Non-ACT Study Protocol and Statistic Analysis Plan (SAP)

Clinical Trial Gov ID.	NCT06091982
Protocol Number	01.202308.101
Title	Renal Replacement Therapy and In-Hospital Mortality Incidence in Cardiac Surgery Associated Acute Kidney Injury
Study title	CSA AKI - RRT and Mortality Risk
Date of last Version of protocol	August 22nd, 2023
Research question and objectives	The purpose of this study is to evaluate the risk of patients with cardiac surgery associated acute kidney injury (CSA-AKI) with renal replacement therapy requirement RRT in related to in-hospital mortality event compared to CSA-AKI patients without the need of RRT.

Primary objective

- To analyze the association between AKI with RRT and intra-hospital postoperative mortality in cardiac surgery patients compared with AKI patients without RRT

Secondary objectives

- To analyze the risk of intra-hospital post-surgical mortality in cardiac surgery patients who complicated with CSA AKI
- To compare the risk of intra-hospital post-surgical mortality in cardiac surgery patients who complicated with CSA AKI with requirement of RRT and without RRT
- To Identify and analyze perioperative factors that play an important role in the incidence of mortality in AKI patients after cardiac surgery

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2 List of Abbreviations

ACE-I	*Angiotensin-converting enzyme inhibitors*
AKI	*Acute Kidney Injury*
APACHE	*Acute Physiology and Chronic Health Evaluation*
ARF	*Acute Renal Failure*
ARB	*Angiotensin Receptor Blocker*
CABG	*Coronary Artery Bypass Graft*
CI	*Confident Interval*
CKD	*Chronic Kidney Disease*
CPB	*Cardiopulmonary bypass*
CRRT	*Continuous Renal Replacement Therapy*
CSA-AKI	*Cardiac Surgery Associated- Acute Kidney Injury*
CVVH	*Continuous Veno-Venous Hemofiltration*
CVVHD	*Continuous Veno-Venous Hemodialysis*
CVVHDF	*Continuous Veno-Venous Hemodiafiltration*
DM	*Diabetes Mellitus*
EF	*Ejection Fraction*
ESRD	*End Stage Renal Disease*
EURO-SCORE II	*European System for Cardiac Operative Risk Evaluation II*
GFR	*Glomerular Filtration Rate*
HR	*Heart Rate*
HT	*Hypertension*
IABP	*Intra Aortic Balloon Pump*
ICU	*Intensive Care Unit*
IHD	*Intermittent Hemodialysis*
IRI	*Ischemic Reperfusion Injury*
KDIGO	*Kidney Disease Improving Global Outcomes*
LCOS	*Low cardiac output syndrome*
LOS	*Length Of Stay*

LVEF	*Left Ventricle Ejection Fraction*
OR	*Odd Ratio*
RAAS	*Renin-Angiotensin-Aldosterone System*
RIFLE	*Risk Injury Failure Loss and End Stage*
ROS	*Reactive Oxygen Species*
RRT	*Renal Replacement Therapy*
RR	*Risk Ratio*
SCr	*Serum Creatinine*
UO	*Urine Output*

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4 Abstract

The prevalence of acute kidney injury (AKI) varies up to 30% in post-cardiac surgery patients. Of the patients who suffer from AKI, around 1 - 10% will require renal replacement therapy (RRT). Cardiac surgery associated-AKI patients who require renal replacement therapy/dialysis have higher risk of mortality. The purpose of this study was to assess the risk of AKI-RRT on intrahospital mortality, and other factors that have an association with postoperative mortality. The method was non-experimental research design as retrospective cohort analysis. Dependent variable, in-hospital mortality was determined first and then the independent variables were examined to see the relationship between the variables.

Keywords: Acute Kidney Injury (AKI), Renal Replacement Therapy (RRT), cardiac surgery, intrahospital mortality

5 Rational and Background

The overall incidence of mortality post-cardiac surgery in some literatures varies between 2-8%. Cardiac surgery associated - acute kidney injury (CSA-AKI), a common postoperative complication, has increased risk for post-operative mortality. The incidence of mortality in patients complicated with CSA-AKI is up to 60%. The most severe stage of CSA-AKI, which requires dialysis therapy, is an independent risk factor. The prevalence of acute kidney injury is ranged up to 28% in cardiac surgery patients, of which around 1 – 10% of those patients required renal replacement therapy (RRT). [1-5]

The term of Acute Kidney Injury was developed by the Kidney Disease Improving Global Outcomes (KDIGO) organization in 2012, which is defined it as a sudden decrease (≤ 24 hours) in renal function characterized by an increase in serum creatinine (≥0.3 mg/dL or ≥ 50% [1.5 times baseline]), or reduction in urine output <0.5 mL/kg/hour for >6 consecutive hours. Based on these criteria, AKI stage 3 is categorized as acute renal failure or ARF.[1, 6, 7]

In a study conducted by Bove *et al*. in 2018, AKI is a serious complication after cardiac surgery that increases the incidence of morbidity and mortality. Renal replacement therapy (RRT) has been used as one of the important therapies in patients with severe AKI. Although the incidence of CSA-AKI requiring RRT is reported in about 1-10% of all AKI events after cardiac surgery, it is also shown that patients with severe AKI who require RRT therapy suffer a higher post-operative mortality rate. Previous studies reported intra-hospital mortality up to 43.5% in patients with AKI-RRT. Recent research found that from 412 CSA AKI-RRT patients, 174 patients (42.2%) died intra-hospital, with a EuroScore > 7, intraoperative bleeding > 1 liter and mechanical ventilation time > 70 hours as other independent risk factors. Meanwhile, post-operative use of furosemide was considered as protective factor in this study (OR 0.48). This information is similar with the results of our previous study regarding the use of diuretics for CSA-AKI patients. **[8-11]**

Considering the significant impact of AKI on the outcomes of patients' post-cardiac surgery, this study aimed to conduct an analysis of the risk factors that contribute to the incidence of post-operative mortality in patients with CSA-AKI, particularly regarding those cases in stages which required RRT. Based on the above background, this study's primary purposes was to analyze association between patients with CSA-AKI with RRT and in-hospital postoperative mortality risk compared to patients with CSA-AKI without RRT.

Study Rationale

Acute reduction in kidney function post cardiac surgery is the initial mechanism for acute kidney injury. Reduced blood flow, ischemia and reperfusion, hemolysis, activation of the inflammatory response, vascular redistribution and embolism are some of the etiologies that play an important role. The prevalence of acute kidney injury in the patient population with valve cardiac surgery is approximately 28%, with 1 – 10% requiring renal replacement therapy. Acute Kidney Injury/AKI is a strong independent predictor of post-operative mortality, particularly in patients with the requirement of renal replacement therapy. Postoperative AKI is not only increasing mortality, but also reduces long-term survival, extends the length of stay (LOS) in the intensive care unit, increases the risk of chronic kidney disease (CKD), and increases the financial burden on health facilities. Although cardiac surgery associated AKI is not a rare postoperative complication, when it reaches a severe stage that requires renal replacement therapy/RRT, the risk of postoperative mortality will increase several-fold. Apart from that, there are also other factors that increase the risk of mortality. Based on the explanation above, the formulation of the problem in this study is what is the relationship between AKI post-cardiac surgery patients with RRT on the incidence of intra-hospital mortality compared with AKI patients without RRT.

6 Research Question and Objectives

The purpose of this study is to evaluate the risk of patients with cardiac surgery associated acute kidney injury (CSA-AKI) with renal replacement therapy requirement RRT in related to in-hospital mortality event compared to CSA-AKI patients without the need of RRT.

6.1 Primary Objective

- To analyze the association between AKI with RRT and intra-hospital postoperative mortality in cardiac surgery patients compared with AKI patients without RRT

6.2 Secondary Objectives

- To analyze the risk of intra-hospital post-surgical mortality in cardiac surgery patients who complicated with CSA AKI
- To compare the risk of intra-hospital post-surgical mortality in cardiac surgery patients who complicated with CSA AKI with requirement of RRT and without RRT
- To Identify and analyze perioperative factors that play an important role in the incidence of mortality in AKI patients after cardiac surgery

7 Research Methods

7.1 Study Design

This research is a non-experimental study with a retrospective cohort analysis design. Data were secondary collected from patient's registry.

The dependent variable is intra-hospital post-surgical mortality, while the independent variables are cardiac surgery patients with complication of Acute Kidney Injury (AKI) and Renal Replacement Therapy (RRT).

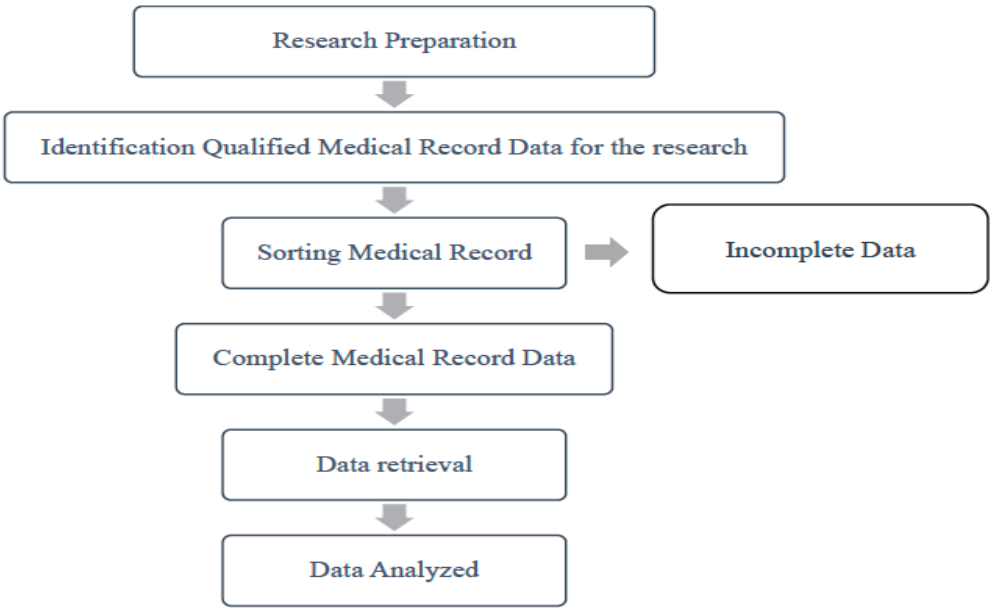
Analysis was carried out to determine the relationship between these variables.

7.1.1 Design Overview

This retrospective study was conducted at a tertiary hospital after obtaining approval from the hospital's institutional review board. Data were secondary collected from patient's registry. There is no direct observation or prospective observation to patients.

The need for informed consent was waived since the data analysis was performed retrospectively using hospital electronic medical records (EMR). The diagram below summarizes the study plan (see Figure 7.1).

Figure 7.1 Study Overview



7.2 Setting

This study will be conducted in tertiary cardiac center in Jakarta, Indonesia. Study began after approval from the ethics committee of Hospital until data collection was completed.

7.2.1 Study Population

Target population for this study is patient aged at least 18 years, who experienced cardiac surgery at adult cardiac surgical unit at tertiary cardiac center from January 2020 to December 2022.

The study population will be identified according to the below inclusion and exclusion criteria.

Inclusion Criteria:

The patient can be included in the study when:

- Data on patients who are at least 18 years old, who experienced cardiac surgery at our tertiary cardiac center from January 2020 to December 2022.

- Data on post-cardiac surgery patients who complicated with Acute Kidney Injury (AKI) which was characterized by an increase in serum creatinine > 0.3 mg/dL or >150% of the pre-operative serum creatinine level, which was checked within 12 hours post-surgery.
- Data is available in the medical records unit of the Harapan Kita National Heart Center.

Exclusion Criteria:

The patient cannot be included when the patient

- Patients with a previous history of dialysis.
- Data on patients who underwent surgery outside the specified period

7.3 Variables

The data collected from EMR included demographic data (age, weight, height, sex), type of surgery, comorbidities (history of diabetes, hypertension, stroke, smoking, renal disease), creatinine level, duration of mechanical ventilation, and ICU length of stay. Clinical variables are obtained that included mechanical ventilation time, ICU length of stay, postoperative diuretic, inotropes, vasopressor therapy, postoperative use of intra-aortic balloon pump (IABP), postoperative RRT, and in-hospital mortality. For the study's purpose, several continuous variables are categorized qualitatively such as mechanical ventilation (>48 hours as a cutoff point), ICU (≥5 days), postoperative diuretic therapy (yes/no), inotropes and vasopressor therapy ≥2 drugs (yes/no), and postoperative use of IABP (yes/no).

7.3.1 **Variables Operational Definition**

Table 7.1 Dependent Variable

No.	Variable	Definition	Measured with	Scoring	Scale
1	*In-hospital mortality*	Patient dies in hospital during treatment after cardiac surgery (patient has never gone home or been discharged from hospital)	Medical record	0 = Not Died 1 = Died	Categorical

Table 7.2 Independent Variables

No.	Variable	Definition	Measured with	Scoring	Scale
1	Acute Kidney Injury	Patients with an increase in serum creatinine more than 1.5 times or > 0.3 mg/dL with urine output < 0.5 cc/kg/hour for 6 consecutive hours.	Medical record	0 = No AKI 1 = With AKI	Categorical
2	Renal Replacement Therapy	Use of a renal replacement therapy machine, either continuous (CVVH) or intermittent (HD), during the period the patient is treated post-operatively until discharge from the hospital.	Medical record	0=Not required 1=Required	Categorical
3	Age	calculated from the day of birth to the day the surgery was performed in years	Medical record	0 = ≤60 years 1 = >60 years	Categorical

4	Type of surgery	These are surgical procedures undertaken by patients, divided into 5 categories: 1. Coronary Artery Bypass Graft (CABG) is a coronary heart bypass surgery 2. Valves or heart valve surgery is surgery performed on heart valves 3. Mixed valves are heart valve surgery performed simultaneously with other heart surgical procedures (for example coronary or vascular) 4. Congenital is surgery for congenital heart defects suffered by the patient 5. Other is for surgery that is not included in the 4 categories above (for example Vascular)	Medical record	1 = CABG 2 = Valves 3=Mixed Valves 4= Congenital 5 = Others	Categorical
5	Diabetes Mellitus	Obtained from the history of the disease suffered and blood sugar laboratory results.	Medical record	0= No 1= Yes	Categorical
6	Hypertension	Obtained from the history of the disease suffered by the patient/which was diagnosed	Medical record	0= No 1= Yes	Categorical

		before undergoing surgery, where the increase in systolic blood pressure is above the normal limit, namely more than 140 mmHg and diastolic blood pressure is more than 90 mmHg.			
7	Serum Creatinine	Serum creatinine value > 3.0 obtained last before surgery, in mg/dL	Medical record	0= No 1= Yes	Categorical
8	History of Stroke	History of stroke diagnoses that the patient has experienced, either with or without sequelae	Medical record	0= No 1= Yes	Categorical
9	Smoking History	Smoking history obtained from the patient's history in the medical record	Medical record	0= No 1= Yes	Categorical
10	History of Renal Disease	History of kidney disease in the patient before surgery.	Medical record	0= No 1= Yes	Categorical
11	Prolonged Ventilation	Use of a ventilator > 48 hours after surgery	Medical record	0= No 1= Yes	Categorical
12	Prolonged ICU stay	Length of stay in ICU > 5 days after surgery	Medical record	0= No 1= Yes	Categorical
13	Post operative IABP	Use of the IABP machine post-surgery	Medical record	0= No 1= Yes	Categorical
14	Use of more	Use of more than 2 types of	Medical	0=No or less	Categorical

	than 2 types of inotropic and vasoactive drugs	inotropic (Adrenaline, Dobutamine, Dopamine, Milrinon) or vasoactive (noradrenaline, vasopressin) drugs in post-surgical care	record	than 2 types 1=Use 2 or more	
15	Postoperative diuretic therapy	Use of diuretic therapy in the form of furosemide in the form of continuous infusion at a dose of 5 – 40 mg/hour post-surgery	Medical record	0=Not require 1=Required	Categorical

7.4 Data Source

The data to be collected in the study will be obtained from patients' registry, from electronic medical records and manual medical records. Data collection processes consist of this following process:

1. Data checking (editing)
   This is an activity to check the research data form sheet for data completeness so that if there are any discrepancies it can be completed immediately by the researcher.
2. Giving code (coding)
   The activity of changing data into numbers/numbers.
3. Entering data into a computer program (data entry)
   This is an activity of processing data obtained from research data forms and then analyzing it by entering the data into a computer program.
4. Cleaning data (cleaning)
   Data cleaning activities were carried out to check again before further analysis was carried out.

All data collected during this study must be documented on an ongoing basis in a complete, accurate, eligible, and timely fashion. The data in the eCRF should be consistent with the relevant source documents.

7.5 Study Size

The sample size was determined based on time, namely all data on adult heart surgery patients between January 1, 2020 - December 31, 2022, who were selected based on acceptance criteria.

7.6 Data Management

The main purpose of the eCRF is to obtain data required by the non-experimental study protocol in a complete, accurate, legible, and timely manner. The data in the eCRF should be consistent with the relevant source documents.

Data protection and privacy regulations will be implemented in capturing, forwarding, processing, and storing subject data.

7.7 Statistical Analysis Plan

All analyses will be performed on patients who underwent cardiac surgery in period between 1 January 2020 until 31 December 2022, with complication of acute kidney injury (AKI) postoperative. All data were retrieved from patient medical record retrospectively. There were no active observation or data retrieved directly from patients.

Data analysis will be carried out by the statistical team after the research samples have been taken and the data has been completed. The analysis was carried out using SPSS Version 29. and all statistical analysis plans have been completely documented in this statistical analysis plan.

Data that has been processed correctly is then analyzed by:

a. Univariate analysis

This univariate analysis was carried out to obtain an overview of the frequency distribution of research subjects and the distribution of the proportion of cases and controls according to each independent variable (risk factor) studied.

b. Bivariate analysis

Bivariate analysis was used to determine the relationship between the main risk factors and the incidence of death in hospital while also testing the research hypothesis using the chi square test.

c. Multivariate analysis

Multivariate analysis is carried out with the aim of describing the relationship between the dependent variable and the independent variable simultaneously in the population. Multivariate analysis was carried out by connecting several independent variables with one dependent variable simultaneously. Because the independent variables are categorical, logistic regression was used for the analysis.

7.7.1 Derived and Transformed Data

Missing data on each variable will be recorded in the table and not considered in data analysis.

7.7.2 Statistical Methods

The statistical analyses described in this section will be performed as further outlined in the SAP, which will be finalized prior to database lock and will be included in the clinical study report for this protocol. The final SAP will take into account any amendment to the protocol.

General Statistical Methodology:

Descriptive statistics (mean, SD, median, interquartile range) will be provided for continuous variables according to the results of data normality tests. Frequencies and percentages will be presented for categorical and ordinal variables.

All analyzes will consider the security of the dataset.

Primary Outcome Analysis:

The primary outcome in this study is to look at the incidence of death in the treatment of patients who have kidney problems with CRRT or not.

Bivariate analysis was carried out using the chi square/fisher's exact test to see whether there was a difference in the incidence of death in treatment between groups (CRRT vs Non-CRRT)

which was then continued to the multivariate analysis stage if it had a p value <0.25, multivariate analysis was carried out using regression multiple logistics with a significance level of 0.05 which shows that it is a variable that influences the incidence of death in care.

Secondary Endpoint Analysis:

The secondary outcome in this study is to look at the factors causing CRRT in patients undergoing cardiac surgery with AKI.

Bivariate analysis was carried out using the chi square/ Fisher's exact test to see whether there were differences in patient characteristics between patients who were given CRRT and those who were not, which was then continued to the multivariate analysis stage if it had a p value <0.25. Multivariate analysis was carried out using multiple logistic regression with The significance level is 0.05 which shows that it is a variable that influences the incidence of CRRT use.

7.7.3 Sequence of Analyses

Analysis was carried out after the research data was complete, in this study no interim analysis was carried out.

7.8 Limitations of the Research Methods

There are some limitations that should be considered in this study. First, due to the retrospective design used, there were some predictors of CSA-AKI that could not be included. Second, there were limitations in the capacity to do crosschecking due to inability to access patients directly, which may lead to confusion and heterogeneity of the dataset. Finally, data only included a single center, which may not reflect the actual demographics of patients and cardiac disease as distinguished from other centers.

However, the difference from real-life observational data, which is more essential to assess and improve clinical practice worldwide and complement randomized controlled trials by providing clinically relevant, real-world data and provide considerable health economic information.

7.9 Other Aspects

None

8 Protection of Human Subjects

8.1 Independent Ethics Committee or Institutional Review Board

Prior to commencement of the study at a given site, the protocol will be submitted together to the responsible IEC/IRB for its favorable opinion/approval. The written favorable opinion/approval of the IEC/IRB will be filed by the Investigator.

The IEC/IRB will be asked to provide documentation of the date of the meeting at which the favorable opinion/approval was given, and of the members and voting members present at the meeting. Written evidence of favorable opinion/approval that clearly identifies the study, the protocol version, and the subject information and consent form version reviewed should be provided.

8.2 Subject Information and Informed Consent

Since the data analysis was performed retrospectively derived from hospital electronic medical records (EMRs), the need for informed consent was waived.

Whenever important new information becomes available that may be relevant to the subject's consent, the written subject information sheet and any other written information provided to subjects will be revised by the Sponsor and be submitted again to the IEC/IRB for review and favorable opinion. The agreed, revised information will be forwarded to each subject in the study. The Investigator will explain the changes to the previous version.

8.3 Subject Identification and Privacy

A unique subject number will be assigned to each subject at inclusion. This number will serve as the subject's identifier in the study as well in the study database. The Investigator must ensure that the subjects' anonymity is maintained.

The Investigator should keep a separate log of subjects' identification numbers, names, addresses, telephone numbers and hospital numbers (if applicable). Only authorized persons will have access to identifiable personal details, if required for data verification. The Investigator is responsible for retrieving information from personal medical records. Data protection and privacy regulations will be observed in capturing, forwarding, processing, and storing subject data.

9 Management and Reporting of Adverse Events

This study design is retrospective study. All the events and incidences were already happened in the past period. This study does not interact directly to patients, there are no adverse events were caused directly by the study.

10 Plans for Disseminating and Communicating Study Results

After completion of the study, we shall prepare a final report of study results, in close collaboration with the coordinating Investigator. All publications and presentations should be based on the final study report.

10.1 Study Report(s)

The completed study will be summarized in a final report that accurately and completely presents the study objectives, methods, results, limitations of the study, and interpretation of the findings.

10.2 Publication

The publication will be a publication of the results of the analysis of the Primary Endpoint that will include data from study

11 References

1. Yi Q, Li K, Jian Z, Xiao YB, Chen L, Zhang Y, et al. Risk Factors for Acute Kidney Injury after Cardiovascular Surgery: Evidence from 2,157 Cases and 49,777 Controls - A Meta-Analysis. Cardiorenal Med. 2016;6(3):237-50.

2. Thakar CV, Arrigain S, Worley S, Yared JP, Paganini EP. A clinical score to predict acute renal failure after cardiac surgery. J Am Soc Nephrol. 2005;16(1):162-8.
3. Vives M, Hernandez A, Parramon F, Estanyol N, Pardina B, Munoz A, et al. Acute kidney injury after cardiac surgery: prevalence, impact and management challenges. Int J Nephrol Renovasc Dis. 2019;12:153-66.
4. Olivero JJ, Olivero JJ, Nguyen PT, Kagan A. Acute kidney injury after cardiovascular surgery: an overview. Methodist Debakey Cardiovasc J. 2012;8(3):31-6.
5. Carrascal Y, Laguna G, Blanco M, Paneda L, Segura B. Acute Kidney Injury after Heart Valve Surgery in Elderly Patients: any Risk Factors to Modify? Braz J Cardiovasc Surg. 2021;36(1):1-9.
6. Kellum JA, Lameire N, Group KAGW. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). Crit Care. 2013;17(1):204.
7. Singbartl K, Kellum JA. AKI in the ICU: definition, epidemiology, risk stratification, and outcomes. Kidney Int. 2012;81(9):819-25.
8. Bove T, Calabro MG, Landoni G, Aletti G, Marino G, Crescenzi G, et al. The incidence and risk of acute renal failure after cardiac surgery. J Cardiothorac Vasc Anesth. 2004;18(4):442-5.
9. Liu C, Zhang HT, Yue LJ, Li ZS, Pan K, Chen Z, et al. Risk factors for mortality in patients undergoing continuous renal replacement therapy after cardiac surgery. BMC Cardiovasc Disord. 2021;21(1):509.
10. Adriane P, J; Sugiarto, A; Susilo, AR. Prophylactic low dose furosemide infusion effect on cardiac surgery patients with renal dysfunction- A randomized controlled trial. Crit Care Shock. 2022;25(5):253-62.
11. Oh TK, Song IA. Postoperative acute kidney injury requiring continuous renal replacement therapy and outcomes after coronary artery bypass grafting: a nationwide cohort study. J Cardiothorac Surg. 2021;16(1):315.
12. KDIGOKAKIW G. KDIGO clinical practice guideline for acute kidney injury. Kidney Int. 2012(2):7-28.
13. Mariscalco G, Lorusso R, Dominici C, Renzulli A, Sala A. Acute kidney injury: a relevant complication after cardiac surgery. Ann Thorac Surg. 2011;92(4):1539-47.

14. Bove T, Monaco F, Covello RD, Zangrillo A. Acute renal failure and cardiac surgery. HSR Proc Intensive Care Cardiovasc Anesth. 2009;1(3):13-21.
15. Wang Y, Bellomo R. Cardiac surgery-associated acute kidney injury: risk factors, pathophysiology and treatment. Nat Rev Nephrol. 2017;13(11):697-711.
16. Yuan SM. Acute Kidney Injury after Cardiac Surgery: Risk Factors and Novel Biomarkers. Braz J Cardiovasc Surg. 2019;34(3):352-60.
17. Chikazawa GH, A; Ohshita, T; Kimura, M; Ishii, S; Totsugawa, T; Yoshitaka, H. Continuous Renal Replacement Therapy for Acute Kidney Injuries-after Cardiac Surgery-Insights from a Single Cardiovascular Institute. Journal of Intensive and Critical Care. 2022;8(1.60):1-4.
18. Zou H, Hong Q, Xu G. Early versus late initiation of renal replacement therapy impacts mortality in patients with acute kidney injury post cardiac surgery: a meta-analysis. Crit Care. 2017;21(1):150.
19. Borisov AS, Malov AA, Kolesnikov SV, Lomivorotov VV. Renal Replacement Therapy in Adult Patients After Cardiac Surgery. J Cardiothorac Vasc Anesth. 2019;33(8):2273-86.
20. Matsuura R, Iwagami M, Moriya H, Ohtake T, Hamasaki Y, Nangaku M, et al. The Clinical Course of Acute Kidney Disease after Cardiac Surgery: A Retrospective Observational Study. Sci Rep. 2020;10(1):6490.
21. Bagshaw SM, Berthiaume LR, Delaney A, Bellomo R. Continuous versus intermittent renal replacement therapy for critically ill patients with acute kidney injury: a meta-analysis. Crit Care Med. 2008;36(2):610-7.
22. Fernando M, Paterson HS, Byth K, Robinson BM, Wolfenden H, Gracey D, et al. Outcomes of cardiac surgery in chronic kidney disease. J Thorac Cardiovasc Surg. 2014;148(5):2167-73.
23. Thongprayoon C, Cheungpasitporn W, Shah IK, Kashyap R, Park SJ, Kashani K, et al. Long-term Outcomes and Prognostic Factors for Patients Requiring Renal Replacement Therapy After Cardiac Surgery. Mayo Clin Proc. 2015;90(7):857-64.
24. Palevsky PM, Liu KD, Brophy PD, Chawla LS, Parikh CR, Thakar CV, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for acute kidney injury. Am J Kidney Dis. 2013;61(5):649-72.