

Clarifications on Continuous Renal Replacement Therapy and Hemodynamics

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Abstract

Objective: Continuous renal replacement therapy (CRRT) is a continuous process of bedside blood purification which is widely used in the treatment of acute kidney injury (AKI) and for fluid management. However, since AKI and fluid overload are often found to be associated with hemodynamic abnormalities, determining the relationship between CRRT and hemodynamics remains a challenge in the treatment of critically ill patients. The aim of this review was to summarize key points in the relationship between CRRT and hemodynamics and to understand and monitor renal hemodynamics in critically ill patients, especially those with AKI.

Data Sources: This review was based on data in articles published in the PubMed databases up to January 30, 2017, with the following keywords: “continuous renal replacement therapy,” “Hemodynamics,” and “Acute kidney injury.”

Study Selection: Original articles and critical reviews on CRRT were selected for this review.

Results: CRRT might treat AKI by hemodynamic therapy, and it was an important form of hemodynamic therapy. The targets of hemodynamic therapy should be established when using CRRT. Therefore, hemodynamic management and stability were very important during CRRT. Most studies suggested that renal hemodynamics should be clearly identified.

Conclusions: CRRT is not only a replacement for organ function, but an important form of hemodynamic therapy. Improved hemodynamic management of critically ill patients can be achieved by establishing specific therapeutic hemodynamic targets and maintaining circulatory stability during CRRT. Over the long term, observation of renal hemodynamics will provide greater opportunities for the progression of CRRT hemodynamic therapy.

Key words: Acute Kidney Injury; Continuous Renal Replacement Therapy; Hemodynamics

INTRODUCTION

Continuous renal replacement therapy (CRRT) is a continuous process of bedside blood purification that originated from hemodialysis. With the improvement of its techniques and methods, CRRT is currently widely used in the treatment of acute kidney injury (AKI) and for fluid management, metabolic solute management, and exogenous solute management. CRRT has good hemodynamic tolerance, especially suitable for patients with severe hemodynamic instability, so it plays an important role in the field of critical care medicine. Since AKI and fluid overload are often found to be associated with hemodynamic abnormalities such as shock and heart failure, determining the relationship

between CRRT and hemodynamics remains a challenge in the treatment of critically ill patients. Therefore, the aim of this review was to summarize key points in the relationship between CRRT and hemodynamics and to understand and monitor renal hemodynamics in critically ill patients, especially those with AKI.

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Received: 13-02-2017 **Edited by:** Peng Lyu
How to cite this article: Wang XT, Wang C, Zhang HM, Liu DW. Clarifications on Continuous Renal Replacement Therapy and Hemodynamics. Chin Med J 2017;130:1244-8.

Access this article online

Quick Response Code:



Website:
www.cmj.org

DOI:
10.4103/0366-6999.205863

CONTINUOUS RENAL REPLACEMENT THERAPY CAN BE USED TO TREAT ACUTE KIDNEY INJURY BY HEMODYNAMIC THERAPY

Although it is well established that the occurrence of AKI in critically ill patients can significantly increase mortality, the incidence of AKI in the intensive care unit (ICU) remains high. The kidneys are vital organs, and appropriate preload (flow and pressure) and afterload (central venous pressure [CVP] and venous congestion) are required to maintain their normal functions.

Renal blood flow is autoregulatory under healthy conditions. That is, regardless of fluctuations in blood pressure, the autoregulatory mechanisms of the kidneys maintain renal blood flow at a relatively stable level if arterial pressure is within the average range of 80–180 mmHg (1 mmHg = 0.133 kPa). However, this autoregulation is no longer effective when blood pressure is outside of normal range and in some critical situations. A study examining the factors that contribute to the occurrence of AKI in critically ill patients found that direct circulation dysfunction (including hypovolemia and cardiogenic shock)-induced AKI accounts for 47.3% of all cases of AKI.^[1] In addition, Poukkanen *et al.*^[2] showed that time-adjusted mean arterial pressure (MAP) below 73 mmHg, the use of dobutamine within the first 24 h in the ICU, and the highest lactate value during the first 24 h can accelerate the progression of AKI in patients with severe sepsis. These findings clearly demonstrated that renal injury is closely associated with hemodynamics, and the use of CRRT for accurate quantitative volume management can therefore provide prompt improvement in renal perfusion.^[3] Since CRRT reduces further deterioration of renal function, and consequently the dependence on dialysis through maintenance of hemodynamic stability, the application of CRRT is highly recommended in severe AKI patients, especially for those with hemodynamic instability.^[4]

CVP is the backward-pressure target for organ protection, and “MAP-CVP” is commonly used to represent renal perfusion pressure. Renal perfusion pressure gradually decreases along the path of blood flow. Since the average glomerular capillary pressure is around 50 mmHg and renal tubular capillary pressure is 10 mmHg, greater CVP (renal afterload) indicates greater renal resistance. High CVP increases renal afterload but not perfusion flow, and therefore reduces renal perfusion. A previous study showed that high CVP might increase the occurrence and morbidity of AKI in patients with septic shock. In addition, an excessively high CVP should be prevented, especially when it approaches 10 mmHg.^[5] Another study found that the occurrence of AKI is linearly correlated with CVP in patients with severe sepsis such that the risk of AKI increases with increasing CVP.^[6] A study of 105 septic shock patients by Wang *et al.*^[7] showed that CVP is closely associated with renal function. Patients with septic shock with high CVP (CVP >12 mmHg) had higher levels of serum creatinine (SCr) compared with those with low CVP (CVP <8 mmHg) on day 5, and patients whose

CVP dropped to <8 mmHg within 7 days had a higher 28-day survival rate. This suggests that maintaining CVP <8 mmHg during the early phase of septic shock can prevent further damage to renal function and improve the survival rate of critically ill patients.

Venous congestion, commonly caused by right-sided heart failure, can also lead to obstruction of venous reflux, which results in elevated renal vein pressure and reduced glomerular filtration rate and ultimately leads to the occurrence of AKI. Using transthoracic echocardiography, Guinot *et al.*^[8] assessed the right ventricular function of patients with AKI undergoing cardiac surgery. They found that the occurrence of early postoperative right ventricular dysfunction was significantly associated with elevated SCr, indicating that the main cause of AKI is not reduced cardiac output but venous congestion.

Fluid overload (defined as fluid accumulation of over 10% of baseline weight within a given period of time) is a phenomenon that commonly occurs in critically ill patients. It not only causes renal vein pressure elevation and renal interstitial edema, but also leads to reduced renal perfusion, which increases intraglomerular pressure and leads to sustained AKI.^[9] In “Critical Hemodynamic Therapy-Beijing Consensus,” Liu *et al.*^[10] indicated that volume overload can lead to impaired renal perfusion and deterioration of AKI. A recently serial research indicate fluid status abnormalities were common among patients receiving CRRT. Different types of fluid status corresponded to different clinical conditions and treatment outcomes, and in patients with AKI, a higher degree of fluid overload at RRT initiation predicts worse renal recovery at 1 year.^[11,12] Similarly, a study on patients with acute respiratory distress syndrome demonstrated that positive fluid balance is closely associated with the occurrence of AKI.^[13] In contrast, when negative fluid balance increases during CRRT, the probability of renal function recovery in AKI patients also increases.^[14] Therefore, by precise titration of fluid balance using CRRT during the volume management of severe AKI patients, renal interstitial edema is reduced. In turn, the rate of recovery of renal function and survival in these patients can improve significantly.

Finally, CRRT can timely correct solute abnormalities (such as hyperchloremia, and hypernatremia caused by various factors). All these contributes to the maintenance of a stable internal environment in critically ill patients and reduces further renal injury.^[15]

In summary, CRRT can be used to treat AKI by hemodynamic therapy.

CONTINUOUS RENAL REPLACEMENT THERAPY IS AN IMPORTANT FORM OF HEMODYNAMIC THERAPY

“Volume” often refers to the total volume in the circulatory system, including cardiac preload. However, volume management of critically ill patients not only includes fluid in the circulatory system, but also those in interstitial fluid.

A previous study demonstrated that up to 70% of critically ill patients in the ICU have fluid overload.^[16] In critically ill patient immediate reverse resuscitation is required for those with fluid and volume overload. In cases of postoperative congestive heart failure and patients with pericarditis, rapid elevation of the circulating volume in these patients causes rapid expansion of the right ventricle, which then pushes the interventricular septum leftward and restricts left ventricular filling, which results in reduced cardiac output and inadequate tissue perfusion. If urine output decreases and diuretics are ineffective in removing the excess fluid, emergency mechanical fluid removal (i.e., CRRT) should be performed.^[17]

CRRT precisely regulates fluid, and is simple to operate. Therefore, it is suitable for precise adjustments of fluid removal rate in the management of fluid overload in different diseases. For example, in patients with cardiorenal syndrome, negative fluid balance should be established as early as possible, and dehydration can be slowed once lung edema is reduced. For septic shock patients, slow dehydration should only be performed after they are clinically stable to limit further accumulation of body fluids. Dehydration of patients with kidney damage can be conducted at a faster rate than that of patients with severe sepsis or septic shock. While CRRT can maintain fluid balance, it is also an indispensable method for correcting fluid overload, an outcome that is especially vital for the fluid management of critically ill patients with complications from cardiac insufficiency.

In summary, CRRT is not only a treatment for AKI and a substitute for organ function, but it is also an important technique in hemodynamic therapy that focuses on managing fluid overload and stabilizing hemodynamics in critically ill patients.

TARGETS IN HEMODYNAMIC THERAPY SHOULD BE ESTABLISHED WHEN USING CONTINUOUS RENAL REPLACEMENT THERAPY

CRRT is a powerful tool for hemodynamic therapy, and corresponding therapeutic hemodynamic targets should be established when it is used.^[8]

CVP is a simple indicator for evaluating preload. Although CVP is not a perfect indicator, its value is easily obtained, and it is always the first indicator to be examined and intervened. Dynamic changes in CVP can accurately reflect relative changes in blood volume and provide guidance for adjustment of dehydration rate during CRRT. Therefore, CVP might represent a preferred target in hemodynamic therapy during CRRT. Moreover, the degree of venous congestion can be immediately observed by measurement of changes in the diameter of the inferior vena cava before and after volume therapy and its variability during respiration using ultrasonography. Such changes in inferior vena cava diameter prompt adjustments of the dehydration rate.

Previous studies found that heart failure is a major risk factor of AKI, as 30% of patients with heart failure are also accompanied by renal insufficiency. Hence, greater care should be taken

when conducting fluid management by CRRT in patients with cardiac insufficiency,^[18,19] especially those with right ventricular dysfunction. When the right ventricular end-diastolic pressure becomes greater than the left ventricular end-diastolic pressure, the interventricular septum bends toward the left ventricle, leading to decreased left ventricular filling and reduced cardiac output that ultimately result in circulatory fluctuations. However, if dehydration therapy is conducted immediately to reduce the right ventricular pressure, cardiac output will elevate again. During this process, critical ultrasound can be used to monitor immediate changes in the right ventricle and interventricular septum to allow prompt reverse volume resuscitation and maintain hemodynamic stability. Reverse volume resuscitation also plays an important role in special cardiac cases, such as valvular vegetation, the identification of which is equally reliant on the use of critical ultrasound.

Furthermore, lung ultrasound has a role in volume monitoring. When lung tissue fluid increases, “comet-tails” perpendicular to the pleura, otherwise known as the B-lines, can be observed by lung ultrasound. The number, density, and distribution of B-lines are closely associated with the extent of extravascular lung water, and different B-line characteristics represent different levels of water content in the lungs.^[20] A study using lung ultrasound to predict pulmonary arterial wedge pressure (PAWP) showed that patients with A-predominance have lower PAWP, while patients with B-predominance have higher PAWP, which indicates interstitial edema.^[21] Since changes in B-lines occur with negative fluid balance during the treatment of lung edema, continuous assessment of their changes can help to determine treatment efficacy and guide treatment speed and effectiveness. In addition, ongoing studies have demonstrated that continuous assessment of B-lines in the lung during fluid therapy allows for early identification of increasing extravascular lung water, which prevents excessive fluid resuscitation.

Fluid overload can induce edema in abdominal organs and reduce abdominal wall compliance, resulting in high intraperitoneal pressure that affects not only renal venous return, but induces or exacerbates AKI. However, the use of CRRT in these cases can reduce edema through dehydration and achieve lower intraperitoneal pressure. Therefore, intraperitoneal pressure becomes the target of hemodynamic therapy at the moment.

In summary, corresponding therapeutic hemodynamic targets should be established when using CRRT.

HEMODYNAMIC MANAGEMENT AND STABILITY ARE VERY IMPORTANT DURING CONTINUOUS RENAL REPLACEMENT THERAPY

Reduction of blood pressure and further deterioration of renal function are sometimes inevitable during CRRT. A previous study demonstrated that 43% of critically ill patients undergoing initial CRRT presented with new onset hypotension within 1 h of beginning treatment.^[22] As previously mentioned, the duration of MAP <73 mmHg can

accelerate the progression of AKI.^[21] Therefore, maintaining circulatory stability is especially important during CRRT.

It is important to note that the fluid therapy phase of patients (recovery phase, optimal phase, stable phase, and withdrawal phase) must be known before conducting fluid management.^[23] Body fluid distribution should be accurately evaluated to select appropriate fluid therapy measures and goals. A previous study suggested using bioelectrical impedance vector analysis (BIVA) in the clinical evaluation of volume balance.^[24] Samoni *et al.*^[25] also demonstrated that the prognostic prediction of patients in the ICU who had been evaluated by BIVA for body fluid distribution was superior to conventional methods of recording fluid balance. Hence, it can be used to accurately guide fluid therapy by CRRT.

Close monitoring of hemodynamics should be conducted. Due to the unpredictable nature of hemodynamic changes in some patients undergoing CRRT, close hemodynamic monitoring is advised to reduce hemodynamic fluctuations as much as possible. This relates to the issue as to how monitoring should be conducted. A previous study showed that the use of monitoring tools, such as transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE), can provide better management of fluid therapy, etiology, and speed.^[17] Another study found that ultrasound determination of the inferior vena cava diameter (IVCD) and its collapsibility index (IVCCI) could be used to optimize the fluid removal rate while avoiding hypotension during slow continuous ultrafiltration (SCUF). Therefore, they can be used in the management and monitoring of circulation during CRRT.^[26]

Effective preventative measures should be taken. As a form of establishing extracorporeal circulation, the occurrence of hemodynamic stability during CRRT is closely associated with changes in blood flow and circulating volume. Therefore, circulatory fluctuations might be prevented if the time for increasing the blood pump speed is reduced appropriately at the beginning of CRRT. Eastwood *et al.*^[27] compared the effect of two different sets of parameters for regulating pump speed at the beginning of CRRT (blood pump speed increases of 50 ml/min over 1–4 min vs. 20–50 ml/min over 3–10 min) on circulation and found that slower adjustment of pump speed at the start of CRRT was not only better for stabilizing circulation compared with the conventional method, but also reduced the incidence of low blood pressure and prevented further damage to renal function.

Finally, monitoring of CRRT-related fluid balance should be performed. The set of replacement and dehydration speed during CRRT should be reassessed periodically by monitoring cardiac output and volume status so that timely adjustments can be made in response to reduced or excessive circulating volume.

RENAL HEMODYNAMICS SHOULD BE ACCURATELY ASSESSED

It was reported in “Critical Hemodynamic Therapy-Beijing Consensus”^[10] that organ specificity is an important basis

for establishing the targets of hemodynamic therapy. Moreover, the targets of hemodynamic therapy differ for different organs because of their specific requirements. As the most susceptible organs under pathophysiological conditions (such as during shock), the kidneys have more stringent requirements for the maintenance of hemodynamic stability. Changes in renal function are also somewhat reflective of changes in hemodynamics. Therefore, close assessment of renal blood flow and perfusion represents an organ-directed target for hemodynamic therapy.

It is an important issue how to more accurately assess renal blood flow. As a noninvasive method, ultrasound is commonly used by ICU physicians to assess renal blood flow in critically ill patients. Renal blood flow can be examined by various types of ultrasound, including color Doppler ultrasound, pulse Doppler ultrasound, power Doppler ultrasound (PDU), and contrast-enhanced ultrasound. Moreover, researchers in the field of AKI and CRRT are investigating the potential application of the newly developed ultrasonic dynamic evaluation perfusion technique.

Changes in renal perfusion can be detected by monitoring renal blood flow using color Doppler ultrasound.^[28] By monitoring renal blood flow in AKI patients using PDU, Chen *et al.*^[29] confirmed that PDU is a suitable technique for monitoring renal blood flow in AKI patients, and the PDU score can be used for assessing the severity and prognosis of AKI. In addition, Doppler ultrasound can also be applied to measure resistance index (RI) to reflect renal artery blood flow to a certain degree. A previous study found that changes in RI (measured by ultrasound) during fluid challenge were associated with increased urine volume and appeared earlier than changes in urine volume.^[30] In contrast, another study showed that there was no correlation between RI and stroke volume before and after the fluid challenge in sepsis patients.^[31] A study by Zhang *et al.*^[32] indicated that increasing cardiac output and MAP, without significantly increasing CVP, can increase renal blood flow score, and therefore improve renal perfusion. As more studies are being performed on contrast-enhanced ultrasound using microbubbles as contrast agent, many investigators are beginning to recognize its value in evaluating renal microcirculation and blood perfusion.^[33]

Although there are a considerable number of studies related to renal hemodynamics, further studies are still required to help and guide the development and improvement of hemodynamic therapy.

CONCLUSION

CRRT is closely associated with hemodynamics. It is not only a replacement for organ function, but also an important form of hemodynamic therapy. Improved hemodynamic management of critically ill patients can be achieved by establishing clear therapeutic hemodynamic targets and maintaining circulatory stability during CRRT. Finally, close observation of renal hemodynamics will provide greater

opportunities for the development and progression of CRRT associated hemodynamic therapy.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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