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Practical considerations for the dosing and adjustment of continuous renal replacement therapy in the intensive care unit

Samuel M. Galvagno Jr., DO, PhD [a,b,*], Caron M. Hong, MD, MSc [c], Matthew E. Lissauer, MD, FACS [d,e], Andrew K. Baker, MBBS, MRCP, FRCA, DICM [f], Sarah B. Murthi, MD, FACS [d,e], Daniel L. Herr, MD, MS, FCCM [g], Deborah M. Stein, MD, MPH, FACS FCCM [h]

[a] Division of Critical Care Medicine, Department of Anesthesiology, University of Maryland Medical School, Baltimore, MD
[b] Division of Trauma Anesthesiology, Program in Trauma, R Adams Cowley Shock Trauma Center, University of Maryland Medical School, Baltimore, MD
[c] Division of Critical Care Medicine, Department of Anesthesiology, University of Maryland School of Medicine, Baltimore, MD
[d] Division of Acute Care Surgery, Department of Surgery, University of Maryland Medical School, Baltimore, MD
[e] Program in Trauma, R Adams Cowley Shock Trauma Center, University of Maryland Medical School, Baltimore, MD
[f] ST7 in Anaesthesia and Intensive Care Medicine, Dorset County Hospital, Dorchester, UK
[g] Departments of Medicine and Surgery, University of Maryland School of Medicine, Baltimore, MD
[h] Department of Surgery, Program in Trauma, R Adams Cowley Shock Trauma Center, University of Maryland Medical School, Baltimore, MD

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ABSTRACT

Familiarity with the initiation, dosing, adjustment, and termination of continuous renal replacement therapy (CRRT) is a core skill for contemporary intensivists. Guidelines for how to administer CRRT in the intensive care unit are not well documented. The purpose of this review is to discuss the modalities, terminology, and components of CRRT, with an emphasis on the practical aspects of dosing, adjustments, and termination. Management of electrolyte and acid-base derangements commonly encountered with acute renal failure is emphasized. Knowledge regarding the practical aspects of managing CRRT in the intensive care unit is a prerequisite for achieving desired physiological end points.

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1. Introduction

Approximately 5% to 25% of all intensive care unit (ICU) patients develop acute renal failure (ARF) [1-3]. Once continuous renal replacement therapy (CRRT) is required, mortality may exceed 50%, [3-5] and the need for CRRT is associated with a marked increase in the patient's severity of illness and the complexity of ICU management. In many ICUs, the intensivist makes decisions regarding the initiation, dosing, adjustment, and termination of CRRT. A description of the physiology, equipment, and data supporting outcomes is beyond the scope of this review; the reader is referred to comprehensive reviews by Tolwani [3], John and Eckhardt [6], and Ghossein et al [5] for more information. The purpose of this review is to describe practical aspects for the management of CRRT by intensivists. Initiation, dosing, adjustment, and termination of CRRT will be extensively discussed.

2. Indications for CRRT

The decision regarding when to initiate CRRT is a fundamental question faced by intensivists. Although no controlled trials exist to establish clear indications for early versus late initiation of CRRT, it is a widely established practice to start CRRT for severe acidosis, uremia, hyperkalemia, or pulmonary edema when other therapeutic measures have failed for these conditions [6-8]. Established indications for the initiation of CRRT are listed in Table 1.

The principal indication for CRRT, as opposed to intermittent hemodialysis, is to correct metabolic or fluid derangements associated with ARF, in patients who are hemodynamically unstable [6,7]. Additional benefits of CRRT are the ability to continuously remove volume, customize replacement solutions for different clinical conditions, and use ICU staff instead of relying on specialized dialysis support staff. Established definitions for acute kidney injury (AKI) and ARF should be used to diagnose the condition [9,10].

3. Continuous renal replacement therapy modalities

There are 4 main modalities used for CRRT. These modalities are slow continuous ultrafiltration (SCUF), continuous venovenous hemofiltration (CVVH), continuous venovenous hemodialysis (CVVHD), and continuous venovenous hemodiafiltration (CVVHDF).

* Corresponding author. Department of Anesthesiology, Division of Trauma Anesthesiology, Program in Trauma, R Adams Cowley Shock Trauma Center, University of Maryland School of Medicine, Baltimore, MD 21230. Tel.: +1 410 328 3246.
E-mail addresses: sgalvagno@anes.umm.edu, sam_galvagno@yahoo.com (S.M. Galvagno).

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Table 1
Indications for CRRT

Indications	Comment
Life-threatening acidosis	Typically pH <7.0
Severe uremia	With associated neuropathy, myopathy, encephalopathy, or pericarditis
Hypervolemia	With pulmonary edema, bowel edema, associated with oliguria or anuria
Hyperkalemia	Usually >6.5 mmol/L with or without electrocardiographic changes
Intoxications	For clearance of *dialyzable* toxins (eg, salicylates, contrast media—agents that are water soluble and not highly protein bound)
Other severe electrolyte derangements	For example, hypernatremia or hyponatremia, usually occurring in conjunction with other electrolyte derangements
Severe sepsis	Controversial; see text for explanation
Rhabdomyolysis	May consider more liberal indications for starting CRRT in crush injury patients in anticipation of potential problems [22]

Table 3
The RIFLE criteria [9]

RIFLE stage	GFR criteria	Urine output criteria	Sensitivity/ Specificity for AKI/ARF
Risk	Increased creatinine × 1.5 Decreased GFR >25%	< 0.5 mL kg^{-1} h^{-1} × 6 h	High sensitivity
Injury	Increased creatinine × 2 Decreased GFR >50%	<0.5 mL kg^{-1} h^{-1} × 12 h	High sensitivity
Failure	Increased creatinine × 3 Decreased GFR >75% or creatinine ≥4 mg/100 mL (acute rise of ≥0.5 mg per 100 mL/dL)	<0.5 mL kg^{-1} h^{-1} × 24 h or anuria × 12 h	High specificity
Loss	Persistent ARF (complete loss of renal function >4 wk)		
End-stage renal disease	End-stage renal disease (dependent on dialysis)		

GFR indicates glomerular filtration rate.

In practice, the most commonly used modality in most ICUs is CVVH (Table 2).

The CRRT modality should be selected based on the indication and goals of clearance and/or volume removal. Although a discussion of the physiological principles is beyond the scope of this review, a few key concepts and definitions should be understood. When blood passes through the dialysis filter, solute clearance is achieved by diffusion, convection, or a combination of both. Convective clearance refers to filtration and occurs when water driven by hydrostatic or osmotic force is pushed through a membrane; solute clearance is therefore dependent on ultrafiltration. Ultrafiltration refers to the process in which hydrostatic pressure forces a liquid against a semipermeable membrane; the "ultrafiltrate" (UF) refers to the fluid collected distal to the membrane, or hemofilter. Solutes that can pass easily through the membrane pores are swept along with the water (ie, "solute drag"). Diffusive clearance refers to dialysis and occurs because of movement of solutes as the result of random molecular motion. If the solute molecule encounters a pore of sufficient size, the molecule will pass through the filter. Diffusive clearance can occur in either direction. In dialysis (diffusive clearance), solute clearance is dependent on dialysate infusion rate and blood flow rate because the faster blood flows across a dialysis membrane, the greater the opportunity to maintain a diffusion gradient across the length of the filter. The same machine and filters can be used for the different modalities (Tables 3-5).

Clearance of solutes depends largely on molecular size. Diffusive clearance of solutes by hemodialysis decreases rapidly with increasing molecular weight. For example, in rhabdomyolysis, myoglobin has a molecular weight that exceeds the pore size of standard CVVH filters and is poorly cleared [11-13]. Dialysis membranes (eg, Polyflux series; Gambro Lundia AB, Lund, Sweden) with larger pores have been shown to improve clearance of myoglobin compared with conventional dialysis [11]. Similarly, with drugs, the capacity of a drug to pass through a dialysis filter membrane is governed by the sieving coefficient. A sieving coefficient represents the ratio of drug concentration in the UF to the drug concentration in the plasma. A coefficient of 1 indicates full passage of solute through the filter (eg, sodium and potassium), whereas a coefficient of 0 (eg, albumin) indicates that the solute does not pass through the filter at all [14]. Filter age and protein binding are factors that influence the sieving coefficient. Overall clearance of larger molecules such as drugs is dependent on both the sieving coefficient and the dialysis flow rate.

For smaller solutes (<300 d) such as urea, creatinine, or amino acids, convection or diffusion is the mechanism of clearance. For middle-size solutes (500-50 000 d) or large proteins (<50 000 d) such as myoglobin, vitamin B_{12}, vancomycin, or albumin, convection is the mechanism of clearance; CVVH can be used to clear these molecules. Low-molecular-weight proteins (5000-50 000 d) such as inflammatory mediators are cleared by both convection and adsorption; CVVHDF is an appropriate modality to clear these molecules.

In both SCUF and CVVH, no dialysate is used. Slow continuous ultrafiltration simply involves running blood through the filter without replacement fluid, to allow fluid removal. Conversely, with CVVH, blood is run through the filter with a replacement fluid added either before and/or after the filter. Molecules that are small enough (<50 000 d) pass through the semipermeable CVVH filter membrane through the process of convection. The filtered fluid (UF) is removed and replaced to create the desired fluid balance (ie, "even" or "negative 50 mL/h"). In CVVH, the replacement fluid is used to replace the volume of fluid removed, as opposed to hemodialysis, where blood is separated from a crystalloid solution by a semipermeable membrane, and clearance is affected by diffusion. Continuous venovenous hemofiltration is indicated for the removal of middle or large molecules (ie, blood urea nitrogen, creatinine, myoglobin) when precise control of fluid management is needed.

Continuous venovenous hemodialysis involves the addition of dialysate after blood is separated by diffusion across a semipermeable membrane (ie, haemodiafilter; Fig. 1). For example, bicarbonate moves from dialysate to blood, whereas urea and potassium move from blood to dialysate. The dialysate flows countercurrent to the flow

Table 2
Definition of AKI

AKI is defined as *any one* of the following: [7]
1. Increase in serum creatinine by >0.3 mg/dL; OR
2. Increase in serum creatinine by >1.5 times baseline, which is known or presumed to have occurred within the prior 7 d; OR
3. Urine volume <0.5 mL kg^{-1} h^{-1} for 6 h

Table 4
The 4 principle modalities used for CRRT

Modality	Urea clearance (g/d)	Replacement fluid	Dialysate	Solute transport	UF flow (mL/h)	Dialysate flow (mL/h)
SCUF	1-4	No	No	Convection	100-400	0
CVVH	22-24	Yes	No	Convection	500-4000	0
CVVHD	24-30	No	Yes	Diffusion	0-350	500-4000
CVVHDF	36-38	Yes	Yes	Convection + diffusion	500-4000	500-4000

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