Prediction Scores for Acute Kidney Injury following Adult Cardiac Surgery

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Abstract

Background In the development of scoring systems for acute kidney injury (AKI) following cardiac surgery, previous investigations have primarily and solely attached importance to preoperative associated risk factors without any consideration for surgery-derived physiopathology. We sought to internally derive and then validate risk score systems using pre- and intraoperative variables to predict the occurrence of any-stage (stage 1-3) and stage-3 AKI within 7 days.

Methods Patients undergoing cardiac surgery from Jan 1, 2012, to Jan 1, 2019, were enrolled in our retrospective study. The clinical data were divided into a derivation cohort (n= 43799) and a validation cohort (n= 14600). Multivariable logistic regression analysis was used to develop the prediction models.

Results The overall prevalence of any-stage and stage-3 AKI after cardiac surgery was 34.3% and 1.7%, respectively. Any-stage AKI prediction-model discrimination measured by the area under the curve (AUC) was acceptable (AUC = 0.69, 95% CI: 0.68, 0.69), and the prediction model calibration measured by the Hosmer-Lemshow test was good (P = 0.95). The stage-3 AKI prediction model had an AUC of 0.84 (95% CI 0.83, 0.85) and good calibration according to the Hosmer-Lemshow test (P = 0.73).

Conclusions Using pre- and intraoperative data, we developed two scoring systems for any-stage AKI and stage-3 AKI in a cardiac surgery population. These scoring systems can potentially be adopted clinically in the field of AKI recognition and therapeutic intervention.

Background

Acute kidney injury (AKI) following cardiac surgery is a common and serious complication[1, 2]. It can evolve into a variety of chronic kidney diseases, prolong the length of intensive care unit (ICU) and hospital stay, and carry a high risk of increased medical expenditure and even mortality[3]. The incidence of postoperative any-stage AKI (stage 1, 2, 3) is 25% -35%[4, 5]. Renal replacement therapies (RRTs) following cardiac surgery secondary to AKI are required for approximately 1% of adult patients but are associated with in-hospital mortality rates of 50–80%[6, 7]. It has been postulated that any-stage AKI, even mild, reversible AKI, has important clinical indications, including increased short- and long-term poor outcomes after cardiac surgery[8]. Currently, efforts to alleviate AKI and its associated poor outcomes are primarily focused on the early detection of compromised kidney function, as effective practical clinical measures to prevent or treat AKI remain controversial. Prediction models or scoring systems for AKI in the field of cardiac surgery have proliferated in recent years. Additionally, clinicians and policy-makers have increasingly recommended the use of prediction models in clinical practice guidelines to make informed decisions at various AKI stages[9].

Although several scoring systems for AKI risk prediction after cardiac surgery have been published[10–17], they carry several limitations. First, the definitions of AKI in previous studies are different. In 2012, the definition and diagnostic criteria of AKI were significantly revised by the Kidney Disease: Improving Global Outcomes (KDIGO) organization, which made scoring systems developed before 2012 imprecise,

outdated and even likely to be eliminated[18]. Second, in previous models, dialysis induced by AKI was the most widely used endpoint. However, we cannot ignore the impact of milder forms of AKI; hence, risk models for any-stage AKI are also needed. Third, only two published scores (the Cleveland clinic score and the Mehta score) have undergone independent external validation by investigators. However, neither has demonstrated adequate discrimination and calibration in non-North American patient populations[19–22]. Fourth, the sample sizes of previous prediction models were relatively limited. Finally, to date, innovative AKI predictors have been widely explored, but some indicators such as hyperuricaemia have not been incorporated into these risk score systems.

In 2013, the International Society of Nephrology launched a worldwide target of “0 by 25”—no patient deaths due to untreated acute kidney failure by 2025—to improve the diagnosis and treatment of AKI globally[23]. An important step to achieve this target is to establish an ideal risk prediction model for AKI after cardiac surgery. We sought to derive and validate scoring systems that can predict the risk of any-stage and stage-3 AKI following cardiac surgery based on the KDIGO criteria.

Material And Methods

The research was approved by the Ethics Committee of Fuwai Hospital (20191308), and written informed consent from participants was waived for this retrospective analysis.

Objectives

The primary purpose of this study is to derive and then internally validate scoring systems that can predict the risk of any-stage and stage-3 AKICS based on KDIGO criteria. The secondary purpose is to further elucidate the association between AKI occurrence and postoperative clinical outcomes.

Study Design

A total of 58469 adult patients underwent cardiac repair at our institute from Jan 1, 2012, to Jan 1, 2019. Digital clinical data were provided by Fuwai Hospital Information Center. We monitored and checked the collected perioperative data. All data were checked twice by postgraduates and engineers who work for the Hospital Information Center. Thus, quality and accuracy were guaranteed. Patients were included if they were aged more than 18 years and had undergone open cardiac surgery (including coronary artery bypass grafting (CABG), valve surgery, great vessel operations, congenital heart disease repair, cardiac tumour surgery and combined surgery). Patients who received RRT prior to surgery were excluded (n = 70). Finally, 58399 patient charts were enrolled retrospectively.

Patient Outcomes

The diagnosis of AKI was based on the KDIGO criteria, listed as follows:

Stage 1: an increase in creatinine from baseline of ≥ 26.5 μmol/L (0.3 mg/dl) within 48 hours or to 1.5 to 1.9 times the baseline level within 7 days;

Stage 2: an increase in creatinine to 2.0 to 2.9 times the baseline level

Stage 3: an increase in creatinine to ≥ 3 times the baseline level or to ≥ 354 μmol/L or when the patient required RRT.

The baseline creatinine level was defined as the latest obtained prior to surgery. Urine output speed, although a reliable indicator of AKI as defined by the KDIGO criteria, was not included to evaluate AKI onset due to its unavailability at our institute for the majority of patients.

Variable Definitions

A list of 27 candidate variables was selected based on our clinical experience and other evidence obtained by previous investigations. The definitions of risk factors were mainly referenced from the STS website (www.sts.org). The rationale for using these variables in the scoring model was based on the results of univariable analysis and clinical relevance.

Statistical Analysis

Descriptive statistics are expressed as frequencies (n), percentages (%) or medians, and interquartile ranges (IQRs) as appropriate. Categorical variables were analysed using Pearson's chi-square test or Fisher's exact test. We transformed some continuous variables into categorical variables according to clinically meaningful cut-off values or previous literature reports. A single imputation was used for variables missing less than 2% of their values (defaulted to the most common value). Missing data for the history of peripheral vascular disease (accounting for 2.2% of the data) were modelled as unknown categories. Statistical significance was considered for P values less than 0.05.

The data set was randomly divided into a derivation and a validation cohort. Any-stage AKI and stage-3 AKI predictive systems were formulated after using multivariable logistic regression analysis. The final models were assessed by the Hosmer-Lemeshow goodness-of-fit test for calibration and the area under the receiver operating characteristic (ROC) curve (AUC) for discrimination. Next, the predictive utility was assessed by calculating the AUC using the validation cohort data. The final scores, obtained by a linear transformation of the regression coefficients, were calculated by dividing the regression coefficient of each risk factor by the absolute value of the sex coefficient.

Statistical analysis was performed with SPSS software, version 25.0.

Results

Characteristics of Patients

A total of 58399 patients (43799 in the derivation cohort and 14600 in the validation cohort) were retrospectively analysed during the 7-year period. The most common procedure was CABG (44.6%), followed by valve surgery (22.5%), combined surgeries (18.3%), great vessel surgery (7.8%), congenital heart repair and cardiac tumour surgery (6.6%). The prevalence of any-stage AKI and stage-3 AKI in the whole cohort after cardiac surgery was 34.3% and 1.7%, respectively. Baseline clinical characteristics of

the patients for both the derivation cohort and the validation cohort are illustrated in additional file 1 in the Supplement.

Pre- and intraoperative information for patients in the derivation group is shown in Table 1. Patients with any-stage or stage-3 AKI were older and had a greater likelihood of previous cardiac surgery, intra-aortic balloon pump (IABP) use, atrial fibrillation, urine protein, New York Heart Association (NYHA) classification ≥ 4, blood transfusion product use,hyperuricaemia, and left ventricular ejection fraction (LVEF) damage before surgery. Emergency surgery, cardiopulmonary bypass, haemorrhage volume and greater amounts of red blood cell (RBC), platelet, or plasma transfusion during surgery were also significant characteristics of the AKI cohorts.

Table 1
Clinical Characteristics of Derivation Cohort(N = 43799)(%)

Preoperative variable	No any-stage AKI (n = 28659,65.4%)	Any-stage AKI(n = 15140,34.6%)	P Value	No stage-3 AKI (n = 43046,98.3%)	Stage-3 AKI (n = 753,1.7%)	P Value
Age(year)			< 0.001			0.080
< 60	16685(58.2)	7800(51.5)		24075(55.9)	410(54.4)	
60–74	10763(37.6)	6554(43.3)		17021(39.5)	296(39.3)	
≥ 75	1211(4.2)	786(5.2)		1950(4.5)	47(6.2)	
Gender			0.003			< 0.001
Female	9943(34.7)	5038(33.3)		14673(34.1)	308(40.9)	
Male	18716(65.3)	10102(66.7)		28373(65.9)	445(59.1)	
Obesity(BMI ≥ 30 kg/m²)	1867(6.5)	1674(11.1)	< 0.001	3483(8.1)	58(7.7)	0.698
Previous COPD	402(1.4)	264(1.7)	0.006	654(1.5)	12(1.6)	0.765
History of cardiac surgery	542(1.9)	507(3.3)	< 0.001	1002(2.3)	47(4.5)	< 0.001
History of peripheral vascular disease			0.003			0.258
Yes	3182(11.1)	1841(12.2)		4929(11.5)	94(12.5)	
Unknown	626(2.2)	342(2.3)		946(2.2)	22(2.9)	
IABP use	48(0.2)	49(0.3)	0.001	92(0.2)	5(0.7)	0.026
Infective endocarditis	235(0.8)	109(0.7)	0.259	338(0.8)	6(0.8)	0.971
Atrial fibrillation	3389(11.8)	3031(20.0)	< 0.001	6259(14.5)	161(21.4)	< 0.001
Urine protein	274(1.0)	371(2.5)	< 0.001	611(1.4)	34(4.5)	< 0.001
Hypertension	10193(35.6)	5409(35.7)	0.739	15335(35.6)	267(35.5)	0.925
Type 2 diabetes	5672(19.8)	3052(20.2)	0.360	8588(20.0)	136(18.1)	0.198
NYHA classification ≥ 4	648(2.3)	553(3.7)	< 0.001	1150(2.7)	51(6.8)	< 0.001

Preoperative variable	No any-stage AKI (n = 28659,65.4%)	Any-stage AKI(n = 15140,34.6%)	P Value	No stage-3 AKI (n = 43046,98.3%)	Stage-3 AKI (n = 753,1.7%)	P Value
Blood transfusion products	26(0.1)	47(0.3)	< 0.001	67(0.2)	6(0.8)	0.002
hyperuricemia	6297(22.0)	4513(29.8)	< 0.001	10564(24.5)	246(32.7)	< 0.001
dyslipidemia	21406(74.7)	11184(73.9)	0.061	32083(74.5)	507(67.3)	< 0.001
LVEF(> 60%,reference group)			0.001			0.006
Mild damage (46%-60%)	451(1.6)	267(1.8)		699(1.6)	19(2.5)	
Moderate damage (30%-45%)	112(0.4)	86(0.6)		192(0.4)	6(0.8)	
Severe damage(< 30%)	9(0.0)	14(0.1)		21(0.0)	2(0.3)	
Serum creatinine (umol/L)			0.062			0.346
< 70	9077(31.7)	4844(32.0)		13680(31.8)	241(32.0)	
70–100	16543(57.7)	8560(56.6)		24666(57.3)	428(56.8)	
101–120	2015(7.0)	1149(7.6)		3106(7.2)	58(7.7)	
121–150	601(2.1)	346(2.3)		937(2.2)	10(1.3)	
> 150	432(1.5)	241(1.6)		657(1.5)	16(2.1)	
eGFR (mL/min/1.73 m2)			0.400			0.386
≥ 90	13598(47.4)	7133(47.1)		20377(47.3)	354(47.0)	
60-89.9	11749(41.0)	6205(41.0)		17649(41.0)	305(40.5)	
30-59.9	2873(10.0)	1586(10.5)		4382(10.2)	77(10.2)	
< 30	439(1.5)	216(1.4)		638(1.5)	17(2.3)	
Emergency surgery	1164(4.1)	714(4.7)	0.001	1819(4.2)	59(7.8)	< 0.001
The type of surgery			< 0.001			< 0.001
Others *	2381(8.3)	736(4.9)		3094(7.2)	23(3.1)	

Preoperative variable	No any-stage AKI (n = 28659,65.4%)	Any-stage AKI(n = 15140,34.6%)	P Value	No stage-3 AKI (n = 43046,98.3%)	Stage-3 AKI (n = 753,1.7%)	P Value
CABG	14190(49.5)	5633(37.2)		19696(45.8)	127(16.9)	
Valve Surgery	6141(21.4)	4167(27.5)		10165(23.6)	143(19.0)	
Great vessel surgery	1764(6.2)	1699(11.2)		3187(7.4)	276(36.7)	
Combined surgery	4183(14.6)	2905(19.2)		6904(16.0)	184(24.4)	
Bypass time (min)			< 0.001			< 0.001
Off-pump surgery	9425(32.9)	2541(16.8)	< 0.001	11910(27.7)	56(7.4)	< 0.001
≤ 120 min	14619(51.0)	7478(49.4)		21872(50.8)	225(29.9)	
> 120 min	4615(16.1)	5121(33.8)		9264(21.5)	472(62.7)	
Hemorrhage volume			< 0.001			< 0.001
≤ 600 mL	24732(86.3)	12506(82.6)		36762(85.4)	476(63.2)	
600 mL	3927(13.7)	2634(17.4)		6284(14.6)	277(36.8)	
Intraoperative RBC use	4276(14.9)	3621(23.9)	< 0.001	7555(17.6)	342(45.4)	< 0.001
Intraoperative platelet	1013(3.5)	1487(9.8)	< 0.001	2221(5.2)	279(37.1)	< 0.001
Intraoperative plasma	2646(9.2)	2626(17.3)	< 0.001	5002(11.6)	270(35.9)	< 0.001

Data presented as numbers and percentages. AKI, acute kidney injury; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate, calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula; IABP, intra-aortic balloon pump; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association ; RBC, red blood cell.*included congenital heart disease repair, cardiac tumor surgery.

Development of Risk Prediction Score

Coefficients, point scores, odds ratios (ORs) and 95% confidence intervals (CIs) are presented in Table 2 (any-stage AKI scoring system) and Table 3 (stage-3 AKI scoring system). There were 20 variables included in the any-stage AKI prediction model and 17 in the stage-3 AKI model. Next, we developed point score systems for any-stage and stage-3 AKI after cardiac surgery.

Table 2
Preoperative and intraoperative risk variables in the prediction model for postoperative any-stage AKI after cardiac surgery.

Preoperative	Coefficient	Scores	OR	95%CI	P value
Age(<60 years, reference group)					< 0.001
60–74	0.434	3	1.544	(1.474, 1.617)	< 0.001
≥ 75	0.670	4	1.954	(1.765,2.164)	< 0.001
Male	0.165	1	1.179	(1.123, 1.238)	< 0.001
Obesity(BMI ≥ 30 kg/m²)	0.687	4	1.987	(1.846, 2.139)	< 0.001
History of cardiac surgery	0.371	2	1.449	(1.291, 1.626)	< 0.001
History of peripheral vascular disease					< 0.001
Yes	0.169	1	1.184	(1.109,1.263)	< 0.001
Unknown	0.032	0	1.032	(0.896,1.189)	0.663
IABP use	0.519	3	1.680	(1.088,2.593)	0.019
Atrial fibrillation	0.348	2	1.417	(1.331, 1.508)	< 0.001
Urine protein	0.832	5	2.297	(1.994,2.714)	< 0.001
Hypertension	0.094	1	1.099	(1.048,1.152)	< 0.001
Type 2 diabetes	0.061	0	1.062	(1.008,1.120)	0.024
NYHA classification ≥ 4	0.150	1	1.162	(1.026,1.315)	0.018
Blood transfusion products use	0.663	4	1.940	(1.158,3.251)	0.012
hyperuricemia	0.229	1	1.257	(1.197,1.320)	< 0.001
LVEF(> 60%,reference group)					0.029
Mild damage(46%-60%)	0.062	0	1.064	(0.905,1.252)	0.453
Moderate damage(30–45%)	0.321	2	1.379	(1.023,1.858)	0.035
Severe damage(< 30%)	0.913	6	2.491	(1.029,6.034)	0.043
The type of surgery(Others* ,reference group)					< 0.001
CABG	0.183	1	1.201	(1.088,1.326)	< 0.001
Valve Surgery	0.354	2	1.424	(1.292,1.570)	< 0.001
Great vessel surgery	0.693	4	2.000	(1.775,2.255)	< 0.001
Combined surgery	0.505	3	1.656	(1.497,1.832)	< 0.001

Preoperative	Coefficient	Scores	OR	95%CI	P value
Intraoperative					
Bypass time (Off-pump surgery, reference group)					< 0.001
≤ 120 min	0.676	4	1.967	(1.853, 2.087)	< 0.001
> 120 min	1.269	8	3.557	(3.322, 3.809)	< 0.001
Hemorrhage volume≥600 ml	0.064	0	1.067	(1.005,1.132)	0.003
Intraoperative RBC use	0.186	1	1.204	(1.132, 1.281)	< 0.001
Intraoperative platelet use	0.293	2	1.340	(1.207, 1.487)	< 0.001
Intraoperative plasma use	0.355	2	1.426	(1.329, 1.529)	< 0.001
Intercept	-2.301				< 0.001

Minimum score = 0; maximum score = 52. AKI, acute kidney injury; BMI, body mass index; CABG, coronary artery bypass grafting; CI, confidence interval; LVEF, left ventricular ejection fraction; OR, odds ratio; RBC, red blood cell.*included congenital heart disease repair, cardiac tumor surgery.

Table 3
Preoperative and intraoperative risk variables in the prediction model for postoperative stage-3 AKI after cardiac surgery.

Preoperative	Coefficient	Scores	OR	95%CI	P value
Age(<60 years, reference group)					< 0.001
60–74	0.318	1	1.374	(1.165, 1.621)	< 0.001
≥ 75	0.871	2	2.389	(1.713, 3.331)	< 0.001
Male	-0.367	-1	0.693	(0.585, 0.821)	< 0.001
History of cardiac surgery	0.372	1	1.451	(1.117, 1.886)	0.005
History of peripheral vascular disease					0.003
Yes	0.377	1	1.458	(1.158,1.837)	0.001
Unknown	0.332	1	1.393	(0.881,2.204)	0.156
IABP use	0.977	3	2.655	(1.002,7.038)	0.050
Atrial fibrillation	0.257	1	1.293	(1.050,1.592)	0.016
Urine protein	0.844	2	2.326	(1.578, 3.427)	< 0.001
NYHA classification ≥ 4	0.361	1	1.434	(1.043, 1.972)	0.026
hyperuricemia	0.224	1	1.251	(1.057,1.482)	0.009
dyslipidemia	-0.232	-1	0.793	(0.674, 0.933)	0.005
LVEF(> 60%,reference group)					0.025
Mild damage(46%-60%)	0.342	1	1.408	(0.863, 2.298)	0.171
Moderate damage(30–45%)	0.472	1	1.604	(0.679, 3.790)	0.282
Severe damage(< 30%)	1.942	5	6.973	(1.560,31.166)	0.011
The type of surgery(Others* ,reference group)					< 0.001
CABG	-0.040	0	0.961	(0.600,1.537)	0.867
Valve Surgery	0.061	0	1.062	(0.671,1.682)	0.796
Great vessel surgery	1.501	4	4.487	(2.840,7.088)	< 0.001
Combined surgery	0.778	2	2.177	(1.389,3.411)	0.001
Intraoperative					
Bypass time (Off-pump surgery, reference group)					< 0.001
≤ 120 min	0.485	1	1.625	(1.187, 2.224)	0.002

Preoperative	Coefficient	Scores	OR	95%CI	P value
> 120 min	1.625	4	5.079	(3.726, 6.922)	< 0.001
Hemorrhage volume > 600 ml	0.540	1	1.716	(1.451, 2.028)	< 0.001
Intraoperative RBC use	0.355	1	1.427	(0.170, 1.740)	< 0.001
Intraoperative platelet use	0.776	2	2.173	(1.725, 2.736)	< 0.001
Intraoperative plasma use	0.308	1	1.361	(1.110, 1.668)	0.003
Intercept	-5.821				< 0.001

Minimum score = -2; maximum score = 30. AKI, acute kidney injury; CABG, coronary artery bypass grafting; CI, confidence interval; LVEF, left ventricular ejection fraction; OR, odds ratio; RBC, red blood cell.*included congenital heart disease repair, cardiac tumor surgery.

Risk Variables Associated with Postoperative AKI

The details for the any-stage AKI and stage-3 AKI prediction models are shown in Table 2 and Table 3, respectively. The risk variables that contributed to any-stage AKI were age, male sex, obesity, history of cardiac surgery, history of peripheral vascular disease, IABP use, atrial fibrillation, urine protein, hypertension, type 2 diabetes, NYHA classification, blood transfusion product use, hyperuricaemia, LVEF damage, cardiopulmonary bypass, haemorrhage volume and greater amounts of RBC, platelet, or plasma transfusion during surgery. Among the variables mentioned above, obesity, hypertension, type 2 diabetes, and blood transfusion products used could not be included in the stage-3 AKI model. The remaining variables as well as dyslipidaemia were incorporated into the stage-3 AKI model. However, female rather than male sex was included as the risk factor for stage-3 AKI onset.

Diagnostic Utility

1. Any-stage AKI model from pre- and intraoperative variables

For the derivation data set, the performance of the any-stage AKI risk prediction model, which was derived from pre- and intraoperative variables, was as follows. The AUC was 0.69 (95% CI, 0.68, 0.69; Fig. 1), indicating an acceptable discriminability. The Hosmer-Lemshow test showed that the calibration of the any-stage AKI model from the pre- and intraoperative variables was good (P = 0.95). The model sensitivity, specificity, positive predictive value, and negative predictive value were 29.3%, 90.0%, 60.7%, and 70.7%, respectively. The AUC with the validation cohort was very similar (AUC = 0.69, 95% CI, 0.68, 0.70), with a sensitivity, specificity, positive predictive value, and negative predictive value of 27.5%, 91.0%, 60.5%, 71.4%, respectively.

2. Stage-3 AKI model from pre- and intraoperative variables

The AUC for the stage-3 AKI risk prediction model with the derivation cohort was 0.84 (95% CI, 0.83, 0.85, Fig. 1). The Hosmer-Lemshow test demonstrated good calibration for the derivation cohort (P = 0.73). The model sensitivity, specificity, positive predictive value, and negative predictive value were 0.4%, 100%, 42.9%, and 98.3%, respectively. The performance with the validation cohort also indicated good discriminability (AUC = 0.82, 95% CI, 0.80, 0.85), and the model sensitivity, specificity, positive predictive value, and negative predictive value were 1.8%, 100%, 100%, and 98.5%, respectively.

3. Any-stage or stage-3 AKI model from preoperative variables

After using only preoperative variables to construct the AKI prediction models, the AUC for the any-stage AKI model was 0.64 (95% CI, 0.64, 0.65), and that for the stage-3 AKI model was 0.79 (95% CI, 0.77, 0.80). Nevertheless, the calibration from the Hosmer-Lemshow test was poor for both models (P < 0.001, P = 0.015, respectively, Additional file 2).

AKI Score Classification

Figure 2 shows the predicted and observed incidences of AKI, which were based on the risk prediction scores for the validation cohorts. According to the scores observed in the validation cohorts, the predictive risk of AKI could be grouped into three classifications: low, medium, and high (Additional file 3 in the Supplement). For the validation cohorts, the incidence of AKI onset predicted by the model was similar to that observed clinically. The risk score and its associated predictive risk charts are presented in additional file 4 and additional file 5 in the Supplement.

Secondary Outcomes

AKI was associated with greater medical expenditure and a prolonged length of hospital stay (Additional file 6). Patients developing any degree of AKI incurred a significantly greater cost during their treatment in the hospital (P < 0.001). Patients with AKI had a significantly longer length of stay than those without AKI (P < 0.001). In the whole cohort (N = 58399), any degree AKI was associated with higher odds of agitated delirium, pulmonary complications, re-intubation, and death in the hospital (Additional file 7).

Discussion

We developed two scoring systems for AKI risk prediction following cardiac surgery, primarily for any-stage AKI and stage-3 AKI. Scores were evolved from pre- and intraoperative risk variables with a large cohort of cardiac patients. The scoring systems were also well internally validated.

The prominent strengths of our study are listed as follows.

In addition to preoperative variables, intraoperative parameters were also incorporated to investigate the risk score for AKI. Comparatively, previous predictive scores primarily and solely attached importance to preoperative associated variables without any consideration for surgery-derived physiopathology induced by cardiopulmonary bypass (CPB), transfusion product use and excessive bleeding[10–17]. Additionally,

we failed to construct a predictive model for AKI using preoperative variables alone because the calibration assessed by the Hosmer-Lemshow test was not good.

Other risk scores have been derived from information collected from all phases, including pre-, intra-, and postoperation[12, 15, 16]. However, it is arduous to disentangle whether morbidities occurring in the postoperative period can truly contribute to AKI onset. For example, low cardiac output syndrome can lead to compromised renal function and vice versa. Furthermore, at present, the number of postoperative parameters investigated following cardiac surgery is apparently limited. Postoperative central venous pressure > 14 cmH_2O and low cardiac output syndrome are perceived as prognostic factors in the AKICS score[12]. Ng scores[14] only include intra-aortic balloon pump use in the postoperative period. The Jiang dynamic predictive score[16] only includes low cardiac output syndrome following cardiac surgery. However, pre-, intra- and postoperative models are limited in clinical effectiveness and utility because it is not easy to distinguish the causal relationship between postoperative variables and AKI. Given the differences in AKI definition and race, no statistical comparison can be performed among the abovementioned models.

Our research represents a meaningful attempt to include atrial fibrillation in the prediction models. Atrial fibrillation commonly occurs in patients with kidney disease[24]. Previous studies have indicated that by inducing myocardial fibrosis, atrial fibrillation contributes to the decline in left ventricular function and the alteration of cardiac haemodynamics and then accelerates the progression of kidney disease. Atrial fibrillation also induces renal fibrosis by downregulating neutral endopeptidase expression[25]. Our research innovatively found that atrial fibrillation could predict postoperative AKI after cardiac surgery. Additionally, there is evidence that higher uric acid levels can induce AKI through fibroblast expansion, the inflammatory cascade and an increase in endothelin-1[26, 27]. Similar to previous investigations, our research found that hyperuricaemia prior to surgery was a risk factor for postoperative AKI[28, 29]. Meanwhile, we found that sex differences can significantly contribute to postoperative AKI. Male patients had a greater likelihood of developing any-stage AKI, whereas female patients were prone to develop stage-3 AKI; the underlying mechanisms remain to be elucidated.

The AKI endpoint was defined by the KDIGO criteria in our study, which is consistent with that by Birnine et al[15] and Jiang et al[16]. Compared with investigations carried out by Birnine et al[15] (n = 30854) and Jiang et al[16](n = 7233), our study is characterized by an unprecedentedly larger sample size. In fact, the criteria for defining AKI following cardiac surgery varied greatly in previous studies on risk scores[12–16]. In 2012, based on evidence review and appraisal, the KDIGO organization compiled the first international and multidisciplinary clinical practice guidelines for AKI. At present, these guidelines are recognized as a consensus on the AKI definition from all over the world[30]. However, due to differences in race, religious belief, living habits and medical level, foreign prediction models cannot be effectively applied to other individual, local patient cohorts. Previous models have demonstrated poor discrimination and calibration in non-local populations[19–22]; hence, it is necessary to build prediction models for AKI for individual populations after cardiac surgery. For the Asian population, Jiang et al. developed a dynamic predictive score for any-stage AKI after cardiac surgery. However, in this study, we not only provided a robust

predictive scoring system for any-stage AKI after cardiac surgery in the Chinese population but also developed a separate system for postoperative stage-3 AKI.

In the future, both the any-stage AKI and stage-3 AKI scoring systems will be available as online calculators, which not only will be freely available and accessible by any computer system but can also be completed in a short time. Our model can even be integrated into hospital information management systems as a module to reduce labour costs in predicting AKI.

As a retrospective analysis that is pending prospective validation, our research has intrinsic limitations as a result of unmeasured confounders. Variables such as the Canadian Cardiovascular Society (CCS) class, contrast-induced nephropathy, aorta cannulation and cross-clamping time were not included as potential predictive factors because records on these variables were not completed for a majority of the recruited patients. Additionally, the AKI diagnosis currently used in the study is not strictly consistent with the KDIGO criteria because it lacks the urinary output criteria due to its unavailability at our institute for the majority of patients. This may not be a very detrimental problem, however, because urinary output criteria often perform poorly in diagnosing clinically relevant AKI. Furthermore, it is generally accepted that the sicker the patient, the longer the length of stay and the higher the cost are, so the long-term outcome is more important than the calculated administrative cost. Our study is characterized by a large sample size, but data about long-term outcomes are unavailable at our institute for the majority of patients. The AUC of the any-stage AKI risk prediction model was 0.69, which is acceptable. We will focus on updating and optimizing the existing models by exploring new biomarkers and using smarter modelling methods in future work. Finally, data were obtained from a single centre, which could lead to bias in the results; hence, there is a need to validate this scoring system with clinical data from other cardiac centres.

Conclusion

Using pre- and intraoperative data, we developed individual scoring systems for any-stage AKI or stage-3 AKI in a cardiac surgery population in accordance with KDIGO criteria. These scoring systems are beneficial for guiding clinicians towards decision-making for AKI detection and therapy after surgery. This study will contribute to AKI-predicting software development and further explorations into effective clinical interventions for AKI.

Declarations

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Authors' contributions

Yuefu Wang provided the idea for this study. Xiaolin Diao and Weiwei Wang provided Digital clinical data of patients. Yuchen Gao and Sudena Wang monitored and checked the collected data. Yu Tian and Wei

Zhao wrote and edited the paper. Chunrong Wang was responsible for revision in this paper. The authors read and approved the final manuscript.

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Availability of data and materials

The data-sets generated during and/or analyzed during the current study are not publicly available due to IRB provisions but are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The research was approved by the Ethics Committee of Fuwai Hospital (20191308), and written informed consent from participants was waived for this retrospective analysis.

Consent for publication

Patients agreed to allow all the manuscript data to be reported.

Competing interests

Authors declare no conflicts of interest related to this manuscript content.

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Figures

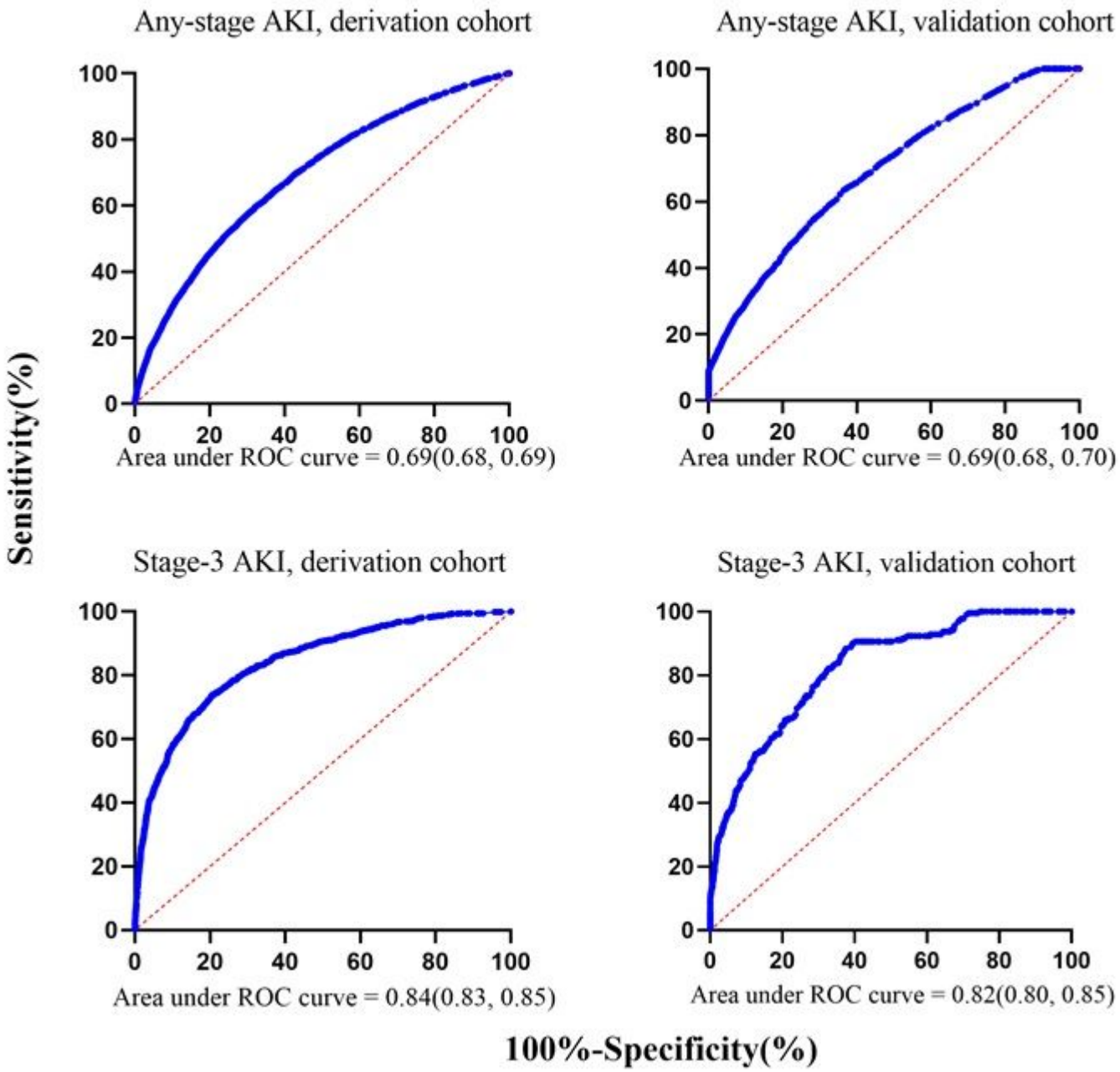
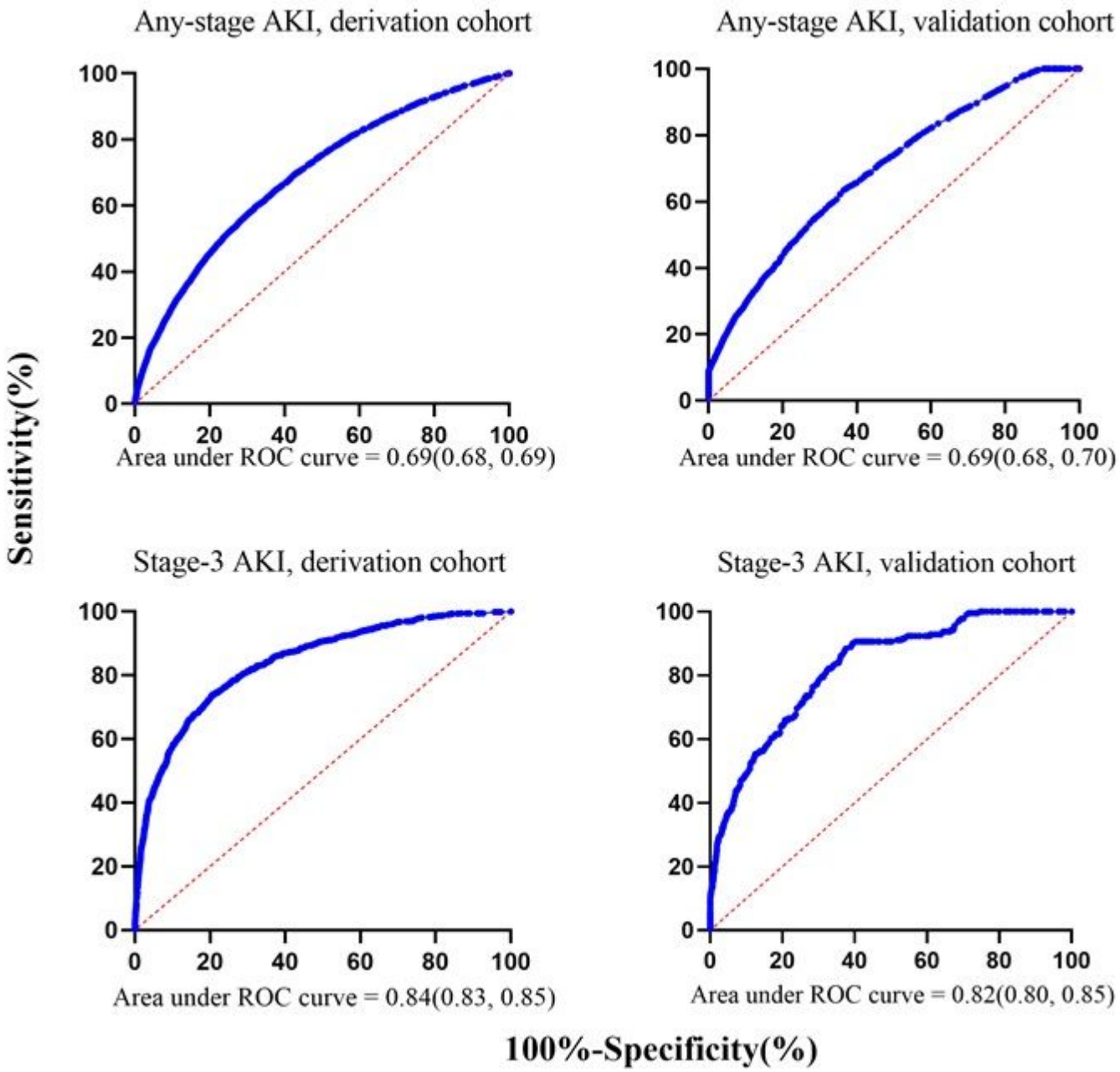


Figure 1

Receiver operating characteristic curves (ROC) for any-stage AKI and stage-3 AKI prediction models in the derivation cohort and validation cohort. AKI: acute kidney injury



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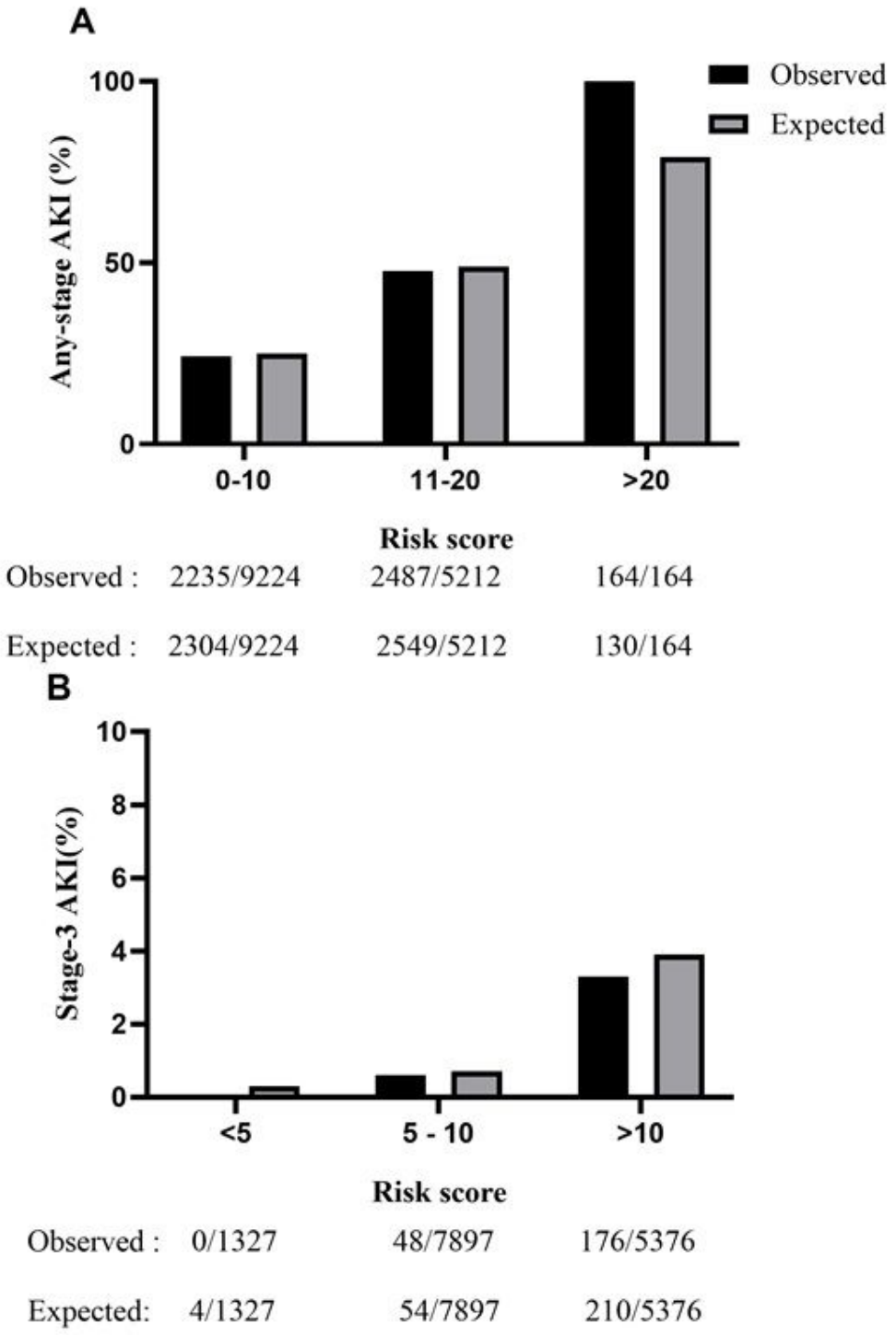

Figure 2

Observed and predicted risk of any-stage AKI (A) and stage-3 AKI (B) in the validation cohorts. AKI: acute kidney injury

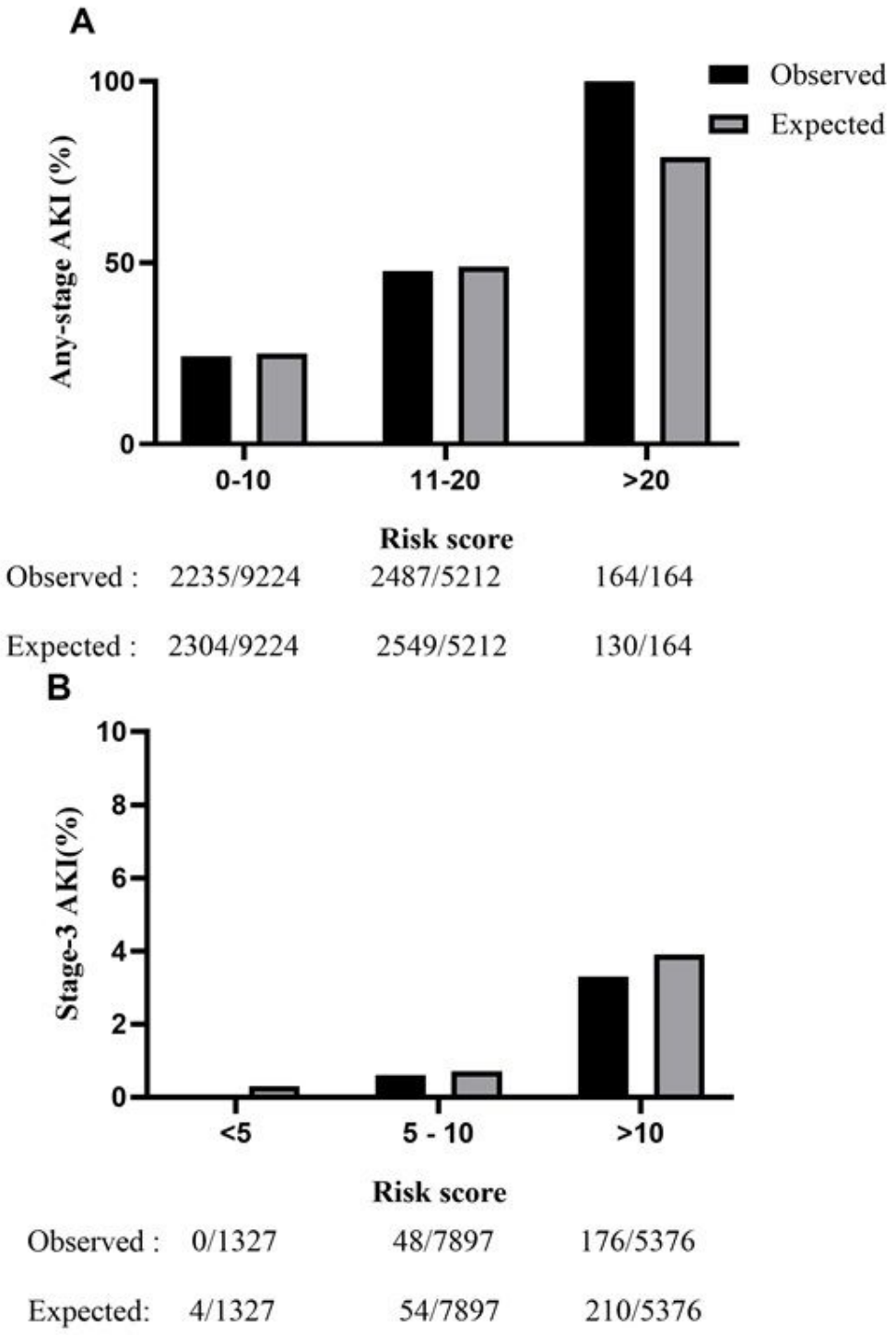

Figure 2

Observed and predicted risk of any-stage AKI (A) and stage-3 AKI (B) in the validation cohorts. AKI: acute kidney injury

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