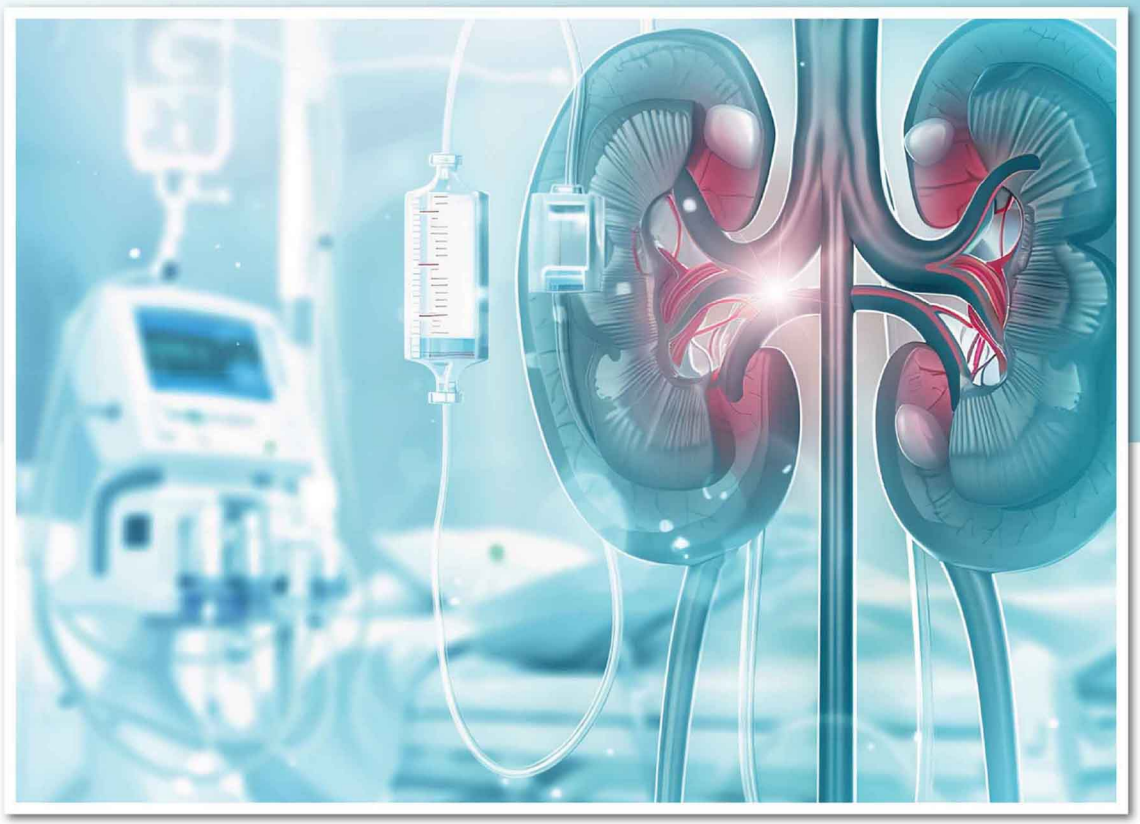
Handbook in Critical Care Nephrology

A Bedside Guide



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Contents

CHAPTER

11

Dose and Prescription in Continuous Renal Replacement Therapy

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INTRODUCTION

Continuous renal replacement therapy is an essential component of critical care management in contemporary intensive care units of critically ill patients. It manages a wide range of complications, including acute kidney injury (AKI), metabolic acidosis, electrolyte disturbance, and fluid overload. In comparison with intermittent hemodialysis (IHD), this modality has an advantage since it can continuously remove fluid and solute from the patient, including in hemodynamically unstable patients. Thus, continuous renal replacement therapy (CRRT) may also be termed *continuous organ support therapy (COST),* which reflects its broader systemic stabilization effect.[1]

Continuous renal replacement therapy dosing is much more complex than IHD. Unlike IHD, urea clearance (kt/V urea) is not always the only factor determining the dose; in CRRT, the dosage is determined based on effluent volume rate.[2] This is also required due to dynamic fluid distribution and metabolic alterations observed in ICU patients. However, despite its benefits, CRRT presents challenges such as filter clotting, nutrient loss, hypophosphatemia, and increased resource intensity compared to IHD. While CRRT is widely considered a standard treatment for critically ill patients with renal dysfunction globally, its use should be carefully evaluated based on each patient's specific needs and condition.

CASE SCENARIO

A 63-year-old lady was admitted to the ICU with septic shock associated with a urinary tract infection. Subsequently, she developed an acute kidney injury along with fluid overload and metabolic acidosis. The ICU team decided on CRRT using continuous venovenous hemodiafiltration (CVVHDF).

The initial dose of 25 mL/kg/h for CRRT was reasonable, but this dose was continuously interrupted by the filter clotting and hemodynamic instability. The delivered dose fell below the target, and downtime adjustments and alterations in the filtration fraction (FF) were made for dose optimization for CRRT.

DOSING EVOLUTION AND KEY TRIALS

The optimal dose of CRRT has been the object of passionate research. Initially, high effluent rates–up to 40 mL/kg/h, were believed to confer survival benefits. However, many key trials have reshaped this perspective.

Acute Tubular Necrosis Trial

In the critical illness, acute tubular necrosis (ATN) trial compared intensive (35 mL/kg/h) versus less intensive (20 mL/kg/h) renal replacement therapy in acutely critically ill patients. Both groups underwent intermittent hemodialysis or CRRT. The study did not indicate any statistically significant difference in 60-day mortality, thereby disproving the idea that larger doses are related with favorable outcomes.[3]

Randomized Evaluation of Normal versus Augmented Level Trial

The RENAL study further compared CRRT parameters of 25 mL/kg/h versus 40 mL/kg/h

in patients with AKI. Extending survival over a period of 90 days as the primary endpoint, the trial also did not show a significant advantage with higher doses. These findings defined 25 mL/kg/h as the reference dose for CRRT.[4]

Practical Implications

However, practical challenges such as downtime frequently prevent patients from receiving the full prescribed dose. The DO-RE-MI (Dobutamine compared to milRInone in Milrinone (or Management of) Cardiogenic Shock) study highlighted this issue, showing that only 22% of patients prescribed a total effluent flow rate of ≥35 mL/kg/h actually received the intended dose.[5] Consequently, to achieve the desired therapeutic target, clinicians must consider prescribing a higher effluent dose to compensate for these interruptions.

During CRRT, the FF must be kept below 20%. This prevents complications such as hypotension, lowered renal perfusion, and filter clotting. High FF can result in too much fluid being removed, leading to a steep drop in blood pressure and a reduction in renal blood flow that risks impairing overall hemodynamic stability and renal function. To control for this risk, the ultrafiltrate flow rate (UFR) and plasma flow rate (PFR) need to be monitored constantly and adjusted closely by the clinician. The FF formula is:

$$FF = \left(\frac{UFR}{PFR}\right) \times 100$$

Example

A clinician observes the following settings:

- *UFR* = 180 mL/h
- *PFR* = 1,200 mL/h

The FF is calculated as: FF= (180/1,200) × 100 = 15%

This value is below 20%, indicating the current settings are safe for fluid removal.

Now imagine the patient experiences a drop in blood pressure, reducing the PFR to 900 mL/h.

The new FF becomes: FF= (180/900) × 100 = 20%

While the FF is at the upper safe limit, further reductions in *PFR* could result in complications like filter clotting or hypotension.

Adjustment options:

- *Reduce UFR:* To maintain the FF below 20%, the UFR can be adjusted to:

  New UFR = PFR × 0.18 = 900 × 0.18 = 162 mL/h
- *Increase PFR:* Alternatively, increasing the PFR will lower the FF. For example:

  New PFR = UFR/0.18 = 1800/.18 ≈ 1,000 mL/h

  New FF will be: (162/1,000) ×100 = 16.2%

Outcome

By making than ese adjustments, the FF is maintained within a safe range, reducing risks and ensuring effective fluid removal. This is, however, an oversimplification of the CRRT dose. The dosing pattern changes as per the disease and the patients' clinical presentation.

CONTINUOUS RENAL REPLACEMENT THERAPY MODALITIES IN PRACTICE

The continuous form of renal replacement has many modalities. It works on the principles of diffusion, ultrafiltration, convection, and adsorption. Understanding these principles is essential for optimizing therapy **(Fig. 1)**.

Continuous Venovenous Hemodialysis

Continuous venovenous hemodialysis (CVVHD) relies on diffusion, where solutes move across a semipermeable membrane down a concentration gradient. This modality is particularly effective in patients with hyperkalemia and uraemia.[6] For instance, a patient with refractory hyperkalemia due to tumor lysis syndrome can be benefited with CVVHD, with potassium levels normalizing within hours.

Continuous Venovenous Hemofiltration

In CVVHF, convection drives solute removal. This modality is ideal for managing sepsis-induced AKI with significant inflammatory mediator loads.[7] A septic patient with a cytokine storm can show clinical improvement after CVVHF, where high ultrafiltration rates remove excess inflammatory mediators.

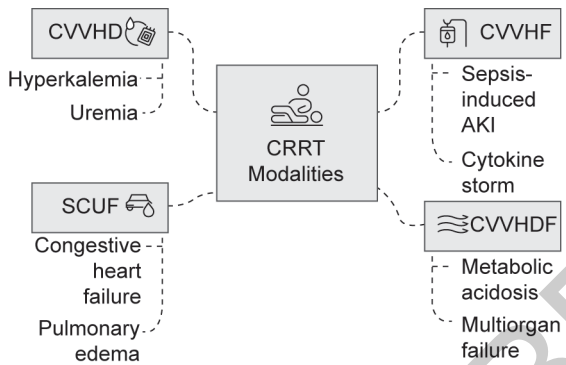

Fig. 1: CRRT modalities. (CRRT: continuous renal replacement therapy; CVVHD: continuous venovenous hemodialysis; CVVHF: continuous venovenous hemofiltration; CVVHDF: continuous venovenous hemodiafiltration; SCUF: slow continuous ultrafiltration)

Continuous Venovenous Hemodiafiltration

Continuous venovenous hemodiafiltration combines diffusion and convection, making it adaptable for various solutes.[8,9] For example, a patient with severe metabolic acidosis and multiorgan failure can achieve rapid acid-base correction with CVVHDF.

Slow Continuous Ultrafiltration

Slow continuous ultrafiltration (SCUF) focuses solely on fluid removal. It is often used in patients with congestive heart failure and pulmonary edema.[10] A patient with refractory pulmonary edema, unresponsive to diuretics, can have significant symptom relief and better oxygenation within 24 hours of initiating SCUF.

Prescribing Continuous Renal Replacement Therapy Dose: A Patient-centered Approach

Optimal CRRT dosing is not fixed but has to be adjusted to the dynamic state of the patient. Factors to be taken into account are the FF, the blood flow, and fluid balance **(Table 1)**.[11,12]

TABLE 1: Key points for prescribing CRRT dose.

Factor	*Optimal range*	*Considerations*	*Example*
FF	20–30%	Avoid high FF to prevent hypotension and filter clotting	Reducing the ultrafiltration rate from 300 to 150 mL/h decreased FF from 30% to 18%, stabilizing a hypotensive patient
Blood flow rate	Five to six times the ultrafiltration flow (for CVVHDF)	Higher blood flow enhances efficiency and reduces filter clotting	Increasing blood flow from 120–180 mL/min can improve solute clearance and decrease thrombus formation in a hypovolemic patient
Fluid balance	Individualized based on patient needs	Accurate fluid removal for volume-overloaded patients	Adjusting net ultrafiltration to 250 mL/h in a 70-year-old man with severe ascites can achieve gradual weight reduction
CRRT dose	20–25 mL/kg/h (delivered)	Prescribe 25–30 mL/kg/h to account for interruptions	Frequent assessment and adjustment of the prescription to achieve the target delivered dose

(CRRT: continuous renal replacement therapy; CVVHDF: continuous venovenous hemodiafiltration; FF: filtration fraction)

CONTINUOUS RENAL REPLACEMENT THERAPY IN SPECIALIZED CONDITIONS

Acute Brain Injury

Brain-kidney interaction is often complicated in ABI patients, such as the syndrome of inappropriate antidiuretic hormone (SIADH) and cerebral edema. CRRT can help manage these complications.

In these situations, prompt implementation of continuous venovenous hemofiltration (CVVH) is advised. Cerebral edema, an ABI complication widely treated, can be effectively treated by switching to slow continuous ultrafiltration (SCUF), where the ultrafiltration rate is <13 mL/kg/h. In order to improve the results, the CRRT circuit may be primed with albumin, and the dialysate quality may be adjusted with higher sodium levels and lower bicarbonate amounts to better meet the fluid and electrolyte requirements of ABI patients.[13]

For example, A 45-year-old man with traumatic brain injury and AKI initially received CVVH treatment to resolve metabolic alterations. After stabilization, SCUF was used to reduce intracranial pressure (ICP) through the negative fluid balance of 500 mL/day by SCUF. This transition enabled focused control of cerebral edema with the preservation of systemic stability.

Acute Liver Failure

Hyperammonemia in ALF poses unique challenges. Aggressive ammonia clearance by CVVHDF at a rate of 50 mL/kg/h can improve neurologic function in a case of an adolescent female with fulminant hepatic failure.[14] Additional manipulation of dialysate composition (increasing sodium concentration to prevent cerebral edema and reducing bicarbonate levels to avoid worsening ammonia production) may further improve results, stabilizing ammonia levels in 48 hours.

PRACTICAL CONSIDERATIONS FOR QUALITY AND SAFETY

Ensuring the quality of CRRT involves consistent monitoring and adjustments.[15-18]

Key Indicators

- *Effluent urea nitrogen/blood urea nitrogen ratio:* Maintain >0.8 for effective clearance.
- *Downtime:* Prescribe 10–15% higher doses to compensate.
- *Sieving coefficient:* Aim for >0.9 for small solutes like urea.
- *Setting flow rates* ***(Table 2):***
- *Patient fluid removal*: Patient fluid removal rate (to be set on machine) = Net fluid removal (hourly) + non-CRRT intake—non-CRRT output.

TABLE 2: Key aspects of setting flow rates in CRRT.

Parameter	*CVVHD*	*CVVHDF/CVVHF (Postfilter)*	*CVVHDF/CVVHF (Prefilter)*	*Additional considerations*
Blood flow rate	≥2.5–3 times dialysate flow/minute	≥5 times UF rate/min	≥6 times ultrafiltration rate/min	Typically, 150–250 mL/min
Dialysate and replacement rates	17–33 mL/min	17–33 mL/min	17–33 mL/min	UF: Dialysate ratio in CVVHDF is usually 1:1
Replacement fluid infusion	N/A	Postfilter	Prefilter	Often divided in a 1/3:2/3 ratio between pre- and postfilter

(CVVHD: continuous venovenous hemodialysis; CVVHDF: continuous venovenous hemodiafiltration; CVVHF: continuous venovenous hemofiltration; UF: ultrafiltration)

Clinical Example

Patient fluid removal calculation for continuous renal replacement therapy

Mr Y is a 60-year-old male on *CRRT-CVVHDF*, currently on day 3 of treatment. The intensivist has prescribed a net fluid removal rate of 250 mL/h based on the patient's fluid status from the previous 24 hours. In the last hour, the patient has received the following fluids:

- *Tube feed*: 120 mL.
- *IV ceftriaxone*: 60 mL.
- *IV normal saline*: 80 mL.

Additionally, the patient's outputs for the last hour include:

- *Drain output*: 180 mL
- *Urine output*: 90 mL

Now, calculate the patient's fluid removal rate that needs to be set on the CRRT machine.

Solution:

- *Net fluid removal (as per intensivist order)* = 250 mL/h.
- *Non-CRRT intake* (fluids received in the last hour):
  - *Tube feed*: 120 mL
  - *IV ceftriaxone*: 60 mL
  - *IV normal saline*: 80 mL

  Total non-CRRT Intake = 120 + 60 + 80 = 260 mL.
- *Non-CRRT output (fluids removed in the last hour)*:
  - *Drain output*: 180 mL
  - *Urine output*: 90 mL

  Total non-CRRT output = 180 + 90 = 270 mL
- *Patient fluid removal rate to be set on the machine*:

Patient fluid removal rate = (Net fluid removal) + (Non-CRRT intake) – [Non-CRRT output = (250 mL/h) + (260 mL) – (270 mL) =240 mL/h]

Thus, the *patient's fluid removal rate* to be set on the CRRT machine is *240 mL/h*.

CONTINUOUS RENAL REPLACEMENT THERAPY PRESCRIPTION SETUP AND EXAMPLE (CASE SCENARIO)

Patient details: Mrs X

- *Age:* 63 years; weight: 60 kg
- *Hematocrit (Hct):* 0.3
- *Condition:* Severe Sepsis with Metabolic Acidosis (KDIGO III) due to UTI

CONTINUOUS RENAL REPLACEMENT THERAPY MODE SELECTED: CONTINUOUS VENO-VENOUS HEMODIAFILTRATION

Prescription Setup

See **Table 3**.

Example Calculation

- *Total dose (effluent rate calculation)*: The effluent rate is the sum of the dialysate rate (DR) and UFR. In this case: Effluent rate (EFR) = DR + UFR = 1,200 mL/h + 1,200 mL/h = 2,400 mL/h.
- *Prescribed dose (mL/kg/h)*: The prescribed dose is calculated by dividing the effluent rate by the patient's weight:

Prescribed dose =

$$\text{EFR/Weight} = \frac{2400\ \text{mL/h}}{60\ \text{kg}} = 40\ \text{mL/kg/h}$$

TABLE 3: Prescription parameters in CRRT and their clinical significance.

Parameter	*Value*	*Explanation*
Dialysate rate (DR)	1,200 mL/h	The rate at which dialysate is infused for solute clearance in the CRRT circuit
Ultrafiltrate rate (UFR)	1,200 mL/h	The rate at which fluid is removed from the patient (also the replacement rate)
Effluent rate (EFR)	2,400 mL/h	The total effluent rate is calculated as the sum of DR and UFR (dialysate + ultrafiltrate)
Prescribed dose (mL/kg/h)	40 mL/kg/h	The total dose of CRRT is calculated as the effluent rate divided by patient weight
PFR	200 mL/h	The rate at which fluid is removed from the patient, which is the net ultrafiltration rate

(CRRT: continuous renal replacement therapy; DR: dialysate rate; PFR: patient fluid removal rate; UFR: ultrafiltration rate)

- *Patient fluid removal (including PFR)*: If the patient fluid removal rate (PFR) is 200 mL/h, then the effluent rate becomes:

  New effluent rate = EFR + PFR = 2,400 mL/h + 200 mL/h = 2,600 mL/h
- *New prescribed dose with PFR*:

  The new prescribed dose after including the PFR is calculated as:

$$\text{New dose} = \frac{2600\ \text{mL/h}}{60\ \text{kg}} = 43.3\ \text{mL/kg/h}$$

The final prescribed dose for Mrs X is 43.3 mL/kg/h, based on an effluent rate of 2,400 mL/h for a 60 kg patient. Several factors can reduce the effective dose:

- *Predilution effect*: Predilution of replacement fluids can reduce the clearance efficiency by *7.5%*. Therefore, the effective dose after predilution is:

  Effective dose after predilution = 43.3 mL/kg/h × (1 – 0.075) = 40.1 mL/kg/h
- *Downtime or stoppage*: If there are interruptions in the CRRT circuit (such as filter clotting or technical issues), the total effluent volume delivered will be less than prescribed. Assuming a *40% decrease* due to stoppage, the effective dose becomes:

  Effective dose after downtime = 40.1 mL/kg/h × (1 – 0.40) = 24.1 mL/kg/h
- *Sieving coefficient*: The sieving coefficient, which measures the efficiency of CRRT in removing small solutes like urea, is *0.9*. Applying the sieving coefficient reduces the dose further:

  Final effective dose = 24.1 mL/kg/h × 0.9 = 21.7 mL/kg/h

Final Calculation

Thus, the prescribed dose of 43.3 mL/kg/hr is effectively reduced to 21.7 mL/kg/h after considering:

- *7.5% reduction* due to predilution
- *40% reduction* due to downtime
- *90% reduction* due to the sieving coefficient

This example illustrates how the effluent rate, patient fluid removal, and prescribed dose are calculated for a patient on *CVVHDF* mode in CRRT. The calculations take into account fluid removal (ultrafiltration), dialysate flow, and adjustments based on patient needs, such as patient fluid removal (PFR).

CONCLUSION

Continuous renal replacement therapy is frequently utilized in patients with severe AKI, fluid overload, and hemodynamic instability with the goal of optimizing solute control, acid–base, and volume status. CRRT dosing necessitates a dynamic, individualized strategy, combining evidence-based standards with practice-based personalization. Although a maximum dose of 25 mL/kg/h can be considered as a reference, therapy needs to be determined on a patient-by-patient basis, as well as on-demand practice. Continued research is essential to refine dosing strategies and improve patient outcomes in critical care settings.

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Handbook in Critical Care Nephrology
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The book has been based on the principles of *"Stick to Basics"* and *"Common Things are Common"*.

- Clinically relevant topics related to renal dysfunction in critically ill patients
- Case-based scenarios in each chapter
- Practical points related to the management of such patients
- Current updates and evidence-based practices feasible in resource-limited set-ups
- Drug dosing, especially antibiotics in acute kidney injury and chronic kidney disease
- Nutrition in renal dysfunction
- Continuous renal replacement therapy (CRRT) machine description and various fluids used
- Easy and simple language
- Design is kept simple and easy to comprehend for all healthcare personnel.

Sharmili Sinha MD DNB EDIC FICCM FCCM PGDHM has been working as a Senior Consultant, Department of Critical Care Medicine, Apollo Hospitals, Bhubaneswar, Odisha, India, with more than 20 years of experience. She is also Associate Professor, Department of Critical Care, The Apollo Hospitals Educational and Research Foundation (AHERF), India. After completing MBBS from Srirama Chandra Bhanja Medical College and Hospital, Cuttack, Odisha, she joined Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, for postgraduate studies. She has gained valuable experience from various institutes, including Grant Medical College and Sir JJ Group of Hospitals, Tata Memorial Hospital, and PD Hinduja Hospital, Mumbai, Maharashtra. She spent a few years in Australia in advanced training in intensive care and served at Bankstown Hospital, Liverpool Hospital, and St George Hospital in New South Wales, Australia. She has been closely associated with the Indian Society of Critical Care Medicine (ISCCM) and has been elected as National Executive Member (2020–2024), Vice President (2024–2026), and General Secretary Elect (2026 onward). She is a well-acclaimed academician at national and international forums. She is a Fellow of the Indian College of Critical Care Medicine (FICCM) and American College of Critical Care Medicine (FCCM). She is a strong protagonist of growth and spread of critical care education and training to the peripheral parts of the country. Her vision is to strengthen critical and emergency care training across India with concerted team efforts and collaboration.

Shelving Recommendations
CRITICAL CARE AND NEPHROLOGY

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