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# Continuous Renal Replacement Therapy for Acute Kidney Injuries after Cardiac Surgery-Insights from a Single Cardiovascular Institute

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## ABSTRACT

**Background:** Acute kidney injury (AKI) is not an unusual clinical complication after cardiovascular surgery. The aim of this study was to investigate the clinical significance of continuous renal replacement therapy (CRRT) in managing postoperative AKI.

**Material and methods:** 243 patients who received cardiovascular surgery complicated with postoperative AKI in cardiovascular intensive care (CVICU) were enrolled. Patients were divided into two groups: those requiring CRRT (Group A, n=64) and those not administered CRRT (Group B, n=179).

**Results:** Preoperative backgrounds showed there were more surgically at-risk patients complicated with a poorer renal profile in Group A. Procedure-related data identified cardiopulmonary bypass (CPB) and aortic cross clamp (ACC) times were significantly longer in Group A. Also, in-hospital mortality and hemodialysis transition rates were significantly higher in Group A. Preoperative renal profile and male gender was identified as risk factors for hemodialysis transition post cardiovascular surgery.

**Conclusion:** CRRT is expected to play a vital role in managing AKI post cardiovascular surgery. Further investigation is warranted to clarify the efficacy of CRRT for the improvement of long-term outcomes of patients complicated with postoperative AKI.

**Keywords:** Acute kidney injury; cardiopulmonary bypass; continuous renal replacement therapy

## INTRODUCTION

Acute kidney injury (AKI) is not an unusual postoperative complication after cardiac surgery and is independently associated with increased mortality and morbidity [1]. The incidence of AKI following cardiac surgery varies between 20% and 50%, depending on the diagnostic criteria used to define renal injury [2]. Therapeutic strategies to prevent AKI are imperative in improving clinical outcomes of cardiac surgery as AKI can eventually lead to multi-organ failure if not appropriately treated once AKI is diagnosed [3-7]. Continuous renal replacement therapy (CRRT) has been reported to be an effective treatment for AKI following cardiac surgery. The primary purpose of this study was to examine the clinical significance of prompt initiation of continuous renal replacement therapy (CRRT) under the diagnosis of AKI following cardiovascular surgery, based on the experience of a single cardiovascular institute [8-10]

## METHODS

A total of 243 patients who had undergone elective or emergency cardiovascular surgery with cardiopulmonary bypass (CPB) complicated with postoperative AKI at our institute's

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cardiovascular intensive care unit (CVICU) between 2012 and 2020 were enrolled. Those on dialysis preoperatively or with a functioning renal transplant were excluded. Surgeries included: isolated ischemic heart procedure, such as coronary artery bypass grafting (CABG); isolated heart valve operation, repair or replacement; thoracic aortic fixation for aneurismal or dissecting disorders; and, combinations of those isolated procedures stated above. AKI was confirmed by the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines which define AKI as an increase in sCr concentration ≥ 0.3 mg/dL within 48 hours or an increase in sCr concentration ≥ 1.5X baseline that is known or presumed to have occurred within the prior 7 days, or urine output <0.5 ml/kg/h for 6 hours [11-14] The initiation of CRRT was routinely introduced as promptly as possible after surgery to prevent and treat volume overload unresponsive to diuretics or systemic administration of Atrial Natriuretic Peptide (ANP), uremic symptoms and signs, exacerbated metabolic acidosis, and hyperkalemia in establishing AKI.8-10 All the enrolled cases were divided into two groups: those requiring CRRT (Group A, n=64) and those without CRRT (Group B, n=179).

## Statistical Analysis

Continuous data are presented as a median and interquartile range. Normally distributed data were analyzed using 2-tailed t-tests, and non-normally distributed data were compared with the Mann-Whitney test, as appropriate. Categorical variables are given as a count and percentage of patients and compared using the $\chi 2$ test. When any expected frequency was less than 1, or 20% of expected frequencies were less than or equal to 5, Fisher's exact test was used. Clinical outcomes between both groups and the risk factors of chronic hemodialysis transition among the surviving cases were analyzed by multivariate analysis of variance (MANOVA). A p-value of <0.05 was considered significant. All data were analyzed using the Statistical Analysis Systems software JMP 12.0 (SAS Institute Inc., Cary, NC, USA). All of the enrolled patients underwent elective or eme
ncy surgery after written informed consent was obtained from them or their families. In proceeding with this study, approval from our Institutional Review Board was granted [15-18]

# RESULTS

Preoperative backgrounds are listed in (**Table 1**). There were significant differences between the groups using the Logistic EuroSCORE for 30-day mortality (6.5 ± 3.6% vs. 4.3 ± 3.1%, p<0.001), left ventricular ejection fraction (LVEF) on preoperative echocardiography (50.8 ± 17.5% vs. 57.6 ± 14.0%, p=0.002), serum creatinine (sCr) (1.73 ± 0.91 mg/dl vs. 1.12 ± 0.37 mg/dl, p<0.001), or estimated Glomerular Filtration Rate (eGFR) (36.3 ± 18.2 ml/min vs. 50.0 ± 15.6 ml/min, p<0.001). Those in Group A were revealed to be at a surgically higher risk, complicated with reduced left ventricular function (LVEF) and poorer renal profiles. Procedure-related data is shown in (**Table 2**). Although there were no significant differences between the groups with regard to systemic perfusion pressure, minimum bladder temperature during CPB, and intraoperative total amount of urination, the aortic cross clamp (ACC) time (143.9 ± 50.0 min vs. 126.6 ± 42.6 min, p=0.009) and CPB time (222.6 ± 86.7 min vs. 184.1 ± 59.0 min, p<0.001) were significantly longer in Group A than in Group B. In addition, the total amount of blood transfusion (BTF) (1785 ± 1308 ml vs. 1032 ± 1026 ml, p<0.001) during the entire procedure was much higher in Group A than in Group B. In the present study, both redo and specific type of surgery, or the complexities of more than two isolated procedures, was not significantly associated with the requirement of CRRT for postoperative AKI. Postoperative data is shown in (**Table 3**). Postoperative hospital stay (POH) (52.3 ± 41.4 days vs. 30.2 ± 22.9 days, p<0.001), CVICU stay (52.3 ± 41.4 days vs. 30.2 ± 22.9 days, p<0.001), and intubation time following operation (148.0 ± 253 hours vs. 26.7 ± 37.6 hours, p<0.001) were significantly longer in Group A than in Group B.

It was not unusual that hospital death was markedly higher in Group A (12.5% vs. 26.7 ± 1.7%, p=0.001). Regarding the surviving cases at discharge in both groups, the hemodialysis (HD) transition rate was 32% in Group A and 0% in Group B, which was statistically significant (p<0.001). Risk factors of chronic HD transition are shown in (**Table 4**). While male gender and preoperative sCr or eGFR were revealed significant on univariate analysis, only preoperative sCr was identified on multivariate analysis.

**Table 1:** Preoperative backgrounds

| Variables | Group A (n = 64) | Group B (n = 179) | P value |
|---|---|---|---|
| Age (year) | 72.5 ± 10.6 | 73.0 ± 10.7 | .67 |
| Female sex (n) | 21 (33%) | 63 (35%) | .76 |
| Logistic Euro-score (%) *mortality | 6.5 ± 3.6 | 4.3 ± 3.1 | <.001 |
| BSA (m2) | 1.58 ± 0.20 | 1.62 ± 0.19 | .09 |
| LVEF (%) | 50.8 ± 17.5 | 57.6 ± 14.0 | .002 |
| Redo Surgery(%) | 13 (20%) | 21 (12%) | .22 |
| sCre (mg/dl) | 1.73 ± 0.91 | 1.12 ± 0.37 | <.001 |
| Hgb (g/dl) | 12.0 ± 2.9 | 12.7 ± 1.8 | .009 |
| eGFR (ml/min/1.73m2) | 36.3 ± 18.2 | 50.0 ± 15.6 | <.001 |
| DM(n) | 38 (59%) | 85 (47%) | .11 |
| COPD(n) | 9 (14%) | 39 (22%) | .20 |
| HT(n) | 31 (48%) | 90 (50%) | .88 |

**Table 2:** Procedure related data

| Variables | Group A (n = 64) | Group B (n = 179) | P value |
|---|---|---|---|
| CPB time (min) | 222.6 ± 86.7 | 184.1 ± 59.0 | P<.001 |
| ACC time (min) | 143.9 ± 50.0 | 126.6 ± 42.6 | .009 |
| Perfusion Pressure (mmHg) | 57.7 ± 11.2 | 55.3 ± 9.5 | <.001 |
| Min BT (degree) | 33.5 ± 1.1 | 33.6 ± 1.0 | .48 |
| Urine Output (ml) | 703.6 ± 1095.9 | 510.6 ± 517.2 | .07 |

**Table 3:** Postoperative data

| Variables | Group A (n = 64) | Group B (n = 179) | P value |
|---|---|---|---|
| Hospital LOS (day) | 52.3 ± 41.4 | 30.2 ± 22.9 | P<.001 |
| ICU LOS (day) | 14.2 ± 14.4 | 4.4 ± 3.6 | P<.001 |

| | | | |
|---|---|---|---|
| Intubation Time (hour) | 148.0 ± 253.0 | 26.7 ± 37.6 | <.001 |
| In-hospital Death (%) | 12.5%<br>*8 cases | 1.7%<br>*3 cases | .001 |
| HD transition Rate (%) | 32%<br>*survival case | 0 | P<.001 |

**Table 4:** Risk factors for HD transition

| | Univariate Analysis OR(CI) P value | Multivariate Analysis Adjusted OR(CI) P value |
|---|---|---|
| Male gender | 4.05(1.1-9.6) 0.034 | |
| sCre value | 6.91(2.6-26.3) <.001 | 6.87(1.01-66.1) .049 |
| eGFR value | 0.92(0.86-0.97) <.001 | |

## DISCUSSION

Postoperative administration of prompt CRRT for AKI following cardiac surgery was reported to be effective in decreasing operative mortality, reducing the CVICU length of stay (LOS) as well as hospital LOS, and reducing the duration of CRRT.13 The benefits for early introduction of CRRT are considered to be effective in decreasing the chance of life-threatening complications including uremia, acidemia, volume overload, and hyperkalemia. Also, initiation of CRRT as promptly as possible, which balances electrolyte, solute, and fluid levels before exacerbation to a more serious stage can effectively reduce the risk of kidney-specific and non-kidney vital organ injury, compared to a late introduction of CRRT. Once AKI is confirmed, we routinely initiate CRRT for postoperative AKI which is unresponsive to diuretics and systemic administration of renal-protective agents, such as ANP [19].

However, there are some negative or controversial studies which are opposed to early initiation of CRRT because it could expose patients to potential harms, such as hemorrhage, bacteremia derived from the placement of the dialysis catheter, and thrombosis, intradialytic hypotension, clearance of trace elements, and hypersensitivity to the extracorporeal circuit or antibiotics, which could add to resource utilization.21 Thus, the optimal treatment strategy for AKI is not only the prompt initiation of CRRT after the operation but also the careful intraoperative management which can help avoid the need for CRRT introduction [20,21].

Maintaining renal perfusion during CPB is key to the prevention of AKI.2 Typical hemodynamic goals during CPB are to support normal organ function and maintenance of a mean perfusion pressure of 50 to 70 mmHg, and these values are based on experimental studies of minimum blood flow required to deliver adequate oxygenation.11,12 In the present study, mean perfusion pressure during CPB between the groups was not significantly different, and perfusion pressure settings and determination by our institute perfusionists was considered to be appropriate so as to preserve renal perfusion. Karkouti K. demonstrated BTF in excess of 2 units consistently increased the risk of patients developing AKI [22]. considering the amount of BTF was significantly higher in Group A than in Group B in our study, secure and complete hemostasis during surgery should be attained in order to prevent the initiation of CRRT for exacerbated AKI. Also, needless to say CBP time under cardiac arrest should be shortened to as little as possible to avoid the use of CRRT because ACC times as well as CPB time were significantly longer in Group A than in Group B. In short, a sophisticated surgical technique is an important factor for the prevention of AKI requiring CRRT following cardiac surgery.

Regarding postoperative management, hemodynamic instability such as low cardiac output is a primary cause of AKI after cardiac surgery. This can occur from multiple factors, including hypovolemia, acute ventricular dysfunction such as perioperative myocardial infarction, prolonged ACC time, persistent hemorrhage, or cardiac tamponade. Prompt diagnosis is crucial, and the main aspects of treatment strategies, including goal-directed fluid management and administration of renal protective agents, such as ANP and dexamethasone,2,10,18-19 can be implemented prior to the initiation of CRRT [22]. In the present study, those in Group A were identified as more surgically high-risk, with worse renal profile, and poorer clinical outcomes, including significantly higher rates of hemodialysis transition and in-hospital mortality. Accordingly, in the real setting of postoperative management, prompt determination to initiate CRRT for AKI unresponsive to those conservative treatments stated above should be performed, especially for more severe and complicated cases.

Our study has several limitations. Data are derived from a small sample size at a single cardiovascular institute. Therefore, our models need to be evaluated at multi-centers to be validated. Further investigation is needed to clarify the long-term outcomes of all the surviving cases at discharge for conclusive clinical significance of CRRT introduction after cardiovascular surgery using CPB.

## CONCLUSION

AKI following cardiovascular surgery is not an unusual complication, and a comprehensive approach, including goal-directed fluid management, administration of renal protective agents, and CRRT initiation should be implemented. Of these treatments of choice, CRRT has the potential to improve early clinical outcomes of those cases complicated with AKI. Thus, prompt initiation of CRRT should be considered, especially for more surgically severe and complicated cases.

## CONFLICT OF INTEREST

All of the authors have nothing to disclose and also state no conflict of interest in the submission of this manuscript.

## AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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