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Continuous renal replacement therapy in intensive care unit

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Abstract

Acute renal failure (ARF) requiring dialysis is a common complication of patients in intensive care unit (ICU). Dialysis can be performed with either intermittent hemodialysis (IHD) or continuous renal replacement therapy (CRRT). CRRT is associated with less hemodynamic instability. Therefore, it is preferred in critically ill and hypotensive patients in ICU. However, current evidence does not demonstrate the superiority of CRRT over IHD. Both methods for renal replacement therapy are complementary and the choice of dialysis in ICU should be individualized based on hemodynamic stability of patients and local expertise.

Keywords: acute renal failure, renal replacement therapy, dialysis, hemofiltration

Introduction

ARF is usually diagnosed by elevation in blood urea nitrogen and creatinine, and decrease in urine output. ARF is a frequent complication of patients admitted to ICU. It often presents as part of multiple organ failure (MOF). The mortality of ARF in an ICU setting is 50% to 80% [1-5] compared to 7% in patients admitted to a hospital with ARF due to prerenal azotemia [6]. Survival after ARF is influenced by the severity of the underlying illness and number of failed organs. The mortality of patients with ARF increases with the number of failed organ systems both in ICU and non-ICU settings [5]. Despite advances in dialysis and supportive care in the last 30 years, the mortality of ARF in ICU settings is still unacceptably high [7]. Pending recovery of renal function, temporary renal replacement therapy is required in most cases. In addition to ARF, acute renal replacement therapy is also indicated for other reasons (**Table 1**).

Table 1. Indications for Acute Renal Replacement Therapy

- Oliguria (urine output <400 ml/day) or anuria (urine output <100 ml/day)
- Diuretics resistant pulmonary edema
- Severe hyperkalemia (serum potassium >6.5 mmol/L)
- Azotemia (serum urea >30 mmol/L)
- Severe metabolic acidosis (pH<7.1)
- Suspected uremic pericarditis or encephalopathy
- Drug overdose due to dialyzable toxins
- Severe hypothermia (core temperature <32°C) or hyperthermia (core temperature >40°C)

Choice of Renal Replacement Therapy

In clinical practice, there is a large variation in the way renal replacement therapy is performed in ICU. Apart from IHD, other techniques including CRRT and slow low-efficiency daily dialysis (SLEDD) are commonly used as renal replacement therapy in ICU. Each modality has advantages and disadvantages (**Table 2**). CRRT is most often selected for patients with ARF, who have hemodynamic instability and for patients in whom continuous removal of volume or uremic toxins is thought desirable [8-10]. In addition, CRRT offers more rapid improvement and control of metabolic acidosis and hyperphosphatemia [11]. However, serum phosphate level needs to be monitored since hypophosphatemia can occur during CRRT. Beyond renal support, CRRT also provides a degree of cytokine removal via filtration and adsorption [12]. However, the clinical significance of such removal is still unknown since multiple studies have shown that CRRT does not lead to the expected reduction in the serum concentrations of these mediators [13-15].

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Table 2. Characteristics of IHD compared with CRRT

IHD	CRRT
Mainly diffusive	Mainly convective (CVVH), diffusive (CVVHD), or both (CVVHDF)
High dialysate flow (500-800 mL/min)	Low dialysate flow (1-2 L/hr) as in CVVHD or CVVHDF or no dialysate at all (CVVH)
On-line dialysate production	Use commercial fluid
Usually 4 hr per dialysis session	In theory continuous
Technically demanding	Technically less demanding
Less labor-intensive	Labor intensive
Usually used in patients who are hemodynamically stable	Usually used in patients with hemodynamic instability or increased intracranial pressure

For a long time, it has been claimed that CRRT was superior to IHD. However, several recent trials failed to confirm the superiority of CRRT over IHD [16,17]. A recent meta-analysis also showed no difference in mortality between IHD and CRRT [18]. Unfortunately, study quality included in the meta-analysis was poor and only a few studies were randomized.

However, secondary analyses after adjusting for severity of illness suggest that mortality was lower in patients treated with CRRT. In addition, none of the retrospective or prospective comparisons published in the literature has ever shown any trend in favor of IHD and all have shown a trend in favor of CRRT [19]. In addition, CRRT is recommended over IHD for patients at risk of or who have increased intracranial pressure since CRRT has been shown to prevent the surge in intracranial pressure that is associated with intermittent therapies [20-23].

Initiation and treatment dosage of CRRT

Dialysis has been shown to improve short-term survival in severe ARF [24]. Nonrandomized study suggests that earlier initiation of CRRT might increase survival [25]. However, a recent prospective randomized study failed to confirm the benefit of early over late CRRT [26]. Currently there is still no consensus regarding the timing of initiation of dialysis in ARF [8]. The minimum of delivered dialysis dose in patients with end-stage renal disease is well known. It is recommended that a Kt/V of at least 1.2 should be delivered for patients on hemodialysis [27]. Unfortunately, little is known about the minimum of dialysis dose for patients with ARF. Ronco et al showed in a prospective randomized study that patients, who were treated with ultrafiltration volume of 35 and 45 ml/hr/kg of body weight had a lower mortality rate than patients who were treated with ultrafiltration volume of 20 ml/hr/kg of body weight [28]. However, two recent studies did not show any significant survival benefit for high volume haemofiltration [26,29]. Currently, there is no consensus on what the minimum dialysis dose should be for ARF [8].

Different Formats of CRRT

Kramer et al described the first use of continuous arteriovenous haemofiltration (CAVH) for treatment of patients with fluid overload in 1977 [30]. Initially, CAVH is used since it does not require a blood pump. However, CAVH has serious shortcomings, since it requires arterial cannulation and it is incapable in maintaining adequate solute clearance in most critically ill patients in ICU. Therefore, a venovenous technique of CRRT was developed using a peristaltic blood pump and a double lumen catheter for vascular access. In practice, all CRRT modalities are now venovenous.

There are several formats of CRRT, which are used in the ICU (**Figure 1 and Table 3**). Based on the available data, there is no consensus regarding the preferred type of CRRT. The use of predominantly convective (CVVH), diffusive (CVVHD) or combination therapy (CVVHDF) should be individualized based on the competency of physicians and nurses and the local resources of the health care facilities. Removal of middle- and high-molecular-weight solute is greater with convective therapy. However, there is no evidence that this enhanced solute removal is associated with better clinical outcomes.

Table 3. Summary of CRRT

CVVH	Solute removal is through convection No requirement of dialysate Ultrafiltrate is replaced in part or completely with a replacement fluid (1-2 L/hr). Clearance of solutes equal ultrafiltration Usually used in patients who are septic with hemodynamic instability
SCUF	Solute removal is through convection No requirement of dialysate Removal of ultrafiltrate at rates < 300 ml/hr without the use of a replacement fluid Used only for patients with fluid overload without azotemia such as patients with end-stage congestive heart failure awaiting heart transplantation
CVVHD	Solute removal is through diffusion Dialysate is used countercurrent to blood flow at a rate of 1-2 L/hr Replacement fluid is minimal (<100 ml/hr) and usually not routinely administered Usually used in patients with hemodynamic instability
CVVHDF	Solute removal is through both diffusion and convection Dialysate is used countercurrent to blood flow at a rate of 1-2 L/hr Ultrafiltrate is replaced in part or completely with a replacement fluid (1-2 L/hr) Usually used in patients with hypercatabolism and hemodynamic instability

Vascular Access

The standard vascular access for CRRT is a dual-lumen venous catheter, which is placed in subclavian, internal jugular or femoral veins. The choice of the venous access site is determined by the risks of infection, thrombosis, and ease of placement. The risk of infection is greatest in the femoral position [31]. Due to the risk of central vein stenosis and thrombosis, the subclavian insertion site should be avoided, if possible, for CRRT access in a patient who may need permanent vascular access [32-33]. Catheter insertion in the right internal jugular vein is associated with a lower risk of complications compared to other sites [34-35]. Ultrasound-guided insertion of catheter is recommended to reduce insertion-related complications [36-37].

Replacement fluid, pre- versus post-dilution

Replacement fluids used during CRRT should contain physiologic concentrations of electrolytes and lactate or bicarbonate as buffer. Both lactate or bicarbonate based buffer solutions are able to correct the metabolic acidosis in most ARF patients [38]. A recent clinical study did not show any advantage of bicarbonate-based buffer over lactate buffer solution [39]. Thus, either lactate or bicarbonate can be used as buffer in most CRRT patients. However, bicarbonate buffer is preferred in patients with liver failure [8]. Since liver failure is a relatively frequent complication in ICU patients, many ICUs still choose bicarbonate as buffer solution. At our institution, we use commercial bicarbonate buffer solution as replacement fluid (*Hemosol BO, Hospal*).

The choice between pre- and post-dilution fluid administration depends on several factors. Pre-dilution hemofiltration may be useful in patients with frequent filter clotting since replacement fluid administered prior to hemofilter will decrease the hematocrit of the blood during the passage through the filter with theoretical lower risk of clotting problems. A recent study showed that predilution of replacement fluid was associated with increased filter life [40]. The disadvantage of pre-dilution hemofiltration is decreased efficacy of dialysis and increased requirement of replacement fluid.

Hemofilter

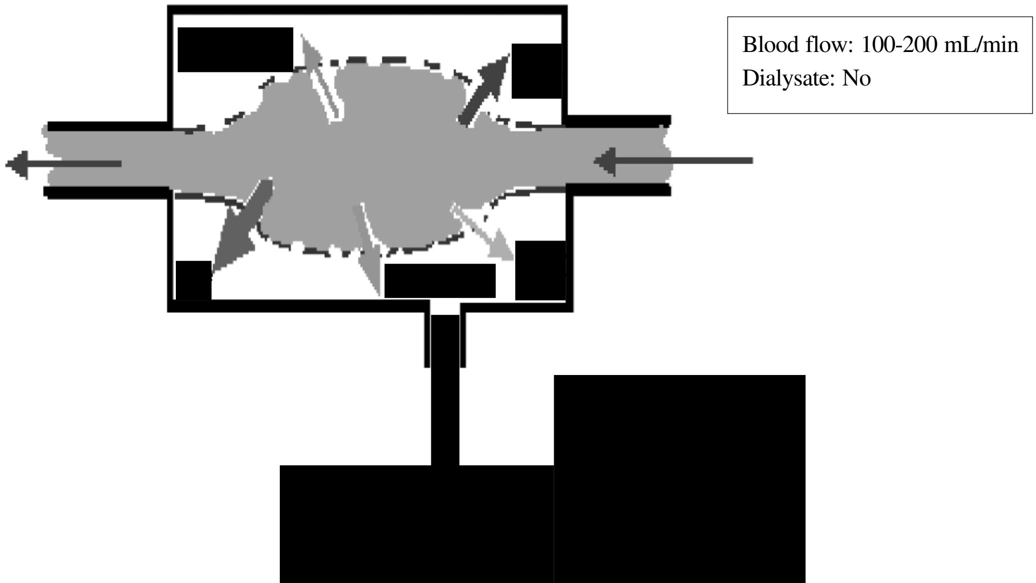
Some studies have suggested that dialysis with bioincompatible membranes is associated with a less favorable patient outcome than dialysis with biocompatible synthetic membranes [41-42]. However, other studies found no differences in the survival rate of ICU patients using cellulose-based or synthetic membrane filters [43-47]. At present time, there is insufficient data to recommend the use of specific membranes in CRRT.

Anticoagulation

Clotting of the filter is one of the most common complications of CRRT. Therefore, continuous anticoagulation needs to be provided to prevent filter clotting and extend filter life. Systemic anticoagulation with heparin is most commonly used in patients not at risk of bleeding. The degree of anticoagulation can be monitored by measurement of partial thromboplastin time (PTT). In addition, routine measurement of platelets should be done to avoid

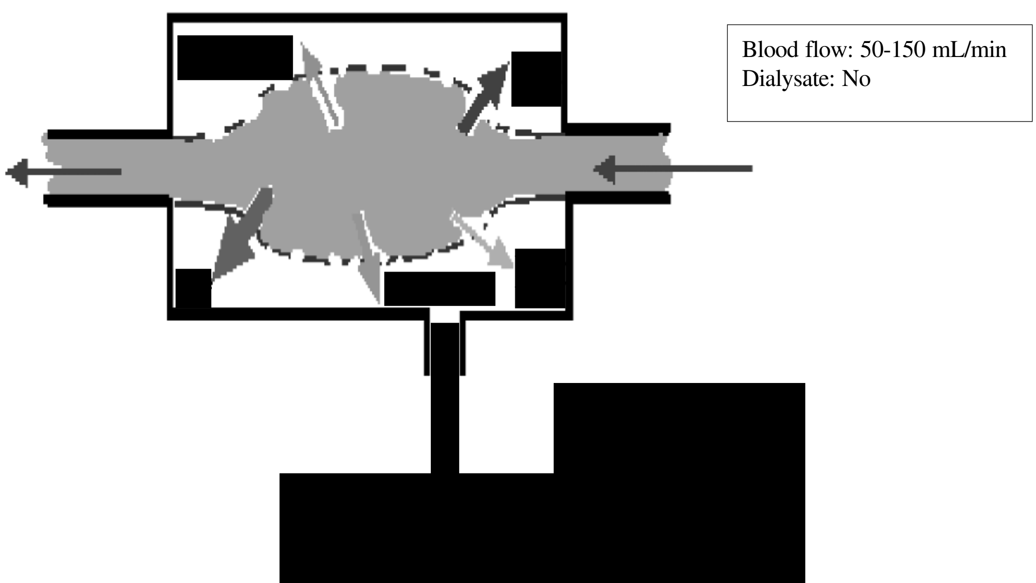
Figure. 1. The different formats of CRRT.

A. CV[redacted]s hemofiltration)



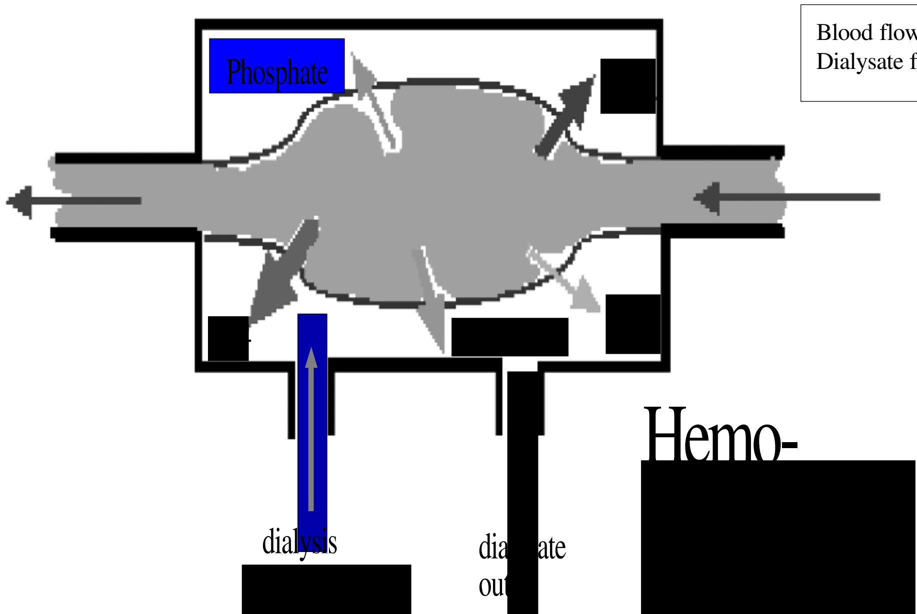
Solute removal is through convec[redacted]cur since no dialysate is used. Removal of lower molecular weight solutes ([redacted]um) is less effective than CVVHD. Large volume of ultrafiltrate (1-2 L/hr) is replaced in part or completely with a replacement fluid.

B[redacted]ltrafiltration)



SCUF is a form of CVVH with rem[redacted]es < 300 mL/hr without the use of a replacement fluid. As in CVVH, no dialy[redacted]m used. The purpose is to prevent or treat volume overload. The ideal indication for SCUF is patient with end-stage congestive heart failure, who is volume overload and awaiting urgent heart transplantation.

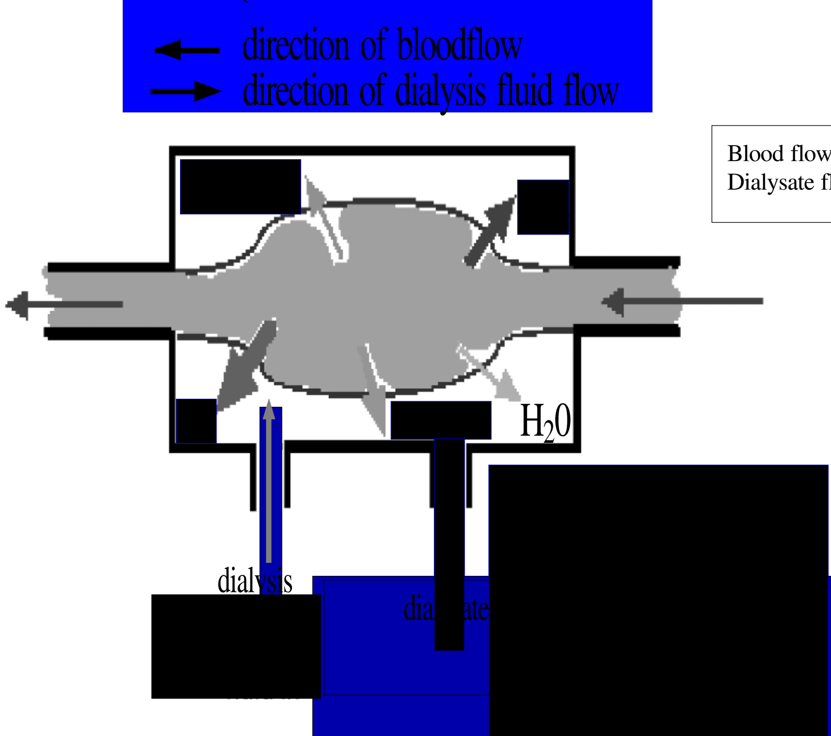
C. [redacted]hemodialysis)



Blood flow: 100-200 mL/min
Dialysate flow: 1-2 L/hr

Dialysate solution is used cou[redacted]lood[redacted]o[redacted]-2 L/hr). Solute removal is by diffusion. Replacement fluid is minima[redacted]nd[redacted]nistered.

D. CVVHDF (Continuous venovenous hemodiafiltration)



Blood flow: 100-200 mL/min
Dialysate flow: 1-2 L/hr

Dialysate solution is used countercurrent to blood flow at a rate s[redacted]te (1-2 L/hr). Large volume of ultrafiltrate (1-2 L/hr) is replaced in part or completely with a replacement solution. Solute removal is through both diffusion and convection.

heparin-induced thrombocytopenia. In patients, who are at high risk of bleeding, CRRT can also be conducted successfully without anticoagulation [48-49]. Regional citrate anticoagulation is an alternative option for patients at high risk of bleeding [50-54]. Frequent monitoring of serum ionized calcium and appropriate calcium substitution is required for regional citrate anticoagulation.

Conclusion

Acute renal failure is a common complication in ICU patients. It is associated with increased morbidity, and mortality. Renal replacement therapy is often required for more severe acute renal failure. Compared with IHD, CRRT offers a potential advantage of enhanced hemodynamic stability. However, current evidence does not demonstrate any clear improved clinical outcomes of CRRT over IHD. A multicenter randomized controlled trial comparing CRRT versus IHD is needed to answer this question, although it may be difficult to design this type of study in view of the complex status of ICU patients.

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