Am J Transl Res 2021;13(4):3418-3426
www.ajtr.org /ISSN:1943-8141/AJTR0127464

Original Article

Timing of continuous renal replacement therapy in patients with acute non-ST-segment elevation myocardial infarction complicated with cardiac and renal insufficiency

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Received December 2, 2020; Accepted January 7, 2021; Epub April 15, 2021; Published April 30, 2021

Abstract: Objective: To explore the efficacy of different timing options for continuous renal replacement therapy (CRRT) in patients with acute non-ST-segment elevation myocardial infarction (NSTEMI) and cardiac and renal insufficiency. Methods: Eighty-eight patients with acute NSTEMI complicated with cardiac and renal insufficiency received PCI treatment after achieving a stable condition and were randomly divided into the control group (n = 44) and the research group (n = 44). The control group was given CRRT after percutaneous coronary intervention (PCI), and the research group was treated with CRRT before and after PCI. The clinical treatment efficacy, cardiac function indexes (left ventricular ejection fraction (LVEF), cardiac output (CO), and left ventricular end diastolic diameter (LVEDD)), renal function indexes (creatinine (Cr), glomerular filtration rate (GFR), neutrophil gelatinase-associated lipocalin (NGAL)), quality of life (QoL) and incidence of major adverse cardiovascular events were compared between the two groups. Results: After treatment, the overall effective rate in the research group was higher than that in the control group ($P < 0.05$); LVEF, CO, GFR and QoL score were higher, while LVEDD value, creatinine level, NGAL level and the incidence of major adverse cardiovascular events were lower in the research group than in the control group ($P < 0.05$). Conclusion: For patients with acute NSTEMI complicated with cardiac and renal insufficiency, the use of CRRT before and after PCI can effectively ameliorate cardiac and renal function, and significantly improve quality of life with a good prognosis.

Keywords: Percutaneous coronary intervention, continuous renal replacement therapy, acute non-ST-segment elevation myocardial infarction, cardiac and renal insufficiency

Introduction

Heart failure is a syndrome of cardiac insufficiency resulting from various heart diseases, and myocardial infarction is one of the most common causes. Percutaneous coronary intervention (PCI) is the main treatment for myocardial infarction with high operability and safety [1]. However, due to the use of a large dose of contrast agent during PCI, the volume of contrast agent may directly damage the kidney or aggravate the injury after renal filtration in patients with renal tubular injury, renal ischemia, etc. So once patients have renal insufficiency, the incidence of contrast-induced nephropathy after PCI can be quite high, and the nephropathy will greatly increase the mortality and the risk of serious complications such as sepsis, bleeding, and respiratory failure [2, 3]. Therefore, the study of how to improve the prognosis of patients with cardiac and renal insufficiency has become the focus of much clinical research. A variety of preventive regimens have been developed for this prevention (e.g., calcium antagonists, N-acetylcysteine, diuretics and hemodialysis). However, due to different doses and types of contrast agents, other agents with nephrotoxicity, etc., the incidence of contrast-induced nephropathy is still about 8%, which is commonly known as one of the three major post-PCI complications (the other two are post-stent thrombosis and post-

stent restenosis). Therefore, it's essential to investigate a scientific method of prevention and treatment for these complications [4, 5].

Continuous renal replacement therapy (CRRT) is a common treatment for renal insufficiency via extracorporeal blood purification technology with the advantages of stability and high efficiency [6]. Nevertheless, it's worth noting that there is still a lack of evidence-based medical information for the timing of CRRT, and many different views are held in clinical practice. In most hospitals, the timing of CRRT is selected based on the best medical resources and clinical experience [7]. If the patient's condition is serious, there can be difficulty in treatment when severe hyperkalemia, severe acid-base balance disorders and other dialysis indications occur. Hence, some scholars advocate early CRRT, but there is still no clear definition for the timing of early CRRT [8]. Based on these research findings, we herein further investigate the efficacy of CRRT at different time points in patients with acute non-ST-segment elevation myocardial infarction (NSTEMI) complicated with post-PCI cardiac and renal insufficiency.

Materials and methods

General data

We selected 88 patients with acute NSTEMI accompanied with cardiac and renal insufficiency treated in The First Affiliated Hospital of Soochow University from May 2019 to May 2020. All the patients required further PCI treatment after achieving stable NSTEMI status, and were divided into the control group and the research group according to a random number table method, with 44 cases in each group. This study was approved by the Medical Ethics Committee of The First Affiliated Hospital of Soochow University.

Inclusion and exclusion criteria

Inclusion criteria: Patients who were diagnosed with acute NSTEMI accompanied with cardiac and renal insufficiency according to the diagnostic and dialysis criteria from the Guidelines for the Diagnosis and Treatment of Unstable Angina Pectoris and Non-ST-segment Elevation Myocardial Infarction, Chinese Guidelines for the Diagnosis and Treatment of Heart Failure 2018, and Clinical Practice Guidelines for Chronic Kidney Disease and Dialysis II; patients with endogenous creatinine clearance < 80 mL/min, serum creatinine > 133 μmol/L, and New York Heart Association (NYHA) functional Class II and above [9-12]. Patients who received PCI treatment with no history of surgical contraindications and no coagulopathy; Patients without a history of dialysis or CRRT before enrollment; patients who signed the informed consent form to participate in this study.

Exclusion criteria: Patients with history of myocardial infarction; patients with severe valvular heart disease, cardiogenic shock, cardiomyopathy, major infectious diseases, or congenital heart disease; patients with abnormal liver function (alanine aminotransferase (ALT) and aspartate aminotransferase (AST) more than 2 times the normal value (8-40 U/L) respectively); patients with malignant tumors, severe trauma, or abnormal mental states or cognition.

Methods

During the two-week study period, the control group was treated with CRRT after PCI, while the research group was given CRRT before and after PCI. The dialysis instrument were Dialog$^+$ hemodialysis machine (B.Braun, Germany) and REXEED-15UC blood purifier (Asahi Kasei Medical (HangZhou) Co., Ltd., China). As for operating steps, jugular or femoral vein puncture was first performed to establish additional sites of vascular access with the replacement rate of 3-6 L/h and blood flow rate of 180-220 mL/min. According to the daily fluid output and central venous pressure of patients, the ultrafiltration volume and clearance rate of CRRT were adjusted, with continuous ultrafiltration for 48 hours, twice a week. Also, argatroban and heparin anticoagulation were selected according to whether there was a bleeding tendency. During the process, the patients' vital signs were closely monitored to prevent adverse effects.

Outcome measures

(1) Clinical efficacy: "Markedly effective" revealed that cardiac function improved to Class 1 or improved by 2 classes and above, urinary albumin level decreased by > 40%, and urine volume increased without blood purification treatment performed. "Effective" indicated that cardiac function improved by 1 class, urinary albumin level decreased by ≤ 40% yet CRRT

was still needed, and urine volume slightly increased. Additionally, "Ineffective" demonstrated unimproved cardiac functional classification and renal function with even aggravated heart failure symptoms, and CRRT was terminated since patients required mechanical ventilation support or had intolerance the therapy. Overall effective rate = (markedly effective cases + effective cases)/n × 100%.

(2) Cardiac function: Before and after treatment, left ventricular ejection fraction (LVEF), cardiac output (CO) and left ventricular end diastolic diameter (LVEDD) were analyzed by GE Vivid E9 echocardiography in both groups.

(3) Renal function: Before and after treatment, a peripheral venous blood sample (4 mL) was collected from each subject. Creatinine (Cr) level was measured by sarcosine oxidase method via semi-automatic biochemical analyzer (BA-90, Shanghai Thermo Biotechnology Development Co., Ltd., China) Glomerular filtration rate (GFR) was calculated with the following formula: GFR = 175 × (Cr-1.1234) × (age-0.179) × gender (male = 1, female = 0.79). Besides, neutrophil gelatinase-associated lipocalin (NGAL) level was determined by enzyme-linked immunosorbent assay through Beckman IAMMGE.

(4) Quality of life (QoL): Before and 3 months after treatment, the patients' QoL was assessed using the Short Form-36 (SF-36), which incorporated 8 dimensions (36 items), namely, physical functioning, bodily pain, role-physical, role-emotional, social functioning, mental health, energy, and general health [13]. The score is 0-100 points, with higher scores indicating better QoL.

(5) Major adverse cardiovascular events (MACE): During the 6-month followed up, cardiogenic death, sudden cardiac arrest, myocardial infarction, target vessel revascularization, instent thrombosis, etc. were recorded.

Statistical analysis

Data analyses were performed with the SPSS 21.0 software. The measurement data were expressed as mean ± standard deviation ($\bar{x}$ ± sd). Independent sample t-test was adopted for the comparison between the two groups, and paired samples t-test was used for the comparison before and after intervention within the same group. Chi-square test (χ^2 test) was applied as to the enumeration data expressed as the percentage (%). *P* values less than 0.05 were considered significant.

Results

Comparison of general data

There was no significant difference in general data such as gender, age, 24 h-U-pro, body mass index, cardiac functional grading, combined underlying diseases, location of myocardial infarction, onset-to-admission time, onset-to-PCI time and medication use before disease onset between the two groups, suggesting the two groups were comparable (P > 0.05). See **Table 1**.

Comparison of clinical efficacy

Table 2 shows that the research group had a significantly higher overall effective rate than the control group (P < 0.05), indicating that the use of CRRT before and after PCI can facilitate clinical treatment efficacy.

Comparison of cardiac function

Before treatment, no significant difference was identified in cardiac function indexes between the two groups (P > 0.05). After treatment, LVEF and CO increased while LVEDD decreased in both groups, and the research group revealed better results than the control group (P < 0.05). It can be seen that the use of CRRT before and after PCI is more conducive to ameliorating cardiac function. See **Table 3** and **Figure 1**.

Comparison of renal function

Before treatment, no significant difference was found regarding renal function indexes between the two groups (P > 0.05). After treatment, GFR increased while Cr and NGAL decreased in both groups, and the research group revealed better results than the control group (P < 0.01). The results suggest that the use of CRRT before and after PCI is more beneficial for renal function. See **Table 4** and **Figure 2**.

Comparison of QoL

Before treatment, no significant difference was revealed in terms of the QoL between the two

Table 1. Comparison of General data ($\bar{x} \pm sd$, %)

Group	Control group (n = 44)	Research group (n = 44)	t/χ^2	P
Gender (male/female)	22/22	24/20	0.182	0.669
Age (years)	59.5±10.3	59.1±10.2	0.064	0.949
24 h-U-pro (g/24 h)	2.09±0.29	2.11±0.31	0.313	0.755
BMI (kg/m^2)	21.68±2.71	22.05±2.88	0.621	0.536
Cardiac functional grading			0.566	0.754
I	14	13		
III	21	19		
IV	9	12		
Combined underlying diseases			0.189	0.910
Diabetes	14	15		
Hypertension	19	17		
Hyperlipidemia	11	12		
Onset-to-admission time (h)	5.24±0.84	5.36±0.95	0.623	0.532
Onset-to-PCI time (h)	10.39±1.36	10.48±1.48	0.297	0.767
Medication use before onset (Yes/No)	28/16	26/18	0.192	0.662
Location of myocardial infarction (anterior wall/inferior wall/anterolateral wall/antero-septal wall)	16/15/10/13	18/12/12/12	0.018	0.978

Note: BMI: body mass index; 24 h-U-pro: 24 h urinary protein; PCI: percutaneous coronary intervention.

Table 2. Comparison of clinical efficacy (n, %)

Group	Markedly effective	Effective	Ineffective	Overall effective rate
Control group (n = 44)	18 (40.91)	17 (38.64)	9 (20.45)	35 (79.55)
Research group (n = 44)	27 (61.36)	15 (34.09)	2 (4.55)	42 (95.45)
Z/χ^2		Z = 2.295		χ^2 = 5.091
P		0.022		0.024

Table 3. Comparison of Cardiac function ($\bar{x}$ ± sd)

Group	Control group (n = 44)	Research group (n = 44)	t	P
LVEF (%)				
Before treatment	36.93±4.56	36.26±4.37	0.704	0.483
After treatment	51.47±7.23***	57.12±9.21***	3.201	0.002
CO (L/min)				
Before treatment	2.37±0.48	2.40±0.49	0.290	0.773
After treatment	4.59±1.12***	5.26±1.35***	2.534	0.013
LVEDD (mm)				
Before treatment	61.36±9.66	60.71±9.53	0.318	0.751
After treatment	46.57±5.63***	42.15±5.01***	3.890	< 0.001

Note: LVEF: left ventricular ejection fraction; CO: cardiac output; LVEDD: left ventricular end diastolic diameter. Compared within the same group before treatment, ***P < 0.001.

groups (P > 0.05). After treatment, QoL scores in each aspect improved in both groups, and the research group showed higher scores than the control group (P < 0.001). It's identified that the use of CRRT before and after PCI is more conducive to improving the QoL. See **Table 5**.

Comparison of MACE incidence

The incidence of MACE was significantly lower in the research group than in the control group (P < 0.05). In the control group, there was one case of cardiogenic death one month after the end of treatment, indicating that the use of CRRT before and after PCI treatment is beneficial to reducing the incidence of MACE. See **Table 6**.

Discussion

Cardiac insufficiency before PCI is an independent risk factor for contrast-induced nephropathy after PCI. Due to the disordered internal environment of the patients, the renin-angiotensin-aldosterone system is activated, thus cardiac output is increased with high cardiac load, reduced renal vascular blood flow, and aggravated renal ischemia [14, 15]. It's reported that the occurrence of acute kidney injury after PCI is closely related to the cardiac function of patients [16]. What's more, patients with acute NSTEMI, who are older, have gradually decreased functional renal reserve, and most of them are accompanied by chronic diseases such as diabetes and hypertension. Generally, PCI treatment for these patients requires an increased dose of contrast agent, which results in unstable renal hemodynamic and further reduced renal function [17]. Therefore, patients with acute NSTEMI complicated with cardiac and renal insufficiency have relatively poor prognosis after PCI and comparatively high risk of postoperative complications. To a certain extent, it also increases the risk of cardiovascular adverse events, making improvement of the cardiac and renal function of great significance to enhance the efficacy of PCI.

In our study, the clinical efficacy was higher, and the incidence of MACE was lower in the research group than in the control group, suggesting that CRRT has a high value on patients with acute NSTEMI complicated with cardiac and renal insufficiency, which can reduce the incidence of cardiovascular adverse events. A previous study revealed that for patients with acute NSTEMI complicated with cardiac and renal insufficiency, the use of CRRT before and after PCI treatment could significantly promote the therapeutic effects, which was basically consistent with the results of this study [18].

In recent years CRRT has been a common method for treating renal diseases. It's mainly used to continuously and slowly remove excess wastes such as solutes and water in the body by extracorporeal blood purification, so that patients have better tolerance and achieve an

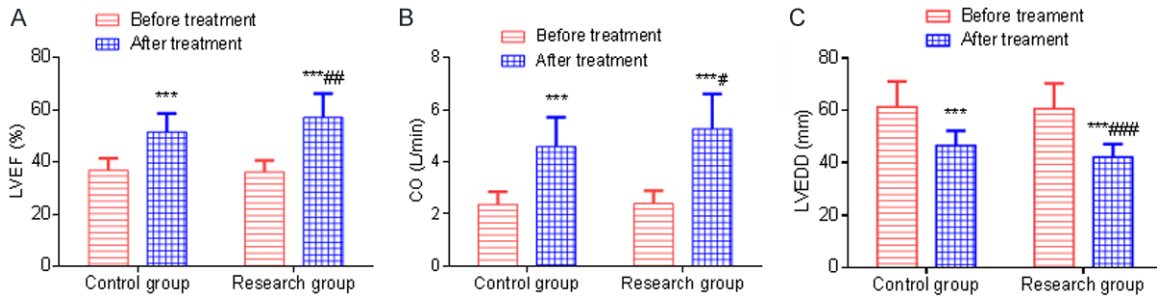

Figure 1. Comparison of cardiac function. A: LVEF level (%); B: CO (L/min); C: LVEDD level (mm). Compared within the same group before treatment, ***P < 0.001; compared with the control group, #P < 0.05, ##P < 0.01, ###P < 0.001. LVEF: left ventricular ejection fraction; CO: cardiac output; LVEDD: left ventricular end diastolic diameter.

Table 4. Comparison of renal function ($\bar{x}$ ± sd)

Group	Control group (n = 44)	Research group (n = 44)	t	P
Cr (μmol/L)				
Before treatment	347.56±50.25	345.10±350.01	0.046	0.963
After treatment	198.62±23.33***	175.19±20.27***	5.029	< 0.001
GFR (mL/min)				
Before treatment	45.29±6.68	44.58±6.51	0.505	0.615
After treatment	62.78±8.54***	69.41±9.91***	3.362	0.001
NGAL (μg/mL)				
Before treatment	50.17±7.34	51.32±7.58	0.723	0.472
After treatment	41.29±6.17***	36.24±5.38***	4.092	< 0.001

Note: Cr: Creatinine; GFR: Glomerular filtration rate; NGAL: neutrophil gelatinase-associated lipocalin. Compared within the same group before treatment, ***P < 0.001.

ideal water load more quickly to fully maintain normal hemodynamics [19]. Compared with drugs such as cardiotonics and diuretics or traditional hemodialysis regimens, CRRT can prolong the treatment time of blood purification, while exerting less of an effect on the hemodynamics, reducing cardiac preload and afterload, improving cardiac microcirculation and cardiac output, and reducing ventricular wall tension, ventricular end-diastolic volume and pressure, so as to minimize the ischemia or reperfusion injury in tissues and organs due to unstable blood flow [20, 21]. Renal blood flow increases with the improvement of cardiac function, which reduces the damage of metabolites to the kidney. Gradually, renal function recovery is facilitated, and the incidences of short-term and long-term complications are thus reduced. Also, the filter with good biocompatibility and high permeability used in CRRT in the treatment process can ensure that the replacement fluid volume is sufficient and macromolecular inflammatory mediators are filtered out. Hence, the inflammatory response in the body is reduced and the metabolic circulation and excretion of the body are increased, to help maintain a stable internal environment such as electrolyte and acid-base balance. In this way, the function of the renal system is protected and the safety of treatment is enhanced [22]. Moreover, CRRT is used before and after PCI treatment to first regulate and improve cardiac and renal function, stabilize the hemodynamics, promote the reserve function and tolerance of the heart and kidney. These methods can effectively relieve the aggravation of cardiorenal injury due to myocardial ischemia, contrast agents and other factors exacerbating hemodynamic changes during PCI, and reduce the incidence of adverse cardiovascular events [23].

Clinically, it was found that cardiac and renal function were significantly lower in patients with acute NSTEMI complicated with cardiac and renal insufficiency than in the normal population. LVEF, CO and LVEDD are important indicators for evaluating cardiac function, while GFR, Cr and NGAL are important indicators for reflecting renal function [24]. NGAL as a lipocalin shows low expression in the liver and kidney of the body under normal physiological conditions, and high expression when renal tubules are damaged, so NGAL can effectively reflect early renal injury [25]. In our study, the LVEF, CO and GFR of both groups were increased after treatment, while the LVEDD, Cr and NGAL were decreased, and the results in the research

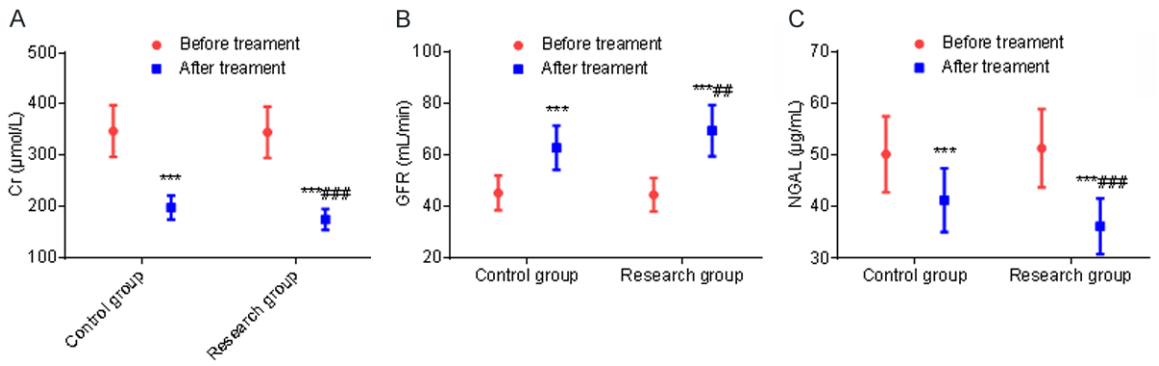

Figure 2. Comparison of renal function. A: Cr level (μmol/L); B: GFR (mL/min); C: NGAL (μg/mL). Compared within the same group before treatment, ***P < 0.001; compared with the control group, ##P < 0.01, ###P < 0.001. Cr: Creatinine; GFR: Glomerular filtration rate; NGAL: neutrophil gelatinase-associated lipocalin.

Table 5. Comparison of QoL ($\bar{x}$ ± sd, point)

Group	Control group (n = 44)	Research group (n = 44)	t	P
Physical functioning				
Before treatment	55.48±6.82	54.59±6.79	0.610	0.544
After treatment	72.48±9.44***	81.25±10.21***	4.158	< 0.001
Bodily pain				
Before treatment	43.59±5.48	44.02±5.12	0.378	0.706
After treatment	75.78±9.36***	85.10±10.32***	4.409	< 0.001
Role-physical				
Before treatment	63.47±7.29	64.02±7.37	0.350	0.727
After treatment	74.26±8.87***	82.48±10.11***	4.028	< 0.001
Role-emotional				
Before treatment	65.05±7.63	66.58±7.76	0.927	0.357
After treatment	75.31±9.33***	82.87±10.03***	3.638	< 0.001
Social functioning				
Before treatment	50.19±7.69	52.70±7.98	1.493	0.139
After treatment	75.49±9.82***	82.65±8.17***	3.700	< 0.001
Mental health				
Before treatment	58.51±7.73	60.04±8.25	0.892	0.375
After treatment	70.89±9.87***	80.32±10.53***	4.307	< 0.001
Energy				
Before treatment	53.27±6.74	52.21±6.29	0.759	0.450
After treatment	75.41±8.57***	83.82±10.39***	4.114	< 0.001
General health				
Before treatment	50.15±6.57	51.04±6.86	0.618	0.538
After treatment	73.52±9.24***	82.17±10.49***	4.078	< 0.001

Note: QoL: Quality of life. Compared within the same group before treatment, ***P < 0.001.

group were better than those in the control group. Wu et al. pointed out that preoperative and postoperative CRRT can strengthen renal function with better prognosis in patients with acute NSTEMI combined with cardiac and renal insufficiency, which was consistent with the results of this study [26]. Furthermore, the prognosis of patients can be effectively understood by observing the changes of QoL before and after treatment. In our study, a 3-month follow-up demonstrated that the QoL in the research group was also better than that in the control group, further indicating that the use of CRRT before and after PCI in treating acute NSTEMI with cardiac and renal insufficiency has a good short-term prognosis and can effectively enhance the QoL of patients.

However, due to the small sample size and short observation time in this study, we have not evaluated the long-term efficacy and prognosis, thus in-depth studies with larger sizes and prolonged observation time will be performed to compensate for the clinical shortcomings in the future.

To sum up, the use of CRRT before and after PCI can effectively improve cardiac and renal function and QoL, and deliver a good prognosis in patients with acute NSTEMI and cardiac insufficiency.

Table 6. Comparison of MACE incidence (n, %)

Group	Control group (n = 44)	Research group (n = 44)	t	P
Cardiogenic death	1 (2.27)	0 (0.00)	0.000	1.000
Sudden cardiac arrest	1 (2.27)	0 (0.00)	0.000	1.000
Target vessel revascularization	3 (6.82)	1 (2.27)	0.262	0.609
In-stent thrombosis	3 (6.82)	1 (2.27)	0.262	0.609
Total incidence of MACE	8 (18.18)	2 (4.55)	4.062	0.044

Note: MACE: major adverse cardiovascular events.

Acknowledgements

This work was supported by the National Natural Science Foundation of China for *Negative regulation of miR-195 promotes the protective effect of MSCs on ischemic cardiomyocytes and its mechanism* (81400200).

Disclosure of conflict of interest

None.

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