ISSN: 1607-8322, e-ISSN: 2220-5799 **Anaesthesia, Pain & Intensive Care**
Vol 28(6); December 2024 DOI: 10.35975/apic.v28i6.2623

ORIGINAL RESEARCH **INTENSIVE CARE**

Continuous renal replacement therapy versus intermittent hemodialysis in intensive care patients: impact on mortality and length of stay

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ABSTRACT

Background: Almost 30-60% of patients treated in the intensive care unit (ICU) experience acute kidney injury (AKI) and approximately 5% of all ICU patients require renal replacement therapy. This study was conducted to determine the difference in length of stay (LOS) and mortality based on continuous renal replacement therapy (CRRT) compared to intermittent hemodialysis (IHD) in AKI patients in the ICU of a tertiary referral hospital in Indonesia.

Methodology: A cross-sectional study was conducted on all patients diagnosed with AKI who were treated in the ICU. The study data included age, sex, comorbidities, The Sequential Organ Failure Assessment (SOFA) score, Acute Physiologic and Chronic Health Evaluation (APACHE) score, treatment modality, LOS, and mortality.

Results: There were 18 patients in each of the IHD and CRRT groups. The number of study subjects with comorbidities was higher in the CRRT group (12 people (66.7%)), compared to the IHD group (11 people (61.1%)). The SOFA score in the IHD group was higher (6.06) than the CRRT group (5.44). APACHE score in the IHD group (18.50) differed greatly from the CRRT group (18.44).

Discussion: Studies have shown no difference in mortality with CRRT compared to IHD. Studies showed higher APACHE scores were associated with shorter LOS, reflecting higher mortality rates.

Conclusion: There is a significant difference in the LOS of AKI patients undergoing CRRT with IHD. However, no significant difference in the mortality rate between the CRRT and IHD groups was found.

Abbreviations: APACHE - Acute Physiologic and Chronic Health Evaluation; CRRT - continuous renal replacement therapy; ICU - intensive care unit; IHD - intermittent hemodialysis; LOS - length of stay;

Keywords: acute kidney injury, continuous renal replacement therapy, intermittent hemodialysis, length of stay, mortality rate

Citation: Kestriani ND, Pradian E, Alifahna MR. Continuous renal replacement therapy versus intermittent hemodialysis in intensive care patients: impact on mortality and length of stay. Anaesth. pain intensive care 2024;28(6):1061-1066; **DOI:** 10.35975/apic.v28i6.2623

Received: August 30, 2024; **Reviewed:** September 15, 2024; **Accepted:** September 15, 2024

1. INTRODUCTION

AKI is defined as a rapid decline in kidney function that develops over hours and days.[1] The global incidence of AKI is 21.6% with a mortality rate of 23.9%. Nearly 30-60% of patients admitted to the ICU experience AKI, with approximately 5% of all ICU patients requiring

renal replacement therapy (RRT). The percentage of mortality in AKI patients requiring RRT varies between 40% and 55%. AKI leads to increased duration of hospitalization, progression of chronic kidney disease (CKD), progression from CKD to end-stage kidney disease (ESKD), and decreased health-related quality of life.[2] Ricci et al mentioned the use of RRT techniques chosen by clinicians is CRRT at 91%, followed by IHD at 69% and slow low-efficiency dialysis (SLED) at 24%.[3]

There are two methods of RRT in patients in the ICU: IHD and CRRT. CRRT is used when hemodynamically unstable patients, critically ill patients with generalized brain oedema, acute brain injury, increased intracranial pressure, and AKI and/or multiorgan failure. In critically ill AKI patients with hyperkalemia, rhabdomyolysis, and intoxication, IHD is preferred.[4] Several studies have compared CRRT and IHD in the literature, but until now it is still controversial in providing better outcomes in patient survival as well as clinical and laboratory parameters.

CRRT is an extracorporeal blood purification therapy (performed with a device outside the body), which is a slow and continuous process. The CRRT process mimics the function of the kidneys in regulate water, electrolytes, and toxic metabolic products, by removing solutes and fluids in a slow but continuous manner. IHD is a conventional dialysis routine. Dialysis is intermittent which means 4-5 hours per dialysis with 2-3 times per week.5 In a meta-analysis of 21 studies by Nash et al., the superiority of groups over each other was not demonstrated in terms of 30-day mortality and duration of ICU stay.6,7 Yuanyuan et al. showed that CRRT has an advantage in hemodynamic stability compared to IHD but there was no significant difference in mortality between the two groups.8 Haiying Ma et al. and Klingele et al. compared the length of stay in the ICU in patients who performed CRRT and IHD in patients with acute renal failure.

The results showed that the CRRT group had a significantly better rate than the IHD group.9,10 Phongphithakchai et al. showed that improvements in laboratory parameters such as CRP values and creatinine clearance as well as clinical parameters such as urine output were found that the CRRT group had a better advantage compared to the IHD group, thus affecting the length of stay of patients in the ICU.11

Objective of Study

The purpose of this study is to compare the mortality rate and length of stay of acute kidney injury patients undergoing CRRT and IHD therapy.

2. METHODOLOGY

This study is an analytic observational study with a cross-sectional design. The data collection method was carried out retrospectively by searching medical record documents of patients admitted to the ICU of a tertiary hospital in Indonesia from 2021 to 2022. Inclusion criteria included patients diagnosed with AKI according to Kidney Disease Improving Global Outcomes (KDIGO) criteria who underwent CRRT and IHD with mean arterial pressure (MAP) >65 mmHg. Patients with CKD or incomplete medical records were excluded from the study.

The independent variables were AKI patients who received CRRT and IHD therapy (categorical-nominal). The dependent variables were the length of stay (numeric-ratio) and mortality (categorical-nominal). The study size was determined based on the formula for determining sample size for unpaired numerical categorical analytical research, by setting a confidence level of 95% and a power test of 80%, a minimum sample size of 18 people per group was obtained (including the possibility of sample exclusion of 10%).

Numeric data including age, SOFA score, APACHE score, and LOS were presented as mean, standard deviation, median, and range. Categorical data, namely gender (male/female), comorbidities (present/absent), RRT therapy modality (IHD/CRRT), and mortality (death/alive) were presented as frequencies and percentages. The significance criterion used was the $P \leq 0.05$ was considered significant. Shapiro Wilk normality test was performed on numerical data, and then unpaired t-test or Mann-Whitney test was used to analyze significance. Categorical data were analyzed with the chi-square test.

3. RESULTS

Two groups of 18 patients each were included, namely those undergoing CRRT and IHD. Subject characteristics in this study were described based on age, gender, comorbidities, SOFA score, and APACHE score (Table 1).

It can be concluded that there are no differences in characteristics at the beginning of the examination. This shows that both groups are homogeneous and suitable for further hypothesis testing except for the sex variable.

Mortality Comparison

The results of the statistical test showed that there was no statistically significant difference in proportion between the mortality rate in the IHD and CRRT groups (Table 2).

Length of Stay Comparison

Table 1: General characteristics of subjects

Variables	RRT Modality		P-value
	IHD (n = 18)	CRRT (n = 18)	
Age			**0.095**
Mean ± SD	61.11 ± 10.764	51.50 ± 21.200	
Median (min-max)	63.00 (41.00-80.00)	55.50 (21.00-85.00)	
Gender			**0.044***
Male	7 (38.9%)	13 (72.2%)	
Female	11 (61.1%)	5 (27.8%)	
Comorbidities			**0.729**
Present	11 (61.1%)	12 (66.7%)	
Absent	7 (38.9%)	6 (33.3%)	
SOFA score			**0.239**
Mean ± Std	6.06 ± 1.259	5.44 ± 1.756	
Median (min-max)	6.00 (4.00-8.00)	5.00 (1.00-9.00)	
APACHE score			**0.964**
Mean ± SD	18.50 ± 3.451	18.44 ± 3.854	
Median (min-max)	18.50 (11.00-24.00)	18.00 (12.00-25.00)	

Significance based on P < 0.05. RRT: renal replacement therapy; IHD: intermittent hemodialysis; CRRT: continuous renal replacement therapy; SOFA: Sequential Organ Failure Assessment; APACHE: Acute Physiologic and Chronic Health Evaluation

Table 2: Comparison of mortality rate

Variable	RRT Modality		P-value
	IHD (n = 18)	CRRT (n = 18)	
Mortality			**0.502**
Death	9 (50.0%)	7 (38.9%)	
Alive	9 (50.0%)	11 (61.1%)	

Significance based on P < 0.05. RRT: renal replacement therapy; IHD: intermittent hemodialysis; CRRT: continuous renal replacement therapy

Table 3: Comparison of LOS

Variable	RRT Modality		P-value
	IHD (n = 18)	CRRT (n = 18)	
Length of stay (LOS)			**0.001***
Mean ± SD	21.67 ± 17.918	9.50 ± 6.879	
Median (min-max)	17.50 (6.00-88.00)	7.00 (3.00-25.00)	

Significance based on P < 0.05. RRT: renal replacement therapy; IHD: intermittent hemodialysis; CRRT: continuous renal replacement therapy

The results of statistical tests in both groups showed that there was a significant mean difference between the LOS variables in the IHD and CRRT groups (Table 3).

4. DISCUSSION

The characteristics of the subjects in this study based on the variables of age, comorbidities, SOFA score, and APACHE score were not found to be significantly different (P > 0.05; Table 1) so the two groups were considered homogeneous and worthy of comparison.

Many studies have reported the relationship between age and survival rate in acute renal failure, due to poor compensatory abilities in the elderly and underlying conditions prone to complications such as diabetes, hypertension, coronary heart disease, and others. Elderly patients are also prone to complications such as severe infections, metabolic acidosis, and hyperkalemia. Acute renal failure in the elderly often requires symptomatic treatment according to the cause of the disease and the patient's condition, as well as improving the patient's electrolyte and acid-base balance.[13]

Other studies have shown no difference in in-hospital mortality between patients treated with CRRT and IHD and this is not related to patient characteristics such as sex, age, and history of previous surgical procedures. When patients were stratified by The Simplified Acute Physiology Score (SAPS) on admission to the ICU, overall mortality was directly related to the severity of the disease. The amount of organ failure did not predict mortality, but the presence of shock and catecholamine therapy were strong predictors of mortality. In the pre-defined subgroup analysis, the selection was based on reported evidence that the subgroup included patients with the most complicated complications,

showing the highest comorbidities and mortality.[14]

4.1. Comparison of mortality rate

The results showed that the mortality rate in the IHD group was 9 patients (50%). While in the CRRT group, the mortality rate was 7 patients (38.9%). The results of statistical analysis in both groups obtained a P = 0.502 means that it is not significant. So it can be concluded that there is no significant difference in mortality rates between the IHD and CRRT groups.

Many studies and randomized trials have shown no difference in survival outcomes with CRRT compared to IHD. Some studies showed hemodynamic stability with CRRT but did not appear to be better than the survival outcomes of IHD patients. The Mehta et al. trial showed higher ICU mortality in CRRT patients compared to IHD, 59.5% vs 41.5%. However, this result was limited to the imbalance of baseline values between the two groups because patients who underwent CRRT had more severe disease severity. Therefore, there was no difference between the two groups in renal recovery. Another study showed that CRRT did not differ from IHD in mortality rates.[4]

Elderly patients at risk of AKI usually have complex comorbidities and age-related abnormalities in renal structure and function. Physiological changes in elderly patients with AKI can be a high risk of hemodynamic instability and are likely to receive CRRT therapy. The results of the study also showed that the outcome was not affected by age and sex, whereas some previous studies have shown an association between age and male sex with outcome. Acute respiratory failure requiring mechanical ventilation is also significantly associated with increased mortality. In this study, the majority of critical patients in the ICU with acute renal failure who received RRT therapy already had multiple organ failure. The underlying condition for multiple organ failure is severe sepsis or sepsis shock. In addition to requiring renal support, most patients required mechanical ventilation and vasopressors, which explains the high mortality rate in these patients. The randomization method in the CRRT or IHD study showed no independent association with mortality. The difference observed between CRRT and IHD may be due to comorbidities and disease severity, rather than dialysis modality.[19]

Mortality in critically ill patients is most likely influenced by several factors unrelated to dialysis. It has previously been shown that the do-not-resuscitate (DNR) status in the ICU affects the level of care provided and the outcome. Mehta et al. found that 7.1% of CRRT patients and 1.2% of I do not resuscitate IHD patients were given DNR before nephrology consultation. This study also aimed to detect a 27% difference (50 vs.70%) in ICU mortality rates. This approach failed to account for the reduction in mortality in the group receiving trial-related IHD care. Had the number of studies been larger, the ability to detect differences between modalities would have been greater, and it is less likely that the studies would have suffered from unbalanced randomization.[14]

4.2. Comparison of Length of Stay (LOS)

The IHD group had a longer average LOS than the CRRT group, namely 21.67 ± 17.918 days with a median value of 17.50 days and a range of 6-88 days. While in the CRRT group, the average LOS was 9.50 ± 6.879 days with a median value of 7 days and a range of 3-88 days. median of 7 days and a range of 3-25 days. Statistical analysis was carried out on both groups with the results of a p-value of 0.001 (P < 0.05) which means statistically significant. This is in line with research conducted in 2016 in China on AKI patients showing the results of LOS in the ICU in CRRT patients being shorter than IHD with a value of 9.54 ± 3.39 and 13.42 ± 3.89 and the results of statistical analysis mean a value of P < 0.001.[25]

One of the main concerns in AKI patients is renal recovery. The presence of hypotensive episodes decreases GFR, causes ischemia in the kidney and delays the recovery time of the renal function. IHD therapy causes high episodes of hypotension and in theory can slow down the recovery process, causing patients to need dialysis for a long time and increasing mortality. Whereas CRRT with its continuous principle (24 hours/day) in fluid replacement, has better results in maintaining homeostasis in unstable patients to improve the recovery of kidney function and reduce mortality. Compared to IHD, CRRT is more efficient in patients with AKI caused by sepsis in removing excess fluid and metabolic waste, reducing proinflammatory cytokine levels, maintaining homeostasis, reducing side effects on the cardiovascular system and significantly improving patient prognosis. CRRT therapy also reduces the need for organ support devices and the duration of ICU stay.[4]

The theoretical advantages of CRRT over IHD are slower fluid removal resulting in better hemodynamic stability and better control of fluid balance, slower solute concentration control, avoidance of large fluctuations and fluid displacement (including decreased risk of worsening cerebral edema), high flexibility (allowing adaptation of treatment to patient needs at any time), and the ability to perform treatment with a relatively simple and easy-to-use machine (allowing ICU nurses to monitor treatment). Disadvantages include the need for immobilization, continuous use of anticoagulants, risk of hypothermia and in some places higher cost.[22]

Conversely, the main advantages of IHD over CRRT are rapid toxin removal and a limited treatment period that allows downtime for diagnostic and therapeutic interventions. IHD may therefore be the therapy of choice in patients who require immediate removal of small solutes such as severe hyperkalemia, some cases of poisoning, and tumor lysis syndrome. Hybrid treatments such as SLED may have the same advantages as IHD and CRRT without having the disadvantages of both.[23]

Due to its continuous nature and high filtration rate, the CRRT method can better control azotemia and fluid overload associated with nutritional support, but may also result in the loss of water-soluble and low molecular weight substances, including nutrients. In CRRT, 0.2 grams of amino acids are lost per litre due to filtration, with a total daily loss of 10-15 grams of amino acids. An additional 5-10 grams of protein is lost per day depending on the type of therapy and dialyzer membrane. Nutritional support should account for losses associated with CRRT, including PD by providing a maximum of 1.7 grams of amino acids/kg/d.[23]

5. LIMITATIONS

This study is a single-center study, and the generalizability of the results may be limited including the limited number of research subjects in the CRRT group in the ICU. The small number of subjects cannot represent the situation and cannot be generalized to a wider population regarding differences in mortality and LOS in the CRRT and IHD groups in the ICU. Another limitation is that the subject characteristics in this study consisted of only five characteristics (age, sex, comorbidities, SOFA score, and APACHE score) while there are still many other characteristics that can be studied that affect differences in mortality and LOS in the CRRT and IHD patients.

6. CONCLUSION

There was a significant difference in LOS between the CRRT and IHD groups with a lower LOS time in the CRRT group compared to IHD. There was no significant difference in mortality rates between CRRT and IHD groups with a lower number of mortalities in the CRRT group compared to IHD. Based on this study, it can be recommended that CRRT has better final results on LOS in ICU compared to IHD.

7. FUTURE DIRECTION

This study is expected to provide clinical considerations for the selection of therapy between continuous renal replacement therapy and intermittent hemodialysis for acute kidney injury patients in the ICU. The results of this study are expected to provide scientific information regarding the comparison of the effectiveness of continuous renal replacement therapy with intermittent hemodialysis on LOS and mortality in patients with acute kidney injury in the ICU.

8. Acknowledgement

This research was supported by Dr. Hasan Sadikin General Hospital Bandung, Indonesia and Faculty of Medicine, Padjadjaran University, Indonesia.

9. Author Contribution

NDK: Supervision, Resources, Writing-Review and Editing

EP: Validation, Supervision, Writing-Review and Editing

MRA: Conceptualization, Methodology, Software, Formal Analysis, Investigation, Data Curation, Writing-Original Draft, Writing-Review and Editing, Visualization, Project Administration, Funding Acquisition

10. Conflict of Interest

The authors have no conflicts of interest to declare.

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