

Evaluation of the Time to Terminate Continuous Renal Replacement Therapy in Patients with Acute Kidney Injury Following Cardiovascular Surgery in Association with or without a Mechanical Ventilation Support

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Abstract

Acute kidney injury (AKI) is a frequent and severe complication after cardiovascular surgery. Indications for continuous renal replacement therapy (CRRT) in patients with AKI have been proposed. However, there is often less discussion of when to terminate CRRT as well as what conditions are required for transferring patients to intermittent hemodialysis (HD). In this retrospective study of electronic medical records, we examined the role of a mechanical ventilator support in determining when to terminate CRRT in patients with AKI. When CRRT was stopped, 32 patients were supported with a mechanical ventilator while 41 patients had no support. Although there were no differences in age, sex, and pre levels of cardiopulmonary between the two groups, the levels of eGFR before the cardiovascular surgery were lower in the patients without a ventilator. Increases in body weight after cardiac surgery were higher, sequential organ failure assessment (SOFA) score was higher, and central venous pressures were higher in patients supported with a ventilator (all were $p < 0.05$). The rate of re-introduction to CRRT was higher ($p = 0.016$) in patients supported with a ventilator. After multiple regression analysis, successful cessation of CRRT was dependent on support of mechanical ventilation (odds ratio, 5.20 (CI: 1.15-23.4)). These data suggest that successful termination of CRRT is closely associated with removing the support of a mechanical ventilator.

Keywords: SOFA score; Urine volume; Fluid therapy

Introduction

The abrupt cessation of homeostasis induces multiple organ failure and cardiac surgery is one of the procedures that results in disturbance of homeostasis. Acute kidney injury (AKI) is a major postoperative complication in cardiac surgery, and is associated with high morbidity and mortality [1]. The reported incidence of cardiac surgery-associated AKI based on its many historical definitions ranges from 0.3 to 29.7% [2,3]. In 1.2 to 3.0 % of those patients, renal replacement therapy (RRT) is required [4,5]. There is a wide variation throughout the world on the indications for, and for when RRT is started [6-8]. Moreover, the termination of continuous RRT (CRRT) is affected by strongly held physician beliefs and organizational aspects of a given institution. Uchino et al. [9] were the first to report that the time of CRRT termination depended on urine output. In addition to low urine output, Wu et al. [10] proposed that older age, higher SOFA scores, and a longer dialysis-dependent period were risk factors for early re-dialysis. In general, patients suffering from AKI after cardiac surgery are treated in intensive care units (ICU). In this situation, all patients are usually intubated and their respiratory function is supported by a mechanical ventilator. Although the effective clinical protocols for the prevention and optimal management for AKI after cardiac surgery are not yet established, generally proposed strategies for its prevention stress optimal support of cardiovascular function and oxygen delivery during and after surgery. For mechanical ventilation, there are several international consensus guidelines that have been proposed, which have been followed by physicians working in ICU [11]. In our practice, the two on renal and respiratory mechanical support might be considered together. In other words, it might be appropriate that weaning from mechanical ventilation and cessation of CRRT are simultaneously carried out for acutely ill patients after cardiac surgery. In the present study, we examined the association of weaning from a mechanical ventilator and its cessation in AKI patients requiring continuous CRRT after cardiac surgery.

Subjects and Methods

This retrospective observational study was performed between July 2008 and September 2012 in a cohort of adult patients who underwent open heart surgery and needed CRRT due to AKI in the International Medical Center Saitama Medical University, Saitama, Japan. This study was approved by the institutional review board of our institution. The inclusion criteria were AKI patients who started CRRT while receiving respiratory support of a mechanical ventilator after cardiac surgery and those who stopped CRRT with or without a mechanical ventilator. The patients were divided into 2 groups: A) patients who were supported by a mechanical ventilator when CRRT was terminated and B) patients who were not supported by a mechanical ventilator when CRRT was terminated. Weaning of mechanical ventilation was decided by the intensivists who followed the guidelines. The cessation of CRRT was determined by integrated assessment of increased urine output, use of vasopressors, improved metabolic/electrolyte state, decreased urea/creatinine, and stable hemodynamics. A successful weaning was defined as the cessation of dialysis for at least 30 days.

AKI was defined according to the Second International Consensus Conference of the Acute Dialysis Quality Initiative Group with

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reference to RIFLE (risk, injury, failure, loss, and end-stage kidney disease) [12]. Continuous venovenous hemofiltration (CRRT) was started when at least one of the following institutional protocol criteria was fulfilled: (i) urine output below 0.5 mL/kg/h in 6 hours despite treatment with fluid transfusion, inotropes, and/or vasoconstrictor infusions aimed at optimization of the hemodynamic parameters and the administration of furosemide 100 mg/h over 3 hours or (ii) more than a 4-fold increase in plasma creatinine concentration was observed. Hemofiltration treatment ceased when patients recovered urine output exceeding 1 mL/kg/h, provided that no indications for RRT were observed subsequently. Patients were accessed through double-lumen catheters (Vas-cath, Medicon Co., Chicago, IL), which were inserted into the right or left femoral vein and connected to a continuous hemodialyzer (KM8600, Kuraray Co. Ltd., Tokyo, Japan). An anticoagulant, nafamostat mesilate (Futhan, Torii Pharmaceutical Co. Ltd. Tokyo, Japan), was used at 30 IU/hr. Dialysis was started under conditions of water elimination rate of 60 mL/hr and a dialysate (HF Solita, Shimizu Pharmaceutical Co., Ltd., Shimizu, Japan) flow rate of 1 L/hr. The dialyzers used in this study were Panflow APF-S (Asahi Medical Co., Ltd., Tokyo, Japan) and Hemofeel SH (Toray Medical Co., Ltd., Tokyo, Japan).

Disease severity was assessed using the Sequential Organ Failure Assessment (SOFA) score [13].

eGFR was calculated using a modified three-variable equation for eGFR in Japanese patients: $eGFR = 194 \times \text{age}^{-0.287} \times \text{SCr}^{-1.094} \times (x0.739, \text{ if female})$, where SCr=serum creatinine [14]. Early redialysis, defined as relapsed need for CRRT within 30 days after cessation of CRRT, was considered the primary outcome variable. The indications for resumption of redialysis were mainly fluid overload and azotemia or its combination. The characteristics of patients were examined with regard to presence or absence of a mechanical ventilator for values of baseline, preoperative, and at cessation of CRRT.

Statistical Analysis

Data were analyzed by using SAS 1999 program (release 8.00 by SAS Institute Inc, Cary, NC). Continuous measures are expressed as mean ± standard deviation and were compared using Student's t test. Categorical variables were compared with Fisher's exact χ^2 test. A multivariate logistic regression analysis with successful cessation of CRRT was carried out as dependent variables (age, preoperative eGFR, organ damage score at the cessation of CRRT, body weight changes, CVP and duration of CRRT). $P < 0.05$ was considered to be statistically significant.

Results

Patient characteristics

The demographics of patients in groups A and B are shown in (Table 1). There were no differences between the two groups in age, sex ratio, body weight, HbA1C, ejection fraction, presence of emergency surgery, types of cardiac surgery, duration of surgery, and use of IABP between the two groups. The only difference was eGFR of patients in group B was lower than in group A ($p < 0.001$). Moreover, at the initiation of CRRT, there were no differences in increases in serum creatinine and body weight, decreasing urine volume, central venous pressure and SOFA score at the initiation of CRRT between the two groups, (Table 2) shows variables at cessation of CRRT. In spite of elevations of serum creatinine in the two groups, group A showed higher urine volume

($P = 0.016$), higher dose of fluid therapy ($P < 0.001$), higher body weights ($P = 0.032$), higher CVP ($P = 0.003$) and greater increases of SOFA scores (cardiovascular: $P < 0.001$; respiratory: $P < 0.001$; and liver: $P = 0.005$) than in patients of group B. On the contrary, renal scores of patients in group B were higher than in group A. In the analysis for SOFA score, neurological score was not counted, because "1" was given for patients of group A. Consequently, SOFA scores in group A were significantly higher than in group B (10.7 ± 2.2 vs. 7.6 ± 2.7 ; $P < 0.01$).

| | Group A(n=32) | Group B(n=41) | p-value |
|----------------------------------|---------------|---------------|---------|
| Age (yr) | 72.5 ± 6.4 | 75.5 ± 6.9 | 0.062 |
| Gender(M/F) | 19/13 | 28/13 | 0.468 |
| Preoperative | | | |
| Body weight(Kg) | 57.6 ± 11.2 | 57.4 ± 12.7 | 0.935 |
| HbA1c(%NGSP) | 6.23 ± 1.17 | 5.93 ± 0.95 | 0.193 |
| Ejection Fraction (%) | 48.5 ± 16.2 | 50.3 ± 17.8 | 0.655 |
| eGFR(mL/min/1.73m ²) | 46.1 ± 19.6 | 32.9 ± 15.3 | 0.001 |
| Intraoperative | | | |
| Emergency surgery(yes/no) | 10/22(31%) | 15/26(37%) | 0.804 |
| Surgery | | | |
| CABG | 19(59%) | 24(59%) | 1 |
| Valve surgery | 8(25%) | 12(29%) | 0.793 |
| CABG + valve | 5(16%) | 5(12%) | 0.739 |
| Duration of surgery(hr) | 8.08 ± 185 | 7.51 ± 1.87 | 0.197 |
| IABP(yes/no) | 17/15(53%) | 18/23(44%) | 0.484 |
| At the start of CRRT | | | |
| Increases in Scr (x) | 1.95 ± 0.79 | 1.65 ± 0.58 | 0.071 |
| Urine volume(mL/hr/Kg) | 0.53 ± 0.44 | 0.67 ± 0.49 | 0.22 |
| Changes in body weight (%) | 9.08 ± 5.41 | 9.49 ± 7.18 | 0.788 |
| CVP(mmHg) | 10.9 ± 3.8 | 9.8 ± 3.9 | 0.209 |
| SOFA score | 12.2 ± 2.4 | 11.2 ± 2.1 | 0.084 |

Values are expressed as mean ± standard deviation. eGFR, estimated glomerular filtration rate; CABG, Coronary artery bypass grafting; IABP, intra-aortic balloon pump; Scr, serum creatinine; CVP, central venous pressure; SOFA, sequential organ failure assessment.

Table 1: Demographic and clinical characteristics of acute kidney injury patients requiring continuous renal replacement therapy (CRRT) who had supported (Group A) or not supported (Group B) by mechanical ventilator at timing of cessation of CRRT.

| | Group A(n=32) | Group B (n=41) | p-value |
|----------------------------|---------------|----------------|---------|
| Increases in Scr (x) | 1.39 ± 0.61 | 1.19 ± 0.34 | 0.107 |
| Urine volume(mL/day) | 2304 ± 1372 | 1608 ± 1061 | 0.016 |
| Fluid therapy(mL/day) | 2457 ± 667 | 1938 ± 472 | <.001 |
| Changes in body weight (%) | 5.12 ± 6.82 | 2.94 ± 6.65 | 0.032 |
| CVP(mmHg) | 6.6 ± 3.4 | 4.2 ± 3.1 | 0.003 |
| SOFA score | 10.7 ± 2.2 | 7.6 ± 2.7 | <.001 |
| Cardiovascular | 2.3 ± 0.7 | 1.5 ± 0.8 | <.001 |
| Respiratory | 1.5 ± 0.7 | 1.1 ± 0.8 | 0.043 |
| coagulation | 1.6 ± 0.8 | 1.3 ± 1.0 | 0.264 |
| Liver | 1.9 ± 1.3 | 1.2 ± 1.1 | 0.005 |
| Renal | 1.1 ± 1.1 | 1.7 ± 1.2 | 0.046 |
| Organ damage | 8.5 ± 2.1 | 6.7 ± 2.5 | 0.001 |
| Dose of dialysis(ml/hr/kg) | 9.6 ± 4.3 | 9.1 ± 2.4 | 0.549 |
| Duration of CRRT(day) | 7.0 ± 6.6 | 7.0 ± 3.8 | 0.148 |

Values are expressed as mean + standard deviation. Scr, serum creatinine; CVP, central venous pressure; SOFA, sequential organ failure assessment; CRRT, continuous renal replacement therapy.

Table 2: Characteristics of patients with (group A) or without (group B) support of mechanical ventilation at the timing of cessation of continuous renal replacement therapy.

Re-introduction of CRRT

There were 15 (47%) patients in group A and 5 (12%) in group B who were re-introduced to CRRT. ($P < 0.001$). (Figure 1).

Adjusted odds ratio after multiple regression analysis for re-introduction of patients free from a mechanical ventilator was 5.20 (95% confidential interval:1.15-23.4: patients with support of a mechanical ventilator as a control).

Discussion

In the present study, the incidence of patients re-introduced to CRRT was higher in those who were, rather than not supported by a mechanical ventilator when CRRT was terminated. Previously, Uchino et al. [9] proposed that urine output at the time of initial cessation of CRRT was the most important predictor of successful cessation, especially if it occurred without the administration of diuretics. In the present study, patients who were supported by a mechanical ventilator had larger urine output and higher SOFA scores with severe organ damage than those patients without support. These findings suggest that patients supported by a mechanical ventilator suffered more severe conditions or were on the way to recovery from damage of AKI after cardiac surgery. This recalls a previous study that claimed urine volume is a simple and early prognostic index for AKI patients requiring dialysis [15]. In ICU patients, the most important risk factors for AKI or mortality from AKI are often present on admission. During the ICU stay, other organ failures (especially cardiovascular) are important risk factors. Instead of urine volume, oliguric AKI was an independent risk factor for ICU mortality, and infection increased the contribution to mortality by other factors. The severity of circulatory shock is known to be the most important factor influencing outcome in AKI patients [16]. This might be related to the use of diuretics, since Van der Voort et al. [17] demonstrated that continuous infusion of furosemide in the recovery phase of hemofiltration-dependent AKI increased urine volume but did not lead to a shorter duration of renal failure. Instead of urine volume, SOFA score may be associated with organ damage. Wu et al. [10] demonstrated that less urine output, longer duration of dialysis, age over 65 years, and higher disease severity score were predictive of a patient's redialysis after initial weaning from acute dialysis. In the present study, organ damage assessed by SOFA score was higher

in patients supported by a mechanical ventilator. This indicates that severity of AKI is not determined by renal score evaluated by urine volume and serum creatinine but that cardiopulmonary failure is an important factor for recovery of AKI in patients after cardiac surgery. In the studies by Uchino et al. and Wu et al. [9,10], the causes of AKI were varied and AKI patients due to cardiac surgery were not the major group. In contrast, 100 % of our study population was comprised of cardiac surgery induced AKI. The difference between the two studies and ours could result in different indicators for terminating CRRT. In the present study, presence or absence of a mechanical ventilator at the time of cessation of CRRT had a greater impact for re-dialysis of patients regardless of age, preoperative renal dysfunction, CVP and organ damage score. These data suggest that successful termination of CRRT in AKI patients after cardiac surgery is closely associated with removing the support of a mechanical ventilator.

A weakness of the present study is the data were derived from a single center. Inherent to the observational study design is the limitation that it establishes association but not causality. Nevertheless, it can improve individual patient care by allowing us to accurately identify when CRRT should be terminated in AKI patients after cardiac surgery. Second, all subjects of this study were patients who had received cardiac surgery. This background as causes of AKI is different from that of AKI due to various other reasons. However, compared with the previous studies that included various underlying patient's characteristics and different needs for dialysis, this study provides a clear cut proposal for successful weaning of CRRT in AKI patients after cardiac surgery. Third, the cessation of CRRT was not based on clearly established criteria and the experience comes from a single center, although general rules were followed.

Our data suggest that the cessation of CRRT was partially dependent on the two factors; the absence of a mechanical ventilator and the levels of eGFR in the patients who were not supported by mechanical ventilator before cardiovascular surgery were lower than those of patients who were supported. This might hold two things; one is a possibility of re-occurrence of AKI in spite of stability of hemodynamics, and another is prolongation of recovery from AKI. Clearly, patients' cardiopulmonary status at the time of withdrawal of mechanical ventilation would clear sufficient requirement for discontinuation of CRRT. In line with this assumption, it is not so difficult to determine when CRRT should be stopped without jeopardizing patients' general conditions.

In conclusion, albeit retrospective, our study is the first demonstration of the role for a mechanical ventilator in determining the time to terminate CRRT in AKI patients after cardiac surgery.

Conflict of Interest

The authors declare no conflict of interest in this study.

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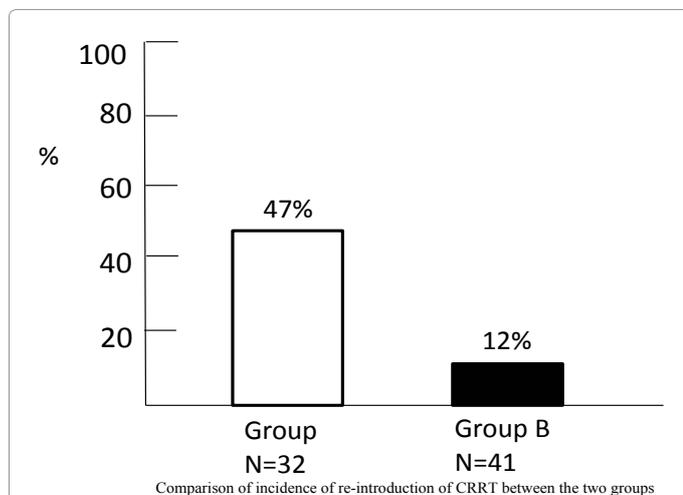


Figure 1: Comparison of incidence of re-introduction to CRRT. In patients who were weaned from a mechanical ventilator (group B), the incidence of re-introduction to CRRT was lower ($P < 0.001$) than in patients who had been supported with a mechanical ventilator until the cessation of CRRT (group A).

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