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ORIGINAL RESEARCH

Risk Prediction Models for Renal Function Decline After Cardiac Surgery Within Different Preoperative Glomerular Filtration Rate Strata

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BACKGROUND: Our goal was to create a simple risk-prediction model for renal function decline after cardiac surgery to help focus renal follow-up efforts on patients most likely to benefit.

METHODS AND RESULTS: This single-center retrospective cohort study enrolled 24 904 patients who underwent cardiac surgery from 2012 to 2019 at Fuwai Hospital, Beijing, China. An estimated glomerular filtration rate (eGFR) reduction of ≥30% 3 months after surgery was considered evidence of renal function decline. Relative to patients with eGFR 60 to 89 mL/min per 1.73 m^2 (4.5% [531/11733]), those with eGFR ≥90 mL/min per 1.73 m^2 (10.9% [1200/11042]) had a higher risk of renal function decline, whereas those with eGFR ≤59 mL/min per 1.73 m^2 (5.8% [124/2129]) did not. Each eGFR stratum had a different strongest contributor to renal function decline: increased baseline eGFR levels for patients with eGFR ≥90 mL/min per 1.73 m^2, transfusion of any blood type for patients with eGFR 60 to 89 mL/min per 1.73 m^2, and no recovery of renal function at discharge for patients with eGFR ≤59 mL/min per 1.73 m^2. Different nomograms were established for the different eGFR strata, which yielded a corrected C-index value of 0.752 for eGFR ≥90 mL/min per 1.73 m^2, 0.725 for eGFR 60–89 mL/min per 1.73 m^2 and 0.791 for eGFR ≤59 mL/min per 1.73 m^2.

CONCLUSIONS: Predictors of renal function decline over the follow-up showed marked differences across the eGFR strata. The nomograms incorporated a small number of variables that are readily available in the routine cardiac surgical setting and can be used to predict renal function decline in patients stratified by baseline eGFR.

Key Words: cardiac surgery ■ glomerular filtration rate ■ prediction nomogram ■ renal function decline

Chronic kidney disease (CKD) is a devastating condition that has a high mortality rate and imposes extreme health care expenditures.[1] The pathologic transition from acute kidney injury (AKI) to CKD is multifactorial and remains poorly understood. Potential causes include vascular dropout, interstitial profibrotic reactions, disordered regeneration, and dysregulated apoptosis.[2] Depending on the definitions used, time frame considered, and populations included, the incidence after cardiac surgery is reported to range from 0.4% to 23%.[3–6]

Several clinical factors have been found to aggravate renal function decline. A transient episode of AKI after

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CLINICAL PERSPECTIVE

What Is New?

- An individual prediction model toward follow-up renal dysfunction after cardiac surgery was achieved in patients stratified by estimated glomerular filtration rate (eGFR) ≥90 mL/min per 1.73 m^2, 60 to 89 mL/min per 1.73 m^2, and ≤59 mL/min per 1.73 m^2 at baseline.

What Are the Clinical Implications?

- The nomograms incorporated a small number of variables that are readily available in the routine cardiac surgical setting and can be used to predict renal function decline in patients stratified by baseline eGFR.
- Predictors of renal function decline over the follow-up showed marked differences across the eGFR strata.
- Within the stratum of baseline eGFR ≥90 mL/min per 1.73 m^2, an increasing trend of baseline eGFR levels indicated a greater likelihood of renal function decline, as well as in the stratum of eGFR 60 to 89 mL/min per 1.73 m^2; however, there was no such association between eGFR levels and renal function decline in those with eGFR ≤59 mL/min per 1.73 m^2.

Nonstandard Abbreviations and Acronyms

AKI	acute kidney injury
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
LASSO	least absolute shrinkage and selection operator

cardiac surgery, regardless of its severity, is recognized as a leading contributor to CKD from a classical view.[4–6] The level of proteinuria and the extent to which renal function recovers from AKI are considered other ideal prognostic indicators for CKD outcome in the field of nephrology,[7–10] but their roles in cardiac surgical settings remain ambiguous. Among patients recovering from AKI after cardiac surgery, CKD can still progress.[5]

A practical prediction score for CKD after cardiac surgery has been proposed but is restricted to patients with a baseline estimated glomerular filtration rate (eGFR) of at least 60 mL/min per 1.73 m^2.[6] The recognition of renal function decline among those with baseline eGFR <60 mL/min per 1.73 m^2 is limited. The clinical prognosis of patients with different baseline eGFRs has been elucidated,[11,12] but whether risk factors contribute to progression of renal function decline in different eGFR strata is still unclear.

The aim of this study, accordingly, was to develop a simple nomogram that is easily used for the prediction of renal function decline in a broad population of patients undergoing cardiac surgery of all baseline eGFR levels. In addition, we planned to explore the prevalence and associated clinical risk predictors of subsequent renal function decline.

METHODS

Data Availability Statement

Because of the strict data regulations by Fuwai Hospital and patient privacy considerations, patient data used for analysis will not be made available to researchers for the purpose of reproducing the results or replicating the procedure.

Data Source

This retrospective cohort study was performed at Fuwai Hospital (Beijing, China). Data on patient characteristics, medical history, surgical procedures, and laboratory measurements from January 1, 2012, to December 31, 2019, were extracted from the electronic health records system, as presented in our last publication on the AKI prediction.[13] All these data had been input by clinical personnel at the time of admission or treatment. The accuracy and completeness of these data from our institute were previously validated.[13–15] Serial follow-up creatinine measurements after the index hospitalization were updated over time in the medical charts if the patient presented at the outpatient clinic or emergency room or was rehospitalized. The follow-up ended on December 20, 2020. The ethics committee of our institute approved this study before it was performed (No. 2019–1308), and patient written consent was waived. This article adheres to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines and the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis statement.

Study Population

A total of 65 077 adult patients (aged ≥18 years) underwent cardiac surgery at our institute over a period of 8 years. For patients with multiple surgical indexes, data associated with the first surgery were entered. Initially, we identified survivors who revisited our institute after discharge. Eligible patients must have had at least 1 follow-up serum creatinine measurement >90 days after the surgical procedure because (1) kidney function loss fluctuates greatly within 3 months postoperatively,[16] and (2) loss of function within 90 days is predominantly considered acute rather than chronic

kidney compromise.[17] Other exclusion criteria consisted of preoperative dialysis support, in-hospital death, and a postoperative hospitalization duration >90 days. Patients who did not have baseline or postoperative measurements of serum creatinine to estimate AKI were not included. More details on the inclusion and exclusion criteria are presented in Figure S1.

Definitions

AKI and eGFR

Postoperative AKI was assessed and staged according to the Kidney Disease: Improving Global Outcomes criteria.[18] It was determined within the first postoperative 7 days after collecting the patient's highest creatinine levels but did not account for urine output. Preoperative creatinine measured at hospital admission was used when possible. Apart from those suspected of having compromised renal function, all patients had only a single serum creatinine test from admission day until the cardiac surgery.

Patient eGFR was separately estimated at the times of admission, hospital discharge, and follow-up. It was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation on the basis of patient serum creatinine level.[19]

Renal Recovery Irrespective of AKI at Discharge

The difference between baseline eGFR and the last eGFR at discharge was used to determine renal recovery irrespective of AKI. Renal function at discharge was categorized as follows: (1) no recovery: eGFR at discharge was at least 10% lower than baseline eGFR; or (2) recovery: eGFR fell by <10%. The cutoff of a 10% change in eGFR has been found to appropriately estimate renal recovery in a clinically meaningful way.[20–22] We assessed renal recovery irrespective of AKI because some patients not meeting AKI criteria could develop unexpected "late" renal injury after the seventh postoperative day, and their renal condition should be updated to include the degree of kidney function recovery when appropriate.[23,24]

Proteinuria Categories

Patient random spot urine samples were collected preoperatively. Proteinuria was examined by the urine albumin : creatinine ratio or the standard semiquantitative urine dipstick test at our institute, most often the latter. The preoperative level closest to surgery was preferred for each patient in this study. We categorized proteinuria as normal (urine albumin : creatinine ratio <30 mg/g or dipstick negative), mild (urine albumin : creatinine ratio 30–300 mg/g or dipstick trace of 1+), or heavy (urine albumin : creatinine ratio >300 mg/g or dipstick ≥2+).

Follow-Up Renal Outcome

The main outcome was an affirmation of a 30% decline or more in eGFR, calculated as the change between the value at baseline and during follow-up. A ≥30% reduction has been proposed as a surrogate end point of renal function decline in clinical trials since 2012, as determined in a scientific workshop conducted by the National Kidney Foundation and the US Food and Drug Administration.[25,26] A diagnosis of renal function decline is entirely dependent on laboratory data. We considered the outcome of 30% reduction to be met if any follow-up measurement showed such a decline, irrespective of any later amelioration. The follow-up time to this outcome was calculated from the date of surgery to the date of the first instance of renal function decline, or the last follow-up date for patients who did not experience a reduction in renal function.

Statistical Analysis

Continuous variables were reported using mean (SD) or median (interquartile range), while categorical variables are presented as frequency (percentage). Missingness of data was assumed to be at random (Table S1). Missing data were handled using multiple imputation techniques with 5 data sets.

Candidate variables potentially associated with follow-up renal function decline were considered on the basis of a literature review, clinical judgment, physiological relevance, and cardiac surgical factors. Collinearity among the covariates was examined using the variance inflation factor, and those having a variance inflation factor >10 were excluded. The cardiopulmonary time and aortic clamping time had collinearity; thus, the latter was not included in the models. Cox hazards regression was used to investigate relationships between a total of 41 candidate variables and outcomes of interest. Corresponding hazard ratios (HRs) and 95% CIs were reported. Cumulative rates of renal function decline were compared with Kaplan–Meier curves.

The relationships of continuous baseline eGFR with serum creatinine and renal function decline were depicted using restricted cubic splines with 5 knots. The least absolute shrinkage and selection operator (LASSO) technique was employed to select candidate covariates to avoid model overfitting and improve model accuracy in each eGFR stratum as well as conform to the rule of events per variable >10. LASSO regression was specifically appropriate for patients with baseline eGFR ≤59 mL/min per 1.73 m^2 and characterized by a relatively large number of candidate covariates but limited events of renal function decline. The ultimate number of variables determined by LASSO regression before multivariable Cox fitting was 14, 12, and 10 in patients stratified into the eGFR ≥90 mL/min

per 1.73 m^2, 60 to 89 mL/min per 1.73 m^2 and ≤59 mL/min per 1.73 m^2 groups, respectively.

To improve the clinical applicability of our models, we constructed a nomogram for each eGFR stratum to predict subsequent renal function decline by replacing the coefficient of each variable with its closest integer. Model discrimination was assessed by Harrell's C-index. A calibration plot was drawn to graphically compare the observed versus predicted probabilities of renal function decline. The final simplified model was internally validated using a bootstrapping technique with 1000 repetitions in both the eGFR ≥90 mL/min per 1.73 m^2 and 60 to 89 mL/min per 1.73 m^2 strata and 200 repetitions in the eGFR ≤59 mL/min per 1.73 m^2 strata to assess the optimism-adjusted C-index. We preferred bootstrap to perform internal validation instead of data splitting because the latter has flaws in inefficiency and not using all the data.[27]

Sensitivity analyses were prespecified for robustness on the basis of the association between baseline eGFR levels and renal function decline in each eGFR stratum: (1) The eGFR change used to define the end point of renal function decline was increased from 30% to 40%; (2) the multivariable association calculation was repeated, which controlled for all selected variables with $P<0.1$ in the univariable regression; (3) a lack of renal function recovery at discharge was redefined as a reduction in eGFR of at least 20%; and (4) the length of intensive care unit stay was introduced into LASSO regression.

R software, version 3.6.1 for Windows (R Project for Statistical Computing, Vienna, Austria), was employed to perform all statistical analyses.

RESULTS

Patient Characteristics

A total of 24 904 patients were eligible for entry into the final analysis. Their mean age was 57.8 (10.7) years, and men predominated (69.0%). The mean patient eGFR at hospital admission and at discharge was 88 (22) mL/min per 1.73 m^2 and 89 (28) mL/min per 1.73 m^2, respectively. During postoperative hospitalization, 8283 (33.3%) patients experienced AKI. Patient baseline characteristics, intraoperative information, and clinical outcomes are shown in Table 1.

Patients With/Without Renal Function Decline

Over a median follow-up of 314 (110, 607) days and a mean follow-up of 499 days, 1855 (7.4%) patients exhibited renal function decline. Patients with renal function decline were 2 years older than those without a decline and were more often women. These patients were also accompanied with more comorbidities, including anemia, diabetes, hyperlipidemia, stroke, hypertension, and prior myocardial infarction (Table 1).

Baseline serum creatinine in patients with renal function decline and those without a decline was 0.82 (0.23) mg/dL and 0.94 (0.22) mg/dL, respectively, and their baseline eGFR was 101 (29) mL/min per 1.73 m^2 and 87 (21) mL/min per 1.73 m^2. The incidence of renal function decline during follow-up increased with higher AKI stages in a graded manner: 5.1% (844/16621) in patients without AKI, 10.7% (782/7278) in stage 1, 21.1% (168/796) in stage 2, and 29.2% (61/209) in stage 3. Compared with patients without renal function decline, those with renal function decline had a lower incidence of full renal function recovery at hospital discharge (60.3% versus 30.8%, respectively). The number of creatinine measurements during postoperative hospitalization (10 [6–17] versus 9 [6–16]; $P<0.001$) and at follow-up (2 [1–4] versus 1 [1–2]; $P<0.001$) were both significantly higher in patients who experienced renal function decline than those who did not.

The Association of Baseline eGFR Levels and Renal Function Decline

The restricted cubic splines displayed that, among patients with eGFR ≥90 mL/min per 1.73 m^2, the hazard of renal function decline increased with greater baseline eGFR levels before and after thorough adjustment for other variables (Figure 1). Compared with patients with eGFR 60 to 89 mL/min per 1.73 m^2, those with eGFR ≥90 mL/min per 1.73 m^2 gained a significantly higher risk of developing renal function decline (HR, 2.470 [95% CI, 2.208–2.764]; $P<0.001$). However, patients with eGFR 45 to 59 mL/min per 1.73 m^2 (HR, 1.006 [95% CI, 0.803–1.261]; $P=0.958$) and those with eGFR ≤44 mL/min per 1.73 m^2 (HR, 0.792 [95% CI, 0.520–1.208]; $P=0.279$) had comparable risks of renal function decline relative to those with eGFR 60 to 89 mL/min per 1.73 m^2 (model 1 in Table S2). Alternatively, using an eGFR 60 to 89 mL/min per 1.73 m^2 as the reference, an eGFR ≤59 mL/min per 1.73 m^2 was not significantly associated with a higher risk of developing renal function decline (HR, 0.961 [95% CI, 0.777–1.188]; $P=0.711$) (model 2 in Table S2). The Kaplan–Meier curves of different baseline eGFR strata are displayed in Figure S2.

Predictive Factors of Renal Function Decline in Each eGFR Stratum

For statistical purposes, the groups of patients with eGFR ≤44 mL/min per 1.73 m^2 and those with eGFR 45 to 59 mL/min per 1.73 m^2 had a limited number of patients and ultimate events, so they were integrated into an isolated eGFR stratum of ≤59 mL/min per 1.73 m^2.

Table 1. Baseline Characteristics and Intra- and Postoperative Information

Variables	Overall (n=24 904)	Without renal function decline (n=23 049)	Renal function decline (n=1855)	*P* value	ASD
Demographics					
Age, y*	57.8 (10.7)	57.7 (10.7)	59.4 (10.4)	<0.001	0.157
Male sex*	17 194 (69.0)	16 053 (70.0)	1141 (61.5)	<0.001	0.172
Body mass index, kg/m^2*	25.3 (3.4)	25.3 (3.4)	25.3 (3.5)	0.836	0.005
Medical history					
Ever/current smoker*	12 214 (49.0)	11 361 (49.3)	853 (46.0)	0.006	0.066
Anemia*	5650 (22.7)	5054 (21.9)	596 (32.1)	<0.001	0.231
Diabetes*	6330 (25.4)	5690 (24.7)	640 (34.5)	<0.001	0.216
Hyperlipidemia*	12 368 (49.7)	11 353 (49.3)	1015 (54.7)	<0.001	0.109
History of stroke*	6593 (26.5)	6014 (26.1)	579 (31.2)	<0.001	0.113
Chronic obstructive pulmonary disease*	320 (1.3)	291 (1.3)	29 (1.6)	0.282	0.025
Liver disease*	1499 (6.0)	1396 (6.1)	103 (5.6)	0.417	0.022
Endocarditis*	186 (0.8)	167 (0.7)	19 (1.0)	0.159	0.032
Hypertension*	13 283 (53.3)	12 119 (52.6)	1164 (62.8)	<0.001	0.207
Atrial fibrillation*	3151 (12.7)	2913 (12.6)	238 (12.8)	0.799	0.006
Prior myocardial infarction*	4967 (19.9)	4546 (19.7)	421 (22.7)	0.003	0.073
Prior heart failure*	5403 (21.7)	5007 (21.7)	396 (21.4)	0.725	0.009
NHYA III/IV*	8899 (35.7)	8230 (35.7)	669 (36.1)	0.763	0.007
Critical status prior to surgery*,†	195 (0.8)	166 (0.7)	29 (1.6)	<0.001	0.079
Echocardiography					
Left ventricular ejection fraction (%)*	61.0 (7.9)	61.0 (7.9)	60.7 (8.1)	0.098	0.039
Preoperative medication					
B Blockers*	17 234 (69.2)	15 926 (69.1)	1308 (70.5)	0.21	0.031
Angiotensin-converting enzyme inhibitors/ angiotensin receptor blockers*	5782 (23.2)	5232 (22.7)	550 (29.7)	<0.001	0.159
Antiplatelet agents*	7426 (29.8)	6754 (29.3)	672 (36.2)	<0.001	0.148
Statins*	11 509 (46.2)	10 572 (45.9)	937 (50.5)	<0.001	0.093
Diuretics*	4609 (18.5)	4250 (18.4)	359 (19.4)	0.335	0.023
Preoperative laboratory measurements					
Hemoglobin, g/L	136.6 (16.3)	137.0 (16.2)	131.9 (16.6)	<0.001	0.308
Albumin, g/L*	41.1 (4.0)	41.1 (4.0)	40.2 (4.0)	<0.001	0.227
Potassium, mmol/L*	4.0 (0.4)	4.1 (0.4)	4.0 (0.4)	<0.001	0.124
Chloride, mmol/L*	104.4 (3.4)	104.4 (3.4)	104.7 (3.5)	<0.001	0.11
Sodium, mmol/L*	139.9 (2.8)	139.9 (2.8)	139.6 (2.8)	<0.001	0.121
Calcium, mmol/L*	2.3 (0.1)	2.3 (0.1)	2.3 (0.1)	<0.001	0.132
Phosphorus, mmol/L*	1.2 (0.2)	1.2 (0.2)	1.2 (0.2)	0.009	0.063
Uric acid, μmol/L*	361.0 (101.5)	362.7 (101.3)	340.1 (101.4)	<0.001	0.223
Urine nitrogen, mmol/L*	5.8 (2.2)	5.9 (2.2)	5.4 (2.0)	<0.001	0.202
White blood cell count, 10^9/L*	6.7 (1.8)	6.7 (1.8)	6.7 (1.9)	0.74	0.008
Platelet count, 10^9/L*	205.0 (57.8)	205.1 (57.6)	204.0 (60.3)	0.406	0.02
Baseline serum creatinine, μmol/L	0.93 (0.22)	0.94 (0.22)	0.82 (0.23)	<0.001	0.525
Baseline kidney function					
Baseline eGFR, mL/min per 1.73 m^2	87.8 (22.1)	86.7 (21.1)	100.8 (28.9)	<0.001	0.555
Baseline eGFR category					
≥90 mL/min per 1.73 m^2	11 042 (44.3)	9842 (42.7)	1200 (64.7)	—	0.459
60–89 mL/min per 1.73 m^2	11 733 (47.1)	11 202 (48.6)	531 (28.6)		
45–59 mL/min per 1.73 m^2	1713 (6.9)	1615 (7.0)	98 (5.3)		

(*Continued*)

Table 1. Continued

Variables	Overall (n=24 904)	Without renal function decline (n=23 049)	Renal function decline (n=1855)	*P* value	ASD
30–44 mL/min per 1.73 m^2	374 (1.5)	353 (1.5)	21 (1.1)		
15–29 mL/min per 1.73 m^2	38 (0.2)	33 (0.1)	5 (0.3)		
<15 mL/min per 1.73 m^2	4 (0.02)	4 (0.02)	0 (0)		
Preoperative proteinuria degrees*					
Negative	22 293 (89.5)	20 680 (89.7)	1613 (87.0)	<0.001	0.119
Mild	2347 (9.4)	2148 (9.3)	199 (10.7)		
Heavy	264 (1.1)	221 (1.0)	43 (2.3)		
Surgery characteristics					
Nonelective procedures*	614 (2.5)	559 (2.4)	55 (3.0)	0.161	0.033
Surgical types*					
Isolated CABG	13 883 (55.8)	12 877 (55.9)	1006 (54.2)	—	0.143
Isolated valve procedures	4151 (16.7)	3887 (16.9)	264 (14.2)	—	
CABG plus valve procedures	1290 (5.2)	1155 (5.0)	135 (7.3)	—	
Aortic procedures	1737 (7.0)	1567 (6.8)	170 (9.2)	—	
Other procedures	3843 (15.4)	3563 (15.5)	280 (15.1)	—	
Cardiopulmonary bypass time, min*	110.4 (45.9)	110.0 (45.6)	115.2 (49.8)	<0.001	0.109
Aortic-cross time, min	77.7 (34.3)	77.6 (34.2)	80.0 (36.1)	0.014	0.069
Duration of surgery, h	4.7 (1.7)	4.7 (1.6)	5.0 (2.7)	<0.001	0.119
Perioperative transfusion of any blood type*[$]	8065 (32.4)	7401 (32.1)	664 (35.8)	—	—
Intraoperative red blood cell transfusion	6278 (25.2)	5755 (25.0)	523 (28.2)	0.002	0.073
Postoperative outcomes					
AKI*					
None	16 621 (66.7)	15 777 (68.5)	844 (45.5)	—	0.518
Stage 1	7278 (29.2)	6496 (28.2)	782 (42.2)	—	—
Stage 2	796 (3.2)	628 (2.7)	168 (9.1)	—	—
Stage 3	209 (0.8)	148 (0.6)	61 (3.3)	—	—
Dialysis support	69 (0.3)	50 (0.2)	19 (1.0)	<0.001	0.103
Creatinine at discharge, μmol/L	0.96 (0.30)	0.95 (0.29)	1.00 (0.45)	<0.001	0.134
eGFR at discharge, mL/min per 1.73 m^2	88.5 (28.0)	88.8 (27.6)	85.6 (31.7)	<0.001	0.106
eGFR ratio of discharge/admission	1.02 (0.27)	1.04 (0.27)	0.85 (0.23)	<0.001	0.731
Nonrecovery of renal function at discharge*	8225 (33.0)	7106 (30.8)	1119 (60.3)	<0.001	0.62
Intra- and postoperative mechanical cardiac support	124 (0.5)	103 (0.5)	21 (1.1)	<0.001	0.077
Duration of mechanical ventilation, h	16.0 (13.0–20.0)	16.0 (13.0–20.0)	17.0 (14.0–22.0)	<0.001	0.123
Length of ICU stay, d	2.0 (1.0–4.0)	2.0 (1.0–3.0)	2.0 (1.0–4.0)	<0.001	0.168
Length of hospital stay, d	6.7 (6.5–8.7)	6.7 (6.5–8.6)	6.7 (6.6–9.7)	<0.001	0.226
No. of postoperative creatinine measurements till discharge (times)	9.0 (6.0–16.0)	9.0 (6.0–16.0)	10.0 (6.0–17.0)	<0.001	0.176
No. of follow-up creatinine measurements (times)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	2.0 (1.0–4.0)	<0.001	0.567

AKI indicates acute kidney injury; ASD, absolute standard difference; CABG, coronary artery bypass graft; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; and NHYA, New York Heart Association.

*Candidate variables that were considered in multivariable Cox analyses.

[†]Defined as mechanical ventilation or mechanical cardiac support before cardiac surgery.

[$]Perioperative transfusion was defined as the transfusion of any blood product: red blood cells, fresh frozen plasma, or platelets.

An overview of the clinical information of patients with and without follow-up renal function decline within the baseline eGFR strata of ≥90 mL/min per 1.73 m^2, 60 to 89 mL/min per 1.73 m^2, and ≤45 mL/min per 1.73 m^2 is summarized in Tables S3 to S5. The crude incidence of renal function decline was 10.9% (1200/11 042), 4.5% (531/11 733), and 5.8% (124/2129) for patients with eGFR ≥90 mL/min per 1.73 m^2, 60 to 89 mL/min per 1.73 m^2, and ≤59 mL/min per 1.73 m^2, respectively. Within the stratum of baseline eGFR ≥90 mL/min per 1.73 m^2, an increasing trend of baseline eGFR levels indicated a greater likelihood of renal function decline

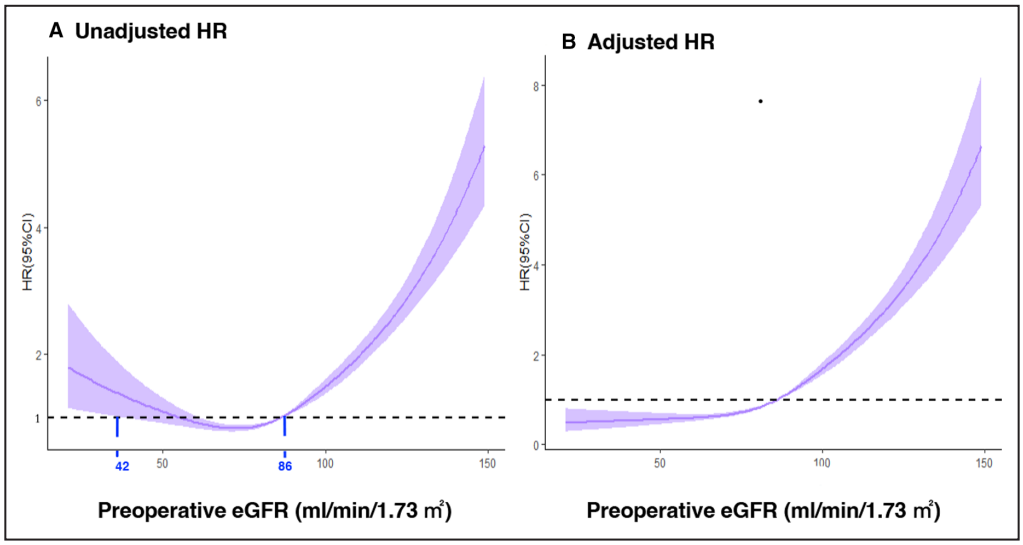

Figure 1. The shapes of association of baseline eGFR and serum creatinine levels as continuous variables and renal function decline depicted by restricted cubic splines.
Patients with eGFR ≥90 mL/min per 1.73 m^2 gained a higher risk of renal function decline than those with eGFR <90 mL/min per 1.73 m^2. The curves are presented with 95% CIs. (**A**) Without adjustment for covariables: There was a J-shaped relationship between baseline eGFR and renal function decline. eGFR of 42 mL/min per 1.73 m^2 and 86 mL/min per 1.73 m^2 were 2 cutoffs with regard to risk of renal function decline, because their HRs of corresponding lower limit of 95% CI were calculated as 1.0; for the sake of clinical utility, we set the cutoffs at 45 mL/min per 1.73 m^2 and 90 mL/min per 1.73 m^2 as consistent with KDIGO guidelines. (**B**) With adjustment for the covariables presented in Table 1 that were labeled *. (**C, D**) Before and after adjustment for the covariables presented in Table 1 that are labeled *. eGFR indicates estimated glomerular filtration rate; HR, hazard ratio; and KDIGO, Kidney Disease: Improving Global Outcomes.

(HR, 1.023 [95% CI, 1.021–1.026]; *P*<0.001), as well as in the stratum of eGFR 60 to 89 mL/min per 1.73 m^2 (HR, 1.029 [95% CI, 1.018–1.040]; *P*<0.001). However, there was no such association between eGFR levels and renal function decline in those with eGFR ≤59 mL/min per 1.73 m^2 (unadjusted HR, 0.988 [95% CI, 0.966–1.011]; *P*=0.301). The different predictive factors associated with renal function decline in each eGFR stratum, which were determined by the LASSO technique before model fitting, are listed in Table 2.

Diabetes and hypertension were recognized as significant contributors to renal function decline in the above 3 eGFR strata (Table 2). Nevertheless, no significant interaction was gained between eGFR strata and diabetes (*P*=0.125) or hypertension (*P*=0.642) toward the end point.

The strongest contributor to renal function decline was increased baseline eGFR levels in the eGFR ≥90 mL/min per 1.73 m^2 stratum, perioperative transfusion of any blood type in the eGFR 60 to 89 mL/min per 1.73 m^2 stratum, and no renal function recovery in the eGFR ≤59 mL/min per 1.73 m^2 stratum (Figure 2). Hypertension, transfusion of any blood type, postoperative AKI stages, and no recovery of renal function at discharge were shared as common contributors to renal function decline in all 3 eGFR categories.

Sensitivity Analysis

The association of eGFR strata and kidney dysfunction progression remained unaltered when we redefined renal decline as a 40% drop in eGFR (eGFR ≥90 mL/min per 1.73 m^2 versus eGFR 60–89 mL/min per 1.73 m^2: HR, 2.188 [95% CI, 1.694–2.827]; *P*<0.001; eGFR ≤59 mL/min per 1.73 m^2 versus eGFR 60–89 mL/min per 1.73 m^2: HR, 1.272 [95% CI, 0.846–1.911]; *P*=0.248). Multivariable Cox analysis, which adjusted for variables with *P*<0.1 on univariable analysis, revealed that the relationships between baseline eGFR and renal function decline within the 3 eGFR strata remained unaltered (Table S6). The results regarding the link between eGFR and renal function decline were still unchanged in the context that the lack of recovery of renal function at discharge was determined as an eGFR drop of at least 20% (Table S7). The most important contributor to renal function decline in each baseline eGFR stratum also remained consistent when the length of intensive care unit stay was additionally incorporated into the models (figure not shown).

Nomograms for Renal Function Decline

Nomograms were built to predict the probability that a patient will develop renal function decline following

Table 2. Multivariable Cox Regression Analysis Using LASSO Technique of Renal Function Decline Over Follow-Up Among Patients Stratified by Baseline eGFR Levels*

eGFR ≥90 mL/min per 1.73 m²		eGFR 60–89 mL/min per 1.73 m²		eGFR ≤59 mL/min per 1.73 m²	
Variables	**Adjusted HR (95% CI), *P* value**	**Variables**	**Adjusted HR (95% CI), *P* value**	**Variables**	**Adjusted HR (95% CI), *P* value**
Baseline eGFR (1 mL/min per 1.73 m² increment)†	1.023 (1.021–1.026), *P*<0.001	Baseline eGFR (1 mL/min/1.73 m² increment)	1.029 (1.018–1.040), *P*<0.001	—	—
Male sex	0.709 (0.628–0.800) *P*<0.001	—	—	Diuretics	0.555 (0.372–0.829) *P*=0.004
Age (1-y increment)	1.031 (1.024–1.037) *P*<0.001	Age (1-y increment)	1.031 (1.020–1.043) *P*<0.001	—	—
Hypertension	1.314 (1.163–1.483) *P*<0.001	Hypertension	1.458 (1.208–1.759) *P*<0.001	Hypertension	2.298 (1.389–3.800) *P*=0.001
Diabetes	1.336 (1.180–1.512) *P*<0.001	Diabetes	1.373 (1.136–1.660) *P*=0.001	Diabetes	1.244 (0.845–1.831) *P*=0.269
Anemia	1.089 (0.954–1.243) *P*=0.209	—	—	Anemia	1.353 (0.904–2.025) *P*=0.142
Myocardial infarction	1.289 (1.119–1.484) *P*<0.001	LVEF (1% increment)	0.979 (0.970–0.989) *P*<0.001	—	—
Stroke	1.502 (1.316–1.714) *P*<0.001	Albumin (1 mg/L increment)	0.980 (0.957–1.003) *P*=0.094	Albumin (1 mg/L increment)	0.979 (0.935–1.026) *P*=0.386
Sodium (1-mmol/L increment)	0.958 (0.938–0.978) *P*<0.001	Chlorine (1-mmol/L increment)	1.033 (1.007–1.061) *P*=0.014	—	—
Calcium (1-mmol/L increment)	0.287 (0.191–0.432) *P*<0.001	Calcium (1-mmol/L increment)	0.213 (0.106–0.427) *P*<0.001	Calcium (1 mmol/L increment)	0.156 (0.031–0.779) *P*=0.023
Preoperative proteinuria levels	—	Preoperative proteinuria levels	—	Preoperative proteinuria levels	—
Negative	1 (reference)	Negative	1 (reference)	Negative	1 (reference)
Mild	1.564 (1.289–1.896) *P*<0.001	Mild	1.512 (1.136–2.012) *P*=0.005	Mild	1.394 (0.857–2.266) *P*=0.181
Heavy	1.253 (0.720–2.180) *P*=0.426	Heavy	2.874 (1.675–4.931) *P*<0.001	Heavy	1.736 (0.914–3.297) *P*=0.092
Perioperative transfusion of any blood type	1.970 (1.725–2.251) *P*<0.001	Perioperative transfusion of any blood type	2.287 (1.885–2.775) *P*<0.001	Perioperative transfusion of any blood type	1.917 (1.265–2.904) *P*=0.002
AKI stages		AKI stages		AKI stages	
None	1 (reference)	None	1 (reference)	None	1 (reference)
Stage 1	1.368 (1.207–1.550) *P*<0.001	Stage 1	1.617 (1.329–1.966) *P*<0.001	Stage 1	1.839 (1.159–2.919) *P*=0.010
Stage 2	1.739 (1.393–2.172) *P*<0.001	Stage 2	2.618 (1.909–3.590) *P*<0.001	Stage 2	1.905 (0.963–3.767) *P*=0.064
Stage 3	1.050 (0.644–1.714) *P*=0.844	Stage 3	3.463 (2.273–5.275) *P*<0.001	Stage 3	3.240 (1.528–6.871) *P*=0.002
Renal recovery		Renal recovery		Renal recovery	
Recovery	1 (reference)	Recovery	1 (reference)	Recovery	1 (reference)
None	1.695 (1.494–1.924) *P*<0.001	None	1.893 (1.573–2.279) *P*<0.001	None	2.809 (1.876–4.206) *P*<0.001
Follow-up time, d, median interquartile range)	335.0 (109.8–671.7)		302.9 (109.1–563.0)		264.1 (110.9–565.0)
C-index	C=0.761		C=0.744		C=0.811

AKI indicates acute kidney injury; eGFR, estimated glomerular filtration rate; HR, hazard ratio; LASSO, least absolute shrinkage and selection operator; and LVEF, left ventricular ejection fraction.

*The variables in each eGFR stratum displayed in this table were specifically selected using the LASSO technique, which incorporated 40 candidate variables in Table 1 labeled * and baseline eGFR levels.

†The unadjusted risk associated with CKD for patients with eGFR ≥90 mL/min per 1.73 m² was HR, 1.021 (95% CI, 1.019–1.023), *P*<0.001; for patients with eGFR 60 to 89 mL/min per 1.73 m² was HR, 1.011 (95% CI, 1.001–1.022), *P*<0.001; and for those with eGFR ≤59 mL/min per 1.73 m² was 0.988 (95% CI, 0.966–1.011), *P*=0.301.

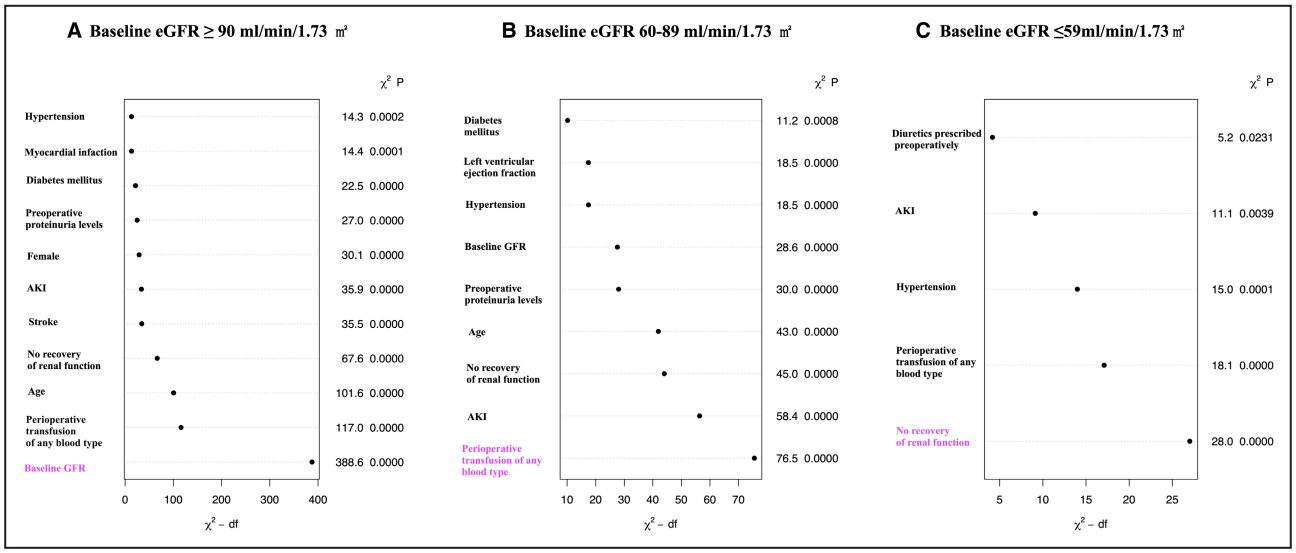

Figure 2. The rank of contributors to renal function decline in individual eGFR stratum.
(**A**) Contributors to renal function decline in patients with eGFR ≥90 ml/min/1.73 m^2. (**B**) Contributors to renal function decline in patients with 60–89 ml/min/1.73 m^2. (**C**) Contributors to renal function decline in patients with eGFR ≤59 ml/min/1.73 m^2. eGFR indicates estimated glomerular filtration rate.

cardiac surgery within each stratum of eGFR (Figure 3A through 3C). An 11-variable nomogram regarding renal function decline prediction was built for patients with eGFR ≥90 mL/min per 1.73 m^2: age; female sex; comorbidities of hypertension, diabetes, stroke, and myocardial infarction; baseline eGFR levels; AKI stages; preoperative proteinuria degrees; transfusion of any blood type; and renal function nonrecovery at hospital discharge. A 9-variable nomogram was developed for patients with eGFR 60 to 89 mL/min per 1.73 m^2: age, hypertension, diabetes, baseline left ventricular ejection fraction values, baseline eGFR levels, preoperative proteinuria degrees, AKI stages, transfusion of any blood type, and renal function nonrecovery at discharge. Finally, another 5-variable nomogram consisting of hypertension, diuretics prescribed before surgery, transfusion of any blood type, AKI stages, and renal function nonrecovery at discharge was built for patients with eGFR ≤59 mL/min per 1.73 m^2.

After internal validation via the bootstrap technique, the corrected C-index was 0.752, 0.725, and 0.791 in patents stratified by eGFR ≥90 mL/min per 1.73 m^2, 60 to 89 mL/min per 1.73 m^2, and ≤59 mL/min per 1.73 m^2, respectively. The cumulative risk of renal function decline by predicted 1-year risk stratification categorized as low, medium, and high within each eGFR stratum is displayed in Figure 4.
Calibration plots are presented in Figure S3.

DISCUSSION

The prominent strength of our analysis was that the prediction of renal function decline in eGFR of 30% differed remarkably across different eGFR strata. An individual prediction nomogram was achieved in patients with eGFR ≥90 mL/min per 1.73 m^2, 60 to 89 mL/min per 1.73 m^2, and ≤59 mL/min per 1.73 m^2, showing good internal consistency. Only a limited number of routine clinical variables were incorporated into each nomogram, making them easy to put into regular practice.

The risk of follow-up renal function decline tended to go unanimously upward with increased baseline eGFR levels in patients without preexisting renal dysfunction, seldom revealed by published studies focusing on cardiac surgery. Patients with ostensibly excellent renal performance may experience hyperfiltration or suffer impaired renal reserve preoperatively. Their renal function subsequently declines in a rapid and progressive fashion, manifesting as a reduction in eGFR of >30% in the context of surgical insults or residual cardiac lesions. To some extent, higher eGFR levels should be interpreted cautiously, as they are not typically perceived as an ideal indicator of promising renal performance. Elevated eGFR at baseline also gained greater odds toward doubling of serum creatinine levels over the follow-up.[28]

Instead of CKD conventionally being diagnosed among French risk score as at least 2 follow-up eGFR values <60 mL/min per 1.73 m^2 separated by an interval of at least 90 days, we have proposed that it be defined as a decline in estimated eGFR by ≥30%.[6] A reduction of 30% in eGFR occurs more frequently, confers benefits such as shorter follow-up episodes and preemptive prediction of CKD and end-stage renal disease,[29,30] and is consistently linked with mortality risk.[30]

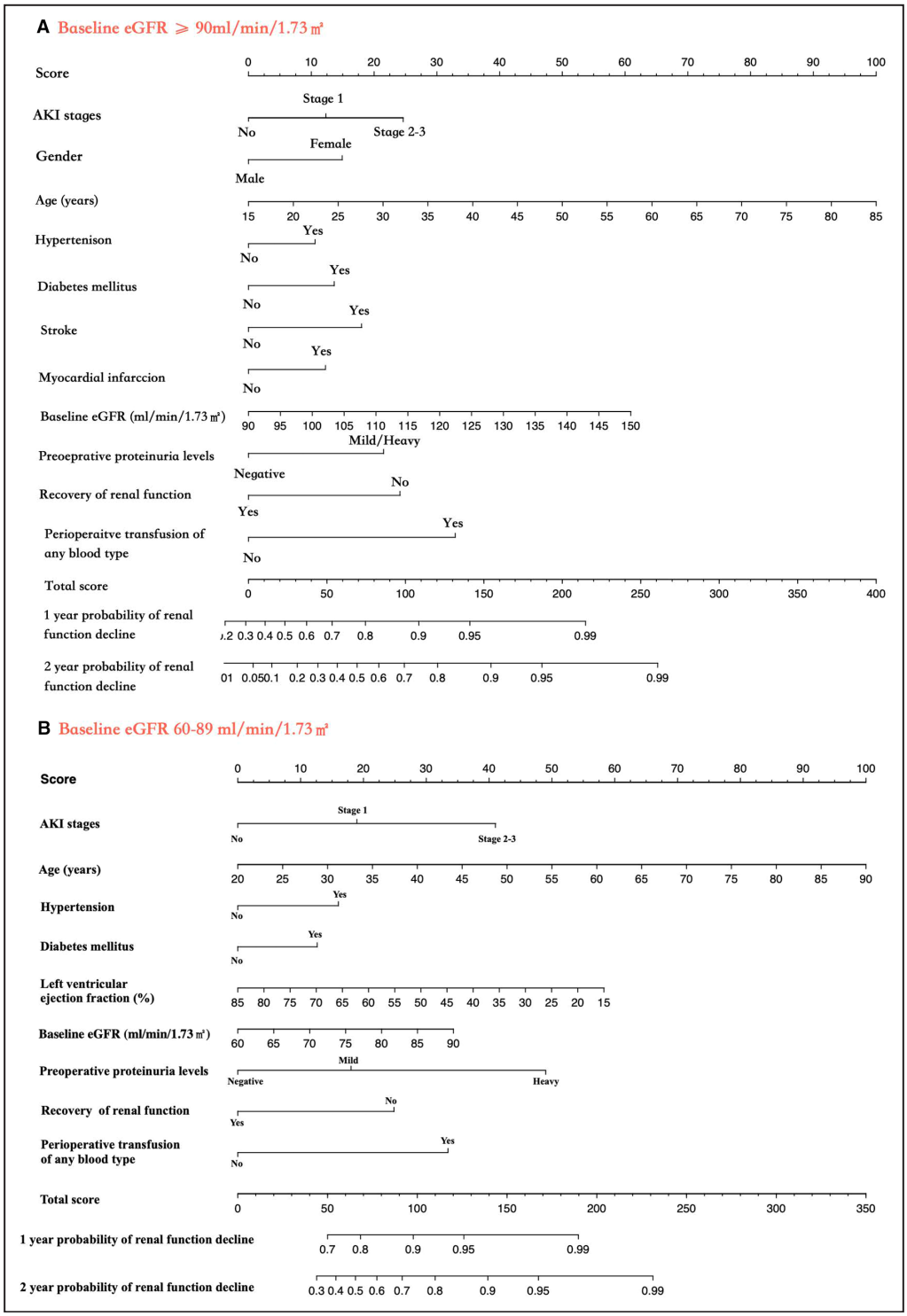

Figure 3. The nomogram to predict the probability that a patient will develop renal function decline.

(**A**) 11-variable prediction nomogram for patients with eGFR ≥90 mL/min per 1.73 m^2. (**B**) 9-variable prediction nomogram for patients with eGFR 60 to 89 mL/min per 1.73 m^2. (**C**) 5-variable prediction nomogram for patients with eGFR ≤59 mL/min per 1.73 m^2. AKI indicates acute kidney injury; and eGFR, estimated glomerular filtration rate.

In patients with eGFR of ≥90 mL/min per 1.73 m^2, the absence of a graded effect of rising AKI stages on the renal function decline burden was identified, as no significant association between stage 3 AKI and CKD was examined by either LASSO regression (Table 2) or univariable regression with the criterion of P<0.1

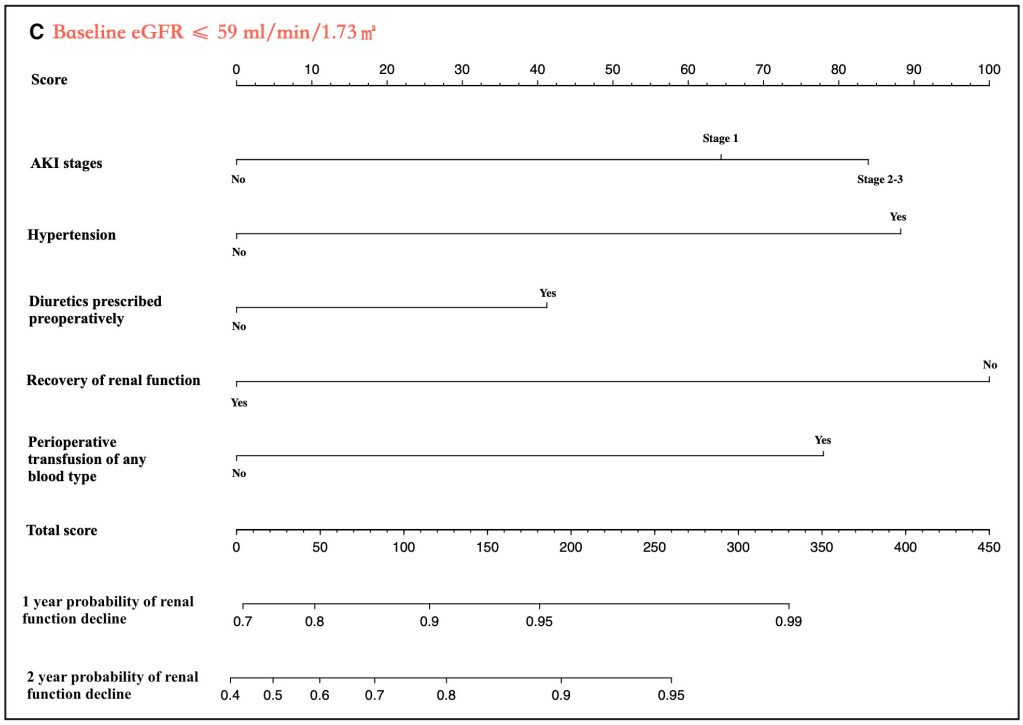

Figure 3. (Continued)

(Table S6), in line with prior studies by Turan et al[31] and Privratsky et al.[32] The likelihood of CKD was already recognized to be somewhat greater in those with baseline eGFR ≥90 mL/min per 1.73 m^2 in conjunction with subsequent mild AKI of stage 1 compared with those having eGFR <90 mL/min per 1.73 m^2 and developing AKI of any stage postoperatively.[32] Clinicians should therefore be aware that the grade-dependent response effects of postsurgical CKD associated with baseline kidney compromise severity or AKI stages may not exist as hypothesized. Meticulous nephrology follow-up and care related to late kidney dysfunction should also be shifted to patients with optimal baseline kidney performance or to those encountering mild/moderate postoperative AKI, when appropriate.

Numerous analyses have iteratively strengthened the conclusion that transfusion has negative effects on AKI and dialysis support,[33–35] specifically in terms of higher red blood cell requirements.[35] Nevertheless, this is the first study to confirm that transfusion with at least 1 type of blood product is also associated with an increased likelihood of renal function decline at 1 year irrespective of the patient's eGFR stratum. Specific mechanisms underlying the renal damage mediated by transfusion remain ambiguous. Higher levels of myeloid-related protein 14 released from packed red blood cells could damage renal structures by increasing the ability of neutrophil influx into the kidney.[36] The red blood cell–derived exosome is another suspected contributor to tubular injury and fibrosis.[37]

The incidence of nonrecovery of renal function at hospital discharge in patients with and without renal function decline was 60.3% and 30.8%, respectively. Despite recovered AKI at discharge after cardiac surgery, renal functional reserve can persistently decrease even 3 months later,[38] and these patients gained a 2.3 times increased likelihood of CKD relative to those without AKI.[5] In the setting of cardiac surgery, much work is still required regarding the relevant assessment of residual renal function at discharge. The confirmation of patient recovery, therefore, relies not only on cardiac performance and physical exercise but also on renal function. Renal recovery may further be referred to as a component of the discharge criteria or of targeted intervention for long-term morbidity and death.

Baseline proteinuria is a well-recognized risk factor contributing to CKD within 1 year following discharge in noncardiac settings.[8] The urine albumin : creatinine ratio was affirmed to indicate long-term renal function decline after inpatient AKI episodes.[7] However, semiquantitative measurement of proteinuria using a urine dipstick is the predominant approach at our institute due in part to its lower cost. In real-life clinical management, the lack of urinalysis assessments for proteinuria either pre- or postoperatively, irrespective of the degrees of baseline creatinine and eGFR, seems somewhat huge.[8,39–41] Interestingly, preoperative proteinuria, whether mild or severe, was not correlated with renal function decline in patients with preexisting kidney dysfunction in our study.

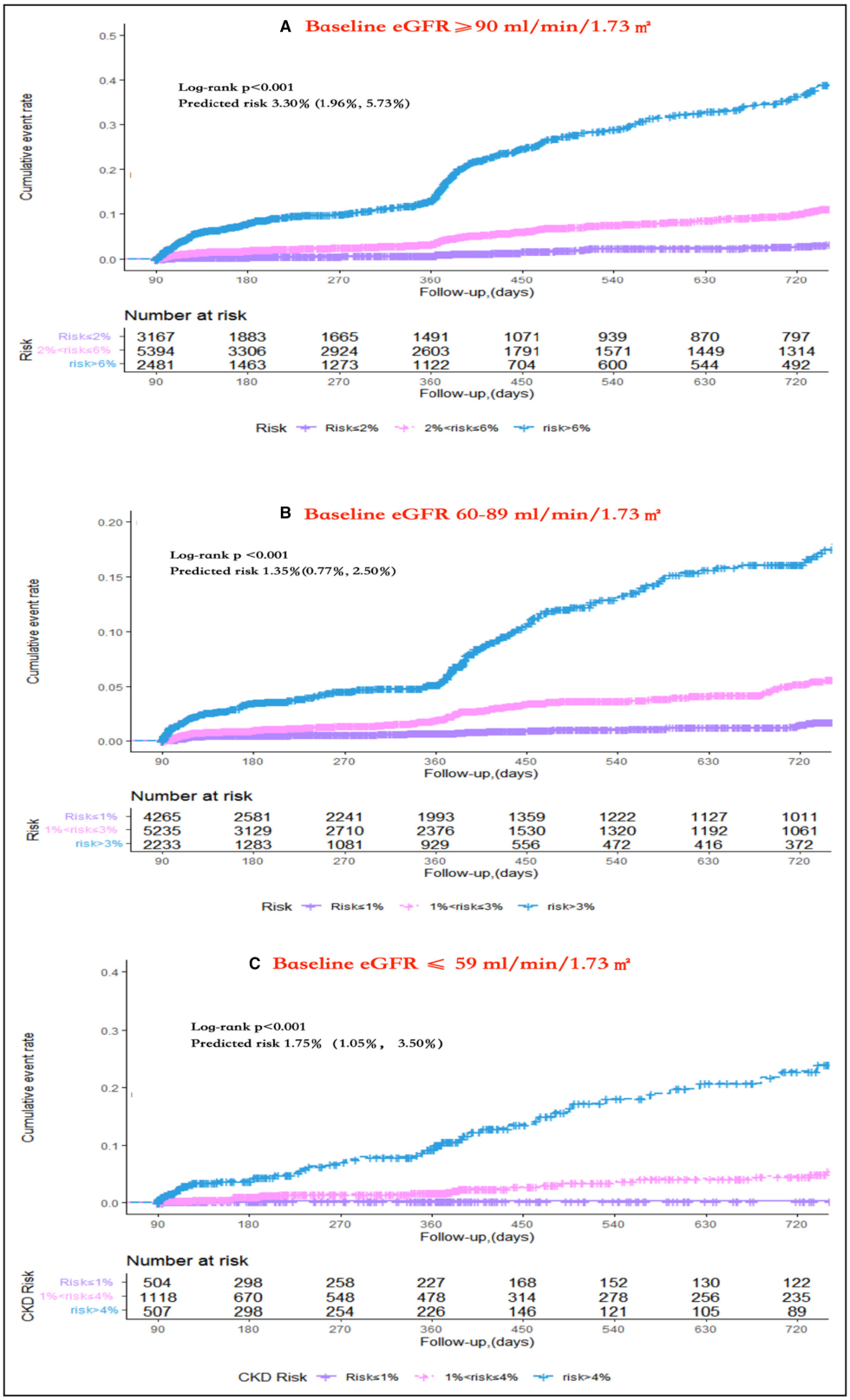

Figure 4. Cumulative risk of renal function decline by the predicted 1-year risk stratification, categorized as low, medium, and high.

Risk categories were created according to interquartile range of individual patient renal function decline risk. (**A**) Cumulative risk of renal function decline in patients with eGFR ≥90 ml/min/1.73 m^2. (**B**) Cumulative risk of renal function decline in patients with eGFR 60–89 ml/min/1.73 m^2. (**C**) Cumulative risk of renal function decline in patients with eGFR ≤59 ml/min/1.73 m^2.

Though an intensive cardiac population was analyzed in our study, the incidence of loss to follow-up serum creatinine was comparably high, at nearly 50% (Table S8). Nevertheless, with the exception of hyperlipidemia and requirement of preoperative medications (absolute standard difference >0.2), the overall demographic and clinical information on patients with and without follow-up serum creatinine was almost well balanced. The discrepancy in kidney function either at baseline (87.0 mL/min per 1.73 m^2 [73.0–103.0] versus 86.0 mL/min per 1.73 m^2 [73.0–101.0]) or at hospital discharge (87.3 mL/min per 1.73 m^2 [69.1–107.1] versus 86.5 mL/min per 1.73 m^2 [69.7–104.4]) was subtle between patients without follow-up creatinine and those with it.

We did not account for any laboratory biomarkers significantly predicting renal function decline, such as calcium, sodium, and chlorine, into the 3 individual nomograms because they are readily modifiable factors during intra- and postoperative management.

This risk model can be readily implemented at the time of hospital discharge to inform about the likelihood of advanced chronic kidney function decline and to aid in enacting and complementing follow-up schemes to design nephrology-based interventions.

Study Limitations

We acknowledge several limitations. First, there were no external data from other medical institutes to further validate the nomogram's performance in each eGFR stratum for renal function decline prediction, which was a primary limitation of this study. Second, no other candidate variables, such as urine assessments, blood pressure, perioperative management, and medications consumed postoperatively, were available in the database. Notably, the kidney-associated parameters we recorded at discharge, such as proteinuria levels, AKI severity, and kidney function recovery, had been fully evident in terms of CKD prediction instead of common clinical characteristics.[8] Third, we obtained a relatively insufficiently long length of follow-up, with a median renal function decline of 314 days, which in part ensured that the renal outcomes were not due to other de novo renal pathogeneses but rather were secondary to cardiac surgical insults. Fourth, definition of renal recovery irrespective of AKI in our research is not flawed because patients with serum creatinine changes without AKI evidence might have body composition changes instead of "recovery of renal function." However, this problem could not be solved by our retrospective monitoring alone.

CONCLUSIONS

Predictors of renal function decline over the follow-up showed remarkable discrepancy in each eGFR stratum of ≥90 mL/min per 1.73 m^2, 60 to 89 mL/min per 1.73 m^2, and ≤59 mL/min per 1.73 m^2. The nomograms for these 3 strata incorporated a limited number of variables that are readily available in the routine cardiac surgical setting and can be used to predict renal function decline in patients stratified by baseline eGFR.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Data S1

REFERENCES

1. Eckardt KU, Coresh J, Devuyst O, Johnson RJ, Kottgen A, Levey AS, Levin A. Evolving importance of kidney disease: from subspecialty to global health burden. *Lancet*. 2013;382:158–169. doi: 10.1016/S0140-6736(13)60439-0
2. Chawla LS, Eggers PW, Star RA, Kimmel PL. Acute kidney injury and chronic kidney disease as interconnected syndromes. *N Engl J Med*. 2014;371:58–66. doi: 10.1056/NEJMra1214243
3. Garg AX, Devereaux PJ, Yusuf S, Cuerden MS, Parikh CR, Coca SG, Walsh M, Novick R, Cook RJ, Jain AR, et al. Kidney function after off-pump or on-pump coronary artery bypass graft surgery: a randomized clinical trial. *JAMA*. 2014;311:2191–2198. doi: 10.1001/jama.2014.4952
4. Ryden L, Sartipy U, Evans M, Holzmann MJ. Acute kidney injury after coronary artery bypass grafting and long-term risk of end-stage renal disease. *Circulation*. 2014;130:2005–2011. doi: 10.1161/CIRCULATIONAHA.114.010622
5. Legouis D, Galichon P, Bataille A, Chevret S, Provenchere S, Boutten A, Buklas D, Fellahi JL, Hanouz JL, Hertig A. Rapid occurrence of chronic kidney disease in patients experiencing reversible acute kidney injury after cardiac surgery. *Anesthesiology*. 2017;126:39–46. doi: 10.1097/ALN.0000000000001400
6. Legouis D, Jamme M, Galichon P, Provenchere S, Boutten A, Buklas D, Hanouz JL, Hertig A. Development of a practical prediction score

for chronic kidney disease after cardiac surgery. *Br J Anaesth*. 2018;121:1025–1033. doi: 10.1016/j.bja.2018.07.033
7. Hsu CY, Chinchilli VM, Coca S, Devarajan P, Ghahramani N, Go AS, Hsu RK, Ikizler TA, Kaufman J, Liu KD, et al. Post-acute kidney injury proteinuria and subsequent kidney disease progression: the assessment, serial evaluation, and subsequent sequelae in acute kidney injury (ASSESS-AKI) study. *JAMA Intern Med*. 2020;180:402–410. doi: 10.1001/jamainternmed.2019.6390
8. James MT, Pannu N, Hemmelgarn BR, Austin PC, Tan Z, McArthur E, Manns BJ, Tonelli M, Wald R, Quinn RR, et al. Derivation and external validation of prediction models for advanced chronic kidney disease following acute kidney injury. *JAMA*. 2017;318:1787–1797. doi: 10.1001/jama.2017.16326
9. Bhatraju PK, Zelnick LR, Chinchilli VM, Moledina DG, Coca SG, Parikh CR, Garg AX, Hsu CY, Go AS, Liu KD, et al. Association between early recovery of kidney function after acute kidney injury and long-term clinical outcomes. *JAMA Netw Open*. 2020;3:e202682. doi: 10.1001/jamanetworkopen.2020.2682
10. Sawhney S, Marks A, Fluck N, Levin A, McLernon D, Prescott G, Black C. Post-discharge kidney function is associated with subsequent ten-year renal progression risk among survivors of acute kidney injury. *Kidney Int*. 2017;92:440–452. doi: 10.1016/j.kint.2017.02.019
11. Mases A, Sabate S, Guilera N, Sadurni M, Arroyo R, Fau M, Rojo A, Castillo J, Bover J, Sierra P, et al. Preoperative estimated glomerular filtration rate and the risk of major adverse cardiovascular and cerebrovascular events in non-cardiac surgery. *Br J Anaesth*. 2014;113:644–651. doi: 10.1093/bja/aeu134
12. Bernardi MH, Schmidlin D, Schiferer A, Ristl R, Neugebauer T, Hiesmayr M, Druml W, Lassnigg A. Impact of preoperative serum creatinine on short- and long-term mortality after cardiac surgery: a cohort study. *Br J Anaesth*. 2015;114:53–62. doi: 10.1093/bja/aeu316
13. Wang C, Gao Y, Tian Y, Wang Y, Zhao W, Sessler DI, Jia Y, Ji B, Diao X, Xu X, et al. Prediction of acute kidney injury after cardiac surgery from preoperative N-terminal pro-B-type natriuretic peptide. *Br J Anaesth*. 2021;127:862–870. doi: 10.1016/j.bja.2021.08.015
14. Qu J, Zhang D, Zhang H, Rao C, Chen S, Zhao Y, Zheng Z. Preoperative clopidogrel and outcomes in patients with acute coronary syndrome undergoing coronary artery bypass surgery. *J Thorac Cardiovasc Surg*. 2022;163:1044–1052.e1015. doi: 10.1016/j.jtcvs.2020.03.118
15. Zhang D, Gu D, Rao C, Zhang H, Su X, Chen S, Ma H, Zhao Y, Feng W, Sun H, et al. Outcome differences between surgeons performing first and subsequent coronary artery bypass grafting procedures in a day: a retrospective comparative cohort study. *BMJ Qual Saf*. 2023;32:192–201. doi: 10.1136/bmjqs-2021-014244
16. Martini A, Cumarasamy S, Beksac AT, Abaza R, Eun DD, Bhandari A, Hemal AK, Porter JR, Badani KK. A nomogram to predict significant estimated glomerular filtration rate reduction after robotic partial nephrectomy. *Eur Urol*. 2018;74:833–839. doi: 10.1016/j.eururo.2018.08.037
17. Cho JS, Shim JK, Lee S, Song JW, Choi N, Lee S, Kwak YL. Chronic progression of cardiac surgery associated acute kidney injury: intermediary role of acute kidney disease. *J Thorac Cardiovasc Surg*. 2021;161(681–688):e683.
18. Kellum JA, Lameire N; Group KAGW. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (part 1). *Crit Care*. 2013;17:204. doi: 10.1186/cc11454
19. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150:604–612. doi: 10.7326/0003-4819-150-9-200905050-00006
20. Bucaloiu ID, Kirchner HL, Norfolk ER, Hartle JE 2nd, Perkins RM. Increased risk of death and de novo chronic kidney disease following reversible acute kidney injury. *Kidney Int*. 2012;81:477–485. doi: 10.1038/ki.2011.405
21. Beohar N, Doshi D, Thourani V, Jensen H, Kodali S, Zhang F, Zhang Y, Davidson C, McCarthy P, Mack M, et al. Association of transcatheter aortic valve replacement with 30-day renal function and 1-year outcomes among patients presenting with compromised baseline renal function: experience from the PARTNER 1 trial and registry. *JAMA Cardiol*. 2017;2:742–749. doi: 10.1001/jamacardio.2017.1220
22. Xu J, Xu X, Shen B, Zhuang Y, Liu L, Wang Y, Fang Y, Luo Z, Teng J, Wang C, et al. Evaluation of five different renal recovery definitions for estimation of long-term outcomes of cardiac surgery associated acute kidney injury. *BMC Nephrol*. 2019;20:427. doi: 10.1186/s12882-019-1613-6
23. Lameire NH, Levin A, Kellum JA, Cheung M, Jadoul M, Winkelmayer WC, Stevens PE, Conference P. Harmonizing acute and chronic kidney disease definition and classification: report of a kidney Disease: improving global outcomes (KDIGO) consensus Conference. *Kidney Int*. 2021;100:516–526. doi: 10.1016/j.kint.2021.06.028
24. James MT, Levey AS, Tonelli M, Tan Z, Barry R, Pannu N, Ravani P, Klarenbach SW, Manns BJ, Hemmelgarn BR. Incidence and prognosis of acute kidney diseases and disorders using an integrated approach to laboratory measurements in a universal health care system. *JAMA Netw Open*. 2019;2:e191795. doi: 10.1001/jamanetworkopen.2019.1795
25. Levey AS, Inker LA, Matsushita K, Greene T, Willis K, Lewis E, de Zeeuw D, Cheung AK, Coresh J. GFR decline as an end point for clinical trials in CKD: a scientific workshop sponsored by the National Kidney Foundation and the US Food and Drug Administration. *Am J Kidney Dis*. 2014;64:821–835. doi: 10.1053/j.ajkd.2014.07.030
26. Yao X, Tangri N, Gersh BJ, Sangaralingham LR, Shah ND, Nath KA, Noseworthy PA. Renal outcomes in anticoagulated patients with atrial fibrillation. *J Am Coll Cardiol*. 2017;70:2621–2632. doi: 10.1016/j.jacc.2017.09.1087
27. Riley RD, Ensor J, Snell KIE, Harrell FE Jr, Martin GP, Reitsma JB, Moons KGM, Collins G, van Smeden M. Calculating the sample size required for developing a clinical prediction model. *BMJ*. 2020;368:m441.
28. Tonelli M, Klarenbach SW, Lloyd AM, James MT, Bello AK, Manns BJ, Hemmelgarn BR. Higher estimated glomerular filtration rates may be associated with increased risk of adverse outcomes, especially with concomitant proteinuria. *Kidney Int*. 2011;80:1306–1314. doi: 10.1038/ki.2011.280
29. Grams ME, Sang Y, Coresh J, Ballew SH, Matsushita K, Levey AS, Greene TH, Molnar MZ, Szabo Z, Kalantar-Zadeh K, et al. Candidate surrogate end points for ESRD after AKI. *J Am Soc Nephrol*. 2016;27:2851–2859. doi: 10.1681/ASN.2015070829
30. Coresh J, Turin TC, Matsushita K, Sang Y, Ballew SH, Appel LJ, Arima H, Chadban SJ, Cirillo M, Djurdjev O, et al. Decline in estimated glomerular filtration rate and subsequent risk of end-stage renal disease and mortality. *JAMA*. 2014;311:2518–2531. doi: 10.1001/jama.2014.6634
31. Turan A, Cohen B, Adegboye J, Makarova N, Liu L, Mascha EJ, Qiu Y, Irefin S, Wakefield BJ, Ruetzler K, et al. Mild acute kidney injury after noncardiac surgery is associated with long-term renal dysfunction: a retrospective cohort study. *Anesthesiology*. 2020;132:1053–1061. doi: 10.1097/ALN.0000000000003109
32. Privratsky JR, Krishnamoorthy V, Raghunathan K, Ohnuma T, Rasouli MR, Long TE, Sigurdsson MI. Postoperative acute kidney injury is associated with progression of chronic kidney disease independent of severity. *Anesth Anal*. 2022;134:49–58. doi: 10.1213/ANE.0000000000005702
33. Karkouti K, Grocott HP, Hall R, Jessen ME, Kruger C, Lerner AB, MacAdams C, Mazer CD, de Medicis E, Myles P, et al. Interrelationship of preoperative anemia, intraoperative anemia, and red blood cell transfusion as potentially modifiable risk factors for acute kidney injury in cardiac surgery: a historical multicentre cohort study. *Can J Anaesth*. 2015;62:377–384. doi: 10.1007/s12630-014-0302-y
34. Karkouti K. Transfusion and risk of acute kidney injury in cardiac surgery. *Br J Anaesth*. 2012;109(Suppl 1):i29–i38. doi: 10.1093/bja/aes422
35. Karkouti K, Wijeysundera DN, Yau TM, McCluskey SA, Chan CT, Wong PY, Beattie WS. Influence of erythrocyte transfusion on the risk of acute kidney injury after cardiac surgery differs in anemic and nonanemic patients. *Anesthesiology*. 2011;115:523–530. doi: 10.1097/ALN.0b013e318229a7e8
36. Vourc'h M, Roquilly A, Foucher A, Retiere C, Feuillet F, Devi S, McWilliam HEG, Braudeau C, Bourreille G, Hachani A, et al. Transfusion-related renal dysfunction after cardiac surgery: the role of myeloid-related Protein_14 in neutrophil-mediated tubular damage. *JACC Basic Transl Sci*. 2022;7:627–638. doi: 10.1016/j.jacbts.2022.02.019
37. Pat B, Oh JY, Masjoan Juncos JX, Powell PC, Collawn JF, Patel RP, Dell'Italia LJ, Clinical WG. Red blood cell exosome hemoglobin content increases after cardiopulmonary bypass and mediates acute kidney injury in an animal model. *J Thorac Cardiovasc Surg*. 2022;164:e289–e308. doi: 10.1016/j.jtcvs.2020.11.102
38. Husain-Syed F, Ferrari F, Sharma A, Hinna Danesi T, Bezerra P, Lopez-Giacoman S, Samoni S, de Cal M, Corradi V, Virzi GM, et al. Persistent decrease of renal functional reserve in patients after cardiac surgery-associated acute kidney injury despite clinical recovery. *Nephrol Dial Transplant*. 2019;34:308–317. doi: 10.1093/ndt/gfy227

39. James MT, Hemmelgarn BR, Wiebe N, Pannu N, Manns BJ, Klarenbach SW, Tonelli M; Alberta Kidney Disease N. Glomerular filtration rate, proteinuria, and the incidence and consequences of acute kidney injury: a cohort study. *Lancet*. 2010;376:2096–2103. doi: 10.1016/S0140-6736(10)61271-8
40. Parr SK, Matheny ME, Abdel-Kader K, Greevy RA Jr, Bian A, Fly J, Chen G, Speroff T, Hung AM, Ikizler TA, et al. Acute kidney injury is a risk factor for subsequent proteinuria. *Kidney Int*. 2018;93:460–469. doi: 10.1016/j.kint.2017.07.007
41. Wahl TS, Graham LA, Morris MS, Richman JS, Hollis RH, Jones CE, Itani KM, Wagner TH, Mull HJ, Whittle JC, et al. Association between preoperative proteinuria and postoperative acute kidney injury and readmission. *JAMA Surg*. 2018;153:e182009. doi: 10.1001/jamasurg.2018.2009