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Postdischarge long-term cardiovascular outcomes of intensive care unit survivors who developed dialysis-requiring acute kidney injury after cardiac surgery

Soojin Lee [a,b], Sehoon Park [a,b], Min Woo Kang [a,b], Hai-Won Yoo [c], Kyungdo Han [d], Yaerim Kim [a], Jung Pyo Lee [b,e], Kwon Wook Joo [a,b,f], Chun Soo Lim [b,e,f], Yon Su Kim [a,b,e], Hyeongsu Kim [c,**], Dong Ki Kim [a,b,f,*]

[a] Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea
[b] Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea
[c] Department of Preventive Medicine, Konkuk University School of Medicine, Seoul, Republic of Korea
[d] Department of Medical Statistics, College of Medicine, Catholic University of Korea, Seoul, Republic of Korea
[e] Department of Internal Medicine, Seoul National University Boramae Medical Center, Seoul, Republic of Korea
[f] Kidney Research Institute, Seoul National University College of Medicine, Seoul, Republic of Korea

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ABSTRACT

Purpose: Dialysis-requiring acute kidney injury (AKI-D) after cardiac surgery is a major cause of in-hospital mortality. However, the long-term outcome has not been previously examined.
Materials and methods: We performed a nationwide, population-based cohort study using the claims data in the Korean National Health Insurance System. Patients who underwent cardiac surgery between 2006 and 2015 were considered.
Results: Among 52,983 patients who underwent cardiac surgery, 1261 underwent dialysis postoperatively. During the median follow-up of 3.33 years, the AKI-D group had increased risk of all-cause mortality, end-stage renal disease (ESRD) progression, and risk of developing major adverse cardiovascular events (MACEs). These results remained consistent after multivariable analysis and propensity-score matching. Even after excluding patients who continued dialysis at discharge, the AKI-D group consistently exhibited worse mortality and an increased risk of MACEs compared to the control group. Patients who underwent continuous renal replacement therapy in the AKI-D group exhibited comparable mortality and risk of MACEs but reduced progression to ESRD compared to those who received intermittent renal replacement therapy.
Conclusions: AKI-D following cardiac surgery was associated with worse long-term postdischarge mortality and elevated risks of dialysis dependency and MACE development. The outcomes were consistent even in the patients who recovered from the dialysis.

1. Introduction

The kidneys and heart are closely interrelated, and dysfunction of either organ may lead to subsequent injury of the other [1,2]. Dialysis-requiring acute kidney injury (AKI-D) occurring after cardiac surgery is associated with a significant increase in in-hospital mortality [3,4] and imposes a considerable medical burden [5-7].

Improvements in dialysis have enabled physicians to adjust dialysis prescriptions to achieve hemodynamic stability in critically ill patients with AKI-D following cardiac surgery during admission to intensive care units (ICUs) [8]. Therefore, a considerable proportion of AKI-D patients recover from dialysis dependency and independently survive after hospital discharge [9]. The in-hospital mortality of patients who have undergone cardiac surgery has decreased over time [10]. It is crucial to assess the long-term outcomes of postdischarge ICU survivors who need dialysis to provide appropriate medical care after hospital discharge because short-term survival is improving. Cardiovascular diseases account for more than half of all causes of death in postcardiac surgery patients [11,12]. AKI is also associated with an increased risk

Abbreviations: AKI-D, dialysis-requiring acute kidney injury; CCI, Charlson-comorbidity index; CRRT, continuous renal replacement therapy; ESRD, end-stage renal disease; ICD, International Classification of Diseases; ICU, intensive care unit; IRRT, intermittent renal replacement therapy; MACE, major adverse cardiovascular adverse events; MI, myocardial infarction; NHIS, National Health Insurance System.

* Correspondence to: D. Kim, Department of Internal Medicine, Seoul National University College of Medicine, 101 Daehak-Ro, Jongno-gu, Seoul 03080, Republic of Korea.
** Correspondence to: H. Kim, Department of Preventive Medicine, Konkuk University School of Medicine, 120 Neungdong-ro, Gwangjin-gu, Seoul 05029, Republic of Korea.
E-mail addresses: mubul@kku.ac.kr (H. Kim), dkkim73@gmail.com (D.K. Kim).

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of cardiovascular events [13-15]. However, the epidemiological data on the long-term risk of major adverse cardiovascular adverse events (MACEs) after severe AKI following cardiac surgery require further investigation.

We performed a nationwide population-based cohort study to examine the postdischarge long-term prognosis of ICU survivors who underwent dialysis for AKI after cardiac surgery. Dialysis dependence after the hospital discharge and MACE occurrence were also examined to determine whether the outcomes differed depending on the need for or modality of dialysis.

2. Material and methods

2.1. Study design and study participants

This study was a nationwide, population-based cohort study performed in Korea. We obtained the data from the Korean National Health Insurance System (NHIS), which provides all covered medical services to Koreans. Patients ≥20 years of age who underwent cardiac surgery and were admitted to an ICU between 2006 and 2015 in 43 government-designated tertiary hospitals were considered. Patients who previously underwent dialysis prior to the index admission were excluded. In addition, if the patients experienced multiple ICU admissions during the study period, the first event of ICU admission was selected as the index admission. Patients who expired within one month after the index admission were also excluded to focus on long-term prognoses. The cardiac surgery was defined as follows; coronary artery bypass graft surgery with or without the application of cardiopulmonary bypass and open-heart valve replacement or repair surgery. Percutaneous intervention of coronary vessels or cardiac valves and heart transplantation were not considered.

The study populations were divided into two groups. Patients who underwent dialysis during the postoperative period of cardiac surgery in an ICU were included in the AKI-D group, and patients who did not undergo dialysis were included in the control group. Patients in the AKI-D group who underwent continuous renal replacement therapy (CRRT) for longer than 24 h were included in the CRRT group, and the remaining patients were included in the intermittent renal replacement therapy (IRRT) group. Demographic data, including age, sex, and the date of index ICU admissions, were collected from the NHIS database. Claims data containing medication usage, past medical history, and the name of surgeries were also included. Comorbidities were collected according to the Charlson-comorbidity index (CCI) [16], and the International Classification of Diseases (ICD)-10 codes [17] were used for the descriptions and analyses. Comorbidities were defined when the diagnosis codes were extracted more than twice per year of the index admission. Principal diagnosis during the index ICU admission was collected and categorized. The implemented ICU treatment, including the application status of mechanical ventilator or the use of intravenous vasopressors, was also collected for analysis.

2.2. Study outcomes

The primary outcome was all-cause mortality. Data of death events were extracted from the database of Statistics Korea, which provided the date of death. The secondary outcome was progression to end-stage renal disease (ESRD), which was defined as a consistent requirement for dialysis for longer than 90 days after hospital discharge [18]. Total number of MACEs were also examined for additional analyses. MACEs included nonfatal myocardial infarction (MI), cardiac revascularization, and acute ischemic stroke events.

MACEs were defined when one of the following codes was issued during the admissions in the following period: acute MI (ICD-10 code I21 or I22), revascularization (claims data of cardiovascular revascularization), and acute ischemic stroke (ICD-10 code I63). We performed subgroup analyses of the AKI-D group to reduce the influence of ESRD on the study outcomes. Progression to ESRD was added as a time-variable covariate during the regression analysis among the subgroups to minimize the confounding effect of ESRD progression on the development of MACEs [19]. The AKI-D group patients were divided into two groups at the time of the hospital discharge of the index admission. Patients who recovered from the dialysis requirement at the hospital discharge of the index admission were placed in the renal recovery group. Patients who consistently required dialysis for longer than 30 days from the hospital discharge were considered as the dialysis-dependent group. The mortality and occurrence of MACE were assessed in each group.

2.3. Statistical analysis

The chi-squared test was used to compare categorical variables, and the data are presented as frequencies (percentages). Comparisons between nonnormally distributed continuous variables were performed using the Mann-Whitney *U* test, and the data are presented as medians (interquartile ranges). Survival curves were obtained using the Kaplan-Meier method. The log-rank test was used to compare the outcomes between the groups and to calculate the *P*-values. Multivariable regression analysis was performed using the Cox proportional hazard model to examine mortality, MACE and ESRD progression. The variables included age, sex, and CCI. Risk factors for MACEs were identified using the Cox regression and backward-elimination approach. A two-sided *P*-value <.05 was considered statistically significant.

The results table consists of three columns, each representing differently adjusted variables. Model 1 presents the results of an unadjusted, univariable analysis. Model 2 was adjusted for age, sex, CCI, application status of a mechanical ventilator, usage of inotropic agents, and the principal diagnosis of the index admission. Model 3 involves 1:1 propensity-score-matched data followed by multivariable Cox regression analysis. Propensity-score-matching analysis used -age, sex, comorbidities and principal diagnosis during the index admission for calculations. Multivariable analysis was performed with the variables

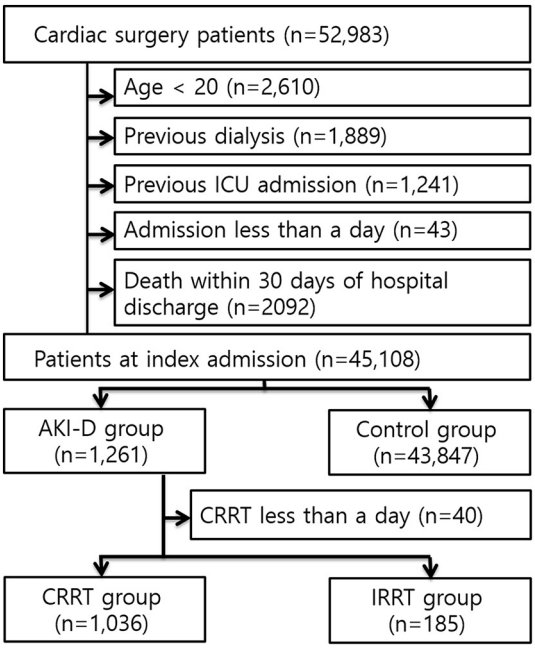

Fig. 1. Flow chart of the study population. ICU = intensive care unit; MACE = major adverse cardiovascular event; CRRT = continuous renal replacement therapy; IRRT = intermittent renal replacement therapy.

Table 1
Baseline characteristics and study outcomes of the subjects.

	Control group ($N = 43,847$)	AKI-D group ($N = 1261$)	*P* value
Age (years (interquartile ranges))	59 (49–68)	64 (54–72)	<0.001
< 40 (N (%))	3375 (7.7)	58 (4.6)	
40–60 (N (%))	15,461 (35.3)	320 (25.4)	
60–80 (N (%))	23,992 (54.7)	822 (65.2)	
≥ 80 (N (%))	1019 (2.3)	61 (4.8)	
Male sex (N, (%))	26,739 (61.0)	716 (56.8)	0.057
Year of admission (N, (%))			<0.001
2015-	18,398 (42.0)	442 (35.1)	
2010–2014	17,435 (39.8)	548 (43.5)	
2005–2009	8014 (18.3)	271 (21.5)	
Charlson comorbidity index score (N (%))			<0.001
≥0 and < 5	41,517 (94.7)	1084 (86.0)	
≥5 and < 10	2276 (5.2)	173 (13.7)	
≥10	54 (0.1)	4 (0.3)	
Implemented treatment during ICU admission (N, (%))			
Ventilator care	42,976 (98.0)	1253 (99.4)	<0.001
Intravenous inotropic agents	42,639 (97.2)	1251 (99.2)	<0.001
Outcomes (N, (%))			
MACE	7085 (16.2)	393 (31.2)	<0.001
Acute MI	2456 (5.6)	196 (15.5)	<0.001
Revascularization	1103 (2.5)	19 (1.5)	0.630
Acute ischemic stroke	3526 (8.0)	178 (14.1)	<0.001
Mortality	5547(12.7)	445 (35.3)	<0.001
Progression to ESRD	817 (1.9)	297 (23.6)	<0.001

ICU = intensive care unit, MACE = major adverse cardiovascular event, MI = myocardial infarction, ESRD = end-stage renal disease.

used in Model 2. All analyses were performed using the SAS 9.4 program (SAS Institute, United States).

2.4. Ethical considerations

The present study received full approval from the Institutional Review Board of Seoul National University Hospital (E-1711-040-897) and Konkuk University (7001355–201,708-E-050). The government approved access to the NHIS database for this study. Informed consent was waived because the present study retrospectively used the data provided by NHIS and no additional medical intervention was performed. All authors followed the latest version of the Declaration of Helsinki throughout the study.

3. Results

3.1. Study population

A total of 52,983 patients underwent cardiac surgery during the study period, of whom 45,108 satisfied the criteria for index admission, between January 2005 and December 2016 (Fig. 1). A total of 1261 patients underwent dialysis during the ICU admission following cardiac surgery and were classified in the AKI-D group. A total of 43,847 patients were assigned to the control group. A total of 1036 patients in the AKI-D group underwent CRRT for longer than 24 h, and 185 patients underwent IRRT during the perioperative period of cardiac surgery.

3.2. Baseline characteristics

Table 1 presents the baseline characteristics of the AKI-D and control groups. Significant differences were identified between the groups. Subjects in the AKI-D group were older ($P < .001$) and exhibited higher CCI scores ($P < .001$) than those in the control group. The AKI-D group required mechanical ventilators ($P < .001$) and intravenous inotropic agents ($P < .001$) more frequently than did those in the control group. Hypertension ($P = .029$), diabetes ($P < .001$), congestive heart failure ($P < .001$) and renal disease ($P < .001$) were more common in the AKI-D group than in the control group (Supplementary Table 1). Principal diagnoses during the index ICU admission revealed that conditions of the circulatory system were the most common diagnosis (93.74%).

3.3. Outcomes of the patients who underwent dialysis

A total of 445 patients (35.3%) in the AKI-D group died, and 393 patients (31.7%) developed MACEs after hospital discharge (Table 1). The AKI-D group exhibited overall worse outcomes than the control group (Fig. 2). The AKI-D group exhibited worse short-term [adjusted hazard ratio (HR) 5.76 (4.33–7.68), $P < .001$] and long-term mortality [adjusted HR 2.72 (2.44–3.02), $P < .001$] than the patients who did not receive dialysis. AKI-D patients more frequently developed MACE within [adjusted HR 3.56 (2.93–4.32), $P < .001$] and after 90 days [adjusted HR 1.97 (1.75–2.23), $P < .001$] from hospital discharge. The risk of progression to ESRD was also higher in the AKI-D group [adjusted hazard ratio (HR) 15.59 (13.89–18.33), $P < .001$] than in the control group. The results remained consistent in comparisons of the propensity-score-matched groups. The patients in the 'renal recovery' subgroup, who were independent of dialysis at the time of the hospital discharge, exhibited worse all-cause mortality [adjusted HR 2.38 (2.13–2.66), $P <$

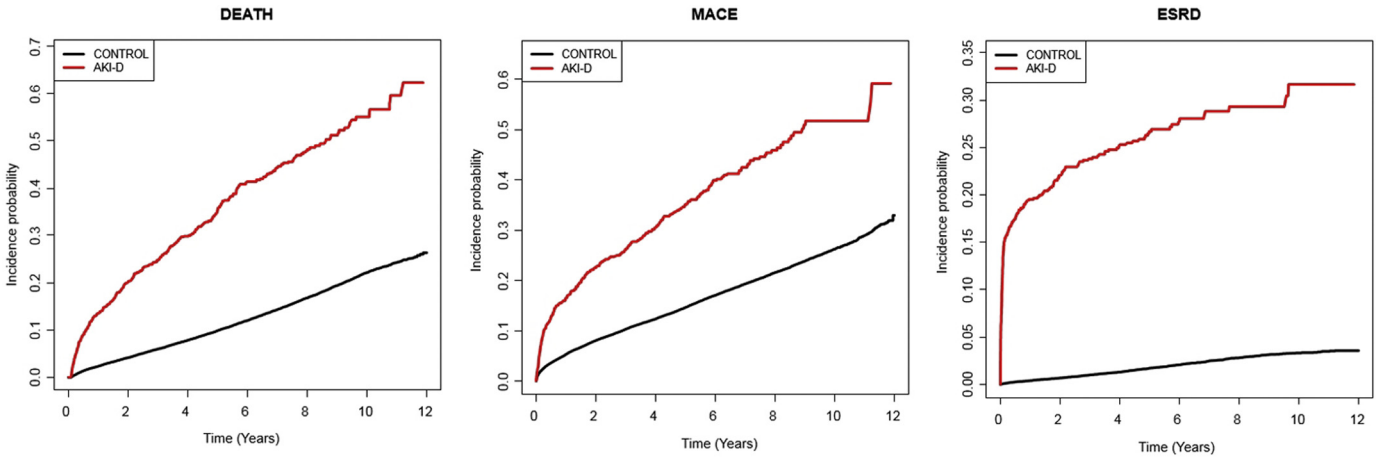

Fig. 2. Kaplan-Meier survival curves of mortality, MACE and ESRD progression: AKI-D vs. control. The x-axes represent time (years), and the y-axes represent the incidence probability. The black and red lines represent the Kaplan-Meier survival curves of the control and AKI-D groups, respectively. MACE = major adverse cardiovascular event; ESRD = end-stage renal disease.

Table 2
Prognosis of patients who underwent dialysis after cardiac surgery.

	Model 1		Model 2		Model 3	
	HR (95% CI)	***P* value**	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**
AKI-D (N = 1261) vs. Control (N = 43,847)						
Mortality	3.99 (3.63–4.40)	<0.001	2.93 (2.65–3.23)	<0.001	2.91 (2.46–3.45)	<0.001
Within 90 days	8.33 (6.32–10.98)	<0.001	5.76 (4.33–7.68)	<0.001	4.61 (2.58–8.25)	<0.001
After 90 days	3.69 (3.33–4.10)	<0.001	2.72 (2.44–3.02)	<0.001	2.76 (2.31–3.30)	<0.001
MACE	2.75 (2.48–3.04)	<0.001	2.26 (2.04–2.51)	<0.001	2.31 (1.96–2.73)	<0.001
Within 90 days	3.96 (3.28–4.78)	<0.001	3.56 (2.93–4.32)	<0.001	4.05 (2.72–6.02)	<0.001
After 90 days	2.43 (2.16–2.75)	<0.001	1.97 (1.75–2.23)	<0.001	2.00 (1.66–2.41)	<0.001
Nonfatal MI	3.84 (3.32–4.44)	<0.001	3.12 (2.69–3.62)	<0.001	3.11 (2.40–4.05)	<0.001
Revascularization	0.89 (0.57–1.41)	0.630	0.81 (0.51–1.28)	0.359	1.12 (0.61–2.07)	0.717
Acute ischemic stroke	2.52 (2.17–2.93)	<0.001	2.03 (1.74–2.37)	<0.001	1.99 (1.57–2.52)	<0.001
Progression to ESRD	20.09 (17.57–22.96)	<0.001	15.95 (13.89–18.33)	<0.001	13.07 (8.96–19.05)	<0.001
Renal recovery (*N* = 1099) vs. Control (N = 43,815)						
Mortality	3.20 (2.87–3.57)	<0.001	2.38 (2.13–2.66)	<0.001	2.58 (2.13–3.13)	<0.001
MACE	2.06 (1.84–2.32)	<0.001	1.73 (1.54–1.95)	<0.001	2.00 (1.66–2.42)	<0.001
Nonfatal MI	2.64 (2.21–3.14)	<0.001	2.18 (1.82–2.60)	<0.001	2.71 (1.99–3.70)	<0.001
Revascularization	0.41 (0.22–0.76)	0.005	0.39 (0.21–0.74)	0.004	0.49 (0.23–1.05)	0.067
Acute ischemic stroke	2.18 (1.85–2.57)	<0.001	1.78 (1.51–2.11)	<0.001	1.97 (1.52–2.55)	<0.001

MACE = major adverse cardiovascular event, MI = myocardial infarction, ESRD = end-stage renal disease, HR = hazard ratio, CI = confidence interval.
Model 1 was an unadjusted simple model.
Model 2 was adjusted for age, sex, the Charlson Comorbidity Index scores, the use of mechanical ventilation, the use of intravenous inotropic agents, and principal diagnosis during the index admission (categorical, the most common six alphabetical ICD-10 diagnostic codes (A, C, I, J, K, N), and others).
Model 3 was a multivariable Cox regression analysis performed in the 1:1 propensity score matched dataset [AKI-D (*N* = 1258) vs. matched control (N = 1258)]. The multivariable analysis was adjusted for all variables included in Model 2. Model 3 of the renal recovery group was a multivariable Cox regression analysis performed in the 1:1 propensity-score-matched dataset [AKI-D (*N* = 1098) vs. matched control (N = 1098)]. The multivariable analysis was adjusted for all variables included in Model 2.

Table 3
Clinical characteristics associated with MACE in the AKI-D group.

	Multiple Cox regression		Backward elimination	
	Adjusted HR	***P* value**	**Adjusted HR**	***P* value valevalue**
Age	1.03 (1.02–1.04)	<0.001	1.03 (1.02–1.04)	<0.001
Sex (Male)	0.99 (0.80–1.23)	0.944		
Underlying comorbidities (CCI)				
Hypertension	0.69 (0.51–0.94)	0.020	0.69 (0.52–0.92)	0.011
Diabetes	1.60 (1.26–2.04)	<0.001	1.62 (1.31–2.01)	<0.001
Diabetic complication	1.02 (0.78–1.33)	0.913		
Connective tissue disease	1.46 (0.80–2.69)	0.221		
Congestive heart failure	0.83 (0.64–1.08)	0.163		
Peripheral vascular disease	0.94 (0.68–1.31)	0.728		
Dementia	1.70 (0.85–3.38)	0.133		
Pulmonary disease	0.86 (0.68–1.09)	0.208		
Peptic ulcer	1.08 (0.85–1.37)	0.551		
Liver disease	0.74 (0.09–5.85)	0.776		
Severe liver disease	1.62 (0.37–7.20)	0.526		
Paraplegia	2.00 (0.98–4.10)	0.059	2.11 (1.05–4.26)	0.037
Renal Disease	1.31 (1.01–1.72)	0.046	1.31 (1.02–1.69)	0.036
Cancer	0.84 (0.46–1.55)	0.579		
Metastatic cancer	2.98 (0.33–27.29)	0.334		
Principal diagnosis, ICD-10 alphabetical index				
Neoplasms or hematological diseases	0.31 (0.02–5.17)	0.418	0.33 (0.02–5.23)	0.429
	2.41 (0.15–39.13)	0.538	1.54 (0.10–24.58)	0.762
Endocrine nutritional and metabolic diseases	1.37 (0.08–22.26)	0.827	1.48 (0.09–23.82)	0.783
Mental and behavioral diseases	0 (0.00–0.00)	0.972	0 (0.00–0.00)	0.973
Diseases of the nervous system	68.18 (4.05–1148.81)	0.003	107.80 (6.52–1781.56)	0.001
Diseases of the circulatory system	1.33 (0.18–9.60)	0.778	1.31 (0.18–9.38)	0.786
Diseases of the respiratory system	1.28 (0.08–20.83)	0.862	1.20 (0.08–19.30)	0.896
Diseases of the digestive system	3.58 (0.21–59.94)	0.375	2.45 (0.15–39.47)	0.527
Diseases of the muscle and connective tissue	0 (0.00–0.00)	0.983	0 (0.00–0.00)	0.982
Diseases of the genitourinary system	1.48 (0.17–12.80)	0.725	1.70 (0.21–14.17)	0.622
Congenital diseases	0.63 (0.06–6.99)	0.704	0.41 (0.04–4.57)	0.472
Abnormal clinical and laboratory findings not elsewhere classified	4.26 (0.24–74.54)	0.321	7.44 (0.46–120.08)	0.157
Injury, poisoning and other consequences of external causes	1.44 (0.12–17.25)	0.773	1.30 (0.12–14.32)	0.832
Unspecified	0 (0.00–0.00)	0.985	0 (0.00–0.00)	0.985
Implemented ICU treatment modalitie				
Ventilator care	1.70 (0.42–6.91)	0.458		
Intravenous inotropic agents	3.86 (0.54–27.60)	0.178		

ICD = International Classification of Diseases, **ICU = intensive care unit.**

.001] and elevated risks of composite MACEs [adjusted HR 1.73 (1.54–1.95), $P < .001$] than those in the control group (Table 2).

Age [adjusted HR 1.03 (1.02–1.04), $P < .001$], diabetes [adjusted HR 1.60 (1.26–2.04), P < .001] and renal disease [adjusted HR 1.31 (1.01–1.72), $P = .046$] were independently associated with an elevated risk of MACE in the AKI-D patients (Table 3).

3.4. Outcomes according to the dialysis modality

Table 4 shows the baseline characteristics of the patients in the AKI-D group who underwent CRRT or IRRT. Male sex ($P < .001$), patients with underlying diabetic complications ($P = .002$), and renal disease (P < .001) were more common in the IRRT group. Patients who underwent CRRT more frequently required intravenous inotropic agents ($P < .001$). CRRT group patients exhibited comparable risks of short-term [adjusted HR 1.93 (0.77–4.83), $P = .161$] and long-term [adjusted HR 1.01 (0.77–1.32), $P = .943$] mortality when compared to patients who underwent IRRT (Table 2). Risk of MACE development was similar between the two groups [adjusted HR 1.25 (0.94–1.67), $P = .126$] (Table 5). In contrast, progression to ESRD was ameliorated in patients who underwent CRRT [adjusted HR 0.60 (0.45–0.79), P < .001] when compared to IRRT patients.

4. Discussion

Patients are often exposed to hemodynamic instability during the perioperative period of cardiac surgery, which leads to ischemic injury of the kidneys [7,20]. Volume overloading, which is also frequently observed during the perioperative period, induces renal dysfunction via the mechanism of the cardiorenal syndrome [1]. Renal dysfunction following cardiac surgery may result in poor survival during the early postoperative period [6,21,22]. However, whether AKI-D affects long-term patient outcomes longitudinally after hospital discharge has not previously been thoroughly examined. AKI-D puts a considerable medical burden on cardiac surgery patients [5-7,23], and we assessed the contribution of AKI-D on long-term postdischarge outcomes. In the present study, we demonstrated that the AKI-D following cardiac surgery was associated with increased postdischarge long-term mortality, progression to ESRD and risk of MACEs. Patients who had dialysis but recovered renal function and were no longer dialysis dependent when discharged from hospital had similar long-term outcomes as those who remained dialysis dependent after hospital discharge. The results for the renal recovery patients suggest that ICU survivors who experience temporary AKI-D following the surgery will continuously require closer attention after hospital discharge, considering the longitudinal impact of AKI-D on adverse outcomes. To our knowledge, the present study is the first report to demonstrate the long-term outcomes including MACE development in critically ill patients who require dialysis after cardiac surgery. Our study includes the following major strengths; 1) we reviewed a nationwide dataset that included all cases of insured cardiac surgeries during the study period; 2) we considered both cardiopulmonary bypass and valve surgery; 3) we assessed potential confounders of adverse outcomes via a review of comorbidities and ICU implementations; and 4) we serially observed postdischarge outcomes using reliable nationwide claims data and death records.

Table 4
Baseline characteristics of the CRRT and IRRT groups.

	CRRT group ($N = 1036$)	IRRT group (N = 185)	*P* value
Age (years (interquartile ranges))	66 (57–72)	66 (58–73)	0.191
< 40 (N (%))	14 (7.6)	42 (4.1)	
40–60 (N (%))	45 (24.3)	257 (24.8)	
60–80 (N (%))	119 (64.3)	686 (66.2)	
≥ 80 (N (%))	7 (3.8)	51 (4.9)	
Male sex (N, %)	127 (68.7)	565 (54.5)	<0.001
Year of admission (N, %)			<0.001
2015-	86 (46.5)	342 (33.0)	
2010–2014	72 (38.9)	457 (44.1)	
2005–2009	27 (14.6)	237 (22.9)	
Charlson comorbidity index (N (%))			0.110
≥ 0 and < 5	151 (81.6)	897 (86.6)	
≥5 and < 10	34 (18.4)	135 (13.0)	
≥ 10	0 (0)	4 (0.4)	
Implemented treatment during ICU admission (N (%))			
Ventilator care	184 (99.5)	1030 (99.4)	0.949
Intravenous inotropic agents	178 (96.2)	1033 (99.7)	<0.001
Outcomes (N (%))			
MACE	56 (30.3)	331 (32.0)	0.090
Acute MI	29 (15.7)	165 (15.9)	0.366
Revascularization	1 (0.5)	17 (1.6)	0.183
Acute ischemic stroke	26 (14.1)	149 (14.4)	0.269
Mortality	73 (39.5)	362 (34.9)	0.530
Progression to ESRD	68 (36.8)	219 (21.1)	<0.001

CRRT = continuous renal replacement therapy, IRRT = intermittent renal replacement therapy, ICU = intensive care unit, MACE = major adverse cardiovascular event, MI = myocardial infarction, ESRD = end-stage renal disease.

The differential clinical characteristics of patients with AKI-D and their risk factors for MACEs are well-known traditional risk factors of cardiovascular disease; these factors include age, underlying hypertension, diabetes and renal disease [24-26]. Therefore, the severity of comorbidities or cardiovascular disease at baseline is a determinant of a poor long-term prognosis. However, the persistence of the increased risk of MACEs in the AKI-D patients even after multivariable adjustment and propensity-score-matched analysis suggests that AKI-D itself plays a direct role in the deterioration of long-term outcomes after discharge. ESRD independently increases patient mortality [27]. Therefore, we performed subgroup analyses of renal recovery group patients to reduce the influence of ESRD on long-term outcomes. Patients who recovered from dialysis at the date of hospital discharge consistently exhibited a risk of poor long-term mortality. The results from the renal recovery group patients further support the hypothesis of a direct effect of AKI-D on long-term outcomes and provide physicians with the following valuable suggestion: ICU survivors who temporarily experienced AKI-D following cardiac surgery longitudinally exhibited elevated risks of adverse outcomes. Therefore, physicians should maintain long-term follow-up for these patients even though they have recovered from AKI-D.

Improvements in dialysis modality have enabled the application of dialysis to critically ill postcardiac surgery AKI-D patients with hemodynamic instability [20,28]. However, the evidence supporting the superiority of the implemented dialysis modality during ICU admission with regard to survival is controversial [29,30], and the effect of dialysis modality on long-term adverse outcomes, including cardiovascular events, must be further examined. Long-term survival and MACE development in the CRRT patients included in the present study were comparable to the outcomes of patients who underwent IRRT. The similar long-term survival of the AKI-D patients regardless of the implemented dialysis modality is an important finding. These results informs clinicians that despite the expectedly high medical acuity of patients undergoing CRRT, CRRT may be safely adjusted for use with postsurgery AKI-D patients and can achieve a reasonable long-term survival, which is comparable to the outcome of IRRT. CRRT patients exhibited reduced ESRD progression, which is consistent with the result of a previous study [31]. The better renal recovery observed in CRRT patients could be explained by the following observations: Compared to CRRT, IRRT had more difficulty in maintaining hemodynamic stability [28]. Moreover, the improved targeted removal of fluid that was achieved in CRRT also contributed to better renal recovery in CRRT because fluid overload in critically ill AKI patients has been associated with reduced renal recovery [32,33]. Dialysis dependence is related to a decrease in health-related quality of life [34,35] and increased medical costs [36]. Therefore, its occurrence requires a thorough assessment of postdischarge

Table 5
Clinical outcomes of cardiac surgery patients according to specific dialysis modality and renal recovery.

	Model 1		Model 2		Model 3	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
CRRT (N = 1036) vs. IRRT (*N* = 185)						
Mortality	1.08 (0.84–1.39)	0.531	1.07 (0.83–1.38)	0.593	1.29 (0.92–1.78)	0.144
Within 90 days	2.09 (0.84–5.22)	0.113	1.93 (0.77–4.83)	0.161	2.78 (0.93–8.29)	0.067
After 90 days	1.01 (0.77–1.31)	0.958	1.01 (0.77–1.32)	0.943	1.18 (0.84–1.68)	0.346
MACE	1.28 (0.96–1.70)	0.090	1.25 (0.94–1.67)	0.126	1.33 (0.93–1.91)	0.118
Within 90 days	1.18 (0.7–2.01)	0.529	1.09 (0.64–1.85)	0.751	1.47 (0.77–2.78)	0.241
After 90 days	1.32 (0.94–1.84)	0.108	1.33 (0.94–1.86)	0.103	1.29 (0.83–2.00)	0.255
Nonfatal MI	1.20 (0.81–1.78)	0.366	1.23 (0.82–1.83)	0.315	1.38 (0.84–2.29)	0.207
Revascularization	3.94 (0.52–29.60)	0.183	4.22 (0.56–31.99)	0.163	5.20 (0.55–48.81)	0.150
Acute ischemic stroke	1.27 (0.83–1.92)	0.263	1.17 (0.77–1.78)	0.470	1.16 (0.679–1.99)	0.583
ESRD progression	0.55 (0.42–0.73)	<0.001	0.60 (0.45–0.79)	<0.001	0.63 (0.43–0.92)	0.017

CRRT = continuous renal replacement therapy, IRRT = intermittent renal replacement therapy, MACE = major adverse cardiovascular event, MI = myocardial infarction, ESRD = end-stage renal disease, HR = hazard ratio, CI = confidence interval.
IRRT group was used as a reference group in the Cox regression analysis.
Model 1 was an unadjusted simple model.
Model 2 was adjusted for age, sex, the Charlson Comorbidity Index scores, the use of mechanical ventilation, the use of intravenous inotropic agents, and the principal diagnosis during the index admission (categorical, the most common six alphabetical ICD-10 diagnostic codes (A, C, I, J, K, N), and others).
Model 3 was a multivariable Cox regression analysis performed in the 1:1 propensity-score-matched dataset [matched CRRT (N = 185) vs. matched IRRT (*N* = 185)]. The model was adjusted for all variables included in Model 2.

patients, and it is essential that this factor be considered by physicians in their choice of the initial dialysis modality.

We thoroughly reviewed a relatively large number of cardiac surgery patients screened from the nationwide database. However, there are several limitations in the study that should be considered during the interpretation of our results, which are due to its retrospective nature. First, the diagnosis of AKI-D was dependent on diagnostic codes rather than on the medical records and laboratory examinations. The claims data of the Korean NHIS are accurately and sensitively collected, but a portion of AKI-D may have been underestimated. Considering the absence of the laboratory results, the present study defined AKI-D based on the accurately collected claims data, issued to all forms of dialysis. As the study specifically focused on the impact of dialysis-requiring AKI, some portion of the AKI patients who did not require dialysis may have been included in the control group. Second, we used propensity score matching using the extensive claims data including the data on medication usage or underlying comorbidities to minimize the difference in medical severity between the groups. However, additional considerations of baseline renal function or hemodynamic change during cardiac surgery or during the ICU admission could not be evaluated because the NHIS data did not contain the results of laboratory examinations or complete medical records. We presented the data obtained from the relatively large cohort with long-term results using the nationwide data, but further prospective studies are warranted to overcome the abovementioned limitations.

5. Conclusions

In conclusion, AKI-D following cardiac surgery is associated with poor short- and long-term mortality and increased risks of MACE development and ESRD progression compared to those in patients who did not receive dialysis. Clinicians must pay meticulous attention to postdischarge ICU survivors who require dialysis following cardiac surgery and to patients who are independent of dialysis because of the long-term impact of AKI-D on adverse outcomes. Effective strategies to prevent or manage AKI-D after cardiac surgery are warranted to improve outcomes in these patients. CRRT was associated with reduced dialysis dependency as well as comparable mortality and risk of MACE development.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2018.11.028.

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