# Effect of early and intensive continuous venovenous hemofiltration on patients with cardiogenic shock and acute kidney injury after cardiac surgery

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**Objective:** Continuous renal replacement therapy (CRRT) is currently the mainstay renal support for critically ill patients. However, the optimal intensity of CRRT remains debated owing to the heterogeneity of the study populations and CRRT techniques across centers. The present study investigated the beneficial effects of early and intensive continuous venovenous hemofiltration (CVVH) on patients with shock after cardiotomy.

**Methods:** Patients who had received CRRT for cardiogenic shock and acute kidney injury after cardiac surgery from January 2003 to December 2007 were retrospectively recruited. They were divided into 2 groups according to the delivered dosage of hemofiltration.

**Results:** The mean duration between intensive care unit admission and initiation of CVVH was $1.4 \pm 0.8$ days. The all-cause mortality by day 30 was 73.3% and 45.4% in the low- and high-dose groups, respectively ($P = .002$). The corresponding in-hospital mortality rate was 82.2% and 61.8% ($P = .02$). No significant difference was seen in the renal recovery of the survivors between the 2 groups.

**Conclusions:** In patients developing postoperative cardiogenic shock and acute kidney injury after cardiac surgery, an early higher CVVH dose was associated with better in-hospital and long-term survival. Moreover, the beneficial effect of intensive treatment might be more critical in the early perioperative period. (J Thorac Cardiovasc Surg 2014;148:1628-33)

Acute kidney injury (AKI) remains a dreaded complication of cardiac surgery, despite substantial advances in surgical techniques, anesthesia management, and cardiopulmonary bypass equipment. The causes of AKI after cardiac surgery have included hypovolemia, systemic inflammation, anemia, hypotension, hypoxemia, and direct ischemia in the case of operations involving vascular interruption.[1] Depending on the population studied and the criteria used for definition, the frequency of AKI after cardiac surgery has ranged from 0.7% to 31%, with 5% to 7% of patients requiring renal replacement therapy (RRT).[2-4] Although tremendous innovations in supportive care and RRT have occurred during the past decade, the mortality rate of AKI necessitating RRT has remained extremely high, in excess of 50%.[5,6]

As an alternative to traditional intermittent hemodialysis, continuous RRT (CRRT) has now emerged as the leading form of RRT for patients with AKI in the intensive care unit (ICU) worldwide owing to less treatment-related hemodynamic instability, more steady acid-base and electrolyte correction, and subtend fluid removal theoretically. In the past decade, several studies of endotoxemic animals have revealed improved hemodynamics and cytokine removal with high-volume CRRT.[7-9] In addition, some single-center clinical studies have advocated a RRT dose–survival relationship, suggesting the beneficial effect of CRRT intensity >35 mL/kg/h.[10,11] However, current large, multicenter, randomized controlled clinical trials have failed to support the putative superiority of intensive CRRT for either survival or renal recovery.[12-14] This discrepancy might have resulted from the clinical heterogeneity of the study populations and practice variations in the application of CRRT across centers. Thus, we conducted a case-control study of patients with shock after cardiotomy, with homogeneity in disease characteristics, timing to the initiation of RRT, and RRT modality. We also analyzed whether intensive CRRT could improve the clinical outcome.

## METHODS

### Study Subjects

The present study was a retrospective case-control study approved by the Taipei Veterans General Hospital institutional review board, which waived the need for written informed consent from the participants.

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**Abbreviations and Acronyms**

AKI = acute kidney injury
APACHE = Acute Physiology and Chronic Health Evaluation
CVVH = continuous venovenous hemofiltration
ECMO = extracorporeal membrane oxygenation
EuroSCORE = European System for Cardiac Operative Risk Evaluation
IABP = intra-aortic balloon pumping
ICU = intensive care unit
RRT = renal replacement therapy
SOFA = Sequential Organ Failure Assessment

From January 2003 to December 2007, adult patients who had developed dialysis-requiring AKI after cardiac surgery at Taipei Veterans General Hospital were recruited. Patients who were hemodynamic stable or receiving chronic dialysis for end-stage kidney disease were ineligible for the present study (Figure 1).

## Data Collection

The demographic data were obtained from the medical records. Biochemistry data, such as hemoglobin, albumin, blood urea nitrogen, and creatinine, were routinely obtained before surgery. The baseline estimated glomerular filtration rate was calculated using the Cockcroft-Gault formula as follows: for men, (140 − age) × (body weight [kg])/(0.814 × serum creatinine [$\mu$mol/L]); for women, the value was multiplied by 0.85.[15] The surgery type, cardiopulmonary bypass duration, postoperative requirement for intra-aortic balloon pumping (IABP), and use of extracorporeal membrane oxygenation (ECMO) were obtained from the surgical records. The Acute Physiology and Chronic Health Evaluation (APACHE) II score, Sequential Organ Failure Assessment (SOFA) score, European System for Cardiac Operative Risk Evaluation (EuroSCORE) II, central venous pressure, interval to CRRT initiation, dosage of inotropic agents and continuous venovenous hemofiltration (CVVH), length of ICU stay, and in-hospital mortality were assessed from the medical records. Sepsis was diagnosed in accordance with the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference guidelines.[16]

## CVVH Setting and Dosage

All patients were admitted to the ICU immediately after surgery. Inotropic support was prescribed when the mean arterial pressure was <60 mm Hg. The indications for RRT were as follows: oliguria (urine output < 240 mL/12 h) despite fluid resuscitation and intravenous diuretic treatment, hyperkalemia > 6.5 mmol/L, severe acidosis (pH < 7.2), or pulmonary edema. The decision to initiate or terminate RRT and the dosage of CVVH were determined by the consulting nephrologists. CVVH was accomplished using blood flow rates of 100 to 150 mL/min through a double-lumen, 12F catheter inserted into a femoral vein. Bicarbonate-based replacement fluid was administered in predilution mode at a dynamically adjusted rate to achieve the desired fluid balance. The amount of effluent was used as a proxy for the treatment dosage. Patients were transitioned from CVVH to intermittent hemodialysis at the judgment of the nephrologists if they became hemodynamically stable. Recovery of renal function was determined from an assessment of urine output and the biochemical data.

During the 6-year enrollment period, 2 types of CVVH machines were used at Taipei Veterans General Hospital. Before 2005, we had only the first-generation, dedicated CRRT machines, which achieved predilutional hemofiltration of about 1000 to 1200 mL/h. The device included an AK-10 hemodialysis machine (Gambro, Lund, Sweden) for blood pumping and an infusion pump for fluid balance. Since January 2005, the Prisma machines (Gambro Hospal, Kilchberg, Switzerland) were available and routinely prescribed predilutional hemofiltration of 3000 mL/h. After a 3-month overlap period, all patients with AKI and unstable hemodynamic data received CVVH using the Prisma machines.

## Patient Follow-up

In June 2010, the renal function and vital status of all patients were collected from the medical records of the outpatient clinic or by telephone interview, or both. When a patient had died during the follow-up period, the date of death was established.

## Statistical Analysis

Normally distributed continuous data are presented as the mean ± standard deviation and analyzed using the Student $t$ test. Numeric data that were not normally distributed are presented as the median and interquartile range and were analyzed using the Mann-Whitney $U$ test. Statistical analysis was performed using the Statistical Package for Social Sciences, version 20.0, software (SPSS, Chicago, Ill). The survival rate of the 2 groups were calculated using the Kaplan-Meier method and compared using the log-rank test. Multivariate stepwise logistic regression analysis was performed to analyze the independent risk factors of in-hospital mortality. Risk factors with $P < .1$ on univariate analysis were entered into the multivariate analysis. All probabilities were 2 tailed.

# RESULTS

## Basic Characteristics of Study Population

A total of 142 patients (mean age, 69.6 ± 12.1 years) were included in the present study. All patients required postoperative support with mechanical ventilation and inotropic agent supplementation. The mean SOFA score, APACHE II score, and EuroSCORE II was 16.4 ± 2.4, 27.8 ± 5.2, and 43.8 ± 18.9, respectively. Of the 142 patients, 45 received a lower dose (18.1 ± 3.6 mL/kg/h) and 97 a higher dose (45.2 ± 7.9 mL/min/h) of CVVH. The mean interval between ICU admission and initiation of CVVH was 1.4 ± 0.8 days. No statistically significant difference was found in the basic characteristics between the 2 groups (Table 1).

## Clinical Outcome

The number of open heart surgery cases and members of the surgical team remained consistent in our hospital during the study period. The mortality rate and CRRT requirement before and after 2005 were comparable (Figure 2). The in-hospital mortality rate was 82.2% (n = 37) in the low-dose group and 61.8% (n = 60) in the high-dose group ($P = .02$). The ICU and hospital length of stay were longer in the high-dose group (Table 2). Univariate logistic regression analysis identified 9 risk factors for in-hospital mortality, including old age, male gender, emergency operation, lower

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