Curative effects of early continuous renal replacement therapy in cardiac failure combined with acute kidney injury

Liang Bai, Li Luo, Weicheng Gao, Chenfeng Bu, Jianfeng Huang

1Department of Urology, The First Affiliated Hospital/School of Clinical Medicine of Guangdong Pharmaceutical University, Guangzhou, Guangdong, China; 2Department of Urology, People’s Hospital of Liannan Yao Autonomous County, Qingyuan, Guangdong, China

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Abstract: Objective: This study was designed to investigate the effects of early continuous renal replacement therapy in the treatment of cardiac failure combined with acute kidney injury. Methods: Seventy-three cardiac failure patients combined with acute kidney injury admitted to our hospital from November 2017 to February 2019 were enrolled for retrospective analysis. Using random number table, they were divided into the observation group and the control group, of which 36 cases in the control group were given conventional treatment + late continuous renal replacement therapy and 37 cases in the observation group were given conventional treatment + early continuous renal replacement therapy. Physiological indicators, Acute Physiology and Chronic Health Evaluation (APACHE) II scores, haemodynamics, length of ICU stay and mortality rate in both groups were recorded. Results: (1) There was no significant difference in the levels of mean arterial pressure (MAP) and heart rate (HR) between the two groups (P>0.05); (2) APACHE II scores obtained at 1, 2 and 3 weeks after treatment in the observation group were lower than those in the control group (P<0.05); (3) Levels of serum creatinine (Scr), brain natriuretic peptide (BNP) and C-reactive protein (CRP) after treatment in the observation group were lower than those in the control group (P<0.05); (4) The length of ICU stay and hospital stay in the observation group were shorter than those in the control group, so was the mortality rate during hospitalization (P<0.05); and (5) Scores in quality of life questionnaire and kidney disease quality of life-short form (KDQOL-SF) assessed at 1, 2, and 3 months after discharge in the observation group were higher than those in the control group (P<0.05). Conclusion: Early continuous renal replacement therapy in the treatment of cardiac failure combined with acute kidney injury can significantly improve patients’ physical conditions and haemodynamics, shorten the length of ICU stay, and lower the occurrence of death, indicating promising application in the future.

Keywords: Cardiac failure, acute kidney injury, early continuous renal replacement therapy, treatment

Introduction

Cardiac failure, as a kind of cardiovascular disease, has a high incidence in the elderly population. With the increase of ageing in recent years, the incidence of cardiac failure has increased clinically, resulting in more deaths [1]. Clinical symptoms of cardiac failure include confined activity, dyspnea, and fluid retention. Studies have found that in the development and progression of cardiac failure, humoral factors, inflammation and neurohormones obviously play important roles [2].

Acute kidney injury refers to a clinical syndrome caused by rapid decline in kidney function that could occur in patients who previously had nephrosis or chronic kidney diseases [3]. Clinical cardiac failure is often combined with renal injury which interacts with the cardiac failure, and if the cardiac and renal injuries or multiple organ failures are continuously aggravated, the mortality rate will increases [4]. Continuous renal replacement therapy allows the substitution of poisonous substance and waste released into the body with substitution fluid, a carrier for clearance, and supplies the body with required energy to ensure a balanced body environment [5]. In case of ineffective drug treatment, continuous renal replacement therapy can be used to ultrafilter the excessive water content from the body, thus to significant-
Early renal replacement therapy can significantly reduce cardiac load and improve cardiac function [6].

In the previous studies, continuous renal replacement therapy was often used in the treatment of renal injury [7, 8]. Few researches have addressed the treatment of renal injury combined with cardiac failure. This study was designed to specifically investigate the effects of early continuous renal replacement therapy in patients with cardiac failure combined with acute kidney injury in order to provide evidence to the clinic treatments of such patients.

**Material and methods**

**Material**

Seventy-three cardiac failure patients combined with acute kidney injury admitted to our hospital from November 2017 to February 2019 were enrolled and divided into the observation group (n=37) and the control group (n=36) according to random number table. Patients in the control group had an age range of 42-67 years old, height 157-178 cm, body weight 52-75 kg, and scores 12-27 points by Acute Physiology and Chronic Health Evaluation Scoring System (APACHE II), while those in the observation group, had an age range of 40-66 years old, height 160-180 cm, body weight 51-74 kg, and scores 13-28 points by APACHE II.

1. **Inclusion criteria**: patient who was over 18 years old; who met the diagnostic criteria for cardiac failure [9] and acute kidney injury [10]; who had cardiac functional grading as III-IV; and who had (or his/her guardian had) signed and submitted the informed consent, were enrolled. The study was approved by the hospital ethics committee.

2. **Exclusion criteria**: patient who had severe arrhythmia, severe valvular heart disease, acute myocardial infarction, acute stroke, and malignant tumor; who had end-stage chronic kidney disease; who had cognitive disorder; who had mental disorders; or who faced a quite high mortality risk, were excluded from the study.

**Methods**

Both groups of patients received conventional treatments. After admitted to ICU, they were given oxygen inhalation and drugs including myocardial nutrition, diuretic, medicines for myocardial circulation improvement, cardiotonic steroids, and nitrate esters, to correct acidoasis and maintain water electrolyte balance. Patients with abnormal haemodynamics were managed with vasoreactive agents such as dobutamine, dopamine, noradrenaline, etc.; patients with eating disorder, risk of aspiration, or in coma were treated with nasointestinal tube indwelling; patients with abnormal digestive function were supported with parenteral nutrition; and those with respiratory failure were assisted with oral trachea cannula respiration. Real-time monitoring of blood gas management was assured so as to adjust the respirator parameters reasonably.

Continuous renal replacement therapy: double lumen dialysis catheter was placed into the body through the femoral vein to create vascular access where the admission passage was the right femoral vein. At the right groin, surface 15 cm surrounded away from the puncture point was disinfected. Later, apertured drapes were unfolded and 2% lidocaine was used for subcutaneous local anesthesia. After femoral vein puncture with the selected puncture needle, the guide wire was imbedded while the puncture needle was pulled out. Along with the guide wire, double lumen dialysis catheter was placed into the femoral vein. The guide wire was pulled out. In acute dialysis and extracorporeal blood treatment machine that have been prepared and connected with a polysulfone hemofilter, the mode of continuous vein-vein blood hemofiltration was applied. With the specific substitution fluid, the blood flow was controlled at 120-150 ml/min and pre-dilution at 2-4 L/h. Net excess was determined based on the liquid in-flow and out-flow, controlling to about 4000 ml every time. Anticoagulant use depended on the patient’s conditions. In case of no significant bleeding or coagulation disorder, unfractionated heparin was allowed. In light of the real-time monitoring of partial thromboplastin time and the results, dose of heparin used was adjusted properly. If patient had significant bleeding and coagulation disorder, in vitro anticoagulation by citric acid was applied. The treatment cycle was 12-24 h and sustained for 4 times subjected to the patient’s conditions.

Patients in the observation group underwent early continuous renal replacement therapy,
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and those in the control group received late continuous renal replacement therapy. Treatment indications for control group included: at least 72 h of persistent oliguria, hyperkalemia, and 200 umol/L serum creatinine (Scr). Treatment indications for observation group included: oliguria within 48 h, no hyperkalemia and serum creatinine not exceeding 200 umol/L. For both groups of patients, continuous monitoring of oxyhemoglobin saturation, heart rate and blood pressure during the treatment was guaranteed to prevent adverse reactions.

**Observed indicators**

(1) Hemodynamic indices: Before and 1 week after treatment, respectively, mean arterial pressure (MAP) and heart rate (HR) of the two groups were measured.

(2) APACHE II score [11]: The scale includes acute physiology, age, and chronic health evaluation scoring. The maximum value is 71 points. Scoring below 15 suggests non-severe, otherwise it indicates severe condition. Before and 1, 2 and 3 weeks after treatment, evaluations were performed.

(3) Physiological indicators: Before and 1 week after treatment, both groups of patients received detections of Scr, brain natriuretic peptide (BNP) and serum C-reactive protein (CRP) by automatic biochemical analyser, radioimmunoassay, and immunoturbidimetry, separately.

(4) The length of ICU stay, hospital stay and mortality during hospitalization were recorded.

(5) Quality of life: China cardiovascular patient quality of life assessment questionnaire (CCQQ) [12] and the kidney disease quality of life-short form (KDQOL-SF) instrument [13] were used to evaluate patients’ quality of life on admission, and 1, 2, and 3 months after discharge. CCQQ includes 6 items of evaluation: general psychosocial function, activity of daily living, state of illness, medical conditions, working conditions, and exercise tolerance. For a total of 24 questions corresponding to the total points of 154, higher score indicates the better quality of life. KDQOL-SF is categorized as SF-36 and End-Stage Renal Disease (ESRD-targeted Areas), containing 79 items related to general health and kidney disease such as sickness impact, sexual function, emotional health and function, social function, pain, physiological function, role-physical, burden of disease, vitality, working conditions, and satisfactory degree, and others among the 19 specific fields. For the total points of 100, higher score indicates the better quality of life.

**Statistics**

SPSS22.0 was applied for statistical analysis. Measurement data were expressed as mean ± standard deviation where comparison of results between groups was based on independent-samples T test, and comparison of results within groups was analyzed by paired samples t test. Enumeration data were expressed as [n (%)] where comparison of the results was based on X² test. P<0.05 indicated statistically significant difference.

**Results**

**Comparison of general information in both groups**

No significant difference was found between the observation group and the control group in gender distribution, average age, average height, average weight, and average APACHE II score (P>0.05) (Table 1).

**Comparison of hemodynamic indices in both groups**

Before treatment, the levels of MAP in the observation group and the control group were 80.49±12.34 mmHg and 81.62±13.26 mmHg, respectively, while after treatment, those in the observation group and the control group were 95.39±20.16 mmHg and 93.35±22.18 mmHg, respectively. Similarly, before treatment, the levels of HR in the observation group and the control group were 119.78±30.25 times/min and 117.52±32.29 times/min, respectively; whilst after treatment, those in the observation group and the control group were 90.16±12.25 times/min and 93.36±13.57 times/min, respectively. Obviously, there was no significant difference between the groups in MAP and HR before treatment (P>0.05). MAP levels increased, while HR levels decreased, in both groups after treatment. The differences were significant compared with those before treatment within the group (P<0.05). In comparison between the groups, MAP and HR levels after
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treatment did not show statistical significance ($P$>0.05) (Figure 1).

Comparison of APACHE II scores in both groups

Before treatment, APACHE II score in the observation group and the control group was 20.18±5.27 points and 20.34±5.49 points, respectively; while 1 week after treatment, that in the observation group and the control group was 17.12±2.13 points and 19.32±1.88 points, respectively; 2 weeks after treatment, that in the observation group and the control group was 16.38±1.86 points and 18.64±1.73 points, respectively; and 3 weeks after treatment, that in the observation group and the control group was 15.24±1.89 points and 17.85±1.24 points, respectively. There was no significant difference between the groups in APACHE II scores before treatment were not significant ($P$>0.05). 1, 2, and 3 weeks after treatment, APACHE II scores of the observation group were significantly lower than those of the control group ($P$<0.05 for all). &Comparison between the two groups of the same temporal point indicates $P$<0.05.

Comparison of physiological indicators in both groups

No significant difference was observed between the groups in terms of Scr, BNP and CRP before treatment ($P$>0.05). After treatment, the levels of Scr, BNP and CRP in both groups decreased
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Table 2. Levels of Scr, BNP and CRP in both groups (X ± s)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Timing</th>
<th>Scr (μmol/L)</th>
<th>BNP (pg/mL)</th>
<th>CRP (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>167.58±44.49</td>
<td>563.38±150.28</td>
<td>28.37±9.56</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>117.52±31.23*</td>
<td>182.59±53.61*</td>
<td>10.82±3.49*</td>
</tr>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>172.89±88.64</td>
<td>581.72±174.69</td>
<td>29.54±10.13</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>136.28±34.68*</td>
<td>239.27±67.58*</td>
<td>17.31±5.62*</td>
</tr>
<tr>
<td>t</td>
<td>2.430</td>
<td>3.976</td>
<td>5.945</td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>0.018</td>
<td>0.000</td>
<td>0.000</td>
<td></td>
</tr>
</tbody>
</table>

Note: t and P are statistical values from variables after treatment. As compared with those before treatment, P*<0.05.

Table 3. Length of ICU and hospital stays and mortality during hospitalization in both groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>Length of ICU stay (X ± s, d)</th>
<th>Length of hospital stay (X ± s, d)</th>
<th>Mortality during hospitalization [n (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>37</td>
<td>10.58±1.46</td>
<td>17.85±2.38</td>
<td>5 (13.51)</td>
</tr>
<tr>
<td>Control</td>
<td>36</td>
<td>15.27±3.66</td>
<td>21.45±4.82</td>
<td>12 (33.33)</td>
</tr>
<tr>
<td>t/χ²</td>
<td></td>
<td>7.227</td>
<td>4.063</td>
<td>4.012</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>0.000</td>
<td>0.000</td>
<td>0.045</td>
</tr>
</tbody>
</table>

Comparison of CCQQ scores in both groups

CCQQ score on admission of the observation group and the control group was 70.15±5.68 and 71.56±6.32, respectively, 1 month after discharge, CCQQ score of the observation group and the control group was 86.69±8.75 and 79.82±6.67, respectively; 2 months after discharge, the score in the observation group and control group was 108.52±10.34 and 95.68±8.37, respectively; 3 months after discharge, the score in the observation group and control group was 113.63±12.2 and 101.23±10.34, respectively. The comparison between the groups of CCQQ scores on admission did not show statistical significance (P>0.05). For both groups, scores at 1, 2, and 3 months after discharge were higher than that on admission (P<0.05). CCQQ scores at 1, 2, and 3 months after discharge in the observation group were significantly higher than those in the control group (P<0.05) (Figure 3).

Comparison of KDQOL-SF scores in both groups

KDQOL-SF score on admission of the observation group and the control group was 48.75±6.29 and 46.35±6.33, respectively, 1 month after discharge, KDQOL-SF score of the observation group and the control group was 57.62±7.22 and 50.46±6.92, respectively; 2 months after discharge, the score was 68.95±8.23 and 60.33±7.05, respectively; 3 months after discharge, the score was 69.83±8.22 and 63.35±7.55, respectively. The comparison between the groups of KDQOL-SF scores on admission did not show statistical significance (P>0.05). For both groups, scores at 1, 2, and 3 months after discharge were higher than that on admission (P<0.05). KDQOL-SF scores at 1, 2, and 3 months after discharge in the observation group were significantly higher than those in the control group (P<0.05) (Figure 4).

Discussions

Continuous blood purification technology has been more widely used in clinical practice for the treatment of various critical illnesses. It serves as not only a replacement therapy for acute and chronic kidney injury, but also a life support for many critical diseases [14, 15]. Continuous blood purification used to manage haemodynamics ensures good stability and slow and continuous removal of circulating water and toxic substances. In case of patients with acute kidney injury accompanied by oligo-
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When patients suffer from renal failure, continuous blood purification is considered as the effective safeguard to the implementation of antibiotics, nutrition and other supports [16, 17]. The larger pore size of the filtration membrane as well as strong convection ensures the efficient adsorption and removal of middle- and macro-molecules including inflammatory mediators and the reestablishment of immunity homeostasis [18]. At present, in the treatment of multiple organ dysfunction syndromes combined with acute kidney injury, although the application of continuous blood purification shows positive effects, the optimal treatment timing is to be unified [19, 20].

Although there are various causes of cardiac failure, it causes fluid retention and increases lung water, which will further lead to circulation congestion and reduce blood supply of organs [21]. After the onset of cardiac failure, the renin-angiotensin-aldosterone system and the sympathetic vasoconstrictor nerve system are activated; atrial natriuretic peptide becomes dysfunctional, and renal hypoperfusion causes retention of water and sodium, which increases cardiac volume load and stimulates the occurrence of metabolic acidosis, high potassium and/or high sodium. In this way, any application of vasoactive agents may not be satisfactory [22, 23]. Continuous renal replacement therapy lowers cardiac load by removing extra body fluids. It is therefore valuable to patients irresponsive to diuretics. Despite the decreased cardiac output and perfusion due to cardiac failure, the application of substitution fluid will not destroy the stability of circulation thanks to the timely removal of excess body fluids. Besides, continuous renal replacement therapy also regulates electrolyte and acid-base equilibrium, which are vital to the treatment [24].

In this paper, APACHE II scores at 1, 2, and 3 weeks after treatment in the observation group were lower than those in the control group \( (P<0.05) \), suggesting that early continuous renal replacement therapy had positive effects on patients’ acute physiology as well as chronic health. As compared with those in the control group, reduced \( (P<0.05) \) levels of Scr, BNP and CRP in the observation group after treatment...
revealed that early continuous renal replacement therapy effectively alleviated the inflammation in patients with cardiac failure combined with acute kidney injury. Also, as compared with those in the control group, shorter length of ICU and hospital stays and lower mortality rates in the observation group (P<0.05) showed that early continuous renal replacement therapy applied to patients with cardiac failure combined with acute kidney injury shortened hospital stays, in addition to lowering mortality and facilitating recovery. In the study of Crescenzi G et al [25], it was not shown that early implementation of continuous renal replacement therapy could significantly reduce the mortality of patients, which was related to the small sample size and fairly short observation period. In our study, CCQQ and KDQOL-SF scores at 1, 2, and 3 months after discharge in the observation group were higher than those in the control group (P<0.05). This indicated that early continuous renal replacement therapy improved patients’ post-discharge quality of life and prognosis.

In conclusion, early continuous renal replacement therapy in the treatment of cardiac failure patients combined with acute kidney injury could improve physical condition, hemodynamics, and length of ICU stay and occurrence of death, which warrant its promising value of applications. However, as a retrospective analysis, this study was subjected to the limitation that advanced selection of objects was infeasible. Moreover, the small sample size restrained it in representativeness. Future study needs a larger sample size and more scientific and representative research directions.

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Disclosure of conflict of interest

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Address correspondence to: Jianfeng Huang, Department of Urology, People’s Hospital of Liannan Yao Autonomous County, No. 95 Chaoyang Road, Sanjiang Town, Liannan Yao Autonomous County, Qingyuan 513300, Guangdong, China. Tel: +86-13602925981; E-mail: huang111f@163.com

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