UNIVERSITY of MARYLAND MEDICAL CENTER

UMMC Clinical Practice Guidelines

Continuous Renal Replacement Therapy

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A. Common Indications for CRRT:

- Refractory Metabolic Acidosis (pH < 7.0)
- Uremia with associated neuropathy, myopathy, encephalopathy or pericarditis
- Hyperkalemia with or without EKG changes
- Electrolyte abnormalities refractory to standard therapy
- Diuretic-resistant Hypervolemia with associated pulmonary edema or bowel edema with oliguria or anuria
- Intoxications for clearance of dialyzable toxins (salicylates, water soluble non-protein bound contrast agents)
  - Intermittent hemodialysis is often the preferred first line treatment to provide the most rapid clearance of toxins
- Severe sepsis with refractory acidemia
- Acute kidney injury secondary to rhabdomyolysis with associated hyperkalemia

B. Mechanism of CRRT Clearance / Definitions

- Convection – filtration, occurs by hydrostatic or osmotic force through a semi-permeable membrane, solute clearance dependent on ultrafiltration. Solutes that can pass through the membrane pores are swept along with water in what is called solute drag
- Diffusion – dialysis, occurs due to movement of solutes as the result of random molecular movement. Molecules will pass through pores based on pore size and molecule size. Diffusive clearance can occur in either direction through the membrane. Solute clearance is dependent on dialysate infusion rate and blood flow rate. Faster blood flow rates expose more solute to the membrane, allowing for a greater opportunity to maintain a diffusion gradient across the membrane.
- Ultrafiltration – hydrostatic pressure forces a liquid against a semipermeable membrane. In this case, liquid is plasma water. Solutes are drawn across the semipermeable membrane.
- Ultrafiltrate (UF) – fluid collected distal to the membrane or hemofilter.
- Clearance – solute clearance depends largely on molecule size and membrane pore size. Larger molecules are less likely to diffuse
- Sieving coefficient – ratio of drug concentration in the ultrafiltrate to drug concentration in the plasma. A sieving coefficient of 1 = full passage of solute through the membrane, whereas 0 = no clearance of solute through the membrane. Filter age and protein binding can also influence sieving coefficient.

C. Solute Size (Table 1)

- Solutes < 300 d (urea, creatinine, amino acids): cleared by convection or diffusion
- Solutes or proteins 500-50,000 d (myoglobin, vitamin B12, vancomycin, albumin): cleared by convection
- Low-molecular-weight proteins 5000-50,000 d (inflammatory mediators): cleared by both convection and adsorption (not discussed in this document)

Table 1: Solute Size

	Molecule	Molecular Mass	Clearance
Small Solutes (< 300 daltons)	Sodium Phosphorus Potassium Urea Phosphate Amino Acids Creatinine Uric Acid Glucose	23 daltons 31 daltons 35 daltons 60 daltons 80 daltons 110 daltons 113 daltons 168 daltons 180 daltons	Convection / Diffusion
Middle Solutes / Molecules / Proteins (500-5,000 daltons)	Myoglobin Vitamin B12 Vancomycin	16,700 daltons 1,350 daltons 1,450 daltons	Convection
Proteins – Low Molecular Weight	Inflammatory Mediators	Variable	Convection / Absorption
Large Proteins (> 50,000 daltons)	Albumin Hemoglobin	66,500 daltons 65,000 daltons	Convection

D. Modalities (Table 2)

- Slow Continuous Ultrafiltration (SCUF)
  - Fluid removal only (ultrafiltration)
- Continuous Venovenous Hemofiltration (CVVH)
  - Replacement fluid added either before and/or after the filter.
  - Molecules < 50,000 d pass through the CVVH membrane through convection.
  - UF is removed and replaced to create the desired fluid balance.
  - Replacement fluid is used to replace the volume of fluid removed.
  - Rate of solute removal is dependent on membrane pore size
  - Indicated for the removal of middle or large molecules (BUN, Cr, Myoglobin)
- Continuous Venovenous Hemodialysis (CVVHD)
  - Involves the addition of dialysate after blood is separated by diffusion across a membrane.
  - Dialysate flows countercurrent to the flow of blood and creates a concentration gradient causing diffusive clearance.
  - Effective at removal of small- to medium-sized molecules.
  - Can be used to reverse acidosis.
  - Solute removal is dependent on the rate of fluid removal in the patient – when attempting to remove fluid, solute removal will occur. Rate of removal is inversely proportional to molecular weight – larger molecules are cleared less efficiently.
  - Effluent volume is equal to amount of fluid removed from the patient plus the amount of dialysate plus the ultrafiltrate.
- Continuous Venovenous Hemodiafiltration (CVVHDF)
  - Involves both convective clearance from filter pressure and diffusive clearance by the dialysate.
  - Effluent volume equals the fluid removed from the patient plus dialysate and replacement fluid.

Table 2: CRRT Modalities

	SCUF	**CVVH**	**CVVHD**	**CVVHDF**
Solute Transport	Convection	Convection	Diffusion	Convection and Diffusion
Replacement Fluid	None or Post	Yes	No	Yes
Blood Flow (mL/min)	10-450	10-450	10-450	10-450
Replacement Flow (mL/hr)	100-400	0-8000	None or 0-350	0-8000
Dialysate Flow (mL/hr)	None	None	0-8000	0-8000
Fluid Removal (mL/hr)	0-2000	0-2000	0-2000	0-2000
Pre Blood Pump (mL/hr)	0-2000	0-4000	0-4000	0-4000

E. Vascular Access

- Site of Vascular Access
  - Right Internal Jugular Vein
    - Preferred site
  - Femoral Veins
    - High risk of infection
  - Left Internal Jugular Vein
  - Subclavian vein
    - Not recommended, as cannulation may lead to central vein stenosis, impeding permanent arteriovenous fistula placement

- Type of Line (Table 3)
  - Avoid triple lumen catheters

Table 3: Types of Lines and Locations

Line Location	**Line Length**	**Line Lumen Diameter**	**Ideal Placement**
Right Internal Jugular	15-20 cm	11-14 Fr	Cavoatrial Junction
Femoral	25 cm	11-14 Fr	Inferior Vena Cava
Left Internal Jugular	20 cm	11-14 Fr	Cavoatrial Junction
Subclavian Vein	20 cm	11-14 Fr	Cavoatrial Junction

F. Vascular Access Maintenance

- In order to maintain patency of vascular access, dialysis catheters should be dwelled with heparin (concentration = 1,000 units / 1 mL) when not in use, unless a specific contraindication to the use of heparin exists, such as Heparin Induced Thrombocytopenia.
- Heparin dwell orders are available in the UMMC MED-CC CRRT Supplemental order set.
  - The supplemental order set contains two orders for “heparin 1000 units/mL injection for dialysis catheter 1-2.5 mL”

        - Each order contains a dosing table with common catheter dwell volumes based on catheter lengths used at UMMC. The amount of heparin dwelled within the catheter is dependent upon the specific lumen volume and must be verified by the nurse prior to administration of the dwell.
        - Each order is needed, as one is for the blue port and the other is for the red port.
        - Before each use of the vascular access, the heparin from within the lumen must be aspirated, as described in the heparin order.
    - Heparin used for the dwell is available as floor stock in the Pyxis machines of each ICU. The heparin dwell vial is a 1,000 unit / 1 mL, 10 mL vial.
    - Vascular access ports with a heparin dwell will not be labeled as such, as it should be assumed that heparin is dwelled within both lumens at all times.

G. Replacement Fluid and Dialysate Fluid Selection (Table 4)

- Fluid selection special circumstances
    - Hyperkalemia
        - Intermittent HD is the preferred modality for the treatment of hyperkalemia
        - If CRRT is needed, recommend using low-potassium replacement fluids such as BK 0/3.5 or BGK 2/0. Of note, BK 0/3.5 contains no potassium and BGK 2/0 contains no calcium.
        - Consider using PrismaSate BGK 4/2.5 as Prefilter replacement and BK 0/3.5 as Postfilter replacement.
    - Citrate Anticoagulation
        - Consider using calcium-free / low bicarbonate formula (Prismasate B22GK 4/0) pre-filter to reduce the amount of calcium that must be bound by citrate and a calcium-containing formula (Prismasate BGK4/2.5 or Prismasate BK 0/3.5) post-filter.
    - Hypocalcemia
        - Consider external replacement with calcium chloride or calcium gluconate.
        - Ensure replacement solutions contain calcium.
    - Hypercalcemia
        - Consider using PrismaSate BGK 4/2.5 as Prefilter replacement and BGK 2/0 as Postfilter replacement
    - Hypophosphatemia
        - PrismaSate replacement solutions do not contain phosphate. Consider adding enteral or IV phosphate supplementation as needed.

Table 4: CRRT Replacement and Dialysate Fluids at UMMC

		Calcium Formulas		***Calcium-Free Formulas***		
	Plasma	**Prismasate BGK 4/2.5**	**Prismasate BK 0/3.5**	**Prismasate B22GK 4/0**	**Prismasate BGK 2/0**	**Plasmalyte**
Potassium (mEq/L)	3.5-5	4	0	4	2	5
Calcium (mEq/L)	2.3-2.6	2.5	3.5	0	0	0
Magnesium (mEq/L)	1.4-2	1.5	1.0	1.5	1.0	3
Sodium (mEq/L)	135-145	140	140	140	140	140
Chloride (mEq/L)	100-108	113	109.5	120.5	108	98
Bicarbonate (mEq/L)	22-26	32	32	22	32	0
Lactate (mEq/L)	0.5-2.2	3	3	3	3	0
Dextrose (mg/dL)	70-110	110	0	110	110	0
Acetate (mEq/L)						27
Gluconate (mEq/L)						23
Osmolarity (mOsm/L)		300	287	296	292	294
Cost						

H. Filter Selection

- Indication for filter selection
  - M 150
    - Preferred filter for all modalities
  - HF 1400
    - Reserved for patients with a prior history of biocompatibility reactions to M150 filters.

Table 5: CRRT Filters at UMMC

	M 150	**HF 1400**
Materials	AN 69 HF Hollow Fiber - Acrylonitrile - Sodium methallyl sulfonate copolymer	PAES Hollow Fiber - PolyarylEtherSulfone
Sterilization Mode	Ethylene Oxide	Ethylene Oxide
Latex	Not made with natural rubber latex	Not made with natural rubber latex
Weight	860 g	820 g
Blood Volume	189 mL	186 mL
Minimal Patient Weight	30 kg	30 kg
Effective Surface Area	1.5 m2	1.4 m2
Fiber internal diameter (wet)	240 micrometers	215 micrometers
Fiber wall thickness	50 micrometers	50 micrometers
Sieving Coefficient **Urea** **Creatinine** **Vitamin B12** **Inulin** **Myoglobin** **Albumin**	 1 1 1 0.95 0.55 <0.01	 1 1 1 1 - <0.01
Minimum Blood Flow Rate	100 mL/min	100 mL/min
Maximum TMP (mmHg/kPa)	450/60	500/66.6
Cost		

I. CRRT Prescription

- Blood Flow Rate:
  - Increased blood flow rate reduces risk of clotting,
  - Decreased blood flow rate increases risk of clotting,
- Dose (Replacement Rate)
  - 25-35 mL/kg/hr
- Replacement Fluid
  - Pre/Post
    - 70/30
    - 50/50
    - 100/0
    - 0/100
  - Pre-Filter Replacement: Dilutes the blood in the filter, reducing clotting.

        - Post-Filter Replacement: Concentrates the blood in the filter, potentially enhancing the risk of clotting.
        - Dialysate (Green Line)
    - Pre Blood Pump
        - White Line
        - Site of anticoagulation infusion when using anticoagulation.
    - Dialysate
    - UF/Qb ratio < 25%
    - Effluent (Yellow Line)

J. Anticoagulation

- Heparin
    - Refer to the UMMC Adult Heparin Protocol for CRRT.
    - Per the UMMC Adult Heparin Protocol for CRRT, contraindications to heparinization include a prior history of heparin-induced thrombocytopenia or heparin allergy, an intracranial hemorrhage within the last 3 months, or a platelet count < 40,000 / mm^3
    - Individual ICUs and providers may identify additional contraindications to heparinization based on their patient population and clinical experience.
- Citrate
    - May be considered in patients with existing bleeding, high risk of bleeding or contraindication to heparin use.
    - Refer to the UMMC Citrate Anticoagulation Guidelines.
    - Monitor closely for electrolyte abnormalities, specifically metabolic acidosis in patients with liver dysfunction due to an inability to metabolize citrate and metabolic alkalosis in the setting of citrate metabolism to bicarbonate.
- Argatroban
    - No specific recommendations for the use of argatroban during CRRT exist. Refer to the UMMC Argatroban Guidelines for the use of argatroban infusions as therapeutic anticoagulation.

K. Laboratory Monitoring

- Baseline levels of parameters of metabolic function, including CMP, ionized calcium, CBC and coagulation parameters (PTT, INR)
- Frequency of monitoring is dependent on the rate of clearance, types of solutions used ad dialysate / replacement and anticoagulation
- More frequent monitoring is initially recommended (every 6-8 hours) to determine if adjustment of dialysate / replacement solutions and rates are needed to improve solute clearance, especially when solutions with less than physiologic amounts of electrolytes are used (e.g. PrismaSate BGK 0/3.5). When citrate is used as an anticoagulant, more frequent monitoring of ionized calcium and bicarbonate is required.

L. Complications / Troubleshooting

- Average filter life reported in the literature is greater than 20 hours. If your filter lasts **less than 12 hours** consider the following:

- Access
    - The access is the most ***CRITICAL*** component in CRRT.

- The barrel of a 10 mL syringe should fill in < 2 sec when the plunger is pulled back. Without adequate access, high blood flow rates will not be achieved.
- Reversing the ports (access from the distal port and return to the proximal port)
  - Should be discouraged. Greatly increases recirculation and reduces clearance.
- Avoid triple lumen catheter whenever possible (12 G lumens vs. 10 G on double lumen catheters)

- Access Sites in Order of Preference
  - Access length depends on the site. A catheter too short may cause the proximal port to suck up to the sidewall of the vessel.
  - Right Internal Jugular – Straight path to the SVC – Atrial Junction
    - Good blood flow with little recirculation
    - 15-20 cm. The tip should reach the SVC – Atrial Junction
  - Femoral – Straight path to the IVC with adequate length
    - Good blood flow with little recirculation
    - 25 cm. The tip should reach the IVC
  - Left Internal Jugular – Tortuous path to the SVC – Atrial Junction
    - Poor blood flow related to curves. Tip may abut the vessel wall creating high return pressure.
    - 20 cm. The tip should reach the SVC – Atrial Junction
  - Subclavian – tortuous path to the SVC – Atrial Junction
    - Poor blood flow related to curves and path between clavicle and ribs. Tip may abut the vessel wall creating high return pressure
    - 20 cm. The tip should reach the SVC – Atrial Junction
- Filtration Fraction
  - The amount of water removed from plasma.
  - Goal filtration fraction < 25%
  - Filtration fraction may be reduced by increasing blood flow rate and the amount of Pre-filter replacement fluid.

- Blood Flow Rate
  - Generally the higher the blood flow rate, the less contact with the hemofilter and risk of clotting. Attempt to increase to 300-400 mL/min
  - Blood flow rate is dependent on the adequacy of the access. The minimum blood flow rate for the M150 and HF1400 is 150 mL/min.
  - Blood flow rate should not affect hemodynamics.
    - Reduction in blood pressure upon initiation of CRRT may be related to biocompatibility issue with the hemofilter.
    - Usually short lived. If persists, may need to switch from M150 to HF1400

- Replacement Flow Rates
  - Pre-filter replacement fluid reduces the risk of clotting by hemodilution.
  - The default order is 70% pre-filter, 30% post-filter. This preferentially provides maximal pre-dilution while protecting the de-aeration chamber from clotting.
  - Reduction to 50/50 reduces pre-filter dilution and may increase risk of clotting.

- Anticoagulation
  - Consider for all patients without a contraindication to anticoagulation.
  - Consider when adequate access is obtained, filtration fraction <25%, and circuit continues to clot.
  - Refer to anticoagulation section above for specific recommendations.

- Resources
  - Clinical support hotline (ICON) available 24/7.
  - Identify superusers and/or clinical mentors at the start of the shift.
  - UMMC CRRT intranet page located under Clinical Staff Resources/Clinical Resources and Information/CRRT

- Communication
  - Label CRRT cassette with date/time and consecutive cassette number. Document circuit change (and blood return) on Portfolio CRRT flowsheet. Notify provider if cassette does not last at least 12 hours.

- Hypophosphatemia
  - Consider adding enteral or intravenous phosphate replacement while on CRRT

- Elevated Transmembrane Pressure (TMP)
  - Initially elevated TMPs may be a sign that the blood flow rate is too high for the catheter
  - TMP will rise throughout treatment, indicating micro-clotting in the filter
  - Rapid rises in TMP may be secondary to a kinked access line or coughing

- Filter Clotting
  - Consider increasing Prefilter replacement

- Access Pressure
  - Negative access pressure may indicate an obstruction in the catheter or that the blood flow rate through the catheter may be too high
  - Positive access pressure may be an indicator that blood flow rates are too low for the catheter size

- Return Pressure
  - Evaluate the line for kinking, clamps, malpositioning or patent coughing
  - If return pressure is initially low, the blood flow rate may be too low
  - Evaluate the patient for disconnection from the machine

- Hemodynamic Instability
  - Consider reducing volume removal or replacing previously removed volume

- Filter Biocompatibility
  - Patients experiencing anaphylactoid-like reactions to M150 filters should be switched to an HF1400 filter is a biocompatibility reaction is suspected

- Hypothermia
  - Utilize the blood warmer to maintain normothermia

- Medication Underdosing
  - Consult your clinical pharmacist regarding medication dosing adjustments when starting, modifying or discontinuing CRRT therapy

M. Required Nursing Documentation

- In the "CRRT/TPE/Aquapheresis" Flowsheets tab
  - At initiation of therapy, every shift, and with changes the nurse should document the "CRRT Settings and Orders".
  - CRRT Circuit Pressures should be documented minimally every 4 hours.
  - The amount of actual patient fluid removal should be documented hourly in the "Ultrafiltrated Volume" box.
- All replacement, dialysate, and pre-blood pump (PBP)/anticoagulation bags should be scanned per hospital policy prior to hanging and connecting to CRRT circuit.
- Patient and family Plan of Care and Education should be completed and individualized.
- Complete a Nursing Note for any events related to CRRT treatment and file an UMMSafe Report.

N. CRRT Termination

- There is no widely accepted strategy for when termination of CRRT therapy is appropriate. Several markers for consideration of discontinuing CRRT therapy include:
  - UOP 400-500 mL/day
  - Correction of metabolic derangement
  - Reduction in need for solute clearance
  - Appropriate fluid balance
  - Conversion to IHD

O. References

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Slowinski T, Morgera S, Joannidis M, et al. Safety and efficacy of regional citrate anticoagulation in continuous venovenous hemodialysis in the presence of liver failure: the liver citrate anticoagulation threshold (L-CAT) observational study. Critical Care. 2015; 19: 349.

Tolwani A. Continuous renal-replacement therapy for acute kidney injury. N Engl J Med. 2012; 367: 2505-14.

P. Additional Resources:

http://222.files.sulli.us/CRRT/Principles.of.CRRT.pdf
http://maryland.ccproject.com/2013/08/28/principles-of-renal-repacement-therapy/

Reviewed by:

UMMC CRRT Committee: December, 2017
Critical Care Operations Committee: December, 2017
Pharmacy & Therapeutics Committee: January, 2018

Last Update:

October 2019