Indian Heart Journal 73 (2021) 594–598

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Original Article

Managing patients of shock and acute kidney injury in tertiary care cardiac ICU: Experience with continuous renal replacement therapy

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ARTICLE INFO

Article history:
Received 20 February 2021
Received in revised form
18 July 2021
Accepted 4 August 2021
Available online 8 August 2021

Keywords:
Continuous renal replacement therapy
Cardiac intensive care unit
Vasoactive-inotropic score
CRRT-Cycle
Mean arterial pressure

ABSTRACT

Background: Clinical experience on details of CRRT initiation and outcomes in cardiac intensive care unit (CICU) patients is not available from developing countries like India. This study shares the 5-year clinical experience of managing CICU patients requiring CRRT in a tertiary care cardiac center of North India.
Materials and methods: Medical records of all CICU patients with acute kidney injury (AKI) managed by CRRT from October 2011 to September 2016 at tertiary referral center in North India were retrospectively reviewed. Multiple logistic regression analysis was used to identify predictors of post-CRRT mortality.
Results: A total of 630 patients received CRRT during the study period. Most commonly AKI developed in patients with acute coronary syndrome (30.2 %) with cardiogenic shock. 55.9 % of the CRRT patients were >60 years of age, and/or on multiple supports in ICU including, mechanical ventilation, high doses of inotropes & vasopressors and other cardiovascular support. Of those on CRRT, 130 (20.6 %) patients had died, 215 (34.1 %) were discharged and 285 (45.2 %) could not complete the desired course. Multivariate regression analysis showed independent association of mortality with high vasoactive-inotropic score, single CRRT cycle and low mean arterial pressure in CRRT patients.
Conclusion: About 34.1 % of patients receiving CRRT were alive at discharge, emphasizing the feasibility and utility of CRRT as a promising modality in this population for improving outcomes.

1. Introduction

Acute kidney injury (AKI) occurs in 18–65 % of intensive care unit (ICU) patients and is commonly associated with multi-organ failure, pre-existing renal disease, sepsis, and renal hypoperfusion.[1] Holland et al reported 15 % AKI prevalence among cardiac ICU (CICU) patients, out of which 20 % required renal replacement therapy (RRT).[2] Continuous renal replacement therapy (CRRT) is a slow form of hemodialysis which provides renal support for hemodynamically unstable and critically ill patients with AKI admitted to ICU.[3]

Kidney Disease Improving Global Outcomes (KDIGO) AKI guidelines (2012) suggested using CRRT over intermittent dialysis options for hemodynamically unstable patients in ICU.[4] Several studies have proven the superiority of CRRT over intermittent therapies in hemodynamic unstable critical patients with higher renal recovery rates because of gradual removal of fluids, superior ability to clear inflammatory mediators, better maintenance of the electrolytes, and hemodynamic stability.[3,5–8] These advantages of CRRT are important, predominantly in CICU patients as AKI after cardiac procedure is often associated with hemodynamic instability.[9,10]

Till today, published clinical experience on details of CRRT initiation and outcomes in CICU patients is mostly available from developed countries and there is scarce data from the developing countries like India. We report our 5-year experience of providing CRRT in the CICU of a tertiary referral center. The goal is to highlight

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https://doi.org/10.1016/j.ihj.2021.08.003

CRRT practices and outcomes from North India, allowing the characterization of similarities and differences in standard CRRT practices.

2. Materials and Methods

This study was undertaken at CICU of the tertiary referral center of North India. This center is an exclusive admitting unit for patients with underlying heart diseases. All patients admitted to CICU and who were treated with CRRT, from October 2011 through September 2016, were included. The RIFLE class (class R, class I, or class F), determined based on the worst of either Creatinine/glomerular filtration rate (GFR)/urine output criteria, was used to classify patients at the time initiation of CRRT. The exclusion criterion was end-stage kidney disease patients, who were undergoing regular dialysis. The study was approved by the Ethics Committee (IEC No. 2017–218), which waived the need for explicit patient consent because no direct contact with study participants was necessary. However, as per the hospital policy, all the patients had implied consent to produce and publish the data at the time of hospital admission.

The primary outcome of the study was survival among CICU patients post CRRT. Also, the factors that were associated with mortality, within seven days of CRRT initiation, were assessed.[11] The RIFLE class (class R, class I, or class F), determined based on the worst of either Creatinine/glomerular filtration rate (GFR)/urine output criteria was used to classify patients at the time initiation of CRRT. We used Prismaflex® (Baxter India) machine to provide CRRT in our patients. Normal saline (0.9 %) solution 5 ml/kg/hour was used for pre blood pump. Prismasol® BO (Baxter India) solution was used for both dialysate as well as replacement fluid.Effluent dose was ranging from 26 to 32 ml/kg/hour. Pre and post dilution were adjusted for replacement fluid as 2/3rd and 1/3rd respectively. Partial thromboplastin time with Kaolin (PTTK) was monitored in cases where anticoagulation was administered and a ratio of 1.5–2 was maintained.

The reasons of discontinuation of CRRT were return of adequate renal function (urinary output $\geq$ 500 ml/24 h), switching to other modalities of renal replacement therapies (SLED or IHD), and premature termination of therapy due to DAMA or death. Patient age, sex, time interval from ICU admission to CRRT initiation, principal diagnosis leading to AKI, CRRT modalities, Mean arterial pressure (MAP), sequential organ failure assessment (SOFA) score, acute physiology and chronic health evaluation II (APACHE II) score, vasoactive-inotropic score (VIS), vasopressor use during CRRT, mechanical ICU support and consecutive number of days of CRRT were collected from the medical records. Mean arterial pressure of 70 mm Hg or more was taken as cut off.

Data was analyzed using SPSS statistical software (version 25; SPSS Inc) and summarized as number and percentage for categorical variables and as mean (SD) for continuous variables. A multiple logistic regression analysis was applied to predict the all-cause mortality after starting CRRT. The following variables were included as covariates in a logistic regression analysis: age, gender, CRRT interval (admission to start), consecutive number of days of CRRT, principal diagnosis, APACHE II score, SOFA score, VIS, mean arterial pressure (MAP) and mechanical ventilation. The level of significance was set as 0.05 and the desired power of the study was 80 %.

3. Results

Over the 5-year period, a total of 642 patients were admitted to CICU and received CRRT at our center. Out of these, data from 630 patients were analyzed and 12 patients with ESRD were excluded.

3.1. Baseline demographic and clinical characteristics

Table 1 shows the baseline demographic and clinical characteristics of the CRRT patients. Four hundred (63.5 %) were male and two hundred thirty (36.5 %) were female. The mean age of the study patients was 61.5 ± 14.3 years. Three hundred fifty-two (55.8 %) were aged $\geq$ 60 years. The development of AKI was associated with cardiovascular diseases (53.2 %), cardiac procedures (33.8 %), non-cardiovascular diseases (4.0 %), and non-cardiac procedures (9.1 %). Acute coronary syndrome with cardiogenic shock (30.2 %)

Table 1
Baseline demographic and characteristics of the CRRT patients (n = 630).

Characteristics	N (%)
Age	
≤40 years	57 (9.0)
40–60 years	221 (35.1)
>60 years	352 (55.9)
Sex	
Male	400 (63.5)
Female	230 (36.5)
Pre CRRT Condition	
Left Ventricular Dysfunction*	305 (48.4)
CPR survivor	47 (7.5)
Sepsis	182 (28.9)
Co-morbidities	
Hypertension	387 (61.4)
Diabetes mellitus	380 (60.3)
Chronic kidney diseases	189 (30.0)
Lung disease	106 (16.8)
Hepatic disease	75 (11.9)
Gastrointestinal diseases	50 (7.9)
Cancer	20 (3.2)
Neurological disorders	9 (1.4)
Obesity	6 (1.0)
ICU Scoring **	
APACHE $II_{CRRTinitiation}$	23 (10–36)**
SOFA $Score_{CRRT\ initiation}$	11[2–20]**
$VIS_{\ CRRT\ initiation}$	32 (0–120)**
RIFLE criteria at the time of CRRT initiation	
Injury	257 (40.8)
Failure	373 (59.2)
CRRT Indications	
Acute kidney injury	424 (67.3)
Metabolic Acidosis	373 (59.2)
Fluid overload	328 (52.1)
Hyperkalemia	39 (6.2)
CRRT Modality	
CVVH	9 (1.4)
CVVHD	257 (40.8)
CVVHDF	333 (52.9)
SCUF	30 (4.8)
Support during ICU Course	
Mechanical Ventilation	584 (92.7)
Intra-Aortic Balloon Pump (IABP)	55 (8.7)
Temporary Pacemaker Insertion (TPI)	13 (2.1)
Extracorporeal membrane oxygenation (ECMO)	6 (0.95)
No. of vasoactive agent	
≤2	233 (37.0)
>2	384 (61.0)
Other Outcomes, No. (%)	
>50 % inotropes reduction after CRRT initiation	459 (72.8)
Discharged against medical advice (DAMA)	285(45.2)
Death	130 (20.7)
Discharged	215 (34.1)

* Left Ventricular Dysfunction was defined as Ejection Fraction (EF) < 35 %
** The values are given as Median (Min-Max)

CPR Cardiopulmonary Resuscitation, ICU Intensive care unit; APACHE II Acute Physiology and Chronic Health Evaluation; SOFA Sequential Organ Failure Assessment; VIS Vasoactive Inotropic Score; CVVH Continuous Veno-Venous Hemofiltration; CVVHD Continuous Veno-Venous Hemodialysis; CVVHDF Continuous Veno-Venous Hemodiafiltration; SCUF Slow Continuous Ultra Filtration.

was the most common cause of AKI. Patients admitted to the CICU for non-cardiac procedures and diseases had chronic cardiac co-morbid conditions (Table 2). The majority of the patients had ≥2 comorbidities, and the median time interval from CICU admission to CRRT initiation was 3 days (0–63).

3.2. Outcomes after CRRT completion

Of 630 patients, 285 (45.2 %) did not complete desired course of treatment in CICU, and all of them had left the CICU against medical advice. Therefore, only 345 (54.8 %) patients were included for the outcome analysis. Overall duration of CRRT cycles was 30.6 ± 19.0 h. The median duration of first CRRT cycle to discharge was 3 days (0–54). 130 patients (37.7 %) died in the 7 days following CRRT initiation (Fig. 1). Out of this, 113 patients (86.9 %) died within 72 h following CRRT initiation, with 57 of those patients dying within 24 h.

In this study, patient's survival and mortality were compared based on number of CRRT cycles for 1, and 2 or more cycles (Fig. 2). In-hospital survival was 49.8 % (107 of 215) among patients undergoing 1 cycle of CRRT, and 83.7 % (108 of 129) among patients undergoing ≥ 2 cycles of CRRT. The mean VIS was higher among patients who died compared with survivors (44.5 ± 12.6 vs. 33.4 ± 15.5; $p < 0.001$). 7 out of 47 CPR survivors (pre-CRRT initiation) got discharged.

3.3. Multivariate logistic regression analysis

Multivariate regression analysis showed significant association of mortality with high VIS (OR: 1.041; 95 % CI, 1.018–1.064) and low MAP (OR: 0.915; 95 % CI, 0.890–0.941). Patients who received one cycle of CRRT showed a trend toward higher mortality (OR: 4.652; 95 % CI, 2.419–8.948) compared to patients who received more than one CRRT cycle (Table 3).

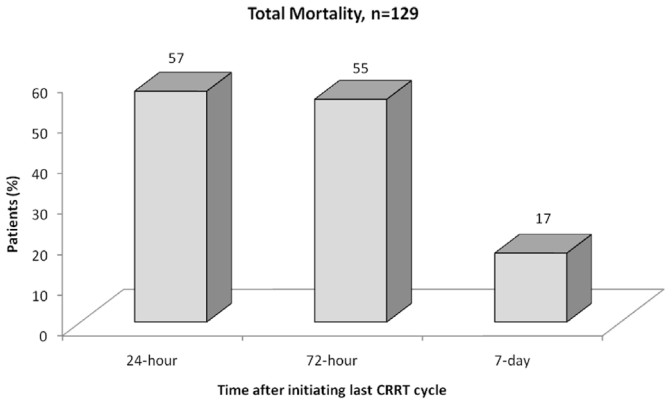

Fig. 1. Overall survival rate after CRRT.

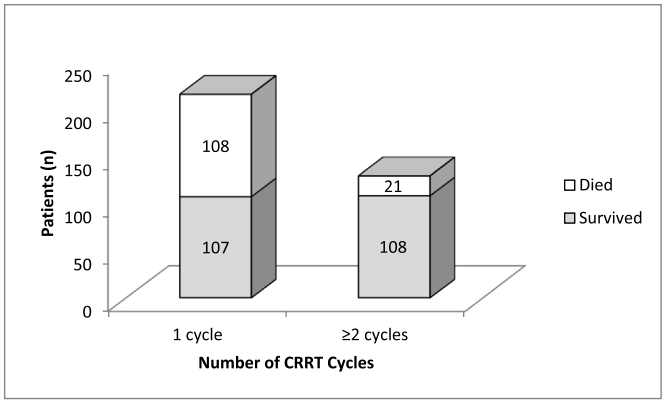

Fig. 2. CRRT cycles and its relation with patient's outcome.

4. Discussion

Acute kidney injury due to sepsis, cardiogenic shock, cardiorenal syndrome, low cardiac output, or ischemic injuries is common in cardiac patients (underwent surgery or having CVDs), often making them too unstable for intermittent hemodialysis.[12,13] CRRT has become the predominant mode of renal replacement therapy used in caring for critically ill patients with renal failure in medical ICUs worldwide.

In our center, 630 cardiac patients with AKI requiring ICU support such as mechanical ventilation, intra-aortic balloon pump (IABP), temporary pacemaker insertion (TPI), extracorporeal membrane oxygenation (ECMO) and vasoactive drugs were treated with CRRT over a period of 5-years. To the best of our knowledge, this is one of the largest contemporary data on CRRT in cardiac patients. For this population in a CICU, we report an overall mortality of 37.5 % (129 of 344 patients). Although this mortality rate does not consider the number of patients excluded from outcome analysis (285 of 630 [45.2 %]) owing to discharge against medical advice (DAMA), it is near the range reported in large studies in the literature. This experience demonstrated high mortality rate within 24-h following CRRT initiation, which decreased with the more number of CRRT cycles. The chances of survival were significantly lower in patients who received only one cycle of CRRT. Furthermore, high VIS as well as low MAP at CRRT initiation was significantly associated with increased risk of mortality in these patients.

Table 2
Principal diagnosis leading to AKI (n = 630).

Principal diagnosis	N (%)
Cardiovascular Disease (CVD)	
Acute coronary syndrome with cardiogenic shock	190 (30.2)
Acute heart failure (including biventricular failure and left ventricular failure)	108 (17.1)
Myocarditis (Viral/Toxic/Septic)	
Cardiomyopathy (Dilated and Ischemic)	25 (4.0)
	12 (1.9)
CV Procedures	
Cardiac (CABG, Valve surgery, combined procedures PTCA etc.)	167 (26.5)
Vascular (aortic root replacement, embolectomy, pulmonary endarterectomy, peripheral vascular stenting)	
	46 (7.3)
Non-cardiac procedures and diseases	
Non-cardiac procedures (Laprotomy, breast surgery, cesarian section, cholecystectomy, joint surgery, amputation etc)	57 (9.1)
Non-cardiovascular diseases	25 (4.0)

Table 3
Independent risk factors of mortality from multivariate logistic regression analysis.

Variables	Odd Ratio	95 % Confidence Interval	P-value
Age	1.015	0.993–1.038	0.189
Gender – F	1.388	0.747–2.579	0.300
Interval time from ICU admission to CRRT initiation	1.001	0.961–1.042	0.974
No. of CRRT cycle			
≥2 cycles[#]	–	–	–
1 cycle	4.652	2.419–8.948	<0.001
Type of primary diagnosis			
Non-Cardiovascular disease[#]	–	–	–
Cardiovascular procedure	1.079	0.212–5.500	0.927
Non-cardiovascular procedure	1.294	0.215–7.789	0.778
Cardiovascular disease	0.930	0.184–4.686	0.930
At CRRT initiation			
SOFA Score	1.024	0.894–1.172	0.734
APACHE Score	1.006	0.928–1.091	0.879
Mean arterial pressure	0.915	0.890–0.941	<0.001
Vasoactive-inotrope score	1.041	1.018–1.064	<0.001

[#] Reference value. As a matter of strategy, the least risky category is to be treated as reference category so that the OR calculated against any other category can be compared with the reference category.

The CICU in this study cares primarily for patients admitted to a hospital before or after cardiac surgery and a second group of patients admitted for treatment of CVDs. AKI is the well-recognized complication of critically ill cardiac patients and is associated with 28–90 % in-hospital mortality, especially in those requiring CRRT.[14] In 2012, a study from Korea on CRRT in septic AKI reported 47.4 % mortality rates for patients who had CRRT after 24 h.[15] In the past few years, several meta-analyses have been published, which show the survival advantage of early initiation (<24 h) of RRT and recommend it for patients with AKI.[16,17] However, the current study showed an overall mortality rate of 37.5 % with median time interval of 72 h for initiating CRRT after CICU admission.

Both APACHE II and SOFA score are the prognostic factors in AKI patients.[18] The patients with lower SOFA and APACHE scores have shown a significantly higher probability of survival at discharge from the hospital.[18] In our study, the SOFA and APACHE scores at CRRT initiation have not predicted mortality in CICU patients, as both the scores do not consider pre-existing cardiovascular disorder & myocardial dysfunction. However, the high VIS and low MAP at CRRT initiation in this study was found to be strongly associated with ICU mortality. This is in line with the previous studies predicting mortality rate in critically ill patients using the VIS score and MAP levels.[19,20] 44 % mortality has been reported by one of the study among patients with VIS <20 and 100 % in those with VIS ≥20. Levels of both VIS and MAP at CRRT initiation may be used as a predictor of mortality.

Studies from Alabama and Denmark have shown sepsis/septic shock as a major cause of AKI.[21,22] A retrospective observational clinical survey from Japan also found sepsis (32.8 %) or severe infectious disease as the main reason for initiating CRRT, followed by heart failure (28.6 %), surgery (21 %), hepatic failure (1.7 %) and renal failure (4.2 %).[23] In contrast, acute coronary syndrome with cardiogenic shock (30.2 %) was the major cause of AKI in our study. An Indian study also reported that out of 22 patients who were due for CRRT, sepsis was present in 68.2%, CKD in 36.4% and diabetes in 27.3%.[24] However, the independent role of non-cardiac complications in determining ICU mortality was also not confirmed by multivariate analysis (HR for survival 0.390, 95 % CI 0.081–1.866 p = 0.005).

Number of CRRT cycles significantly influenced the restoration of kidney function and survival of the patients.[10] Analysis given in Fig. 2 reveals that 84 % of the patients survived after receiving two to three and more than two CRRT cycles respectively. Our results in the cardiac patients suggest survival benefits in continuing CRRT beyond one cycle because majority of these patients were discharged despite the serious clinical situations (Fig. 2). Number of CRRT cycles may be used for risk classification and as a predictor of recovery.

This study has some limitations. First, this study was performed in a single-center and single cardiac intensive care unit and the data were retrospective. Second, in our center, critically ill patients were heterogeneous and were followed up and treated by different clinicians during the study period. Third, 45.2 % discontinued CRRT and left the CICU against medical advice and so were not included in outcome analysis. Fourth, study presents the data for short term follow-up (7 days) post CRRT.

5. Conclusions

This 5-year experience emphasizes the feasibility and utility of CRRT as a promising modality in improving outcomes (survival) in CICU patients with AKI. The need of mechanical ventilation, IABP support or complex surgeries prior to CRRT denotes the severity of illness. High inotropic support at CRRT initiation and low MAP was associated with poor outcome. Overall CRRT has improved the survival rate in CICU patients with AKI.

Funding

No funding was received for this study.

Declaration of competing interest

There was no potential conflict of interest.

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