Continuous renal replacement therapy in Iran; current practice, indications and outcomes in hemodynamically unstable patients

Amirhesam Alirezaei1*, Nilofar Massoudi2, Elham Zare3, Nima Taheri3

1Urology and Nephrology Research Center, Shahid Modarres Hospital, Shahid-Beheshti University of Medical Sciences, Tehran, Iran
2Critical Care Quality Improvement Research Center at Shahid Modarres Hospital, Department of Anaesthesiology, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3Department of Internal Medicine, Shahid-Beheshti University of Medical Sciences, Tehran, Iran

Corresponding author: Amirhesam alirezaei, Email: amirhesam124@gmail.com and Aalirezaei@sbmu.ac.ir

Introduction
Acute kidney injury (AKI) is a dire clinical condition associated with severe consequences and a high rate of mortality (1). The overall incidence of AKI has been reported as 4% to 60% (2). According to the reports of the Iranian Ministry of Health and Medical Education, more than 32000 patients undergo dialysis in Iran (3,4). Continuous renal replacement therapy (CRRT) is the gold standard for management of hemodynamically unstable patients requiring renal replacement therapy (RRT). This approach is increasingly used in intensive care units (ICUs) and cardiovascular care units (CCUs), especially in patients with sepsis (5-10). In comparison with intermittent hemodialysis (IHD), CRRT delivers a slow-acting removal of the waste materials while retaining the hemodynamic stability and intravascular volume (11, 10). In studies investigating the clinical implications of CRRT, better outcomes, as well as higher survival and residual renal function have been reported in long-term follow-up (12-16). Also, CRRT has been associated with reduced risk of mortality in AKI patients after surgery (17, 18). However, some studies reported similar outcomes for CRRT and IHD.

The choice of dialysis method largely depends on the level of knowledge and skill of the staff, as well as the available facilities in the treatment center. Using CRRT as a viable RRT has increased over the past two decades (19-21). A recent study has suggested the CRRT as the...
preferred RRT in AKI patients (24-29). In patients with liver disease and intracranial hypertension, CRRT has provided better control on the fluid balance than IHD (30, 31). Nevertheless, the use of CRRT should be limited only to patients with significant hemodynamic instability (24). CRRT imposes a relatively high cost on the health care system. Furthermore, patients need to remain immobilized during the procedure which is a disadvantage (22,23). Hemodynamic instability is a major complication that may lead to early termination of IHD and increased likelihood of morbidity and mortality in patients undergoing dialysis (2,25,26). Different dialysis methods represent variable therapeutic costs, complications, and limitations.

**Objectives**

There is limited understanding on the characteristics and clinical outcomes of Iranian patients undergoing CRRT. Also, there is no adequate information on the CRRT practice in Iran. In this study, we investigated the characteristics and outcomes of Iranian patients undergoing CRRT.

**Patients and Methods**

**Data collection**

This retrospective study was carried out on the patients undergoing CRRT at the Shahid- Modarres hospital of Tehran (2016 to 2017). The medical archives were reviewed to record the diagnoses, underlying organ involvements, gender, age, admission ward, serum creatinine level at admission, relevant comorbidities, indication for CRRT, duration of CRRT, urine output, history of surgery and finally mortality rate.

**Ethical approval**

The tenets of the Declaration of Helsinki and its later amendments were followed. The objectives of the study were explained to all the participants before obtaining written informed consent from them. This study was the result of a thesis for acquiring M.D. degree of Nima Taheri from Shahid-Beheshti University of Medical Sciences (Thesis # 34).

**Statistical analysis**

The frequency, mean, and standard deviation were used as descriptive statistics. The student t test and chi-square test were used to determine any significant difference in the means of continuous variables and any significant association between the categorical variables respectively. Multivariate analysis was used to determine any significant relationship between the studied variables and mortality. The statistical significance level was designated as P value < 0.05. The statistical procedures were conducted in SPSS, version 21.

**Results**

The mean age of the patients was 65.4 ± 13.16 years old. Eight patients (13.79%) had < 50 years old. Males and females constituted 36 (62.1%) and 22 (37.9%) subjects respectively. The most common underlying diseases were diabetes (23, 39.6%), hypertension (15, 25.8%) and chronic kidney disease (9, 15.5%). The baseline characteristics of the patients and the underlying diseases have been summarized in Table 1. The majority of the patients were admitted to the ICU (23, 39.65%), emergency department (12, 20.7%) and CCU (9, 15.5%). Overall, 20 (34.5%) patients had been admitted for surgery.

The most common underlying conditions at the time of admission were sepsis (10, 17.24%), malignancy (9, 15.5%), cardiovascular surgery (9, 15.5%), and the loss of consciousness (7, 12.06%) (Figure 1). The main indications for CRRT were unstable hemodynamics (46, 79.3%) following by high serum potassium (3, 5.2%), fluid overload (3, 5.2%) and a combination of these indications (6, 10.3%). The continuous venovenous hemodialysis (CVVHD) and continuous veno-venous hemofiltration methods had been used in 72.4% and 27.6% of the patients respectively.

The mean of CRRT dosage and duration were 23.75±2.03 mL/kg/h and 1073 ± 203.6 minutes respectively. The mean serum creatinine level at admission in the hospital was 3.7±2.7 mg/dL. The mean values of serum urea and urine output before initiation of CRRT were 176±47.8 mg/dL and 191±138.1 cc/24 h respectively.

The in-hospital mortality rate was 60.3% (35 patients) at follow up. On the other hand, 23 patients (39.7%) were discharged. Regression multivariate analysis revealed that serum urea level before initiation of CRRT was associated with increased risk of in-hospital mortality. Also, the presence of more than one comorbidity decreased the survival rate in the patients.

**Discussion**

CRRT is a multidimensional procedure with wide range variations on the clinical practice in different global and

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No.</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>36</td>
<td>62.1%</td>
</tr>
<tr>
<td>Female</td>
<td>22</td>
<td>37.9%</td>
</tr>
<tr>
<td>Past medical history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung disease (asthma and COPD)</td>
<td>5</td>
<td>9.61%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>15</td>
<td>28.8%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>23</td>
<td>44.2%</td>
</tr>
<tr>
<td>Malignancy and metastasis</td>
<td>11</td>
<td>21.1%</td>
</tr>
<tr>
<td>Heart failure</td>
<td>8</td>
<td>15.3%</td>
</tr>
<tr>
<td>Renal disease</td>
<td>16</td>
<td>30.7%</td>
</tr>
<tr>
<td>Liver disease</td>
<td>1</td>
<td>1.9%</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>2</td>
<td>3.84%</td>
</tr>
<tr>
<td>Morbid obesity</td>
<td>2</td>
<td>3.84%</td>
</tr>
</tbody>
</table>

Table 1. Demographic characteristics and clinical outcomes in 58 patients undergoing CRRT
Continuous renal replacement therapy

Regional centers (19-23). The application of CRRT in Iran is hindered because of limited facilities, high costs, inadequate experience of health providers, and finally the lack of sufficient data on the patient’s specifications. Therefore, we here aimed to address the characteristics and clinical outcomes of Iranian patients undergoing CRRT. Providing such information can help optimizing resources to effectively implement CRRT in indicated patients. In this study, we examined 58 patients undergoing CRRT in one of the largest nephrology clinics in Iran (2016 to 2017).

Globally, RRT is mainly indicated in patients with sepsis and postoperative complications (7-9, 26). In a research conducted in China, sepsis was the most common indication of CRRT in 43% of patients admitted to ICUs. In other studies, sepsis has been reported to be responsible for 32% to 56% of CRRT procedures worldwide (34-36). Compared with other studies, sepsis accounted for a lower ratio of patients undergoing CRRT (17.24%) in the present report. This may be partly explainable by the lack of facilities for CRRT in the emergency ward (as a major unit for the referral of sepsis patients) in Iran.

Based on the clinical records, the most common underlying diseases leading to RRT in the current study were diabetes (36.9%) and hypertension (25.8%). These results were consistent with the reports of other studies indicating hypertension and diabetes as the underlying causes of RRT in 36.4% to 62.1% of the cases (11,32-34). In some multicenter studies in children, malignancy has been reported as the most common primary diagnosis in patients requiring RRT (11). Overall, special attention must be dedicated to diabetes and hypertension as the main comorbidities leading to RRT.

Other common reasons for RRT were volume overload (67.2%) and tumor lysis syndrome (18.8%) in another study. In other studies, low blood pressure, volume overload and electrolytic disturbances were the most common indications for RRT (37,40-42). Consistent with the mentioned studies, hemodynamic instability also constituted the most common indication for CRRT in the present report. Contrary to the previous studies, however, fluid overload constituted a lower percentage of our patients indicated for CRRT.

At one-year follow-up, the mortality rate was 60.3% in our patients. The mortality rate in patients undergoing CRRT has been reported as 32. 59% to 58% in previous studies (32-34). In addition to the in-hospital mortality, recent studies have reported 15% to 20% mortality rate at two-month follow-up which is somehow in contrast to our results. The mortality rate in patients undergoing CRRT varies between different centers. The factors affecting the mortality rate in these patients include the staff’s experience, timing of dialysis initiation, and the presence of comorbidities. Nonetheless, the global rate of in-hospital mortality has been similar to our study (11,34,37).

Previous studies have asserted a direct correlation between pre-admission creatinine level and mortality rate in patients undergoing CRRT (38,39). However, neither pre-dialysis nor post-dialysis serum creatinine levels were significantly associated with mortality rate in this study. Moreover, we encountered no significant relationship between mortality rate and residual urine output, both pre-dialysis or peri-dialysis.

In pediatrics, the highest rate of recovery following CRRT has been observed in patients with renal insufficiency due to drug toxicity and tumor lysis syndrome (32). Future studies should address the impacts of underlying comorbidities on the survival and outcomes of patients undergoing CRRT. A meta-analysis found no differences in the renal recovery period, volume overload disturbance, mortality rate, and hospitalization period comparing the different methods of CRRT. In the current study, CVVHD was the main method applied in 72.4% of the cases. In other studies, CVVHD had been used in 48-82% of pediatric patients. Nevertheless, recent studies

http://www.jnephropharmacology.com
have indicated a shift toward using CVVHDF as the main CRRT strategy (11,13,32,33), but our CRRT machine does not support this mode of treatment. As the CVVHDF mode of CRRT was not supported by our instrument, neither of our patients underwent this method.

The choice of RRT largely depends on the access to resources, cost-effectiveness, clinical outcomes and the staff’s experience (22,20,37,40,44). The clinical effectiveness of each RRT approach should be further investigated by performing randomized clinical trials on patients with different clinical conditions (37,42).

**Conclusion**

As the CRRT procedure is currently unavailable in many centers in in Iran, our results may not be generalizable to all Iranian medical centers. Finally, due to the nature of the disease and the patients being at high-risk of mortality, it was not applicable to compare the clinical outcomes of CRRT with other methods such as CRRT. In future studies, it is recommended to address variables such as the length of the admission to follow-up (as an indicator for dialysis initiation), as well as the interval between the disease diagnosis and initiation and completion of CRRT. These should be addressed as factors influencing the clinical outcomes of patients in future studies. We here provided a comprehensive view on the characteristics of patients indicated for CRRT at the Shahid-Modarres hospital of Tehran. The patients’ specifications were similar to those in the global reports. It is essential to develop a standard practice for implementing CRRT in Iran.

**Limitations of the study**

Our study has some limitations. The studied population was relatively small and heterogeneous. This was because some patients were excluded from the study due to incomplete clinical records limiting the number of eligible patients. Nevertheless, the heterogeneity rendered the study as a comprehensive research encompassing various etiologies of renal insufficiency.

**Authors’ contribution**

AA designed the study. NT performed the statistical analysis. EZ and NM drafted the manuscript. All authors approved the final version.

**Conflicts of interest**

The authors declared no competing interests.

**Ethical considerations**

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

**Funding/Support**

None.

**References**


9. Morabito S, Pistolesi V, Gibelli L, Pierucci A. A favore delle CRRT: le terapie sostitutive renali continue rimarranno le metodiche prevalenti nelle unita’ di terapia intensiva[Continuous renal replacement therapies (CRRT) will remain the most widely adopted dialysis modality in the critically ill], G Ital Nefrol. 2009;26:13-21


24. Kashani K, Mehta RL. We restrict CRRT to only the most hemodynamically unstable patients. Semin Dial. 2016; 29:268-71. doi: 10.1111/sdi.12507


10.5935/0101-2800.20140067.
43. de Souza Oliveira MA, Dos Santos TOC, Monte JCM. The impact of continuous renal replacement therapy on renal outcomes in dialysis-requiring acute kidney injury may be related to the baseline kidney function. BMC Nephrol. 2017;18:150. doi: 10.1186/s12882-017-0564-z

Copyright © 2019 The Author(s); Published by Published by Society of Diabetic Nephropathy Prevention. This is an open-access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.