Journal of the American Heart Association

ORIGINAL RESEARCH

Long-Term Outcomes of Acute Kidney Injury After Different Types of Cardiac Surgeries: A Population-Based Study

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BACKGROUND: Dialysis-requiring acute kidney injury (D-AKI) is a major complication of cardiovascular surgery that results in worse prognosis. However, the incidence and impacts of D-AKI in different types of cardiac surgeries have not been fully investigated.

METHODS AND RESULTS: Patients admitted for cardiovascular surgery between July 1, 2004, and December 31, 2013, were identified from the National Health Insurance Research Database of Taiwan. The patients were grouped into D-AKI (n=3089) and non–D-AKI (n=42 151) groups. The outcome was all-cause mortality and major adverse kidney event. The long-term outcomes were worse in the D-AKI group than the non–D-AKI group (hazard ratio [HR], 3.89; 95% CI, 3.79–3.99 for major adverse kidney event; HR, 2.89; 95% CI, 2.81–2.98 for all-cause mortality). Patients who underwent aortic surgery had higher risk for D-AKI than other types of surgeries, but they were also more likely to recover. The long-term dialysis rate for the patients who recovered from D-AKI was also lowest in those who underwent aortic surgery. Among all types of cardiac surgeries with D-AKI, patients who had heart valve surgery exhibited the greatest risks of all-cause mortality (HR, 6.04; 95% CI, 5.78–6.32).

CONCLUSIONS: Compared with other heart surgeries, aortic surgery resulted in a higher incidence of D-AKI but better renal recovery, better short-term outcome, and lower incidences of long-term dialysis.

Key Words: acute kidney injury ■ cardiac surgery ■ cardiovascular ■ dialysis ■ prognosis

Acute kidney injury (AKI) is a common complication of cardiac surgery, which affects the different short- and long-term outcomes.[1–3] When AKI progresses, especially in cases in which renal replacement therapy is indicated, AKI is independently associated with mortality.[4,5] The incidence rates of cardiac surgery–related AKI and dialysis-requiring AKI (D-AKI) range from 2% to 50% and from 1% to 6%, respectively.[6–9] Many studies about the pathogenesis, risk triage, and prevention of cardiac surgery–associated AKI have been published.[1,10–13] Although coronary artery bypass grafting (CABG), valve, and aortic surgeries can all induce postoperative AKI, the background pathogenesis for AKI is different for different cardiac surgeries. Few studies have addressed this issue by comparing the outcomes of AKI among different types of cardiac surgery. Relatedly, large-scale, population-based data on the incidence rates of D-AKI associated with different types of cardiac surgery are also scarce. Renal recovery after AKI has been associated with better short-term prognosis,[14,15] but little is known about whether renal recovery affects late outcomes, including postdischarge all-cause mortality and major adverse kidney event

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Supplementary material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.120.019718

For Sources of Funding and Disclosures, see page 8.

This work was presented as a poster at the International Conference on Advances in Critical Care Nephrology, February 25th to 28th, 2020, in San Diego, CA.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- We enrolled a total 45 240 cardiovascular surgery participants who were grouped into dialysis-requiring acute kidney injury (D-AKI) and non–D-AKI groups.
- The incidence of D-AKI for cardiac surgery gradually increased year after year for each type of cardiac surgery, except for aortic surgery.
- Patients who received aortic surgery alone or combination of coronary artery bypass grafting and valve surgery were prone to develop D-AKI; among participants with D-AKI, those who received aortic surgery have better short- and long-term outcomes and higher probability of renal recovery in comparison to other types of cardiac surgery.

What Are the Clinical Implications?

- Our results could help in risk stratification of post–cardiac surgery D-AKI across different cardiac surgery types.
- Patients who received aortic surgery were younger and have fewer comorbidities; the long-term risk for end-stage renal disease among D-AKI survivors with renal recovery were higher in those who received coronary artery bypass grafting surgery alone or combination of coronary artery bypass grafting and valve surgery in comparison to those who received aortic surgery.
- Regular follow-up and intervention might be warranted in high-risk populations.

Nonstandard Abbreviations and Acronyms

aHR	adjusted hazard ratio
AKI	acute kidney injury
D-AKI	dialysis-requiring acute kidney injury
IPTW	inverse probability of treatment weighting
MAKE	major adverse kidney event
NHI	National Health Insurance
NHIRD	National Health Insurance Research Database
STD	standardized difference

(MAKE), in cardiac surgery–associated D-AKI survivors. In this study, we used data from the National Health Insurance (NHI) Research Database (NHIRD) of Taiwan to analyze the prognostic effects of different types of cardiac surgeries, the long-term effects of renal recovery in cardiac surgery–associated D-AKI, and trends in the incidence of D-AKI.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

Ethics Statement

This study was conducted in accordance with the Declaration of Helsinki. This study was approved by the Institutional Review Board of Chang Gung Memorial Hospital (Institutional Review Board No. 104-7990B), and the need for individual informed consent was waived by Institutional Review Board of Chang Gung Memorial Hospital because personal identification data are not included in the NHIRD.

Data Source

This was a retrospective cohort study that used data from Taiwan's NHIRD. Taiwan's NHI system is a mandatory national health insurance program launched in 1995 and covers >99.9% of Taiwan's population. The NHIRD data sets contain anonymized healthcare information, like data on examinations, medications, interventions, surgeries, admissions, and outpatient clinics. Diseases are identified in the NHIRD using *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*), diagnostic codes, whereas procedures or interventions are identified by the *ICD-9-CM* procedure codes or the Taiwan NHI reimbursement codes. Detailed information about the NHI system and NHIRD has been provided in previous publications.[16–18]

Study Population

This study included patients who were first hospitalized for cardiac surgery (including valve, CABG, or aortic surgery) from July 1, 2004, to December 31, 2013, with those patients being identified by using the NHI reimbursement codes in inpatient claims data. The exposure variable of interest was D-AKI, which was defined as an AKI necessitating renal replacement therapy during the index admission and was also identified by using the NHI reimbursement codes. Patients aged <20 years (n=1092), those with missing demographics (n=1), those with a history of AKI (n=2155) or chronic kidney disease/end-stage renal disease (n=6363), and those whose length of hospital stay <7 days (n=1879) were excluded. The eligible study population (n=45 420) was divided into 2 groups: a D-AKI group (n=3089) and a non–D-AKI group (n=42 151) (Figure 1A).

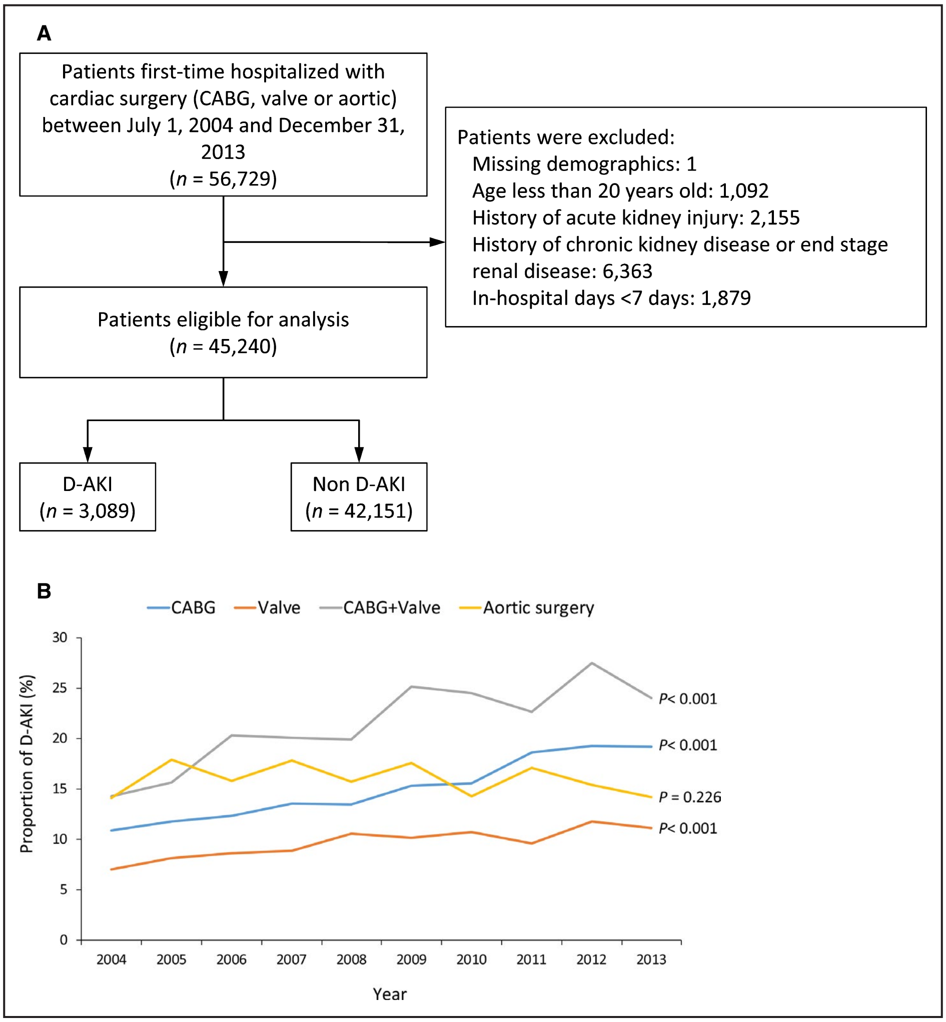

Figure 1. Patient selection process (A) and trends in incidence rate of dialysis-requiring acute kidney injury (D-AKI) during admission from 2004 to 2013 for each type of cardiac surgery (B).
CABG indicates coronary artery bypass grafting.

Covariates

The covariates consisted of patient clinical characteristics and surgical characteristics. The clinical characteristics were age, sex, 10 comorbidities, the Charlson Comorbidity Index score, urgent or emergent surgery, previous cardiac surgery, and hospital level of the index surgery. The surgical characteristics were type of cardiac surgery, number of bypassed vessels for CABG, type of CABG, number of involved valves, type/location of valve surgery, and extensions of aortic surgery. The comorbidities (including the Charlson score) were identified using any inpatient diagnoses made before the index date, which could be traced as far back as the year 1997. Surgical details were generally extracted using the NHI reimbursement codes, whereas the type/location of valve surgery was identified using *ICD-9-CM* procedure codes. Details of the *ICD-9-CM* codes can be found in Table S1.

Definitions of D-AKI and D-AKI Nonrecovery and Outcomes

The definition of D-AKI was an AKI necessitating dialysis during the index hospitalization. A case of D-AKI was identified by reimbursement for renal replacement therapy, similar to previous studies.[19,20] The outcomes of interest consisted of perioperative outcomes and late outcomes after discharge. Perioperative complications during the index admission were identified using either *ICD-9 CM* diagnostic codes or the NHI reimbursement codes. The late outcomes of interest consisted of all-cause mortality, AKI, chronic kidney disease, end-stage renal disease requiring permanent dialysis, and any composite of the aforementioned late outcomes (MAKE). Mortality was defined by a withdrawal from the NHI program.[21] AKI and incident chronic kidney disease were identified on the basis of corresponding inpatient diagnoses during the follow-up period. Cases of end-stage renal disease requiring permanent dialysis during the follow-up period were verified by identifying insured individuals who received an appropriate catastrophic illness certificate >3 months after the index hospitalization. The certification of end-stage renal disease requires authentication by 2 nephrologists. Cases of D-AKI nonrecovery and recovery were identified according to whether a patient obtained a catastrophic illness certificate for end-stage renal disease during the index hospitalization (ie, applied for a catastrophic illness certificate for permanent dialysis during the hospital stay) or within 3 months after discharge, respectively.[19] Patients were followed up from the discharge date to the date of death; date of event occurrence; or December 31, 2013, whichever came first.

Statistical Analysis

To reduce confounding and selection bias when comparing outcomes between the D-AKI and non–D-AKI groups, we calculated the inverse probability of treatment weighting (IPTW) based on the propensity scores. Compared with other propensity score methods, including stratification, matching, and statistical control/adjustment, the IPTW is considered efficient in terms of reducing confounding and having higher statistical power compared with matching.[22] The propensity score was estimated using a logistic regression model in which treatment assignment was regressed on selected covariates listed in Table S2, except that the follow-up year was replaced with the date of index admission. To prevent the impact of extreme values of the estimated propensity score, we used a stabilized weight to mitigate the influence of outliers.[23] The quality of weighting was checked using the absolute value of the standardized difference (STD) between the groups after weighting, where a value <0.1 was considered a negligible difference and a value <0.2 was considered a small effect size of group difference.

The changes in the proportions of patients receiving each type of cardiac surgery across the study period (2004–2013) were tested using the Cochran-Armitage trend test. The incidence rates of D-AKI during the index admission among the different cardiac surgeries were compared using the χ^2 test. Comparisons of the perioperative and in-hospital complications and outcomes during the admission between groups (ie, the D-AKI group versus the non–D-AKI group; the D-AKI nonrecovery group versus the D-AKI recovery group versus the non–D-AKI group) were performed using logistic regression for binary outcomes or linear regression for continuous outcomes. As to the late outcomes after discharge, the mortality rates of the groups were compared using the Cox proportional hazard model. The incidences of nonfatal outcomes among the groups were compared using the Fine and Gray subdistribution hazard model, which considered death a competing risk. The Charlson Comorbidity Index score and surgical type were additionally adjusted in the regression analyses to account for the possibility of residual confounding. To evaluate the effect of D-AKI on in-hospital death and late outcomes (mortality and MAKE) for different cardiac surgeries, we tested the interactions of the different cardiac surgeries with D-AKI. Finally, in patients with D-AKI recovery, the dialysis rates among surgical types were compared using pairwise log-rank tests.

A 2-sided $P<0.05$ was considered to be statistically significant, and no adjustment of multiple testing (multiplicity) was made to avoid low statistical power in this study. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC), including use of the PHREG procedure for survival analysis and the ADJSURV% macro for plotting direct-adjusted survival that was derived from the multivariable Cox model.[24]

RESULTS

Characteristics of Study Cohort

A total of 45 240 participants, treated between July 1, 2004, and December 31, 2013, were included for analysis, including 3089 patients with D-AKI and 42 151 patients with non–D-AKI. Before IPTW, the data indicated that the patients with D-AKI were older; had higher prevalence rates of diabetes mellitus, heart failure, peripheral arterial disease, stroke, and liver cirrhosis; had a higher average Charlson Comorbidity Index score; were more likely to receive urgent or emergent surgery; and were more likely to have had a prior cardiac surgery. After IPTW, however, the group differences in patient characteristics were negligible (STD <0.1) or small (STD ranged from 0.1–0.2) (Table S2).

Before IPTW, the patients with D-AKI were less likely to receive CABG alone and valve surgery alone but more likely to receive the combination of CABG and valve surgery and aortic surgery. When receiving CABG surgery, the patients with D-AKI were more likely to have 2 bypassed vessels, whereas the patients with non–D-AKI were more likely to have 3 bypassed vessels. The patients with D-AKI were also more likely to undergo on-pump CABG. When receiving valve surgery, the patients with D-AKI were more likely to undergo mitral valve replacement and tricuspid replacement, whereas the patients with non–D-AKI were more likely to undergo mitral valve repair. When receiving aortic surgery, the patients with D-AKI were more likely to undergo aortic arch replacement, whereas the patients with non–D-AKI were more likely to undergo ascending aorta replacement. After IPTW, however, the group differences in surgical characteristics were negligible (STD <0.1) or small (STD ranged from 0.1–0.2) (Table S2).

Differences of patient-level characteristics and comorbidities across different surgery groups were also summarized and analyzed (Table S3). In comparison to those who received aortic surgery, participants who received CABG surgery alone or combination of CABG and valve surgery were older and had higher incidence of diabetes mellitus, heart failure, coronary artery disease, and stroke.

Incidence of D-AKI for Cardiac Surgeries in Taiwan

The incidence of D-AKI during admission for cardiac surgery gradually increased year after year for each type of cardiac surgery, except for aortic surgery (Figure 1B). The incidence of D-AKI increased from 10.9% in 2004 to 19.2% in 2013 for CABG, increased from 7.0% in 2004 to 11.1% in 2013 for valve surgery, and increased from 14.2% in 2004 to 27.5% in 2013 for the combination of CABG and valve surgery. Among the aortic surgeries, D-AKI occurred at an overall rate of 14% in 2004 and an overall rate of 15.3% in 2013 (P=0.226). After pooling the study years, the incidence of D-AKI was higher for the combination of CABG and valve surgery and for aortic surgery than for CABG alone and valve surgery alone (Figure 2).

Comparison of In-Hospital and Late Outcomes Between the D-AKI and Non–D-AKI Groups

The patients with D-AKI during admission had higher risks of all the perioperative outcomes than the patients with non–D-AKI, including in-hospital mortality, stroke, sepsis, fasciotomy or amputation, respiratory failure, extracorporeal membrane oxygenation, and massive blood transfusion. The patients with D-AKI had longer ventilator duration, intensive care unit duration, and hospital stays and had higher in-hospital medical expenditures (Table S4). After excluding patients who died during admission, the results showed that the patients with D-AKI had worse outcomes within both the 1-year and overall follow-up periods (Table). Compared with the patients with non–D-AKI, the patients with D-AKI had higher risks of long-term all-cause mortality (Figure S1A), MAKE (Figure S1B), AKI, incident chronic kidney disease, and permanent dialysis (Table).

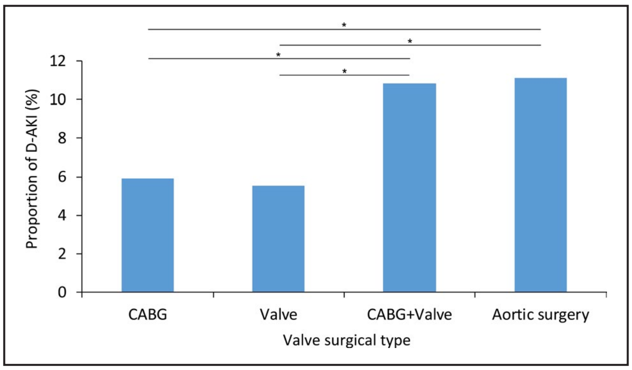

Figure 2. Overall incidence rate of dialysis-requiring acute kidney injury (D-AKI) during admission for different cardiac surgeries.

*Present as statistically significant. CABG indicates coronary artery bypass grafting.

Effect of D-AKI on Outcomes of Different Cardiac Surgeries

The interactions of cardiac surgeries with D-AKI significantly affected the 3 outcomes of in-hospital death, all-cause mortality, and MAKE (P<0.001). The effect of D-AKI on in-hospital death was greatest in the patients who received valve surgery (adjusted odds ratio [OR], 41.62), followed by those who received CABG alone (adjusted OR, 31.63), those who received a combination of CABG and valve surgery (adjusted OR, 19.63), and those who received aortic surgery (adjusted OR, 13.55) (Figure 3A). The effect of D-AKI on all-cause mortality during the follow-up period was greatest in the patients who received valve surgery (adjusted hazard ratio [aHR], 6.04), followed by those who received CABG alone (aHR, 4.61), those who received a combination of CABG and valve surgery (aHR, 4.51), and those who received aortic surgery (aHR, 3.41) (Figure 3B). The effect of D-AKI on MAKE during the follow-up period was greatest in the patients who received valve surgery (aHR, 6.49), followed by those who received CABG alone (aHR, 5.18), those who received a combination of CABG and valve surgery (aHR, 4.68), and those who received aortic surgery (aHR, 3.93) (Figure 3C).

Long-Term Outcome of Non–D-AKI, D-AKI Recovery, and D-AKI Nonrecovery

The incidence of D-AKI nonrecovery was highest in the patients who received CABG alone, followed by those who received a combination of CABG and valve surgery, those who received aortic surgery, and those who received valve surgery alone (Figure S2). The results showed that the D-AKI nonrecovery group had higher mortality rates than did the D-AKI recovery group, which, in turn, had higher mortality rates than the non–D-AKI group (Figure S3A). Likewise, the D-AKI nonrecovery group had higher risks of MAKE during the follow-up period than did the D-AKI recovery group, which, in turn, had higher

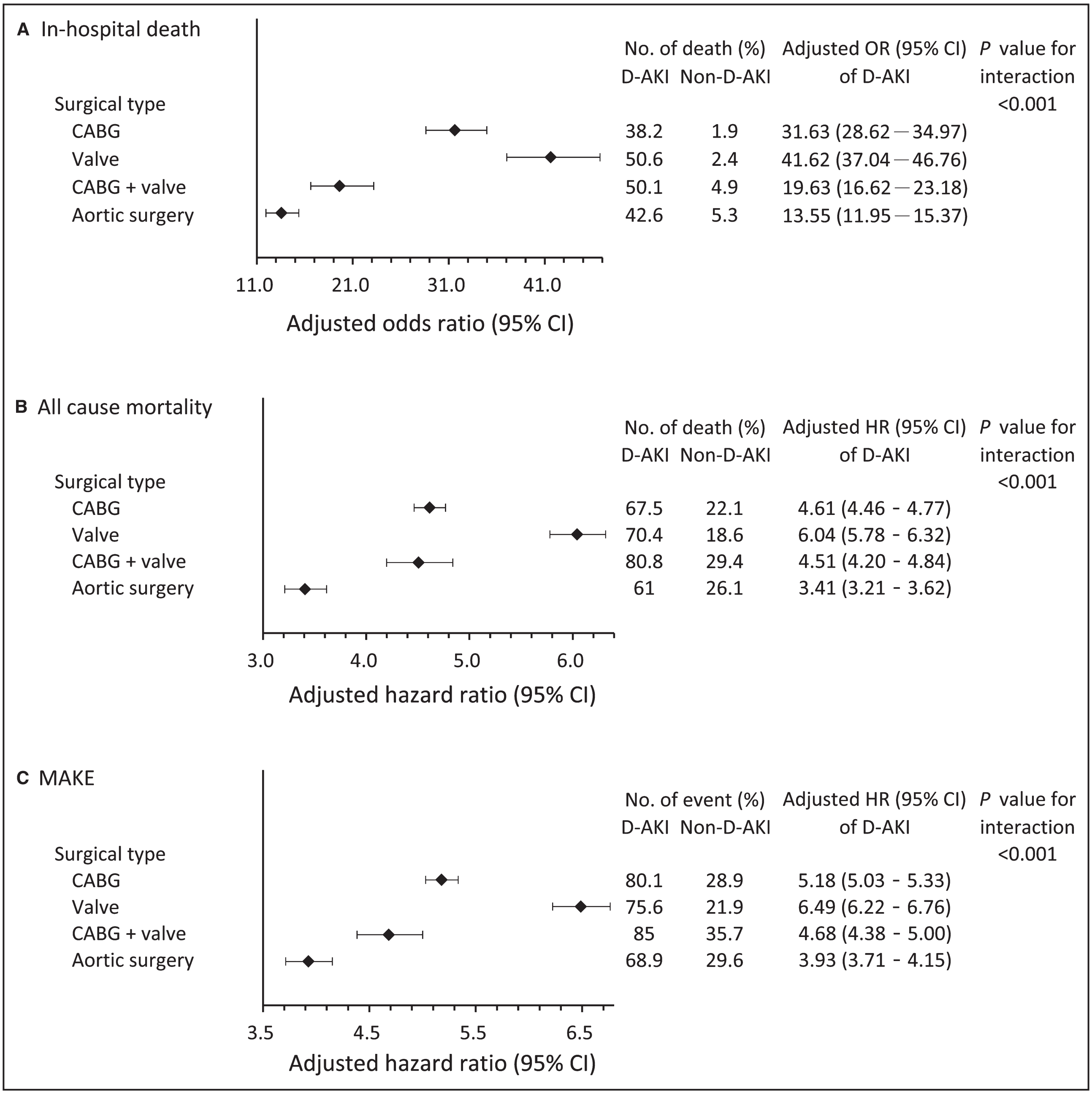

Figure 3. Adjusted odds ratio (OR) or hazard ratio (HR) of dialysis-requiring acute kidney injury (D-AKI) compared with non–D-AKI among different cardiac surgeries in terms of risk of hospital mortality (A), long-term mortality (B), and long-term major adverse kidney event (MAKE) (C).
CABG indicates coronary artery bypass grafting.

mortality rates than the non–D-AKI group (Figure S3B).

Long-Term Outcomes of D-AKI With Recovery Among Different Cardiac Surgeries

The patients who survived cardiac surgery with D-AKI with renal recovery still experienced a gradual decline in renal function. The long-term dialysis-free survival was better among such patients who underwent aortic surgery than among those who underwent CABG (*P*<0.001) or CABG combined with valve surgery (*P*=0.001). Meanwhile, compared with those who had valve surgery alone, the patients who had aortic surgery had a trend of better dialysis-free survival, although the difference was not significant (Figure 4).

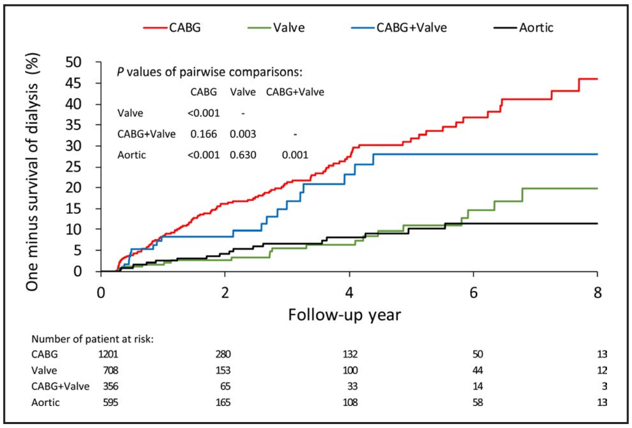

Figure 4. The Kaplan-Meier survival rate of dialysis after discharge in patients with dialysis-requiring acute kidney injury with renal recovery among different cardiac surgery types.
CABG indicates coronary artery bypass grafting.

DISCUSSION

The 6 major findings of this study can be summarized as follows: (1) With the exception of those who received aortic surgery, the incidence of D-AKI increased in patients who received cardiac surgery. (2) Patients who received aortic surgery or CABG combined with valve surgery had higher risks of developing AKI requiring dialysis. (3) In terms of D-AKI, patients who received CABG or CABG combined with valve surgery were less likely to have renal recovery. (4) In terms of D-AKI, patients who received aortic surgery had better prognosis in terms of in-hospital mortality, all-cause mortality, and MAKE. (5) In terms of cardiac surgery–associated AKI, the outcomes were best among the patients with non–D-AKI, followed by those with D-AKI with renal recovery and then those with D-AKI and no renal recovery. (6) In terms of D-AKI with renal recovery, the patients who underwent aortic surgery had better long-term dialysis-free survival.

The population aging and rising disease complexity in Taiwan contributed to the incrementally increasing incidence of D-AKI, which was also noted in other studies.[25–27] A large population study demonstrated that the incidence of AKI after surgical aortic valve replacement had increased slightly but significantly over time.[28]

The different types of cardiac surgery also influence the incidence of AKI. There are several possible explanations for this finding, including different pathogeneses, different populations, and comorbidities. Coronary artery disease and chronic kidney disease share similar risk factors. More congestive heart failure is noted in patients who receive valve heart surgery or CABG than in those who receive aortic surgery, which possibly results in more cardiorenal syndrome. Higher blood transfusion volumes, more instances of circulatory arrest, and more cases requiring emergency surgery immediately after contrast exposure have previously been noted in type A aortic surgery populations.[10,29–32] It has also been noted that aortic surgery populations tend to be younger and have lower rates of diabetes mellitus than the other surgery populations.[31,32] These factors might explain why those who survived aortic surgery–associated D-AKI had better long-term outcomes than those who received other types of cardiac

Table. Follow-Up Outcomes in Patients Who Survived the Index Hospitalization

Variable	Data Before IPTW* D-AKI (n=1661)	Data Before IPTW* Non–D-AKI (n=41 099)	Data After IPTW† D-AKI	Data After IPTW† Non–D-AKI	HR or SHR of D-AKI (95% CI)‡	*P* Value
1-y Follow-up						
MAKE (D-AKI, CKD, ESRD, and mortality)	811 (48.8)	3263 (7.9)	40.5	8.3	6.14 (5.91–6.37)	<0.001
All-cause mortality	486 (29.3)	2245 (5.5)	23.5	5.7	4.45 (4.24–4.66)	<0.001
Acute kidney injury	159 (9.6)	729 (1.8)	8.4	1.8	4.57 (4.21–4.96)	<0.001
Incident CKD	428 (25.8)	1440 (3.5)	21.8	3.7	6.42 (6.07–6.78)	<0.001
ESRD requiring permanent dialysis	204 (12.3)	64 (0.2)	10.3	0.2	65.54 (51.68–83.12)	<0.001
At the end of follow-up period						
MAKE (D-AKI, CKD, ESRD, and mortality)	1102 (66.3)	10 191 (24.8)	59.8	25.5	3.89 (3.79–3.99)	<0.001
All-cause mortality	836 (50.3)	7984 (19.4)	44.0	20.0	2.89 (2.81–2.98)	<0.001
Acute kidney injury	252 (15.2)	2540 (6.2)	14.2	6.3	2.37 (2.25–2.49)	<0.001
Incident CKD	597 (35.9)	4632 (11.3)	33.3	11.5	3.56 (3.43–3.68)	<0.001
ESRD requiring permanent dialysis	317 (19.1)	703 (1.7)	17.9	1.7	11.52 (10.67–12.43)	<0.001

CKD indicates chronic kidney disease; D-AKI, dialysis-requiring acute kidney injury; ESRD, end-stage renal disease; HR, hazard ratio; IPTW, inverse probability of treatment weighting; MAKE, major adverse kidney event; and SHR, subdistribution HR.

*Values are given as number (percentage).

†Values are given as percentage.

‡Additionally adjusted for the Charlson Comorbidity Index score and surgical type.

surgery. Our study is consistent with above mentioned studies. Participants who received CABG surgery alone or combination of CABG and valve surgery were older and more had diabetes mellitus or congestive heart failure in comparison to population who received aortic surgery in our cohort (Table S3). A similar idea was found that post–aortic surgery–associated acute respiratory distress syndrome did not affect in-hospital or long-term prognosis.[33] In contrast, cardiac and renal failure are strong mortality predictors in CABG surgery.[34]

According to published studies, long-term prognosis is determined by pre-AKI renal function and post-AKI renal function.[1,35] However, the relationship between prognosis and renal function has been less discussed in cardiac surgery–associated AKI, and our population-based study demonstrated that renal recovery had positive impacts on long-term outcomes among cardiac surgery–associated AKI survivors.

There were several potential limitations in this study. First, the incidence of D-AKI in the current study was relatively high, a fact that might reflect aging patient population in Taiwan. Furthermore, the costs of renal replacement therapy in Taiwan are covered by the NHI system, such that patients in Taiwan can receive such therapy without socioeconomic concern. Second, after our effort to adjust confounding factors affecting patient outcomes through IPTW, the causal relationships between prognosis and different cardiac surgery types were hard to establish. Several residual confounding factors (eg, baseline renal function and proteinuria) were not measured because of inherent limitations of NHIRD-based studies, which are known to have possible effects on patient outcomes.[10,36–40] Third, the follow-up time may not have been long enough to detect the prognostic effects of milder or subclinical AKI. Fourth, loss to follow-up in participants with milder AKI or non–D-AKI should also be taken into consideration. It could result in underestimation of some late outcome.

Despite these limitations, the strengths of our study included its findings indicating that different cardiac surgery types had various prognostic impacts on cardiac surgery–associated D-AKI, as well as the demonstration of varying incidence trends of D-AKI among different types of cardiac surgery. In this study, we provided an outcome analysis for patients with cardiac surgery who experienced D-AKI. More research would still be necessary, however, to identify the pathogeneses behind our findings.

CONCLUSIONS

D-AKI after cardiac surgery is associated with worse short- and long-term prognosis. Severity of AKI and renal nonrecovery are associated with poor long-term outcome. In contrast to other types of cardiac surgery, patients undergoing aortic surgery experienced a higher incidence of D-AKI but had better outcomes. Survivors from D-AKI with renal recovery still gradually progressed to the point of requiring dialysis, but the aortic surgery group had a lower risk of dialysis during the follow-up period.

ARTICLE INFORMATION

Received October 12, 2020; accepted February 19, 2021.

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Acknowledgments

The authors thank Alfred Hsing-Fen Lin and Ben Yu-Lin Chou for their assistance with the statistical analysis.

Author contributions: Drs S-W Chen and C-H Chang: developed the theory and performed out the plan. Drs Hung, Chu, C-H Chang, and Wu: database preparation and information extraction. Drs J-J Chen, S-H Chang, S-W Chen, and C-H Chang: contributed to the interpretation of the results. Dr J-J Chen took the lead in writing the manuscript. Drs S-W Chen, C-H Chang, and J-J Chen: figure and table formation. All authors provided critical feedback and helped shape the research, analysis, and manuscript.

Sources of Funding

This work was supported by a grant from Chang Gung Memorial Hospital, Taiwan, CORPG5G0081, CMRPG5H0161, and CMRPG5H0162. The authors are grateful for the statistical and data analysis assistance and other support provided by the Maintenance Project of the Center for Big Data Analytics and Statistics (Grant CLRPG3D0048) at Chang Gung Memorial Hospital. This study was based on data from the National Health Insurance Research Database provided by the National Institutes of Health administration, Ministry of Health and Welfare of Taiwan, and managed by the National Health Research Institutes of Taiwan.

Disclosures

None.

Supplementary Material

Tables S1–S4
Figures S1–S3

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Supplemental Material

Table S1. **ICD-9-CM diagnostic codes.**

Variable	ICD-9 CM Code
Acute renal failure	584.xx
Chronic kidney disease	580.xx-589.xx, 403.xx-404.xx, 016.0x, 095.4x, 236.9x, 250.4x, 274.1x, 442.1x, 447.3x, 440.1x, 572.4x, 642.1x, 646.2x, 753.1x, 283.11, 403.01, 404.02, 446.21
Dialysis	585.xx (Catastrophic illness card)
Diabetes mellitus	250.xx
Hypertension	401.xx-405.xx
Heart failure	428.xx
Coronary artery disease	410.xx–414.xx
Myocardial infarction	410.xx, 412.xx
Peripheral arterial disease	440.0x, 440.2x, 440.3x, 440.8x, 440.9x, 443.xx, 444.0x, 444.22, 444.8x, 447.8x, 447.9x
Stroke	430.xx-437.xx
Chronic obstructive pulmonary disease	491.xx, 492.xx, 496.xx
Liver cirrhosis	571.2x, 571.5x, 571.6x
Malignancy	140.xx – 208.xx (Catastrophic illness card)
Ischemic stroke	433.xx-437.xx
Hemorrhagic stroke	430.xx-432.xx
Sepsis	038.xx, 790.7x
Respiratory failure	518.xx

ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification.

Table S2. Demographics, clinical, and surgical characteristics of the D-AKI and Non-D-AKI groups.

	Data before IPTW‡			Data after IPTW†		
Variable	D-AKI (*n* = 3,089)	Non-D-AKI (*n* = 42,151)	STD	D-AKI	Non-D-AKI	STD
Age, Mean, (SD), year	66.2 ± 13.5	62.5 ± 13.1	0.28	63.0 ± 14.8	62.8 ± 13.1	0.01
Male sex	2,107 (68.2)	29,423 (69.8)	-0.03	67.6	69.7	-0.05
Comorbid conditions, No.,(%)						
Diabetes mellitus	1,264 (40.9)	13,741 (32.6)	0.17	34.2	33.2	0.02
Hypertension	1,749 (56.6)	25,497 (60.5)	-0.08	58.7	60.2	-0.03
Heart failure	802 (26.0)	8,654 (20.5)	0.13	22.8	20.9	0.05
Coronary artery disease	2,131 (69.0)	28,865 (68.5)	0.01	64.8	68.5	-0.08
Prior myocardial infarction	488 (15.8)	6,033 (14.3)	0.04	14.5	14.4	<0.01
Peripheral arterial disease	185 (6.0)	1,641 (3.9)	0.10	4.2	4.0	0.01
Prior stroke	484 (15.7)	5,104 (12.1)	0.10	13.5	12.4	0.03
COPD	266 (8.6)	3,212 (7.6)	0.04	8.4	7.7	0.03
Liver cirrhosis	107 (3.5)	646 (1.5)	0.12	2.3	1.7	0.04
Malignancy	135 (4.4)	1,615 (3.8)	0.03	6.0	3.9	0.095
Charlson’s Comorbidity Index score	3.0 ± 2.0	1.9 ± 1.7	0.58	2.2 ± 1.7	2.0 ± 1.8	0.15
Urgent or emergent surgery, No.,(%)	1,125 (36.4)	6,279 (14.9)	0.10	18.8	16.5	0.06
Previous cardiac surgery, No.,(%)	62 (2.0)	578 (1.4)	0.12	1.4	1.4	<0.01
Hospital level, No.,(%)						
Medical center (teaching hospital)	2,232 (72.3)	30,047 (71.3)	0.02	71.2	71.3	<0.01

	Data before IPTW‡			Data after IPTW†		
	D-AKI	Non-D-AKI				
Variable	(*n* = 3,089)	(*n* = 42,151)	STD	D-AKI	Non-D-AKI	STD
Regional / district hospital	857 (27.7)	12,104 (28.7)	-0.02	28.8	28.7	<0.01
Surgical type, No.,(%)						
CABG alone	1,339 (43.3)	21,381 (50.7)	-0.15	45.3	50.1	-0.097
Valve alone	740 (24.0)	12,618 (29.9)	-0.14	30.1	29.5	0.01
CABG + valve	384 (12.4)	3,151 (7.5)	0.17	8.4	7.9	0.02
Aortic surgery*	626 (20.3)	5,001 (11.9)	0.23	16.2	12.5	0.11
CABG details (*n* = 26,255), No.,(%)						
Number of bypass vessels						
1	153 (8.9)	1,973 (8.0)	0.03	8.1	8.1	<0.01
2	339 (19.7)	3,927 (16.0)	0.10	17.9	16.3	0.04
3	998 (57.9)	15,486 (63.1)	-0.11	61.5	62.7	-0.03
4 or more	233 (13.5)	3,146 (12.8)	0.02	12.5	12.9	-0.01
Type of CABG						
On-pump	1,440 (83.6)	18,912 (77.1)	0.16	79.6	77.5	0.05
Off-pump	283 (16.4)	5,620 (22.9)	-0.16	20.4	22.5	-0.05
Valve surgery details (*n* = 16,893), No.,(%)						
Number of involved valves						
1	692 (61.6)	10,093 (64.0)	-0.05	63.0	63.9	-0.02
2	360 (32.0)	4,775 (30.3)	0.04	31.2	30.4	0.02
3	72 (6.4)	901 (5.7)	0.03	5.8	5.7	<0.01

	Data before IPTW‡			Data after IPTW†		
	D-AKI	Non-D-AKI				
Variable	(*n* = 3,089)	(*n* = 42,151)	STD	D-AKI	Non-D-AKI	STD
Type of valve surgery, No.,(%)						
Aortic valve repair or replacement	450 (40.0)	6,669 (42.3)	-0.05	42.0	42.1	<0.01
Mitral valve repair	271 (24.1)	4,496 (28.5)	-0.10	27.1	28.2	-0.02
Mitral valve replacement	544 (48.4)	6,824 (43.3)	0.10	43.4	43.6	<0.01
Tricuspid repair	124 (11.0)	1,488 (9.4)	0.05	11.2	9.5	0.05
Tricuspid replacement	66 (5.9)	428 (2.7)	0.16	3.4	2.9	0.02
Extension of aortic surgery (*n* = 5,627), No.,(%)						
Ascending aorta replacement	435 (69.5)	3,740 (74.8)	-0.12	73.0	74.2	-0.03
Aortic arch replacement	231 (36.9)	1,378 (27.6)	0.20	30.9	28.7	0.05
Aortic root replacement	60 (9.6)	437 (8.7)	0.03	7.3	8.8	-0.06
Follow-up period, Mean, (SD), years	1.4 ± 2.2	4.0 ± 2.8	-1.06	1.7 ± 2.5	4.0 ± 2.7	-0.89

IPTW, inverse probability of treatment weighting; D-AKI, dialysis-requiring acute kidney injury; STD, standardized difference; COPD, chronic obstructive pulmonary disease; CABG, coronary artery bypass graft

‡ Values are given as number (%) or mean ± standard deviation;

† Values are given as % or mean ± standard deviation;

* Ascending aortic replacement.

Table S3. Demographics, clinical and surgical characteristics of patients stratifying by different surgical types.

Variable	CABG alone (*n* = 22,720)	Valve alone (*n* = 13,358)	CABG + valve (*n* = 3,535)	Aortic surgery* (*n* = 5,627)	*P*
Age, Mean, (SD), year	64.9 ± 10.9	58.8 ± 15.0	66.9 ± 11.7	61.1 ± 14.8	<0.001
Male sex	17,898 (78.8)	7,182 (53.8)	2,477 (70.1)	3,973 (70.6)	<0.001
Comorbid conditions, No.,(%)					
Diabetes mellitus	10,920 (48.1)	2,099 (15.7)	1,274 (36.0)	712 (12.7)	<0.001
Hypertension	16,229 (71.4)	5,181 (38.8)	2,120 (60.0)	3,716 (66.0)	<0.001
Heart failure	2,941 (12.9)	4,732 (35.4)	1,280 (36.2)	503 (8.9)	<0.001
Coronary artery disease	22,654 (99.7)	3,561 (26.7)	3,310 (93.6)	1,471 (26.1)	<0.001
Prior myocardial infarction	5,190 (22.8)	427 (3.2)	694 (19.6)	210 (3.7)	<0.001
Peripheral arterial disease	1,102 (4.9)	264 (2.0)	143 (4.0)	317 (5.6)	<0.001
Prior stroke	3,270 (14.4)	1,276 (9.6)	486 (13.7)	556 (9.9)	<0.001
COPD	1,673 (7.4)	1,049 (7.9)	353 (10.0)	403 (7.2)	<0.001
Liver cirrhosis	217 (1.0)	393 (2.9)	57 (1.6)	86 (1.5)	<0.001
Malignancy	802 (3.5)	518 (3.9)	169 (4.8)	261 (4.6)	<0.001
Charlson's Comorbidity Index score	2.1 ± 1.8	1.7 ± 1.6	2.3 ± 1.8	2.1 ± 1.6	<0.001
Urgent or emergent surgery, No.,(%)	3,207 (14.1)	724 (5.4)	396 (11.2)	3,077 (54.7)	<0.001
Previous cardiac surgery, No.,(%)	95 (0.4)	354 (2.7)	35 (1.0)	156 (2.8)	<0.001
Hospital level, No.,(%)					<0.001
Medical center (teaching hospital)	15,398 (67.8)	9,879 (74.0)	2,401 (67.9)	4,601 (81.8)	
Regional / district hospital	7,322 (32.2)	3,479 (26.0)	1,134 (32.1)	1,026 (18.2)	
D-AKI, No (%)	1,339 (5.9)	740 (5.5)	384 (10.9)	626 (11.1)	<0.001

Variable	CABG alone (*n* = 22,720)	Valve alone (*n* = 13,358)	CABG + valve (*n* = 3,535)	Aortic surgery* (*n* = 5,627)	*P*
CABG details (*n* = 26,255), No.,(%)					
Number of bypass vessels					
1	1,183 (5.2)	-	943 (26.7)	-	
2	3,317 (14.6)	-	949 (26.8)	-	
3	15,152 (66.7)	-	1,332 (37.7)	-	
4 or more	3,068 (13.5)	-	311 (8.8)	-	
Type of CABG					
On-pump	16,878 (74.3)	-	3,474 (98.3)	-	
Off-pump	5,842 (25.7)	-	61 (1.7)	-	
Valve surgery details (*n* = 16,893), No.,(%)					
Number of involved valves					
1	-	7,949 (59.5)	2,836 (80.2)	-	
2	-	4,502 (33.7)	633 (17.9)	-	
3	-	907 (6.8)	66 (1.9)	-	
Type of valve surgery, No.,(%)					
Aortic valve repair or replacement	-	5,589 (41.8)	1,530 (43.3)	-	
Mitral valve repair	-	4,031 (30.2)	736 (20.8)	-	
Mitral valve replacement	-	6,291 (47.1)	1,077 (30.5)	-	
Tricuspid repair	-	1,492 (11.2)	120 (3.4)	-	
Tricuspid replacement	-	476 (3.6)	18 (0.5)	-	
Extension of aortic surgery (*n* = 5,627), No.,(%)					

Variable	CABG alone (*n* = 22,720)	Valve alone (*n* = 13,358)	CABG + valve (*n* = 3,535)	Aortic surgery* (*n* = 5,627)	*P*
Ascending aorta replacement	-	-	-	4,175 (74.2)	
Aortic arch replacement	-	-	-	1,609 (28.6)	
Aortic root replacement	-	-	-	497 (8.8)	
Follow-up period, Mean, (SD), years	4.2 ± 2.8	3.7 ± 2.8	3.3 ± 2.7	3.3 ± 2.8	<0.001

CABG, coronary artery bypass graft; D-AKI, dialysis-required acute kidney injury; COPD, chronic obstructive pulmonary disease;

Value are given as number (%) or mean ± standard deviation;

* Ascending aortic replacement.

Table S4. Comparison of in-hospital outcomes between D-AKI and non-D-AKI groups.

	Data before IPTW‡		Data after IPTW†			
Variable	D-AKI (*n* = 3,089)	Non-D-AKI (*n* = 42,151)	D-AKI	Non-D-AKI	B / OR of D-AKI (95% CI)§	*P* value
Categorical parameter						
In-hospital mortality	1,428 (46.2)	1,052 (2.5)	43.6	2.7	27.96 (26.32–29.69)	<0.001
New onset stroke	228 (7.4)	1,522 (3.6)	5.5	3.8	1.38 (1.29–1.47)	<0.001
New onset ischemic stroke	197 (6.4)	1,429 (3.4)	4.7	3.6	1.25 (1.17–1.34)	<0.001
New onset hemorrhagic stroke	54 (1.7)	158 (0.4)	1.3	0.4	3.20 (2.70–3.79)	<0.001
Sepsis	612 (19.8)	1,153 (2.7)	19.2	2.8	8.15 (7.67–8.66)	<0.001
Fasciotomy or amputation	82 (2.7)	165 (0.4)	2.5	0.4	6.00 (5.13–7.02)	<0.001
Respiratory failure	1,317 (42.6)	3,762 (8.9)	39.5	9.3	6.25 (6.02–6.49)	<0.001
ECMO	684 (22.1)	578 (1.4)	22.5	1.4	21.00 (19.37–22.77)	<0.001
Massive blood transfusion	1,725 (55.8)	2,781 (6.6)	52.5	7.0	14.95 (14.34–15.58)	<0.001
Continuous parameter						
PRBC amount (U)	12.0 ± 6.4	4.2 ± 3.8	11.5 ± 6.5	4.3 ± 3.9	7.09 (6.99–7.18)	<0.001
FFP amount (U)	14.1 ± 9.1	6.3 ± 6.9	13.5 ± 9.0	6.4 ± 7.0	6.83 (6.68–6.98)	<0.001
Platelet amount (U)	31.3 ± 19.6	13.4 ± 13.9	30.0 ± 19.8	13.6 ± 14.0	15.96 (15.65–16.27)	<0.001
Ventilator (days)	16.0 ± 11.6	3.7 ± 5.7	14.7 ± 11.5	3.9 ± 5.9	10.53 (10.36–10.69)	<0.001
ICU duration (days)	18.8 ± 11.1	6.2 ± 6.3	17.6 ± 11.1	6.3 ± 6.5	11.00 (10.83–11.16)	<0.001
Hospital stays (days)	42.8 ± 44.2	21.8 ± 16.5	40.0 ± 39.4	22.1 ± 16.9	11.83 (11.53–12.14)	<0.001
Medical expenditure (USD×10^3)	30.6 ± 11.6	14.5 ± 7.0	29.2 ± 11.9	14.7 ± 7.2	18.66 (18.34–18.99)	<0.001

IPTW, inverse probability of treatment weighting; D-AKI, dialysis-requiring acute kidney injury; *B*, regression coefficient; OR, odds ratio; CI, confidence interval;

ECMO, extra-corporeal membrane oxygenation; PRBC, packed red blood cell; FFP, fresh frozen plasma; ICU, intensive care unit

* PRBC >10 Units;

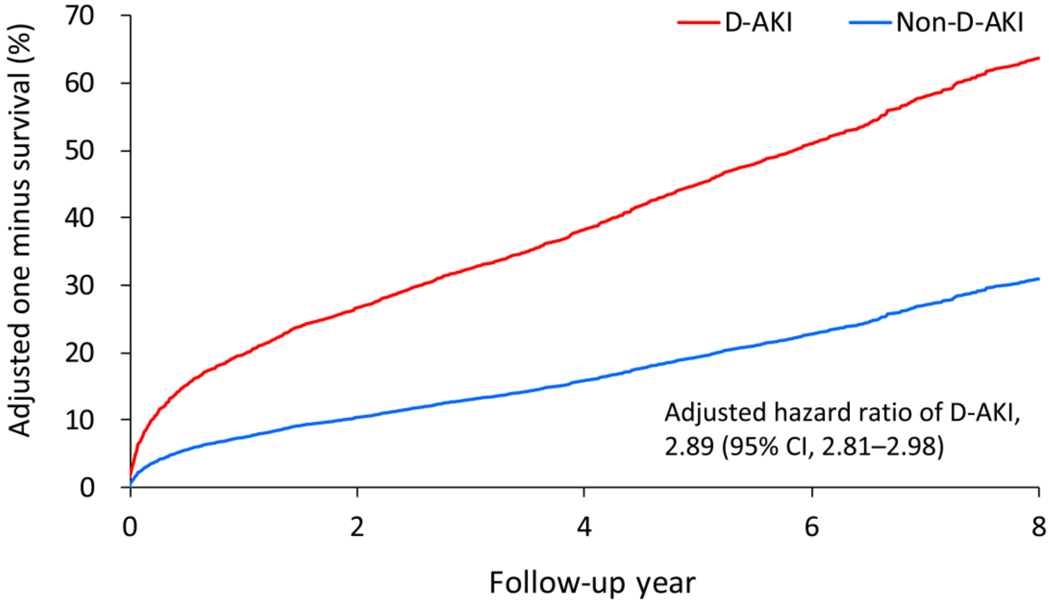
‡ Values are given as number (%) or mean ± standard deviation;

† Values are given as % or mean ± standard deviation;

§ Additionally adjusted for Charlson’s Comorbidity Index score and surgical type.

Figure S1. IPTW-adjusted survival curves of all-cause mortality (A) and major adverse kidney event (B) in patients who survived the index admission and received cardiac surgery with or without D-AKI.

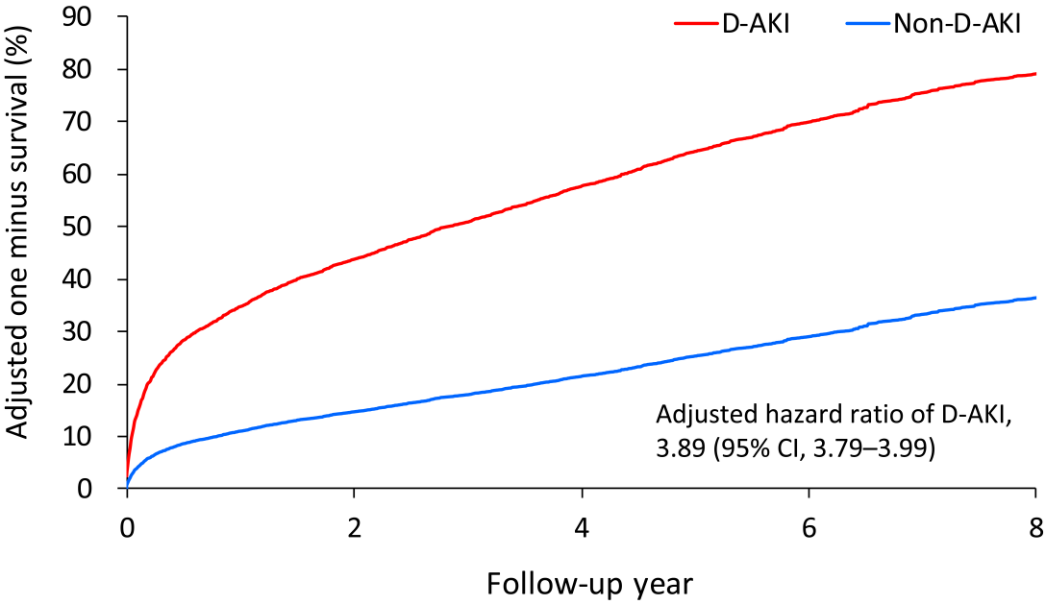
A. Death after discharge



Number of patient at risk (%):

D-AKI	100	56	34	17	5
Non-D-AKI	100	72	49	28	11

B. MAKE



Number of patient at risk (%):

D-AKI	100	42	24	11	3
Non-D-AKI	100	69	46	25	9

IPTW, inverse probability of treatment weight.

Figure S2. Proportions of non-recovery D-AKI among different cardiac surgery types.

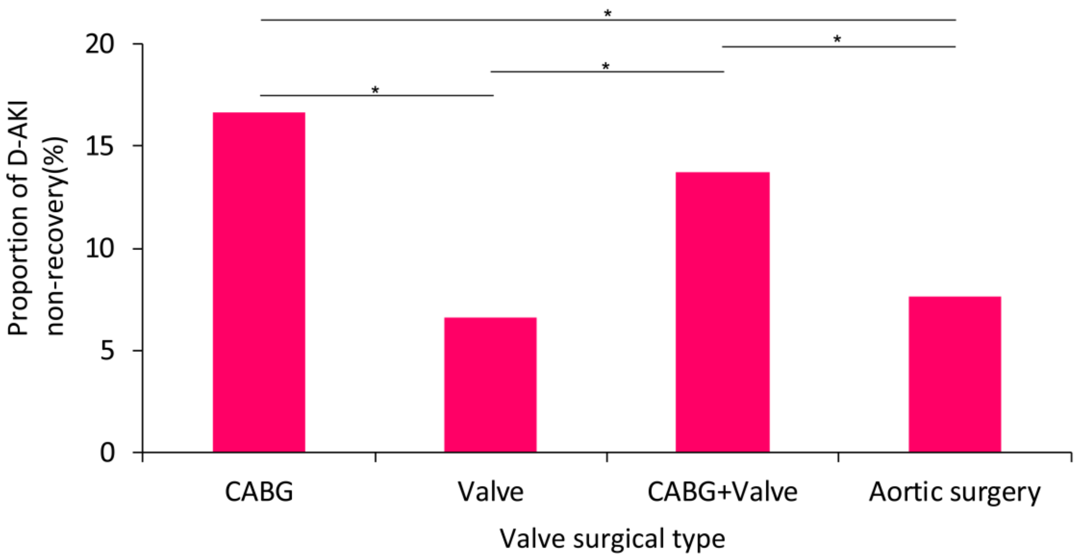
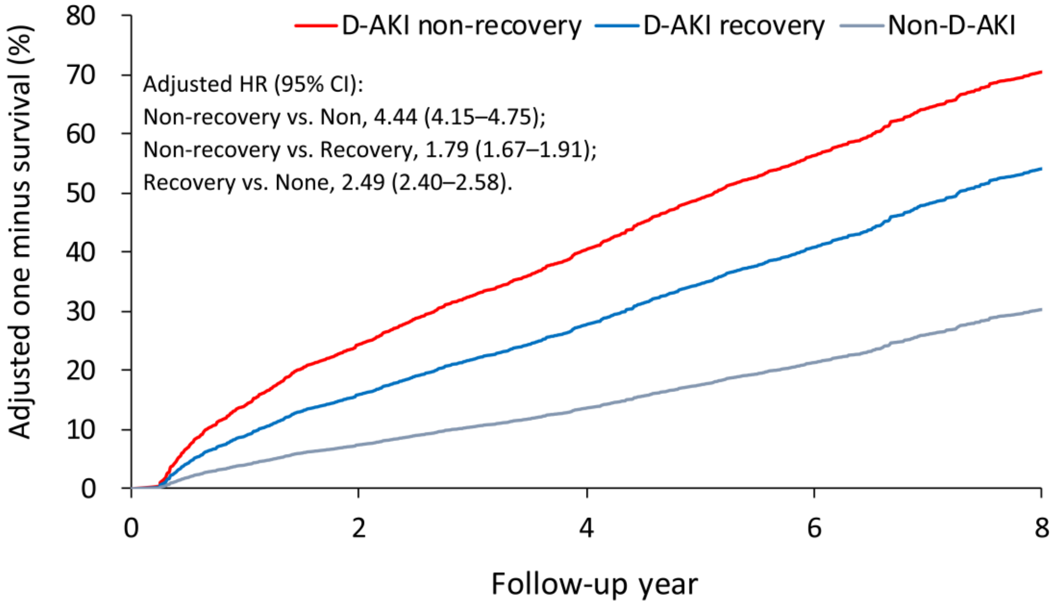


Figure S3. Adjusted survival curves of mortality after discharge (A) and MAKE (B) among D-AKI without recovery, D-AKI with recovery, and non-D-AKI in patients who received cardiac surgery.

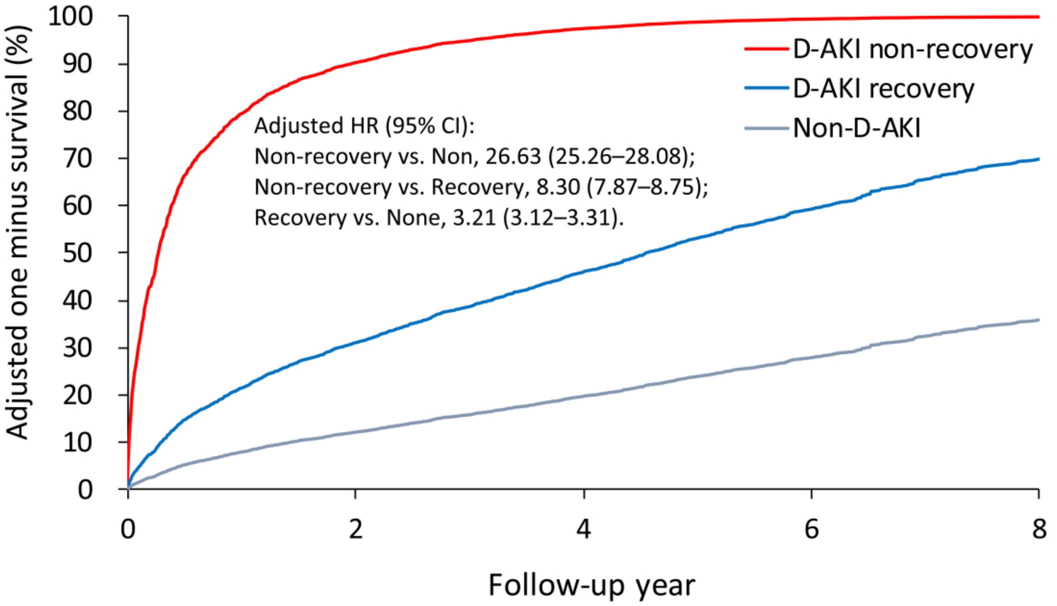
A. Death after discharge



Number of patient at risk (%):

Non-recovery	100	49	24	14	6
Recovery	100	66	41	20	6
Non-D-AKI	100	74	50	28	11

B. MAKE



Number of patient at risk (%):

Non-recovery	100	5	4	3	1
Recovery	100	52	29	14	4
Non-D-AKI	100	70	47	26	10