively. The specificity values were 82.7 (95% CI, 78.4-87.0%) and 75.9 (95% CI, 68.8-82.9%), respectively. The corresponding PPV were 41.4% (95% CI, 31.0-51.7%) and 42.4% (95% CI, 29.8-55.0%), respectively. And NPV were 92.8% (95% CI, 89.6-95.9%) and 92.2% (95% CI, 87.4-97.1%), respectively (Table 4). In addition, patients in high-risk group had higher rate of in-hospital, 30-day, 90-day and 1-year mortality both in derivation and validation cohorts (eTable 3 in the Supplement). And the result of K-M survival analysis also showed that high-risk patients had significantly poorer overall survival (Fig. 5).

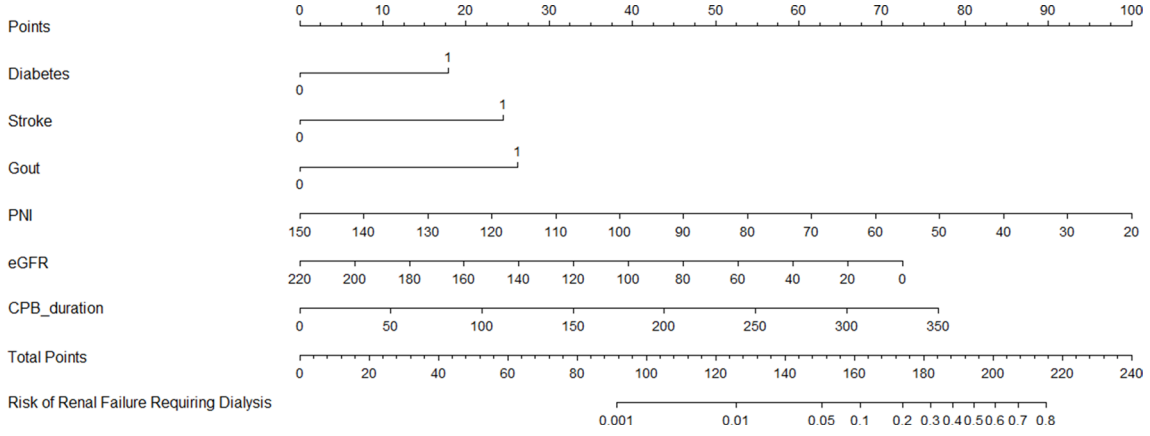

Fig. 2 Nomogram of predicting new-onset post-transplant renal failure requiring dialysis. It was constructed based on the derivation cohort. The points identified on the scale for each indicator were summed and the total points projected on the bottom scales indicate the probabilities of post-transplant renal dysfunction. PNI, prognostic nutritional index; eGFR, estimated glomerular filtration rate; CPB, cardiopulmonary bypass

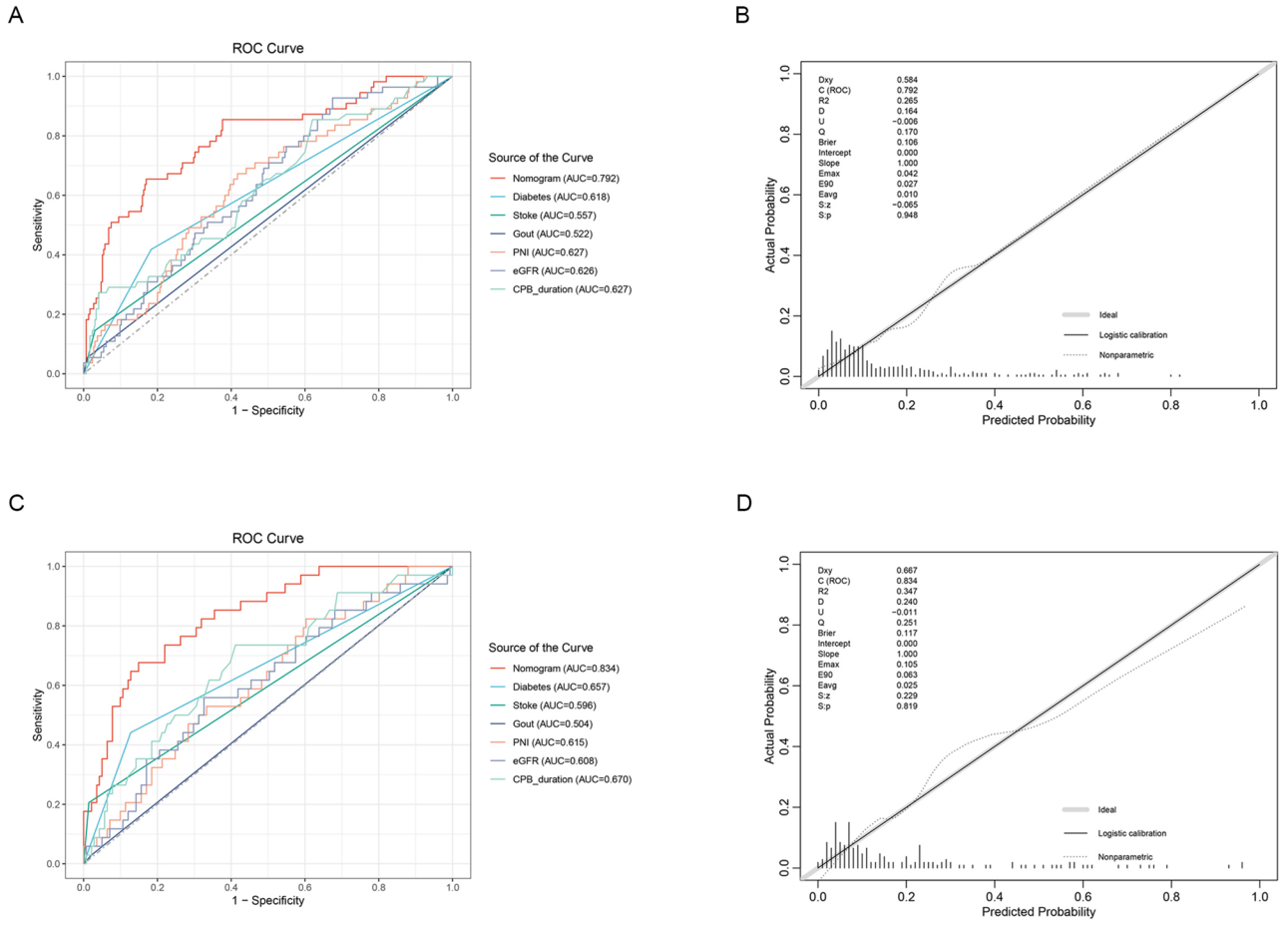

Fig. 3 The nomogram performance. Receiver operating characteristic (ROC) curves for the prediction of new-onset post-transplant renal failure requiring dialysis in the derivation cohort (**A**) and validation (**C**) cohort. Calibration plots for estimating new-onset post-transplant renal failure requiring dialysis probabilities are presented for the derivation cohort (**B**) and validation cohort (**D**). PNI, prognostic nutritional index; eGFR, estimated glomerular filtration rate; CPB, cardiopulmonary bypass

Table 3 The prediction model performance in derivation and validation cohorts, stratified by age, preoperative creatinine and year of surgery

Groups	Age		Preoperative SCr		Year of surgery	
	< 50 years	≥ 50 years	< 90 μmol/L	≥ 90 μmol/L	2015–2017	2018–2021
Derivation cohort						
No. of patients	169	181	185	165	181	169
C-statistics	0.9	0.714	0.858	0.755	0.892	0.767
P value for Z-test	0.913	0.956	0.78	0.909	0.987	0.954
Validation cohort						
No. of patients	88	87	96	79	84	91
C-statistics	0.856	0.859	0.836	0.881	0.951	0.781
P value for Z-test	0.919	0.787	0.847	0.853	0.833	0.928

SCr, serum creatinine

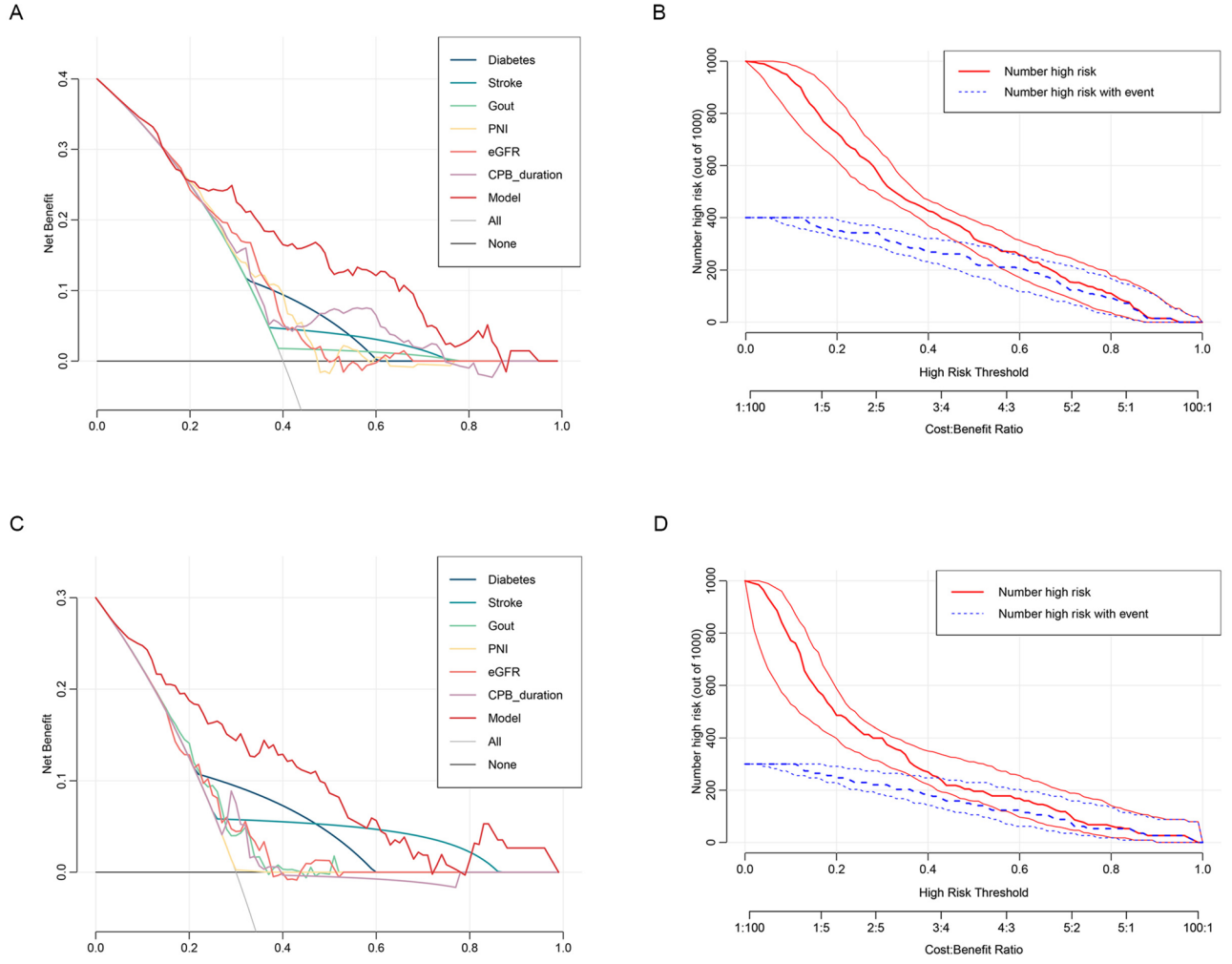

Fig. 4 Clinical utility of the nomogram. Decision curve analysis of the nomogram prediction in the derivation cohort (**A**) and validation cohort (**C**). Clinical impact curve of the nomogram in the derivation cohort (**B**) and validation cohort (**D**). PNI, prognostic nutritional index; eGFR, estimated glomerular filtration rate; CPB, cardiopulmonary bypass

Table 4 Proportion of patients at risk for post-transplant renal dysfunction who are considered for intervention in a range of probability thresholds, and corresponding sensitivity, specificity, positive and negative predictive values

Predicted risk category	Patients (No., %)	Sensitivity (%, CI)	Specificity (%, CI)	PPV (%, CI)	NPV (%, CI)
Derivation cohort					
> 20%	87 (24.9%)	65.5 (52.9–78.0)	82.7 (78.4–87.0)	41.4 (31.0–51.7)	92.8 (89.6–95.9)
Validation cohort					
> 20%	59 (33.7%)	73.5 (58.7–88.4)	75.9 (68.8–82.9)	42.4 (29.8–55.0)	92.2 (87.4–97.1)

CI, confidence interval; PPV, positive predictive value; NPV negative predictive value

Website of the prediction model

The web-based prediction model calculator has been developed and is freely accessible online. It aims to assist patients and physicians in determining the individual risk of new-onset dialysis-requiring AKI following HT. (https://docqianofwuhanunionhospital.shinyapps.io/RiskOfRenalDysfunctionAfterHeartTransplantation/)

Discussion

This study, based on a large single-center Chinese cohort, developed and validated a novel clinical prediction model for predicting new-onset dialysis-requiring AKI following HT. Four key findings emerged: (1) The incidence of new-onset dialysis-requiring AKI following HT was 16.57%, with patients experiencing worse overall survival compared to those without dialysis; (2) Multivariate logistic regression analysis revealed that diabetes, stroke, gout, lower PNI and eGFR, and longer CPB duration were independently associated with an increased risk of

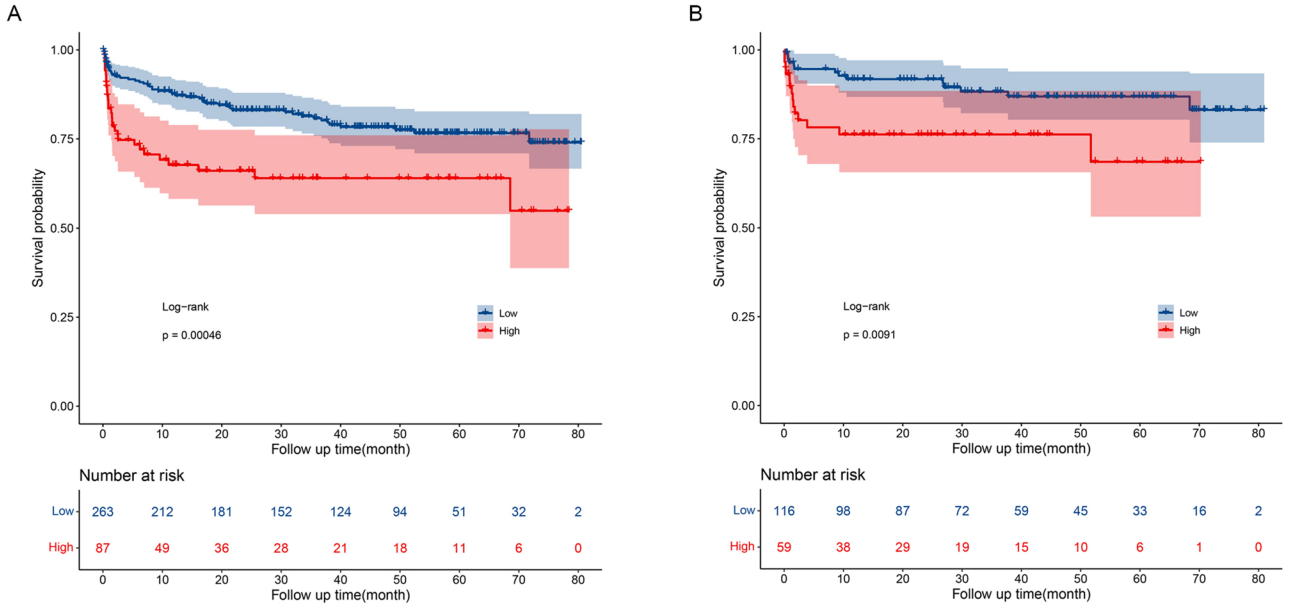

Fig. 5 Comparison of long-term survival between low-risk and high-risk patients. (**A**) In the derivation cohort, high-risk patients (> 20%) stratified by the nomogram had poorer over-all survival. (**B**) In the validation cohort, high-risk patients had poorer over-all survival

postoperative dialysis-requiring AKI; (3) the prediction model demonstrated robust discrimination and calibration utility, as well as effective risk stratification capabilities; (4) the prediction model is accessible online and serves as a valuable tool for guiding prognostic assessments and medical care post-admission.

The prediction model demonstrated excellent discrimination and calibration ability. Subgroup analysis stratified by age, preoperative SCr, and year of surgery further supported the results. A Brier score below 0.1 indicates outstanding model predictive performance, while a score between 0.1 and 0.25 is considered good. In our study, the derivation cohort had a Brier score of 0.106 and the validation cohort had a score of 0.117, indicating good prediction performance of the prediction model. Although precision (PPV) and recall (sensitivity) showed relatively lower values in this study, the prediction model exhibited very high NPV and specificity, demonstrating its strong predictive ability.

The incidence of dialysis-requiring AKI was slightly higher than previous reports in the United States [16, 21], which may be attributed to a greater burden of comorbidities among current heart transplant recipients compared to those in the past. Shoji et al. previously demonstrated the impact of dialysis-requiring AKI on in-hospital mortality [16]. However, their study was based on data from 2009 to 2020 in the United States and may not reflect the contemporary era. Our study provides further evidence that postoperative dialysis-requiring AKI is associated with long-term mortality after HT, using data from China.

The most significant risk predictors for postoperative dialysis-requiring AKI in this study were diabetes and longer CPB duration. A previous study from Taiwan also found that patients with diabetes are at a higher risk of dialysis-requiring AKI [22]. Other notable risk factors included chronic kidney disease, acute kidney injury, and coronary artery disease. Multiple prior studies have linked prolonged CPB time to postoperative AKI [23–26]. Additionally, a prospective study of hospitalized first-ever stroke patients over 10 years revealed that about one third of stroke patients presented with renal dysfunction [27]. Furthermore, renal function upon admission was identified as a significant independent prognostic factor for long-term mortality in stroke patients.

We have observed a significant correlation between malnutrition (lower PNI) and the onset of postoperative acute renal failure. PNI integrates serum albumin and lymphocytes to signify nutritional and inflammatory conditions [28–30]. Recently, several studies have affirmed the efficacy of PNI as a predictive marker for AKI [31–35]. We are the first investigation to explore the diagnostic accuracy of the PNI for dialysis-requiring AKI following HT prediction. However, there is a paucity of literature regarding the pathophysiological mechanisms linking a low PNI to AKI. The likely explanations are that PNI reflects the general physical condition of a patient, and the reduction of PNI indicates a poor overall condition and a decreased protein reserve, which leads to an increased risk of mortality [36]. In addition, Ishikawa et al. [37]. also manifested that the Neutrophil-to-Lymphocyte Ratio (NLR) was a robust and independent predictor of AKI after coronary artery bypass grafting.

The dynamic change in the NLR is ascribed to systemic inflammation. A high NLR significantly augmented the risk of mortality, post-operative re-intubation, limb amputation, and postoperative atrial fibrillation following cardiovascular operations [38].

A prediction model intended for clinical use should be easily calculable. Our prediction model meets this requirement by implementing a web-based platform for simplified data entry and automated computation. Moreover, an essential characteristic of a clinically relevant risk score is its capacity to predict a wide spectrum of outcomes across the low and high ends of the risk continuum. In our investigation, the predicted risk of postoperative acute renal failure necessitating dialysis ranged from 0.06 to 82.96% in the derivation cohort, indicating a diverse range of risk levels. Furthermore, patients classified as high-risk had poorer overall survival and short-term mortality dialysis-requiring AKI, thereby bearing significant implications for patient care and decision-making processes.

This study has the potential to have significant implications for patients, healthcare providers, and decision makers. The assessment of individualized risk of postoperative dialysis-requiring AKI may play a crucial role in treatment decisions and in better preparing patients for potential postoperative complications. Healthcare providers could potentially utilize this tool to identify high-risk patients, enabling targeted counseling and implementation of preventative measures to reduce the risk of dialysis-requiring AKI, as well as more vigilant postoperative monitoring of kidney function in high-risk patients. Furthermore, further research is necessary to determine whether the use of this risk prediction tool leads to improved clinical outcomes.

Limitations

There are several limitations in this study. Firstly, the study did not specifically focus on patients with a history of preoperative dialysis, primarily due to challenges in analyzing the underlying causes of postoperative renal dysfunction. Secondly, despite conducting multivariate logistic regression analysis, it is important to acknowledge that residual confounding and confounding due to unmeasured indicators cannot be entirely eliminated. Thirdly, while the prediction model demonstrated good discrimination and calibration in both derivation and validation cohorts, it is worth noting that external validation was not carried out.

Conclusions

This study has developed and validated a prediction model to predict the occurrence of dialysis-requiring AKI following HT, based on six easily obtainable and objective variables. The prediction model can be utilized by clinicians for prospective assessment of the risk of postoperative dialysis-requiring AKI in HT patients. This visual tool is accessible online and can aid both patients and clinicians in predicting postoperative dialysis-requiring AKI, thereby enhancing clinical management.

Abbreviations

AIC	Akaike Information Criterion
AUC	Area under the receiver operating characteristic curve
CIC	Clinical impact curve
C-index	Harrell concordance index
CPB	Cardiopulmonary bypass
DCA	Decision curve analysis
eGFR	Estimated glomerular filtration rate
HT	Heart transplantation
K-M	Kaplan-Meier
NPV	Negative predictive value
PNI	Prognostic nutritional index
PPV	Positive predictive value
ROC	Receiver operating characteristic
SCr	Serum creatinine

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12893-025-02817-9.

Supplementary Material 1

Author contributions

SQ: Conceptualization, Investigation, Methodology, Formal Analysis, Writing - Original Draft. BC: Data Duration, Investigation, Software, Formal Analysis, Writing - Original Draft. PL: Conceptualization, Resources, Supervision, Writing - Review & Editing. ND: Conceptualization, Funding Acquisition, Writing - Review & Editing.

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Data availability

The original data in the study are included in the article/Supplementary Material. And further information is available upon reasonable request from the corresponding authors.

Declarations

Human ethics and consent to participate

This study was approved by the Ethics Committee of Tongji College, Huazhong University of Science and Technology (No: IORG0003263). Clinical and research activities comply the 'Declaration of Istanbul on Organ Trafficking and Transplant Tourism'. Written informed consent was obtained from individual or guardian participants.

Consent for publication

Written informed consent was obtained from individual or guardian participants.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Cardiovascular Surgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1277 Jiefang Ave, Wuhan 430022, China
[2]Key Laboratory of Organ Transplantation, Ministry of Education NHC, Chinese Academy of Medical Sciences, Wuhan, China

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