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Comparison of hemodynamic indices of dialysis patients in continuous renal replacement therapy and intermittent renal replacement therapy methods with ultrasonic cardiac output monitor in intensive care unit

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ABSTRACT

Introduction: Acute kidney injury (AKI) is a common complication in the intensive care unit (ICU) and is independently associated with end-stage renal disease and higher mortality in the ICU. There are different methods to supporting kidney function in critically ill patients. The renal replacement therapy (RRT) can be conducted continuously, intermittently, or in combination.

Objectives: The purpose of our study is to investigate the hemodynamic indices of dialysis patients in the ICU by two methods high flow continuous renal replacement therapy (CRRT) and intermittently renal replacement therapy (IRRT) of ultrasonic cardiac output monitor (USCOM).

Patients and Methods: In this study conducted at Sina hospital, patients requiring dialysis hospitalized to the ICU were studied. Around 48 patients benefited from rapid CRRT or IRRT in the opinion of a specialist. Basic patient information was recorded. To check hemodynamic parameters during dialysis, USCOM was carried out to check corrected flow time value (FTc) parameters, systemic vascular resistance (SVR) and cardiac output. Results were compared between the IRRT and CRRT groups.

Results: This study was conducted on 48 patients who were candidates for dialysis. Patients were divided into high flow CRRT and IRRT groups based on clinical indications. In CRRT group, 19 patients (79.2%) and in the IRRT group, 20 patients (83.3%) were male (P=0.712). Their mean age was 68.70 ± 8.25 years in the CRRT group and 68.58 ± 7.19 years in the IRRT group. All patients had cardiac output monitored using USCOM or ultrasound. The mean Sequential Organ Failure Assessment (SOFA) score in the CRRT group was 7 and in the IRRT group was 6, with no significant difference among them. FTc value variable or modified flow time in the carotid artery, cardiac output, cardiac index, SVR variable and mean arterial pressure in in the two groups at four evaluated times (before dialysis, 15 minutes later, one hour later and end of dialysis) from the study the difference were not statistically significant.

Conclusion: Although previos studies have recommended CRRT, our study showed significant difference may not be existed between IRRT and CRRT.

Original

Implication for health policy/practice/research/medical education:
In our study, continuous renal replacement therapy and renal replacement therapy with an ultrasonic cardiac output monitor (USCOM) had a uniform effect on dialysis patients. For this reason, it is better to make the necessary policies for using each of these two methods according to the conditions of the patient, hospital and insurance.

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Introduction

Acute kidney injury (AKI) is a common complication in the intensive care unit (ICU) and is independently associated with end-stage renal disease and increased ICU mortality (1). Despite significant advances in health care management, AKI requiring renal replacement therapy (RRT) in the ICU has been associated with increasing in-hospital mortality by up to 50% (2,3). Therefore, this problem is one of the most important and costly complications for patients in ICU (1).

There are various ways to support renal function in critically ill patients. RRT can be used in a continuous, intermittent, or combined methods (4). Very serious ill patients suffering from AKI or acute renal failure along with multiple organ failure, need to take large amounts of fluids in the form of nutrition, medicine and blood products (5). This condition often results in fluid volume desturbance and upsets the patient's acid/base status. Initially, such patients were treated with the conventional RRT technique, which was intermittently renal replacement therapy (IRRT) (4).

In the 1980s, Kramer et al, continuous renal replacement therapy (CRRT) was conducted as an alternative to IRRT, which allows 24-hour blood purification (6). CRRT used a simple pumpless continuous arteriovenous hemofiltration technique; however, the idea was inefficient and recent developments in this technique performed a blood pump known as continuous veno-venous hemofiltration (CVVH). CRRT is a continuous technique that removes a liquid extrafiltration solution from a large hole and replaces it with an alternative liquid. The diffusion method was also used in CRRT by creating an additional pump in the dialysis machine (7).

Continuous renal replacement therapy provides better urea control, electrolyte balance, maintenance of acid/base status and higher hemodynamic stability compared to traditional IRRT. CRRT includes slow continuous ultrafiltration, CVVH, CVVHD (continuous venous-venous hemodialysis) and CVVHDF (continuous venous-venous hemodiafiltration) (8). CRRT dialysis is performed over a long-period of time (average 19 hours) and over several consecutive days and also the removal of solutes and toxins has made it the preferred method of treatment, superior in several studies (9).

Despite the above and the existence of clinical guidelines for AKI, treatment protocols and outcomes are very different from one center to another (7). The debate surrounding the choice of RRT for critically ill patients with AKI is ongoing and there are no comprehensive data to conclusively support a specific clinical approach (8). One of the most important concerns regarding the use of RRT in AKI patients is the risk of hemodynamic instability during treatment and its effect on morbidity and mortality, especially when intermittent RRT methods are used (10). A few studies have previously measured the effects of RRT on hemodynamic indices; however the results are still controversial (10).

Objectives

We decided to measure the hemodynamic indices of dialysis patients in the ICU by CRRT and IRRT using ultrasonic cardiac output monitor (USCOM).

Patients and Methods

Study design

This comparative and cross-sectional study was conducted in the dialysis department of Sina hospital affiliated to Tehran University of Medical Sciences. The study sample size for each study group was 22 patients, considering the probability of dropping a sample was 10%, 24 patients were calculated for each group for a total of 48 patients.

In this study, patients requiring dialysis hospitalized in ICU were examined. Patients on routine dialysis and CRRT were divided into two groups after checking for entry and exit criteria. In the CRRT group, blood flow of 150-200 mL/min or more, dialysis flow rate 2500 ml/h and ultrafiltration flow 200-300 rpm (12-15 liters per hour) were taken into account. In the IRRT group, the blood flow was set at 150-200 mL/min or more and dialysis flow was set at 500 cc/min. To maintain maximum hemodynamic stability, high (150 mmol/L) and low (35) sodium concentrations were used in the dialysate. In addition, the potassium, sodium, calcium, phosphorus, blood urea nitrogen and arterial blood gas (ABG) levels were checked at the beginning of dialysis, one hour later and two hours later.

The patient's baseline information as well as the blood pressure, heart rate and body temperature of the patients were recorded before starting the dialysis. To check hemodynamic parameters during dialysis, USCOM was conducted to check corrected flow time value (FTc) parameters, systemic vascular resistance (SVR) and cardiac output. Side effects of patients such as hypotension, bleeding, thrombocytopenia, hypoglycemia, hypophosphatemia, hypothermia, arrhythmia, air embolism or catheter infection have been reported. Results were compared between the IRRT and CRRT groups. It should be noted that the consumables are provided by the importing company, but the company made no profit or loss in this study.

Continuous renal replacement therapy is usually conducted in a longer period than IRRT. To reduce bias, the time required to perform both studies was the same and the CRRT was carried out in a shorter time frame. In addition, the effectiveness of CRRT is higher if the dialysis rate is high (11) Therefore, in this study, we used high flow CRRT (CVVHD) for a short-period of time.

Statistical analysis

Data analysis was conducted using SPSS version 25 software. To compare the results in separate age groups or type of specialization, the results were compared on

the basis of t-test or chi-squared test by variable type. Correlation was calculated between the different variables of the study. Statistical significance level $P>0.05$ was considered.

Data entry criteria included patients who were candidates for hemodialysis, patients referred for dialysis and patients who consented to participate in the study. Data exclusion criteria included patient dissatisfaction and patient leaving the hospital with personal consent, pregnant patients, age below 18 years, platelets below 30 000/μL, severe coagulation disorders, central vessel thrombus and subclavian and jugular thrombosis.

Results

This study was carried out on 48 patients who were candidates for dialysis. Patients were divided into CRRT and IRRT groups based on clinical indications. As shown in Table 1, in the CRRT group, 19 patients (79.2%) and in the IRRT group, 20 patients (83.3%) were male ($P=0.712$). Their mean age was 68.70 ± 8.25 years in the CRRT group and 68.58 ± 7.19 years in the IRRT group.

The patient's body mass index (BMI) showed its mean as 26.58 ± 4.07 kg/m^2 in the CRRT group and 24.99 ± 4.63 kg/m^2 in the IRRT group. It was also observed that in the CRRT group, 12 patients (50%) were in the overweight range (25.1-30) and in the IRRT group 11 patients (45.8%) were in the normal range (19.5-25). Data analysis with chi-square test showed no significant difference ($P=0.318$).

The results of the patient's cardiac history showed that 20 patients (83.3%) in the CRRT group and 17 patients (70.8%) in the IRRT group had a positive history of heart disease. Data analysis showed, no statistically significant difference between the two groups in terms of heart disease ($P=0.303$).

All patients had cardiac output monitoring using USCOM or ultrasound. The mean Sequential Organ Failure Assessment (SOFA) score in the CRRT group was 7 and in the IRRT group was 6, while no significant difference was observed.

In addition, Table 2 shows that the FTc variable was not significantly different in the two groups at the four time points evaluated (before dialysis, 15 minutes later, one hour later and the end of dialysis).

There were no significant differences in cardiac output before dialysis, during dialysis and at the end of dialysis in the two groups.

Cardiac index or cardiac index, SVR index or SVR and mean arterial pressure were not significantly different between the two groups during the four study periods.

The results show that the change in ultrasonic variables in each group is significant. Of note, the observed changes are not frequent decreases or increases; however, the overall changes in these variables are significant.

The administration of serum to patients in two groups and at four different time points was studied. Results showed that none of the participants in both groups had received fluids before dialysis. About 15 minutes after dialysis starting, seven patients received fluids, of which three were in the IRRT group and four were in the CRRT group. Then one hour after dialysis starting, only two patients received 100 cc of fluid, both in the IRRT group. Finally, at the end of dialysis, only three patients (two patients in the CRRT group and one patient in the IRRT group) received fluids.

During dialysis, norepinephrine was administered in case of blood pressure drop in patients. In the CRRT group,

Table 1. Baseline characteristics and prevalence of CRRT and IRRT (n = 48)

	Overall, No. (%)	Prevalence of CRRT and IRRT		*P* value
		CRRT (mL/kg/h) No. (%)	IRRT (mL/kg/h) No. (%)	
Gender				
Men	39 (81.6)	19 (79.2)	20 (83.3)	0.712
Women	9 (18.4)	5 (20.8)	4 (16.7)	
Age (y)				
<60	3 (6.25)	1 (4.17)	2 (8.33)	0.067
60-69	30 (62.5)	16 (66.7)	14 (58.3)	
70-79	11 (22.9)	4 (16.7)	7 (29.2)	
≥ 80	4 (8.33)	3 (12.5)	1 (4.17)	
BMI (kg/m^2)				
<19.5	3 (6.25)	1 (4.17)	2 (8.33)	0.318
19.6-25	17 (35.4)	6 (25.0)	11 (45.8)	
25.1-30	21 (43.8)	12 (50.0)	9 (37.5)	
≥30	7 (14.6)	5 (20.8)	2 (8.33)	
CVD				
Yes	37 (77.1)	20 (83.3)	17 (70.8)	0.303
No	11 (22.9)	4 (16.7)	7 (29.2)	

CRRT, Continuous renal replacement therapy; IRRT, Intermittently renal replacement therapy; BMI, Body mass index; CVD, Cardiovascular disease.

Table 2. Hemodynamic parameters for CRRT and IRRT and between and in group difference evaluation

	CRRT (mL/kg/h)		IRRT (mL/kg/h)		Between groups difference
	Mean	SD	Mean	SD	
FTC					
Before dialyze	409.08	56.24	394.62	58.66	0.388
15 min before dialyze	273.62	46.14	267.2	45.58	0.630
One hour after dialyze	299.62	42.09	297.25	54.19	0.866
After dialyze	326.4	38.85	315.7	39.73	0.350
In group difference	<0.001		<0.001		
Co					
Before dialyze	3.33	1.14	3.88	1.23	0.117
15 min before dialyze	3.80	1.37	4.08	1.16	0.439
One hour after dialyze	4.07	1.16	4.52	1.26	0.202
After dialyze	5.73	1.13	6.07	1.11	0.299
In group difference	<0.001		<0.001		
CI					
Before dialyze	1.28	0.42	1.46	0.53	0.197
15 min before dialyze	1.63	0.48	1.74	0.62	0.483
One hour after dialyze	1.98	0.47	2.23	0.53	0.088
After dialyze	2.52	0.73	2.52	0.53	0.998
In group difference	<0.001		<0.001		
CVR					
Before dialyze	2457.9	819.6	2180.2	601.1	0.187
15 min before dialyze	3495.6	1100.4	3070.2	875.2	0.145
One hour after dialyze	3174.8	994.1	2741.6	785.2	0.101
After dialyze	2849.4	895.2	2545.1	706.5	0.198
In group difference	<0.001		<0.001		
MAP					
Before dialyze	89.79	22.04	85.12	16.58	0.412
15 min before dialyze	80.08	14.53	78.16	12.43	0.626
One hour after dialyze	83.37	12.61	81.25	9.77	0.517
After dialyze	87.54	13.8	84.04	10.11	0.322
In group difference	<0.001		<0.001		
Norepinephrine					
Before dialyze	29	18.53	22.5	6.21	0.257
15 min before dialyze	23	15.56	24.16	7.68	0.811
One hour after dialyze	25.33	16.84	24.16	11.64	0.849
After dialyze	14	4.7	13.75	4.33	0.888
In group difference	<0.001		<0.001		

FTC, Flow time corrected; CO, Cardiac output; CI, Cardiac index; CVR, Cardiovascular risk; MAP; Mean arterial pressur.

15 patients (62.5%) and 12 patients (50%) in the IRRT group received norepinephrine during dialysis; however, this difference was not statistically significant ($P=0.383$). In addition, the results showed a slight difference in the amount of norepinephrine administration in both groups in four study periods and no significant difference was observed in terms of the amount of norepinephrine used.

Electrolytes including potassium, phosphorus, and calcium and also blood urea nitrogen were checked in all patients. The tests were checked at three times before dialysis, one hour after and after dialysis. Finally, it was only seen that the amount of potassium in the patients after the completion of CRRT was significantly lower than the IRRT group and no significant difference was observed in other times and other electrolytes (Figure 1).

Discussion

Most patients with acute renal failure need RRT. The two main methods of conducting RRT in maintaining renal function in AKI are CRRT and IRRT.

This study was performed on CRRT patients with high dose and high velocity, therefore patients with high volume and high velocity should undergo dialysis within four hours. High-dose (CRRT) and low-dose (IRRT) dialysis did not show a significant difference. The study by Ricci et al (12), reported a mean dose of CRRT of 35 mL/

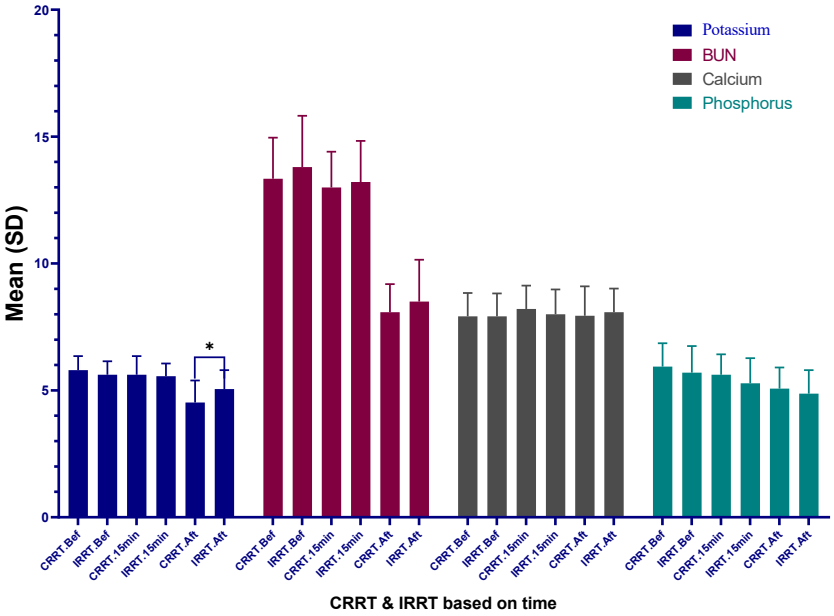

Figure 1. Electrolytes of patients in two CRRT and IRRT groups.

kg/h and a high dose of 45 mL/kg/h could significantly reduce mortality compared with a low-dose of 20 mL/kg/h. However, Tolwani et al (13) reported , no significant relationship between the effect of CRRT dose (20 and 35 mL/kg/h) on renal function and patient mortality (14). Furthermore they showed that a dose of 20 and 30 mL/kg/h of CRRT treatment had no significant effect on 60-day mortality, duration of treatment and renal function recovery. On the other hand, Li et al found that high-dose and low-dose dialysis produce similar results in terms of mortality and duration of ICU hospitalization in patients with AKI (15).

The superiority of IRRT and CRRT varied between studies based on different patient aspects. For example, in terms of hemodynamic status, patients with fluid overload are more likely to benefit from CRRT than IRRT (9). The hemodynamic benefit of CRRT is due to hypothermia, which can lead to improved blood pressure and venous return. On the other hand, a high rate of fluid clearance in IRRT (more than 500 mL/min) can lead to hemodynamic instability. In the study by Augustin et al (16), a significant difference in terms of hemodynamic superiority in patients receiving CRRT compared with the IRRT group was detected. However, in another study conducted by Uehlinger and colleagues prospectively, they did not show any hemodynamic superiority in these two methods (17). In this study, no superiority of hemodynamics was observed in the above two methods.

Regarding solute removal, studies have shown that the speed of IRRT to solute removal is very high. This condition leads to significant removal of the drug from the patient's serum and can cause a decrease in the effectiveness of the drug as well as the lack of a therapeutic levels of the drug in the serum. A high speed of removing electrolytes can lead to electrolyte imbalance (18). CRRT conducts a slow and continuous removal of water and solutes from plasma (17-34 mL/min) and is considered as an appropriate option for the management of hemodynamically unstable patients (19,20). In the present study, no superiority in terms of electrolyte and solute conversion in the CRRT method compared to the IRRT method was detected. However, in acute life-threatening conditions such as AKI with hyperkalemia, rhabdomyolysis and in poisonings, rapid elimination of solutes is critical, where IRRT is the main RRT option (21).

The study by Schneider et al, showed a better ability to improve renal function in patients with unstable status and AKI with CRRT (22). Nevertheless, not all studies demonstrate the superiority of CRRT in this field (16,18,20). In this study, ultrasound examination did not show any hemodynamic superiority of the two existing methods. Mehta et al (20), reported that among the patients who undergoing RRT, a percentage of patients became dependent on dialysis at the time of discharge, which was assessed as 14% in the CRRT group and 7% in the IRRT group. Other studies, including the study of Augustine et al (16), and Uehlinger et al (17) also stated similar results, which reported no relationship between dialysis dependence and RRT method.

In AKI patients, it is important to improve the condition and function of the kidneys. With each episode of low-blood pressure, glomerular filtration rate decreases, which causes ischemic damage to the kidney and delays the recovery of renal function (16). IRRT hemodialysis causes more episodes of hypertension and therefore, theoretically, may slow down the recovery process of the

kidney. Thereby, patients require chronic dialysis and this condition can lead to an increase in the death rate and dies. Hence, hemodialysis by CRRT method, due to fluid exchange (24 hours a day), better maintains blood pressure in unstable patients and prevents it from falling, as a result, theoretically it could lead to improved kidney function and reduced mortality in patients (23).

Similar to our study, some studies have demonstrated that, when comparing IRRT and CRRT methods, no significant difference in survival and prognosis of patients was seen. Few studies have shown more favorable hemodynamic stability in CRRT, but therefore survival is not different from IRRT (8,24). Meanwhile Mehta et al (20), reported that the mortality rate in the ICU was 59.5% in patients who undergoing CRRT and 41.5% in patients who undergoing IRRT. No significant difference was observed between the IRRT and CRRT groups regarding the improvement in renal function.

Dialysis by CRRT method is carried out in patients with renal failure along with liver failure, intracranial trauma, brain edema, lithium toxicity, since hemodynamic stability is of great importance in these patients (25). Compared with IRRT, CRRT may be more effective in removing excess water and metabolic disorders in patients with AKI caused by sepsis and can reduce the level of pro-inflammatory cytokines, maintain homeostasis and also reduce the harmful effects on the cardiovascular system. Reduce and significantly improve the prognosis. It also shortens the time needed to support the organs and the length of stay in the ICU. On the other hand, IRRT is used more commonly used in patients at risk of bleeding, acute hyperkalemia and rhabdomyolysis (25).

Conclusion

The results of current study showed that despite the previos studies which recommended CRRT, or in some studies which showed IRRT is a more suitable option for rapid removal of vital solutes, our study highly significant results have not been observed for the difference between IRRT and CRRT. We absereved the two methods may give found similar effects in patient care.

Limitations of the study

This study was conducted on a limited number of patient and requiers further assessment by larger studies.

Authors' contribution

Conceptualization: AVA, AN and ZA.
Methodology: AVA, AN, ZA and HSH.
Validation: AN, ZA and HSH,
Formal analysis: AN, ZA and HSH.
Investigation: AN, ZA and HSH.
Resources: AVA.
Data curation: AVA.
Writing–original draft preparation: AVA.
Writing–review and editing: AVA.
Visualization: AN and AVA.
Supervision: AN.
Project administration: AVA.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research conducted in accordance with the tenets of the Declaration of Helsinki. The Ethics Committee of Tehran University of Medical Sciences approved this study (IR.TUMS.SINAHOSPITAL.REC.1398.008). Accordingly, written informed consent was taken from all participants before any intervention. Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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