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Continuous renal replacement therapy in intensive care: When is the optimal timing?

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Abstract

Aim: Acute kidney injury is one of the most widespread problems in critical patients in intensive care. It leads to severe morbidity and mortality. Although the indications for emergency dialysis are well known, the timing for initiating continuous renal replacement therapy (CRRT) in the critical patient is still unclear. The purpose of this study was to evaluate the effect on mortality of the timing of CRRT in patients follow-up in intensive care and receiving renal replacement.

Materials and Methods: Patients' medical records were reviewed and analyzed retrospectively. Aged over 18, with no previously known chronic kidney disease, and receiving only CRRT was included in this study who were treated in intensive care over a one-year period. The patients were divided into two groups, an early group consisting of KDIGO stages 1 and 2, and a late group consisting of KDIGO stage 3. These were than evaluated in terms of 28-day mortality.

Results: Forty-eight patients with a mean age of 65.94±19.61 years were included in the study. Twenty-eight (58.3%) patients were men. Cardiovascular diseases were the most frequent diagnoses, in16 (33.3%) patients and comorbidity was detected in 32 (66.7%). SOFA, blood urea nitrogen, creatinine, and procalcitonin values differed between the groups, but no difference was observed in 28-day mortality.

Conclusion: The study results showed that early or late application of CRRT has no positive effect on survival, but further randomized studies on the subject are now needed.

Introduction

Acute kidney injury (AKI) is a frequently encountered entity in intensive care units (ICUs) and leads to significant morbidity and mortality. The incidence in ICUs is 5-7%, and 70% may require renal replacement therapy (RRT) [1]. This was first described in 1861, and began being employed in kidney failure. RRT indications are quite clear in chronic kidney failure, but the situation in AKI is much less certain. Although RRT is frequently used in ICUs, the time of commencement, dosage, and modality are still controversial [2, 3]. The purpose of this study was to evaluate the effect on mortality of the timing of continuous renal replacement therapy (CRRT) in patients follow-up in intensive care and receiving renal replacement.

Materials and Methods

Adult patients aged over 18 admitted to our ICU within the previous year (January 2022 to January 2023) and receiving renal replacement were included in this retrospective study. Approval for the study was granted by the Inonu University Health Sciences Non-Interventional Clinical Research Ethical Committee (2023/4890). The patients' demographic data, ICU admission diagnoses, and co-morbidities were recorded retrospectively from patient's electronic medical data. APACHE II and SOFA scores, the day on which RRT was initiated, and lengths of stay in the ICU were also noted. Serum blood urea nitrogen (BUN), creatinine, albumin, total and direct bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactatedehydrogenase (LDH), sodium (Na), potassium (K), white blood cell count (WBC), hemoglobin, platelet, C-reactive protein (CRP), procalcitonin (PCT), and brain natriureticpeptide (Pro-BNP) values and pH in arterial blood, bicarbonate (HCO_3) and lactate levels immediately prior to RRT were recorded in standard data sheets. Patients receiving CRRT for less than 24 hours, with previous diagnoses of chronic kidney disease (CKD), or receiving intermittent hemodialysis (HD), either alone or together with CRRT, were excluded from the study.

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Table 1. A comparison of the groups' clinical and laboratory mean±standard deviation and median (minimum-maximum) values and p values.

Variables	Mean±SD	Median (Min-Max)	Group		p
			E (n=21) (Mean±SD)	L (n=27) (Mean±SD)	
Age (years)	65.94±19.61	71(18-93)	69(40-93)	72(18-92)	0.967*
RRT timing (days)	7.35±10.06	3(1-61)	3(1-61)	3(1-26)	0.621*
APACHE II	24.73±10.37	22.5(8-52)	19(10-52)	28(8-44)	0.067*
SOFA	6.31±3.12	6(1-14)	5.05±2.36	7.3±3.33	**0.012****
Length of admission (days)	22.73±20.34	17.5(3-110)	17(3-75)	20(4-110)	0.567*
BUN (mg/dL)	74.44±39.74	66.5(17-200)	52(17-195)	71(38-200)	**0.028***
Creatinine (mg/dL)	3.21±1.44	3.1(1.2-8.3)	1.9(1.2-3)	3.8(3.1-8.3)	**<0.001***
Albumin (g/dL)	2.58±0.57	2.5(1.2-4.3)	2.67±0.7	2.51±0.45	0.339**
Total bilirubin (mg/dL)	3.37±13.34	0.875(0.2-93)	1(0.2-93)	0.8(0.2-11.3)	0.435*
Direct bilirubin (mg/dL)	0.71±1.2	0.215(0.04-7.28)	0.3(0.07-2.4)	0.19(0.04-7.28)	0.582*
AST (U/L)	864.85±1970.83	138(12-9030)	120(16-6065)	185(12-9030)	0.473*
ALT (U/L)	384.79±988.77	62.5(4-4838)	63(11-2456)	62(4-4838)	0.884*
LDH (U/L)	1,587.71±2,722.6	670.5(4.2-13,321)	473(4.2-6,723)	762(176-13,321)	0.132*
Na^+ (mmol/L)	456.31±2,171.	141.5(125-15,190)	147(125-15,190)	139(125-167)	0.086*
K^+ (mmol/L)	89 4.92±1.51	4.78(3-10.3)	4.57(3-10.3)	5(3-8.8)	0.411*
WBC (10^3/μL)	16,260.23±8,361.1	15,090(141-40,960)	15,010(141-34170)	15,130(4,900-40,960)	0.811*
Hemoglobin (g/dL)	13.98±15.05	10.4(1.4-84)	9.7(1.4-84)	12.1(7.4-84)	0.084*
Platelet (10^3/μL)	164.01±107.52	147(10-437)	176.59±119.85	154.22±98.08	0.481**
INR	1.95±1.37	1.34(1-7.25)	1.23(1-7.25)	1.36(1-6.1)	0.602*
aPTT (sec)	41.36±21.31	35.45(17.6-121.2)	32.9(17.6-121.2)	36.9(21.6-79.3)	0.216*
Ph	7.15±0.44	7.2(4.3-7.45)	7.2(4.3-7.45)	7.2(6.96-7.42)	0.731*
HCO_3(mmol/L)	17.2±6.4	17.4(3.46-37)	18.12±8.25	16.49±4.51	0.421**
Lactate (mmol/L)	4.8±4.95	2.8(0.5-26)	3.2(0.5-14.3)	2.5(0.7-26)	0.739*
CRP mg/dL)	14.64±9.94	14.5(0.3-38.3)	14.55(0.3-38.3)	13.8(1-37)	0.824**
PCT (ng/mL)	11.88±22.29	2.35(0.02-100)	1.2(0.02-29.3)	3.9(0.1-100)	**0.022***
Pro-BNP (pg/mL)	13,642.61±12422.86	8,708.5(377-35000)	4,992(377-30,183)	11,765.5(1,461-35,000)	0.247*

SD: Standard deviation; Min: Minimum; Max: Maximum.Data are expressed as mean ± standard deviation or median (minimum–maximum) depending on normality of distribution; SD: Standard Deviation; *: Mann Whitney U test, **: Independent samples t-test, RRT: Renal replacement therapy, BUN: Blood urea nitrogen, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, LDH: lactate dehydrogenase, Na: Sodium, K: Potassium, WBC: White blood cell, INR: International normalized ratio, aPTT: HCO3: Bicarbonate, CRP: C-reactive protein, PCT: procalcitonin, BNP: Brain natriuretic peptide.

Diagnosis and staging of AKI were performed in line with the KDIGO guidelines [4]. Patients were divided into two groups, those with stages 1 and 2 being classified as the early group (E), and stage 3 as the late group (L), and these were subsequently compared. The primary endpoint of the study was 28-day mortality.

Statistical analysis

Qualitative data were summarized as numbers (percentages). The normality of distribution of quantitative data was assessed using the Shapiro-Wilk test. Non-normally distributed quantitative data were summarized as median (minimum-maximum) values and normally distributed data as mean± standard deviation. The Mann-Whitney U test, independent samples t-test, Pearson's chi-square test, the Yates-corrected chi-square test, and Fisher's exact chi-square test were applied as appropriate during statistical analyses. p values <0.05 were regarded as statistically significant. All analyses were performed on IBM SPSS Statistics for Windows version 26.0 (New York, USA).

Results

Ninety-nine patients aged over 18 underwent renal replacement between January 2022 and January 2023. CKD was detected in 14 patients, intermittent HD in 21, both CRRT and intermittent HD in four, and hospitalization for less than 24 h in 12, and these were excluded from the study. Forty-eight patients receiving CRRT alone were thus enrolled. Twenty-eight (58.3%) of the 48 patients were men, and the mean age of the entire patient group was 65.94±19.61 years. Evaluation of diagnoses on admission to the ICU showed that the largest proportion were admitted due to cardiovascular system diseases (n=16, 33.3%), followed by trauma (n=11, 22.9%), and infection (n=8, 16.7%). Co-morbidity was detected in 32 (66.7%) patients, the three most common co-morbidity are hypertension (n=19, 39.6%), diabetes mellitus (n=16, 33.3%), and coronary artery disease (n=10, 20.8%), respectively. Thirty-six (75%) patients had received vasoactive or inotropic therapy. Eleven patients (22.9%) had pulmonary edema before CRRT. The 28-day mortality rate was 58.3%. Analysis of the early and late CRRT initiation

groups revealed no significant differences in terms of age, diagnosis, comorbidity, inotropic/vasoactive therapy, pulmonary edema, or mortality (p>0.05). In terms of laboratory and clinical values, significant differences were found between the groups' SOFA (p=0.012), BUN (0.028), creatinine (<0.001), and procalcitonin (p=0.022) values, but none between the other values. Table 1 shows the patients' clinical and laboratory values and a comparison there of together with p values.

Discussion

Early use of CRRT caused no decrease in 28-day mortality compared to late treatment in this retrospective study of critical patients with AKI. Length of stay in the ICU was also no shorter.

The optimal time for initiating CRRT in critical patients with AKI is still unclear. Early initiation of CRRT may be advantageous for the perspective of toxin elimination, achievement of acid-base balance, and control of hypervolemia. However, it creates additional risks for patients whose kidney functions are capable of spontaneous recovery. The ELAIN study randomized critically ill patients with AKI into an early group, KDIGO stage 2, started on RRT within 8 h and a late group, stage 3, started on RRT after 12 h or not receiving any RRT. The authors concluded that early RRT improved 90-day survival, and that lengths of hospital stay were also shorter in those patients [5]. Sugahara et al. reported that the initiation of early RRT in the treatment of AKI developing following coronarybypass had a positive impact in survival rates [6]. Demirkilic et al. investigated the timing of RRT in patients with AKI developing following coronary bypass and reported that it improved the likelihood of survival if AKI is detected and treated early [7]. Bouman et al. [8] evaluated the effect on survival and kidney function of high-volume CRRT initiated early in critical patients in intensive careand concluded that this had no improving effect on 28-day mortality and kidney function. However, the patients in the early disease group received CRRT late in that study, which represents a limitation. In the present study, the patients were diagnosed with AKI and staged on the basis of KDIGO criteria. Patients with stages 1 and 2 were included as the early group and those with stage 3 as the late group. No improvement was observed in 28-day mortality between early or late initiation of RRT.

Creatinine and BUN values were significantly higher in the late stage disease group. This is an expected finding since the patients were subjected to KDIGO staging. In addition, the patients differed in terms of SOFA scores, but no difference was observed in terms of APACHE II scoring. InPan et al.'s [9] meta-analysis investigating the effect of early RRT on survival in critical patients, early initiation of RRT had no effect on survival, although at subgroup analysis they found that a SOFA score of 11 or higher was associated with permanent kidney injury. A study examining the timing of CRRT in patients with septic shock and AKI reported a correlation between SOFA and APACHE IV scores at the commencement of CRRT and improvement in organ function, and that the change in SOFA scores 48 h after CRRT was correlated with improved organ function [10]. Although mortality rates were similar in the two groups in the present study, initial SOFA scores were higher in the late group.

PCT is an inflammatory factor with no hormone activity and a good marker of endotoxemia [11]. It provides useful information in the differentiation of septic patients and in prognosis [12]. In their CRRT study of patients with severe acute pancreatitis, Gao et al. [13] reported a severe decrease in PCT and other inflammatory parameters following the application of CRRT. In the present study, initial PCT levels were significantly higher in the late group and also PCT levels did not decrease in spite of CRRT. We thought that, although the mortality rates were similar, this difference is due to patients in the late group having a more severe clinical manifestation and greater organ failure. SOFA sores were also higher among the patients in that group.

Limitations

The principle limitation of this study is in its retrospective nature. In addition, improvement in SOFA scores was not evaluated, and the time of RRT was unclear.

Conclusion

Early initiation of CRRT identified no decrease in survival in this study. Further randomized studies are needed to clarify the effects of early or late RRT.

Financial disclosures

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Conflict of interest

The author declare that they have no competing interest.

Ethical approval

Before the study, ethical approval was obtained from the Inonu University Health Sciences NonInterventional Clinical Research Ethics Committee (No: 2023/4890).

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