Continuous Renal Replacement Therapy (CRRT): Principles, Dosing & Evidence

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Definition & Indications

CRRT = Renal replacement therapy applied continuously (24 hours/day) in ICU setting

Key feature: Slow, continuous removal of solutes & fluid (vs. intermittent HD's rapid cycling)

Indications: - **Acute kidney injury in critically ill** (hemodynamic instability) - **Fluid overload** (pulmonary edema, HF, sepsis) - **Severe hyperkalemia** (unresponsive to medical management) - **Uremia** (if intermittent dialysis inadequate or unstable) - **Severe acidosis/alkalosis** (buffer adjustment via CRRT dialysate) - **Toxin removal** (theophylline, aspirin, phenobarbital — slower than HD but continuous) - **Thermal management** (hypothermia or hyperthermic correction via dialysate temperature)

> [!important] **CRRT for AKI:** - Better tolerated in unstable patients (gradual fluid/electrolyte changes) - No mortality advantage vs. intermittent HD in randomized trials (ATN/RENAL trials) - **Choice driven by hemodynamic stability, not efficacy**

CRRT Modalities: How They Differ

CVVH: Continuous Venovenous Hemofiltration

Mechanism: Convection (solvent drag) - Blood passes through filter - Hydrostatic pressure forces fluid + solutes across semipermeable membrane (ultrafiltration) - Ultrafiltrate removed directly - "Replacement fluid" infused either pre- or post-filter to maintain blood volume

Solute removal: - **Good small solute clearance** (urea, creatinine, electrolytes via convection) - **Excellent large solute clearance** (β2-microglobulin, middle molecules)

Fluid removal: - **Precise**: Accurate UF controlled by pump

CVVHD: Continuous Venovenous Hemodialysis

Mechanism: Diffusion (concentration gradient) - Blood on one side of filter; dialysate on other - Solutes move by concentration gradient (like regular hemodialysis but slower) - Minimal ultrafiltration (no replacement fluid)

Solute removal: - **Good for small solutes** (diffusion-dependent) - **Slower for large molecules** (convection absent)

Advantage: Less fluid replacement needed (cheaper)

CVVHDF: Continuous Venovenous Hemodiafiltration

Mechanism: Convection + Diffusion (BEST of both) - Combines hemofiltration (convection) + hemodialysis (diffusion) - Ultrafiltrate removed + dialysate run in counter-current - **Highest total solute clearance**

Advantages: - Best small + large molecule removal - Most "efficient" in clearing uremia

Disadvantage: Highest fluid replacement cost; requires highest vascular access flow

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Vascular Access for CRRT

Central Venous Catheter (CVL) Requirements

Catheter type: - **Dual-lumen or triple-lumen** non-tunneled CVL - Preferably 20 cm length; flow needs adequate lumen diameter - **Preferred sites:** IJ (right) > subclavian (avoid left) > femoral (last resort; infection risk)

Flow requirements: - **Minimal:** 80–100 mL/min - **Typical:** 150–300 mL/min - **Better clearance:** 300–400 mL/min

Complications

- **Infection:** Bacteremia, catheter-related bloodstream infection (CRBSI)
  - Risk ↑ with femoral access, prolonged duration
  - Prevention: Sterile technique, minimize line days, remove when no longer needed
- **Stenosis/thrombosis:** Catheter partially occludes
- **Hemolysis:** Catheter malposition or obstruction
- **Central vein stenosis:** Long-term catheter use (rare in acute setting)

CRRT Dosing: How Much is Enough?

Dose Definition

Effluent flow rate = replacement fluid + dialysate + net ultrafiltration

Expressed as: mL/kg/hour (normalized to body weight)

Landmark Trials: ATN & RENAL

ATN Trial (2008): - Compared **standard dose** (35 mL/kg/h) vs **high dose** (45–50 mL/kg/h) - Result: **No difference in mortality** (60% both groups) - Conclusion: Standard dose adequate

RENAL Trial (2009): - Compared **standard dose** (20–25 mL/kg/h) vs **high dose** (35–45 mL/kg/h) - Result: **No mortality benefit for high dose** (56% mortality both groups) - Conclusion: Lower standard dose (20–25 mL/kg/h) sufficient; reduces filter replacement costs

Current Recommendations (KDIGO 2012)

Setting	Dose	Modality
AKI without sepsis	20–25 mL/kg/h	Any CRRT modality
AKI + sepsis	35 mL/kg/h recommended	CVVHDF preferred
Refractory hyperkalemia	Higher dose (>35 mL/kg/h)	CVVHD or CVVHDF
Refractory hypoxemia	Variable; depends on goal	Any modality

> [!tip] **Practical dosing:** Start at 20–25 mL/kg/h; increase to 30–35 mL/kg/h if sepsis, inadequate UF, or persistent hyperkalemia. No benefit beyond 35–40 mL/kg/h in standard AKI.

Dose Calculation Example

Patient: 80 kg male, standard AKI

Dose = 25 mL/kg/h × 80 kg = **2,000 mL/h = 2 L/h total effluent**

If using CVVHDF: - CVVH replacement: 1,000 mL/h - Dialysate: 1,000 mL/h - Net UF: 0 mL/h (can adjust based on fluid status)

Anticoagulation in CRRT

Why Anticoagulation?

Problem: Blood + artificial filter + slow flow → thrombosis → filter clotting - **Filter life:** Without anticoagulation, ~6–12 hours - **Filter life:** With anticoagulation, ~24–48 hours

Options

Agent	Mechanism	Pros	Cons
Heparin (unfractionated)	Thrombin inhibition	Cheap, reversible, monitored	Systemically anticoagulated (bleeding risk)

Agent	Mechanism	Pros	Cons
Citrate (regional)	Local chelation of Ca → inhibits coagulation	No systemic anticoagulation; safer in bleeding; lower thrombosis	Complex; requires Ca reinfusion; hypernatremia risk
Epoprostenol	PGI2 analogue	No systemic anticoagulation	Expensive, flash pulmonary edema risk (vasodilation)
Nafamostat mesilate	Factor Xa inhibitor	Regional anticoagulation	Limited availability (Japan); expensive
No anticoagulation	Tolerate filter clotting	Avoids bleeding risk	Frequent filter changes; expensive

Citrate (Preferred in Most ICUs)

Mechanism: - Citrate chelates Ca in filter circuit - Coagulation cascade inhibited (Ca needed for thrombin) - Citrate metabolized in liver → HCO_3 regenerated - Systemic ionized Ca reinfused post-filter

Advantages: - **Regional anticoagulation** (only filter exposure to anticoagulant) - Safe in bleeding patients - ↓ Systemic anticoagulation-related bleeding - Filter longevity 48 hours typical

Complications: - **Citrate accumulation:** If liver failure; citrate not metabolized → ionized Ca ↓, metabolic alkalosis - **Hypernatremia:** High Na in citrate solution - **Hypomagnesemia:** Mg lost with filtrate; need reinfusion

Monitoring: Check ionized Ca (post-filter), electrolytes daily

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Filter Selection & Management

Types of Filters

Membrane Type	Pore Size	Clearance Profile	Cost
Low-flux polysulfone	Small pores	Small molecules; minimal middle molecules	$
High-flux polysulfone/PEPA	Large pores	Excellent small + large molecule	$\|\| * *Hemodiafiltration−optimized(CVVHDF) *\|Variable\|Bestoverallconvection)\|$

Choice: High-flux filter > low-flux for sepsis, AKI (better cytokine/mediator removal)

Filter Clotting Prevention

1. **Adequate anticoagulation** (citrate preferred)
2. **Adequate vascular access flow** (>150 mL/min minimum)
3. **Avoid catheter kinks** (position check)
4. **Regular flushing** (NS 100 mL q1h or continuous)
5. **Avoid hypotension** (maintain MAP >65 mmHg)
6. **Monitor TMP** (transmembrane pressure)
    - If TMP ↑ rapidly → filter clotting imminent

CRRT Settings & Monitoring

Typical ICU Setup

Hemofilter machine (e.g., Prismaflex, Multifiltrate): - Blood pump: 100–400 mL/min - Replacement fluid pump: 0–1,000 mL/h - Dialysate pump (if CVVHD): 0–1,000 mL/h - Effluent pump (waste removal): automated based on UF goal - Alarms: TMP, line pressure, clotting risk, temperature

Daily Monitoring Parameters

Parameter	Frequency	Target
BMP (Cr, K, Na, HCO3)	Daily	Normal range
Ionized Ca (if citrate)	Daily	0.9–1.1 mmol/L (post-filter)
Mg, PO4	Daily–Q2 days	Replete if low
Citrate level (if accumulation suspected)	As needed	<20 mmol/L
TMP (transmembrane pressure)	Continuous	<300 mmHg; ↑ = clotting
Fluid balance	Hourly	Prescribed UF
CBC (Hgb, platelets)	Q1–2 days	Track for bleeding/transfusion
Fibrinogen, PTT	If citrate	Monitor citrate metabolism

Special CRRT Scenarios

CRRT in Sepsis

Rationale: Continuous removal may clear inflammatory mediators (TNF-α, IL-6)

Evidence: Landmark trials (PRISM, CCM 2020) show **no mortality benefit** of high-dose CRRT vs standard - Some evidence: **Early CRRT (within 6h)** may improve outcomes (inconsistent) - **Recommendation:** Standard dose 25–30 mL/kg/h; high-flux filter preferred

CRRT for Toxin Removal

Best modality: CVVHDF (convection + diffusion)

Examples: - **Phenobarbital:** Long half-life; CRRT helpful for clearance - **Aspirin (salicylate):** Intermittent HD actually better (high dose clearance) - **Theophylline:** CRRT adequate; low urgency - **Methanol/ethylene glycol:** Intermittent HD preferred (faster removal)

CRRT Weaning & Discontinuation

Indicators to stop CRRT: 1. **GFR recovery:** Cr plateau or ↓; patient producing adequate urine 2. **Hemodynamic stability:** Can tolerate intermittent RRT 3. **Electrolyte stability:** No longer need continuous correction

Weaning protocol: 1. **Reduce effluent flow** (from 25 mL/kg/h → 20 → 15 → 10 mL/kg/h) 2. **Reduce frequency** (discontinue intermittently; e.g., 20h/day → 12h → 6h → off) 3. **Trial off CRRT:** If stable 24 hours, can discontinue

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Complications Specific to CRRT

Electrolyte Imbalances

- **Hypokalemia:** ↑ K removal; common; monitor daily; may need K reinfusion
- **Hypomagnesemia:** Mg lost with ultrafiltrate; need repletion
- **Hypernatremia:** Excess Na in replacement/dialysate; manage fluid carefully
- **Hypocalcemia:** Citrate chelation; monitor; reinfuse ionized Ca as needed

Hypothermia

Mechanism: Large fluid volumes at room temperature → core temp ↓

Management: Warm replacement/dialysate to 37°C; insulate tubing

Malnutrition

Problem: Continuous UF removes glucose, amino acids - Patients often require propofol (sedation; lipid calories), high-dose dextrose - Overall: Protein-catabolic state in sepsis; nutrition support critical

Strategy: Early enteral nutrition; if unable, TPN with high amino acids + dextrose

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Related Resources

- Comprehensive CRRT Pathophysiology & Management
- AKI Staging & Classification
- RRT Modality Selection

Self-Test Questions

1. **80 kg male in septic shock, AKI Stage 3, K 6.2, pH 7.22**
   - CRRT modality: CVVHDF (best for sepsis + refractory hyperkalemia)
   - Dose: 30–35 mL/kg/h (ATN/RENAL trials show no benefit >35, but sepsis may warrant higher end)
   - Anticoagulation: Citrate (regional; safer if bleeding risk from sepsis coagulopathy)
2. **CRRT filter clotting at 8 hours despite heparin**
   - Causes: Low vascular access flow? Hypotension? Catheter malposition?
   - Troubleshoot: Check TMP, line pressures, blood flow rate, BP
   - Switch anticoagulation: Try citrate (longer filter life expected)
3. **Mg 1.4 (low), K 3.2 (low), Ca post-filter 0.8 (low)**
   - Abnormalities: Typical CRRT losses
   - Management: Mg reinfusion (1–2 g/day), K reinfusion if continuing RRT, Ca reinfusion post-filter
   - Avoid: Over-replacement (rebound hyperkalemia when RRT stops)

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References: ATN Trial (NEJM 2008), RENAL Trial (NEJM 2009). KDIGO 2012 CRRT Dosing & Modality Guidelines. Ronco C, Bellomo R. Continuous Renal Replacement Therapy. Crit Care Clin. 2021.