Continuous Renal Replacement Therapy

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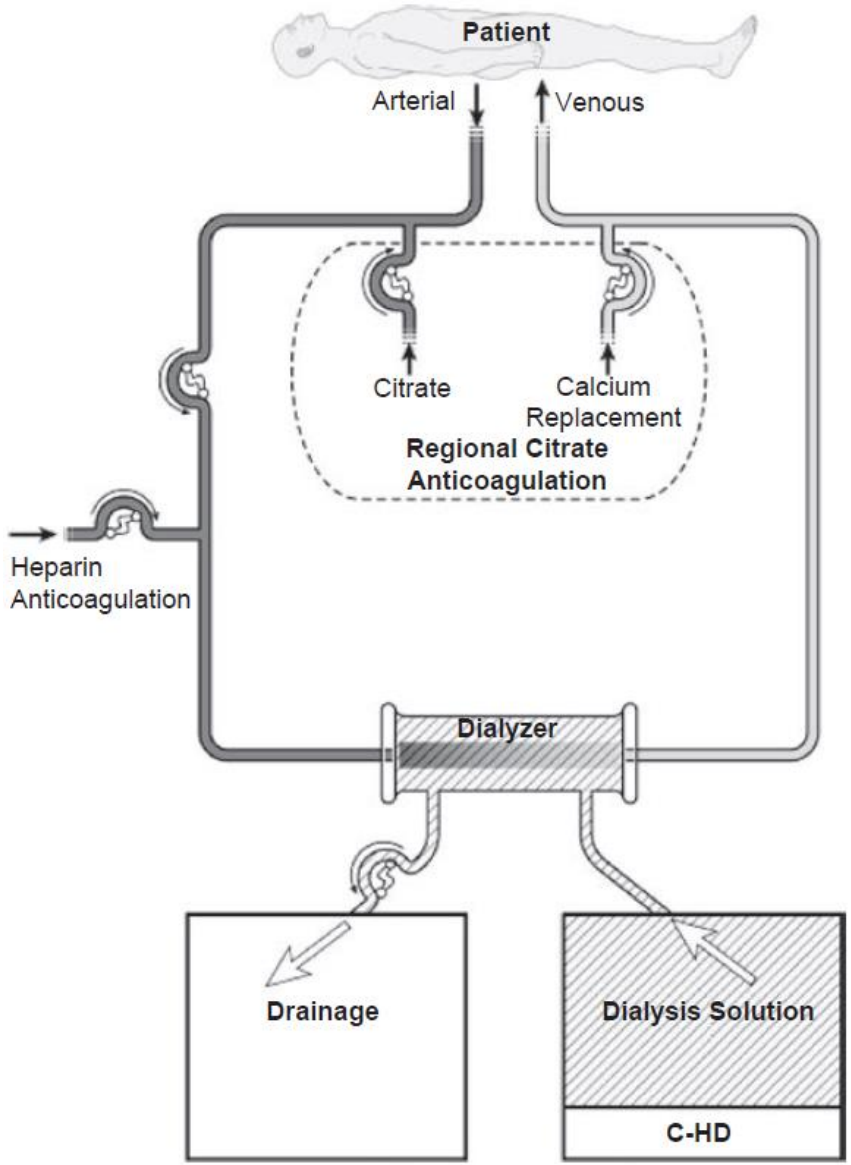
Introduction:

- The most widely used continuous renal replacement therapies (CRRT) for the treatment of critically ill patients in renal failure are continuous hemodialysis and hemodiafiltration.
- Two prolonged intermittent renal replacement therapies (PIRRT), sustained low-efficiency hemodialysis and sustained low-efficiency hemodiafiltration, are also quite popular.
- Continuous hemofiltration and slow continuous ultrafiltration are used, but less commonly.

Continuous hemodialysis **(C-HD).**

- Dialysis solution is passed through the dialysate compartment of the filter continuously and at a slow rate.

- In C-HD, diffusion is the primary method of solute removal.
- The amount of fluid that is ultrafiltered across the membrane is low (usually about 3–6 L per day) and is limited to excess fluid removal.

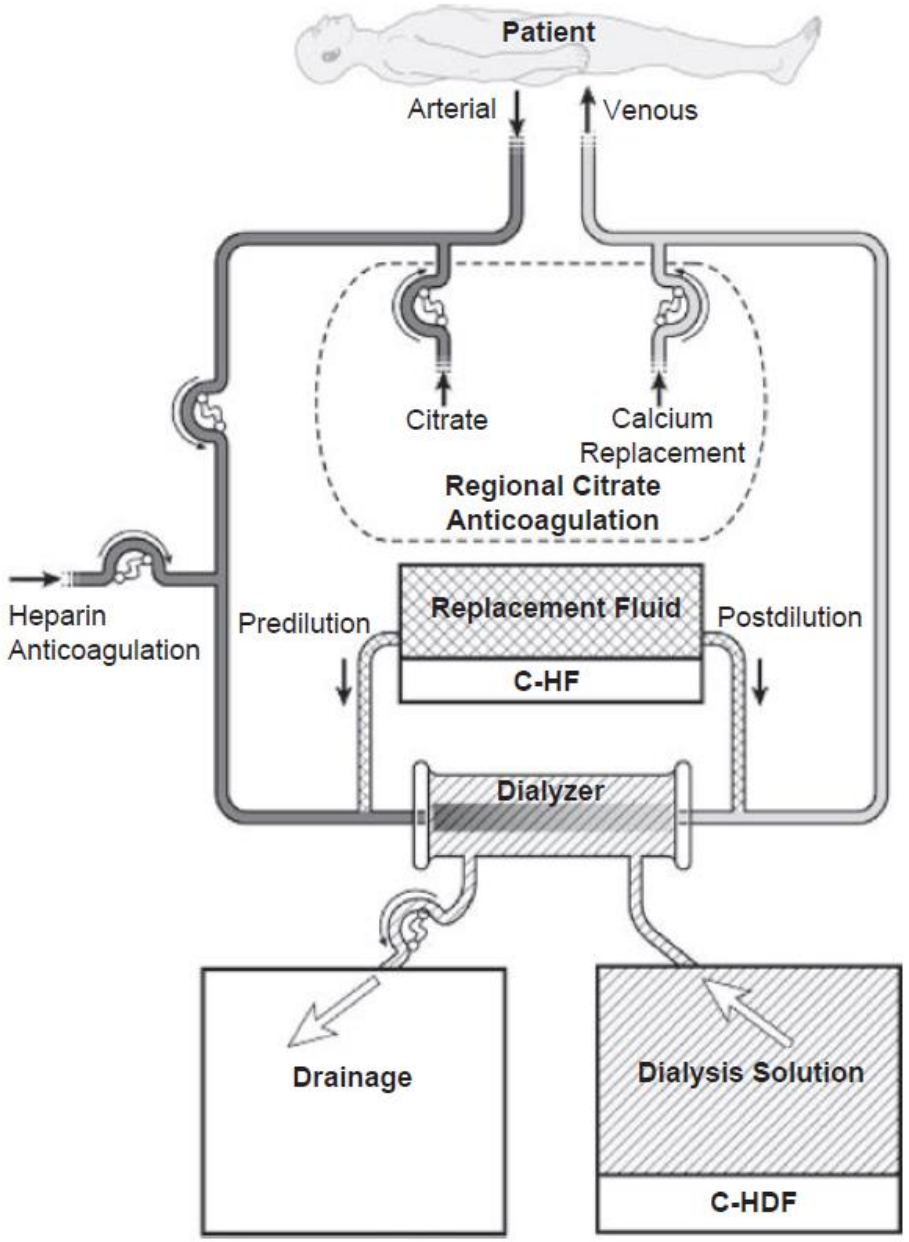

Patient
Arterial
Venous
Citrate
Calcium
Replacement
Regional Citrate
Anticoagulation
Heparin
Anticoagulation
Dialyzer
Drainage
Dialysis Solution
C-HD

Continuous hemofiltration (C-HF).

- In C-HF , dialysis solution is not used.
- Instead, a large volume (about 25–50 L per day) of replacement fluid is infused into either the inflow or the outflow blood line (predilution or postdilution mode, respectively).
- With C-HF, the volume of fluid that is ultrafiltered across the membrane is the sum of replacement fluid and excess fluid removed, and so is much higher than with C-HD.

Continuous hemodiafiltration (C-HDF):

- Is simply a combination of C-HD and C-HF.
- Dialysis solution is used, and replacement fluid is also infused into either the inflow or the outflow blood line.
- The daily volume of fluid that is ultrafiltered across the membrane is equal to the replacement fluid infused plus the net volume removed.


Patient
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Regional Citrate
Anticoagulation
Heparin
Anticoagulation
Predilution
Replacement Fluid
C-HF
Postdilution
Dialyzer
Drainage
Dialysis Solution
C-HDF

Sustained low-efficiency dialysis and hemodiafiltration (SLED)

- SLED is a form of IHD using an extended (6- to10-hour) session length and reduced blood and dialysate flow rates.

Typically, blood flow rates (BFRs) are about 200 mL/min and dialysate flow rate is 100–300 mL/min.

- The same machine used for IHD during the day often can be used for SLED during the night, and hemodialysis nurses can easily be trained to perform SLED, offering some economy of staff instruction.

CLINICAL INDICATIONS FOR CRRT

- **1.** Hemodynamically well tolerated; smaller change in plasma osmolality.
- **2.** Better control of azotemia and electrolyte and acid–base balance; correct abnormalities as they evolve; steady-state chemistries.
- **3.** Highly effective in removing fluid (post surgery, pulmonary edema, ARDS).
- **4.** Facilitates administration of parenteral nutrition and obligatory intravenous medications (i.e., pressor, inotropic drugs) by creating unlimited “space” by virtue of continuous ultrafiltration.
- **5.** Less effect on intracranial pressure.
- **6.** New user-friendly machines available.

DIFFERENCES AMONG C-HD, C-HF, AND C-HDF

- **Solute clearance with C-HD:**
- where the BFR is 150–200 mL/min or more, and dialysate flow rate typically is 25–30 mL/min, clearance of urea and other small molecules is determined primarily by the dialysis solution flow rate.
- BFR in C-HD should be at least three times the dialysate flow rate.
- At this slow BFR and high blood-to-dialysate flow ratio, the outflow dialysate is almost 100% saturated with urea and other small-molecular-weight solutes
- Urea clearance can thus be simply estimated by the effluent volume, which includes the volume of dialysis solution used plus any excess fluid removed.

Continue…..

- The standard dialysis solution inflow rate is now about 20–25 mL/kg per hour.
- In a 70-kg individual, this translates into a flow rate of 23–29 mL/min.
- If we assume a flow rate of 26 mL/min and 100% saturation, this will deliver a urea clearance of 26 mL/min or about 37 L per day, and if we add 3 L per day of excess fluid removal,
- This gives a daily effluent volume and urea clearance of 37 + 3 = 40 L.

VASCULAR ACCESS

- Using a dual-lumen cannula inserted into a large (internal jugular or femoral) vein.

The subclavian vein can be used but is not the site of first choice.

The KDIGO AKI guidelines recommend using uncuffed venous catheters for CRRT).

Uncuffed catheter is easier, that the need for a cuffed catheter might sometimes delay initiation of therapy, and that the average duration of CRRT is only 12–13 days .

- compared use of longer (20–24 cm) soft, versus shorter (15–20 cm) the longer catheters were associated with longer filter life and improved dose of therapy.

- The success rate of CRRT achieved by femoral venous access, filter longevity averaged 15 hours when the venous catheter was inserted on the right side versus 10 hours when the left femoral vein was used

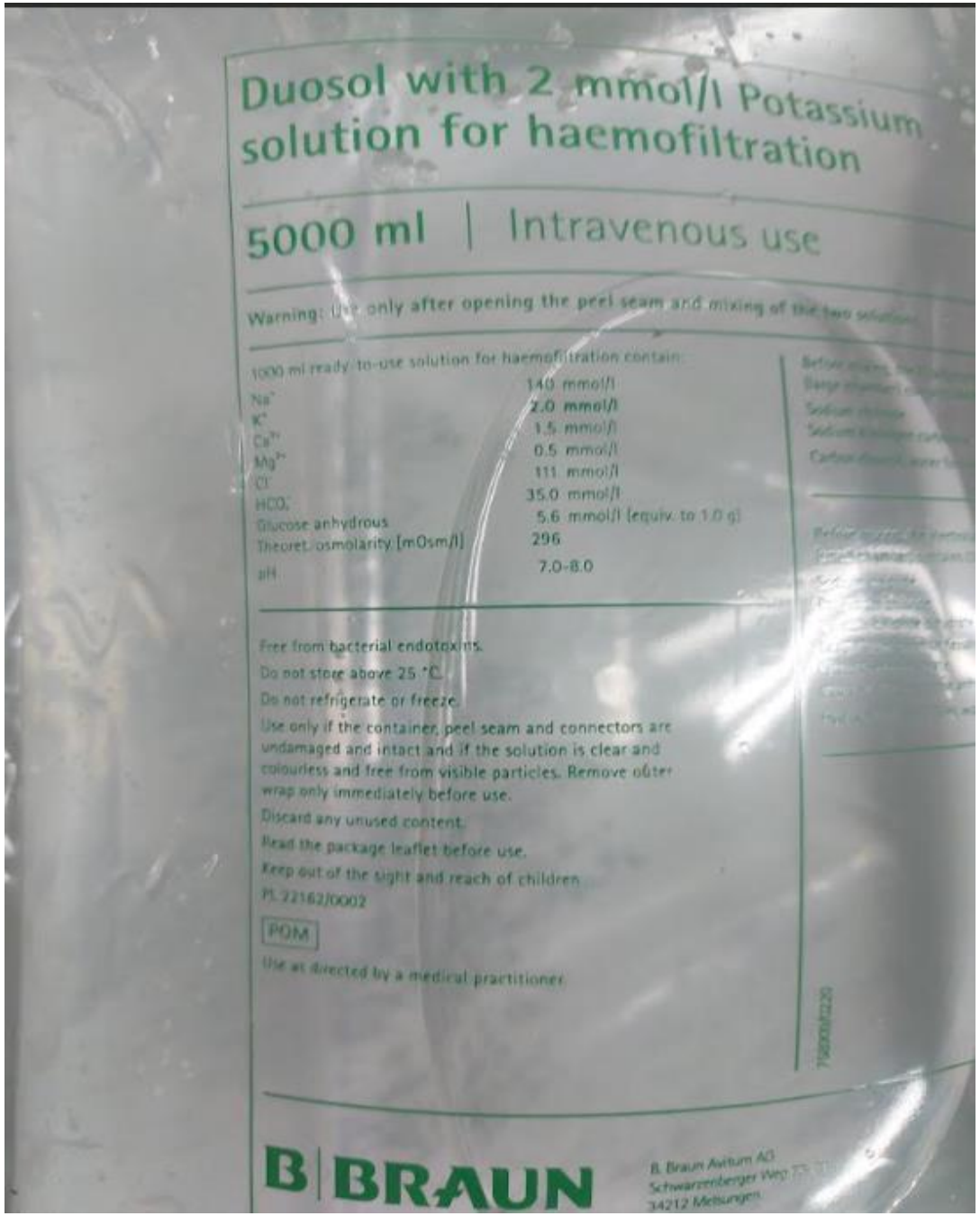
Arteriovenous blood access:

Use of AV blood access for CRRT is no longer widely practiced.

- There is risk of damage to the femoral artery with possible distal limb ischemia, plus AV access will often not deliver high enough blood flows to be able to support the more intensive CRRT therapies in common use today.

TABLE 15.3 Composition of Some Continuous Renal Replacement Therapy Solutions

Component (mM)	Dialysis Machine Generated[a]	Peritoneal Dialysis Fluid[b]	Lactated Ringer Solution	B. Braun Duosol (5-L bag)	Baxter Accusol[b] (2.5-L bag)	Gambro Prismasol[c] (5-L bag)	Nxstage Pureflow[d] (5-L bag)
Sodium	140	132	130	136 or 140	140	140	140
Potassium	Variable	—	4	0 or 2	0 or 2 or 4	0 or 2 or 4	0 or 2 or 4
Chloride	Variable	96	109	107–111	109.5–116.3	106–113	111–120
Bicarbonate	Variable	—	—	25 or 35	30 or 35	32	25 or 35
Calcium	Variable	1.75 (3.5 mEq/L)	1.35 (2.7 mEq/L)	0 or 1.5 (0 or 3.0 (mEq/L)	1.4 or 1.75 (2.8 or 3.5 mEq/L)	0 or 1.25 or 1.75 (0 or 2.5 or 3.5 mEq/L)	0 or 1.25 or 1.5 (0 or 2.5 or 3.0 mEq/L)
Magnesium	0.75 (1.5 mEq/L)	0.25 (0.5 mEq/L)	—	0.5 or 0.75 (1.0 or 1.5 mEq/L)	0.5 or 0.75 (1.0 or 1.5 mEq/L)	0.5 or 0.75 (1.0 or 1.5 mEq/L)	0.5 or 0.75 (1.0 or 1.5 mEq/L)
Lactate	2	40	28	0	0	3	0
Glucose (mg/dL)	100	1,360	—	0 or 100	0 or 100	0 or 100	100
Glucose (mM)	5.5	75.5	—	0 or 5.5	0 or 5.5	0 or 5.5	5.5
Preparation method	6-L bag via membrane filtration	Premix	Premix	Two-compartment bag	Two-compartment bag	Two-compartment bag	Two-compartment bag
Sterility	No	Yes	Yes	Yes	Yes	Yes	Yes


Duosol with 2 mmol/l Potassium solution for haemofiltration
5000 ml | Intravenous use
Warning: Use only after opening the peel seam and mixing of the two solutions.
1000 ml ready-to-use solution for haemofiltration contain:
Na+ 140 mmol/l
K+ 2.0 mmol/l
Ca2+ 1.5 mmol/l
Mg2+ 0.5 mmol/l
Cl- 111 mmol/l
HCO3- 35.0 mmol/l
Glucose anhydrous 5.6 mmol/l (equiv. to 1.0 g)
Theoret. osmolarity [mOsm/l] 296
pH 7.0-8.0
Free from bacterial endotoxins.
Do not store above 25 °C.
Do not refrigerate or freeze.
Use only if the container, peel seam and connectors are undamaged and intact and if the solution is clear and colourless and free from visible particles. Remove outer wrap only immediately before use.
Discard any unused content.
Read the package leaflet before use.
Keep out of the sight and reach of children.
PI: 22162/0002
POM
Use as directed by a medical practitioner.
B BRAUN
B. Braun Avitum AG
Schwarzenberger Weg 73
34212 Melsungen

Lactate-based solutions:

- Pure lactate-based replacement fluid usually contains 40–46 mM of lactate.
- Lactate based solutions effectively correct metabolic acidosis in most patients.
- Lactate is metabolized on a 1:1 molar basis to bicarbonate, but in practice, the dialysis solution lactate concentration needs to be higher than dialysis solution bicarbonate to effect similar degrees of correction of acidosis.

Bicarbonate-based solutions:

- Bicarbonate-containing bags are sold as two-compartment systems, similar to those used to prepare bicarbonate-containing dialysis solution for peritoneal dialysis.
- Bicarbonate is the buffer of choice, and total base concentrations are typically 25–35 mM.
- When a high dialysis solution or replacement solution flow rate (, >30 mL/kg/hour) is prescribed, use of lower bicarbonate solutions may help prevent metabolic alkalosis.

Lower bicarbonate concentration solutions or bicarbonate-free solutions are also indicated when using regional citrate anticoagulation, because citrate is metabolized to bicarbonate by the liver.

When high-lactate solutions should be used with caution:

- Use of solutions using lactate as the primary bicarbonate-generating base has been shown to worsen hyperlactatemia in patients who have severe circulatory instability with tissue hypoperfusion, and in patients with severe liver compromise.

Citrate-based solutions:

- These fluids evolved from attempts to merge the buffering and anticoagulation properties of citrate, and the need to simplify complex regional citrate anticoagulation (RCA) protocols.

- The bulk of citrate-based fluids have to be administered prefilter to allow adequate filter anticoagulation. Forty to 60% of citrate infused in predilution mode is removed in the effluent, and the remainder is mainly metabolized by the liver into bicarbonate (1 mmol citrate yielding 3 mmol bicarbonate).

AJKD

Continuous Kidney Replacement Therapies: Core Curriculum 2025

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Critically ill patients that require kidney replacement therapy (KRT) are among the most ill and complex patients routinely encountered in the intensive care unit (ICU). Continuous KRT (CKRT) is used across many ICUs as the therapy of choice for hemodynamically unstable patients with kidney failure. Though existing trials have not shown superior survival or kidney recovery with CKRT relative to intermittent KRT, CKRT has largely become the standard of care in developed nations for the treatment of acute kidney injury (AKI) in patients with shock, acute brain injury, acute liver failure, and other forms of critical illness. As health care systems provide an ever-widening scope of organ-support therapies to increasingly complicated ICU patients, the use of CKRT is likely to expand. In this Core Curriculum, we review the physicochemical principles of CKRT, provide a comprehensive yet practical review of when and how to prescribe CKRT, and summarize seminal trials that serve as the foundations for our approaches to timing of initiation, dosing, vascular access, and anticoagulation for CKRT. We conclude by briefly highlighting a variety of essential, yet often underappreciated, components of the provision of high-value multidisciplinary care to patients receiving CKRT, including drug dosing, nutrition, physical rehabilitation, and CKRT quality assurance programs.

Complete author and article information provided at end of article.

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Case 1

- A 28-year-old woman is admitted to the ICU after a motor vehicle collision with prolonged extrication.
- She is diagnosed with traumatic brain injury with intraparenchymal hemorrhage and multiple fractures with rhabdomyolysis with an initial creatine kinase (CK) level of 40,000 U/L
- After 48 hours, despite aggressive intravenous fluids followed by intravenous (IV) furosemide at 1 mg/kg, she is:

severely oliguric.

She has required several boluses of sodium chloride to control intracranial hypertension with a goal serum sodium of >150 mEq/L

her blood pressure is 142/91 mm Hg without vasopressor support

She is unresponsive and receiving mechanical ventilation

1- 2+ generalized edema.

Continue…..

- sodium, 154 mEq/L;
- potassium, 6.1 mEq/L;
- creatinine, 3.3 mg/dL (0.9 mg/dL on admission)
- phosphate, 8.2 mg/dL,
- withCK >100,000 U/L (above limit of detection).
- (CT) shows a stable large left frontal hemorrhage with surrounding cerebral edema and persistent 4-mm midline shift.
- Her most recent ICP is 21 mm Hg.

Answer:

- Initiate CKRT with no anticoagulation and a continuous infusion of 3% sodium chloride to generate an effective CKRT bath of 152 mEq/L.

Table 1. Possible Indications for CKRT and Potential Advantages and Disadvantages of CKRT (Relative to IHD or PIKRT) in Critically Ill Patients With AKI

Classic Indications for KRT in the Setting of Hemodynamic Instability	CKRT-specific Indications: Need for KRT in the Setting of Specific Critical Care Scenarios	Advantages of CKRT	Disadvantages of CKRT
• Severe hyperkalemia • Severe metabolic acidosis • Diuretic-resistant volume overload • Life-threatening or severe complications of uremia (eg, bleeding in the setting of uremic platelet dysfunction, pericarditis) • Poisoning with dialyzable toxins (eg, toxic alcohols, salicylates, lithium)[a] • Persistent oliguria or anuria	• Intracranial hypertension or conditions associated with elevated ICP or requiring maintenance of therapeutic hypernatremia (eg, acute liver failure, acute brain injury) • Gradual correction of severe dysnatremia (eg, serum [Na^+] < 120 mEq/L or >165 mEq/L) • Cardiopulmonary failure requiring ECMO or other mechanical circulatory support • Organ support in patients with advanced heart or liver disease unable to tolerate IHD, especially when used as a bridge to transplantation or other destination therapy • Conditions requiring continuous solute removal due to high cell turnover or cell lysis (eg, rhabdomyolysis or tumor lysis syndrome)	• Less hypotension • Less effect on ICP in at-risk patients (eg, acute brain injury; acute liver failure) • Superior volume control • Superior solute control (ie, higher total daily or weekly dose) • Usually permits nutrition without restriction in protein, phosphate, or potassium • Less hemodialysis nurse support[b]	• Decreased (ie, slower) instantaneous clearance • Increased need for circuit anticoagulation due to extended treatment time • Increased risk of hypophosphatemia • Requires catheter placement[c] • Increased risk of immobilization[d] • More ICU nurse support[b] • Increased overall cost

CKRT Principles

- (1) a well-functioning vascular access (duall lumen intravenous hemodialysis catheter)
- (2) a semipermeable membrane (ie, dialyzer/hemofilter)
- (3) a blood pump (ie, roller pump)
- (4) for most CKRT modalities, additional roller pump(s) to circulate dialysate and/or replacement solutions across the membrane or into the circuit
- (5) fluid-balancing and pressure monitoring systems.

Solute Transport and Membrane Characteristics

CKRT can be used to remove solutes via

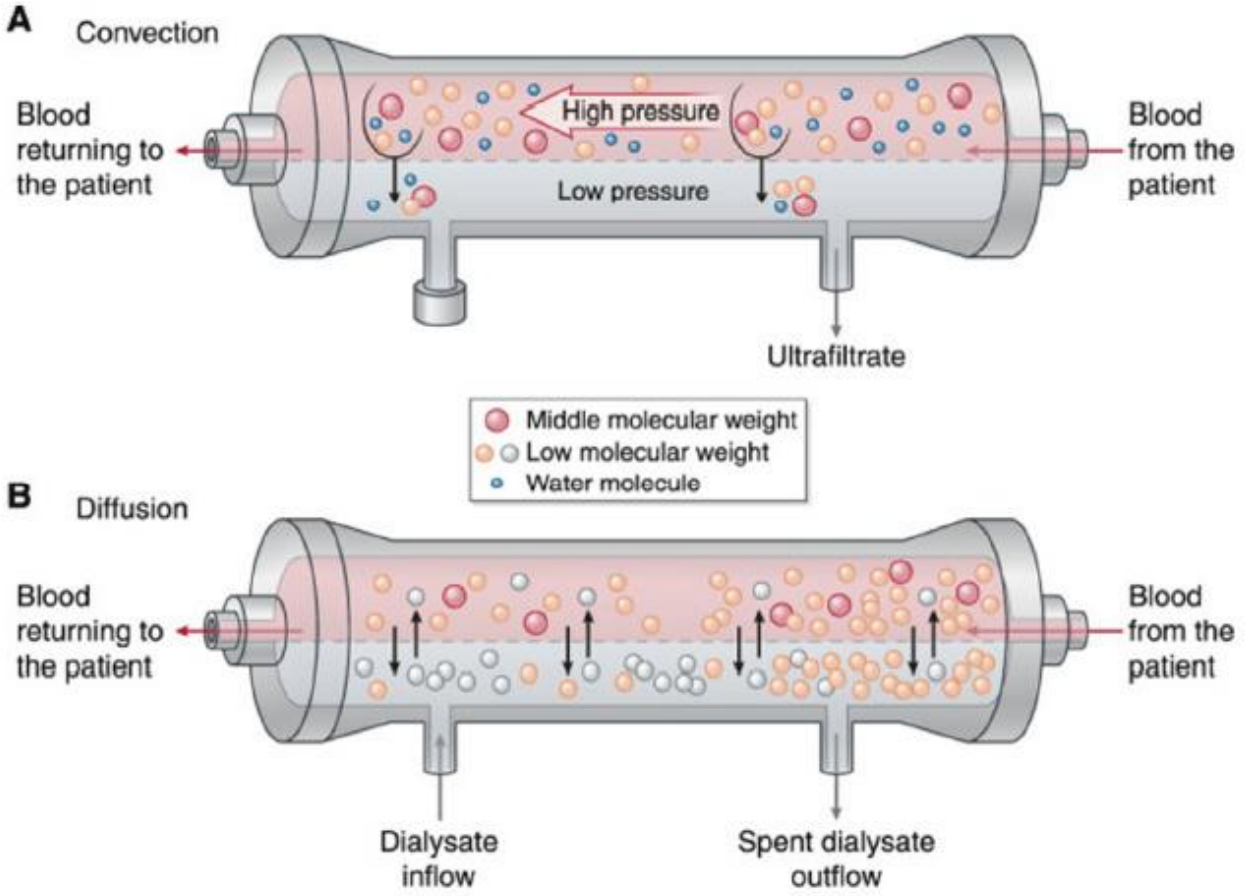
- Convection
- diffusion
- or a combination of both.

Largely depending on membrane characteristics

CKRT circuits, resulting in some large-molecule clearance limited by saturation of membrane-binding sites within several hours of CKRT initiation.

Continue……

- Diffusion, the primary mechanism of solute clearance in IHD, is driven by a difference in solute concentration in plasma water and dialysate across a membrane (dialyzer).
- Convection (or, more precisely, advection) is the bulk movement of solute within fluid across a membrane (hemofilter) due to a hydrostatic pressure difference

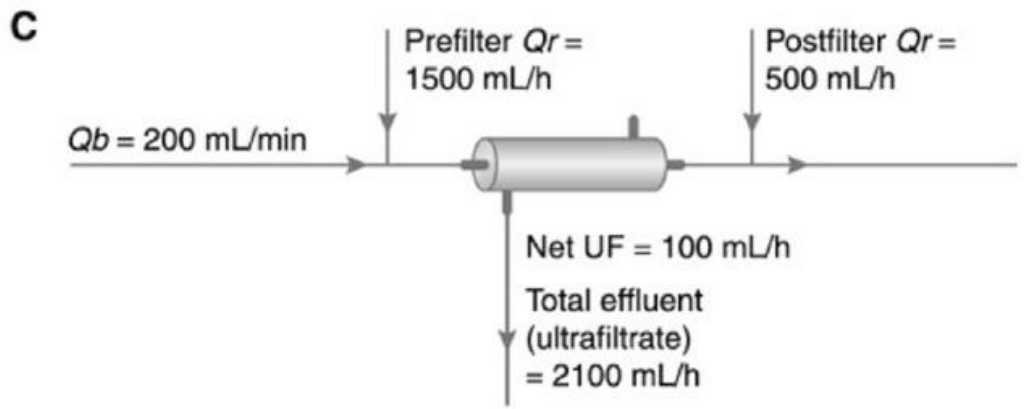

A
Convection
Blood returning to the patient
High pressure
Low pressure
Blood from the patient
Ultrafiltrate
Middle molecular weight
Low molecular weight
Water molecule
B
Diffusion
Blood returning to the patient
Blood from the patient
Dialysate inflow
Spent dialysate outflow

- (A) In hemofiltration, solute clearance occurs primarily by convection.
- In convection, solutes are transported across the hemofilter membrane along with plasma water as a result of a hydrostatic pressure
- (transmembrane pressure) generated on the blood side of the membrane. Solutes cleared by convection include urea and other small molecules along with larger “middle molecules.”

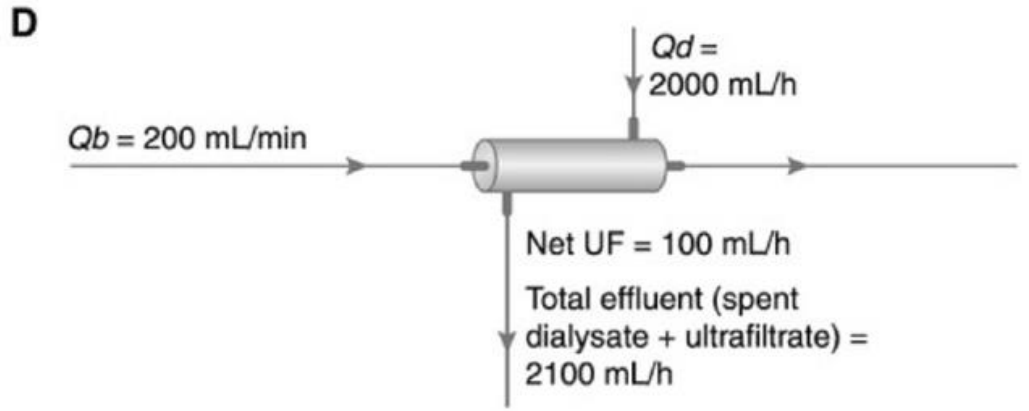
- (B) In hemodialysis, solute clearance occurs primarily by diffusion,

driven by a concentration gradient across the semipermeable membrane. Small solutes in high concentration in the blood diffuse across the membrane into the dialysate, which contains either little (eg, potassium) or none (eg, urea) of the solutes being cleared.

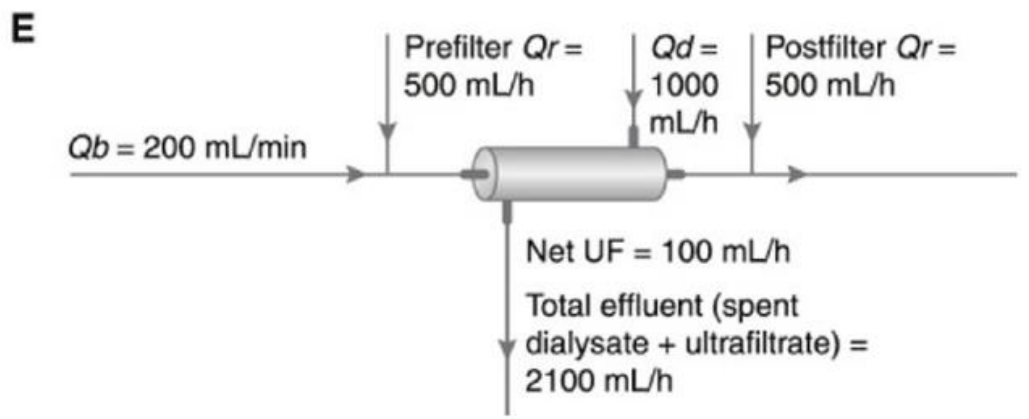
CHF


C
Prefilter Qr = 1500 mL/h
Postfilter Qr = 500 mL/h
Qb = 200 mL/min
Net UF = 100 mL/h
Total effluent (ultrafiltrate) = 2100 mL/h

CHD


D
Qd = 2000 mL/h
Qb = 200 mL/min
Net UF = 100 mL/h
Total effluent (spent dialysate + ultrafiltrate) = 2100 mL/h

CHDF


E
Prefilter Qr = 500 mL/h
Qd = 1000 mL/h
Postfilter Qr = 500 mL/h
Qb = 200 mL/min
Net UF = 100 mL/h
Total effluent (spent dialysate + ultrafiltrate) = 2100 mL/h

- Continuous venovenous hemofiltration (CVVH) only utilizes convection
- continuous venovenous hemodialysis (CVVHD) primarily utilizes diffusion
- continuous venovenous hemodiafiltration (CVVHDF) uses both.
- For CVVH, the total effluent flow rate (Qef) is equal to the machine net ultrafiltration rate (UFnet) plus Qr.
- For CVVHD, Qef is equal to UFnet plus the Qd.
- For CVVHDF, Qef is equal to UFnet plus Qr plus Qd.

Continue….

- Small solutes in higher concentration in the dialysate (eg, bicarbonate) diffuse into the blood.. Modern hemodialyzers are virtually all “high-flux” dialyzers, which clear substances larger than historical low-flux dialyzers.
- unlike hemofiltration, hemodialysis does not effectively clear larger middle molecules.

CVVH

- The machine net ultrafiltration rate (UF) is equal to the difference between the effluent rate and the replacement fluid rate(s) (Qr), and it is adjusted to achieve net volume removal as desired.
- A typical CVVH prescription is shown,which, for a 70 kg patient, would provide a total dose of 30 mL/kg/h and a net ultrafiltration rate of 100 mL/h. To maintain efficient solute clearance in CVVH, blood flow rate (Qb) should be kept approximately 5 to 6 times higher than the replacement fluid rates.

Continuous Venovenous Hemofiltration

- CVVH requires the use of replacement fluid to replace either all or most of the ultrafiltrate, with replacement of less than all the ultrafiltrate resulting in net ultrafiltration .
- Typically, CVVH employs a relatively high rate of ultrafiltration (eg, 20-25 mL/kg/h), with solute cleared at the same rate.

CVVHD

- The dialysate solution used in CVVHD is very similar or identical to the replacement fluid used in CVVH.
- The effluent consists of both the spent dialysate and ultrafiltrate, and the net ultrafiltration rate is equal to the difference between the total effluent flow rate and the dialysate flow rate (Qd).
- A typical CVVHD prescription is shown, which, for a 70 kg patient, again provides a total dose of 30 mL/kg/h and a net ultrafiltration rate of 100 mL/h. To maintain efficient solute clearance in CVVHD, blood flow rate should be kept approximately 2.5 times higher than the dialysate flow rate.

Continue……

- CVVHD removes small solutes primarily by diffusion.
- Dialysate fluid is pumped countercurrent to the direction of blood flow.
- However, because Qd is much lower than Qb (typically 8- 50 mL/min vs 100-200 mL/min), near-complete saturation of dialysate usually occurs during CVVHD.

CVVHDF

- CVVHDF combines a high volume of ultrafiltration coupled with replacement fluid (to achieve solute clearance by convection) with dialysate perfused across the membrane countercurrent to blood flow (to achieve solute clearance by diffusion).

- As in CVVH, ultrafiltrate volume in excess of the desired rate of fluid removal is replaced with a physiologic crystalloid solution that may be infused before the hemofilter (prefilter replacement fluid), into the return line (postfilter replacement fluid), or both.

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Continue…….

- CVVHDF is a hybrid of CVVH and CVVHD, removing solutes using both convection and diffusion, using both
- replacement and dialysate solutions.
- The ultrafiltration rate determines convective clearance, with the use of replacement fluid producing solute dilution.

Parameters	CVVH	CVVHD	CVVHDF	SCUF
Primary solute transport mechanism	Convection[a]	Diffusion	Diffusion + convection[a]	Convection[a]
Blood flow rate (Q_b), mL/min	100-300	100-300	100-300	100-200
Dialysate flow rate (Q_d), mL/h	0	1,000-3,000	1,000-2,000	0
Replacement fluid rate (Q_r), mL/h	1,000-3,000	0	1,000-2,000	0
Net ultrafiltration rate, (UF_{net}), mL/h[b]	0-300	0-300	0-300	50-300
Total ultrafiltration rate (UF_{total}), mL/h	1,000-3,300	0-300	1,000-2,300	50-300
Components of UF_{total}	Q_r+ UF_{net}	UF_{net}	Q_r+ UF_{net}	UF_{net}
Total effluent rate (Q_{ef})	1,000-3,300	1,000-3,300	1,000-3,300	50-300
Components of Q_{ef}	Q_r+ UF_{net}	Q_d+ UF_{net}	Q_r+ Q_d + UF_{net}	UF_{net}

Modality	Examples of typical prescriptions for a patient weighing 70kg and with hourly net fluid intake of 50 mL/h
CVVH	Q_b 200 mL/min, $Q_{r,pre}$ 1,200 mL/h, $Q_{r,post}$ 500 mL/h, UF_{net} = 50 mL/h, UF_{total} = Q_{ef} = 1,750 mL/h (25 mL/kg/min)
CVVHD	Q_b 200 mL/min, Q_d 1,700 mL/h, UF_{net} = 50 mL/h, UF_{total} = 50 mL/h, Q_{ef} = 1,750 mL/h (25 mL/kg/min)
CVVHDF	Q_b 200 mL/min, $Q_{r,pre}$ 400 mL/h, Q_d 900 mL/h, $Q_{r,post}$ 400 mL/h, UF_{net} = 50 mL/h, UF_{total} = 850 mL/h, Q_{ef} = 1,750 mL/h (25 mL/kg/min)
SCUF	Q_b 150 mL/min, UF_{net} = 100 mL/h, UF_{total} = Q_{ef} = 100 mL/h (1.4 mL/kg/min)

Slow Continuous Ultrafiltration

- consisting of ultrafiltration without fluid replacement.
- Qb is typically 100-200 mL/min.
- No diffusive clearance occurs because no dialysate fluid is used.
- SCUF is used to treat isolated fluid overload in patients without any need for solute clearance.
- Notably, the trials assessing SCUF performed using peripheral venous access in patients with heart failure showed no mortality benefit compared with protocolized diuretic use.

Fluid Management

- With CKRT, plasma composition is adjusted by altering the composition of dialysate and/or replacement fluids while the net ultrafiltration rate is adjusted separately, allowing for precise, simultaneous, and independent management of fluid balance and plasma composition.
- For example, the plasma sodium level can be maintained at any targeted level while the fluid balance is kept even, negative, or positive.

Adjusting Plasma Composition

- CKRT solutions most commonly vary in their concentrations of potassium, calcium, and bicarbonate.
- Because the total daily dose of solute clearance provided by CKRT is higher than that provided by thrice weekly or even daily IHD ,The concentration of potassium in CKRT solutions required to control hyperkalemia is typically not as low as is required in IHD (eg, usually 4 mEq/L is sufficient unless hyperkalemia is severe).

Acetate or lactate were historically used as primary buffers in KRT solutions, but modern CKRT solutions are almost exclusively bicarbonate based, with typical bicarbonate concentrations of 22 to 35 mEq/L.

CKRT solutions:

- CKRT solutions used with RCA are usually free of calcium, which facilitates lowering the intrafilter calcium concentration.
- Additionally, these solutions usually have lower concentrations of bicarbonate (typically w25 mEq/L) than other standard CKRT solutions (usually w35 mEq/L)

- Unlike lactate, which generates an equimolar amount of bicarbonate when metabolized, each citrate molecule is metabolized to 3 bicarbonate molecules.

Importantly, although commercially available phosphate-containing CKRT solutions are now available, traditional CKRT solutions are devoid of phosphate.

- With IHD, dialysate sodium concentration can be manipulated in a continuous fashion within a limited range (usually 130-145 mEq/L) by altering the dialysate conductivity, but generating effective sodium dialysate concentrations outside this range is impractical due to the comparatively high Qd used in IHD.

- In contrast, though the sodium concentrations of premanufactured CKRT solutions are set, the relatively low Qd and Qr used in CKRT allow for easier manipulation of the effective sodium concentration, enabling slow and controlled correction of severe hyponatremia or hypernatremia.

- When correcting severe hyponatremia, lowering the effective sodium bath can be achieved by diluting the CKRT solutions by adding sterile water to the bag or replacing some CKRT solution with sterile water.

Continue.....

- Generally, this approach is impractical if commercially available CKRT solutions are used because large volumes of sterile water are not routinely stocked in hospitals due to the safety risk of inadvertent systemic administration, and the addition and removal of fluid from premade sterile bags

Continue…

- Another approach when using commercially available solutions is to provide an additional infusion of dextrose 5% in water (D5W) either into the CKRT circuit, usually in the postfilter position, or via a separate systemic infusion.

- In hyponatremic patients, the additional volume of D5W in liters per hour to administer to achieve a targeted sodium concentration ([Na+]

[Na+]CKRT is the sodium concentration in the dialysate and/or replacement fluid (in mmol/L):

$$V_{D5W} = \left[Q_{ef} \times \left([Na^+]_{CKRT} - [Na^+]_T \right) \right] / [Na^+]_T$$

For example:

- To target a sodium concentration of 125 mmol/L using CKRT with commercially available solutions having a sodium concentration of 140 mmol/L while using 2.5 L/h total effluent rate, VD5W can be calculated as follows:

$$V_{D5W} = (2.5\ \text{L/h} \times (140\ \text{mmol/L} - 125\ \text{mmol/L}))/125\ \text{mmol/L}$$
$$= (350\ \text{mmol/h} - 312.5\ \text{mmol/h})/125\ \text{mmol/L}$$
$$= 0.3\ \text{L/h}$$

- When needing CKRT solutions with a high effective sodium concentration to gradually correct severe hypernatremia or to achieve therapeutic hypernatremia, hypertonic saline can either be added to CKRT solutions or can be infused (usually as 3% sodium chloride) into the CKRT circuit or systemically.

	Maximal Theoretical Clearance (mL/min)	Typical Approximate Total Weekly Dose (ie, Standardized Kt/V_{urea})
IHD, 3 times/wk	280	2
IHD, 7 times/wk	280	5
PD, 7 times/wk	16	2
CKRT, postfilter CVVH, 25 mL/kg/h	25	7
CKRT, prefilter CVVH, 35 mL/kg/h	28	8
CKRT, postfilter CVVH, 35 mL/kg/h	35	10
CKRT, CVVHD, 35 mL/kg/h	35	10
PIKRT	Variable	Variable
Normal kidney	90-140	16

Timing of CKRT Initiation and Discontinuation

- Starting CKRT too late may result in complications from AKI and volume overload.
- However, starting CKRT too early may expose patients who may not have truly needed KRT to its potential harms.
- initiation in AKI "accelerated" (earlier) versus "standard" (delayed) initiation.

➢ some signals of harm with accelerated initiation were observed, including impaired kidney recovery, more catheter-related bloodstream infections (CRBSIs), and higher rates of hypotension and hypophosphatemia.

➢The "more delayed" strategy resulted in a trend toward increased mortality (11% higher 60-day mortality, P = 0.07).

Thus, no clear benefit to accelerated KRT initiation exists, yet, conversely, the results of AKIKI-2 suggest patients may be harmed by excessive delay beyond standard initiation strategies.

➢For most patients, CKRT should be initiated in response to concrete clinical indications:

- Most commonly volume overload
- Hyperkalemia
- Metabolic acidemia unresponsive to medical therapy
- Oliguria persisting ≥48-72 hours

➢Though RCTs are ongoing, no trial data currently exist to guide de-escalation of CKRT

- Observational studies suggest that spontaneous urine output of >500 mL/day
- Diuretic-augmented urine output of >2 L/day

are reasonable criteria for consideration of KRT discontinuation in patients with AKI

Hemodynamic stability

- Ongoing need for vasopressors and higher cumulative fluid balance are associated with intradialytic hypotension in patients who transition to IHD after CKRT.
- In general, hemodynamic stability without vasopressor support is a commonly used trigger for consideration of transition to IHD.
- Experts suggest that volume overload be corrected before discontinuation or transition.

Illness Severity and Patient Characteristics

- AKI severity and trend
- Fluid balance and symptoms of fluid overload
- Presence of oliguria, considering the response to diuretics
- Severity of electrolyte and acid-base disorders, considering the response to medical management
- Presence and severity of cardiopulmonary failure, other relevant nonrenal organ dysfunction, or underlying comorbidities
- Likelihood of recovery of kidney function without KRT, considering the reversibility of the specific etiology of AKI, trends in kidney function and urine output, and baseline kidney function
- Specific scenarios frequently requiring metabolic support from high-dose CKRT (eg, rhabdomyolysis or tumor lysis syndrome)

Risks of CKRT

- Hemodynamic instability from CKRT
- Infection, including catheter-related bloodstream infection
- Other risks associated with vascular access (pneumothorax, procedural bleeding, catheter-associated deep venous thrombosis,
- Clearance of trace elements, water-soluble vitamins, phosphate, amino acids/small peptides, and drugs (especially antibiotics)
- Delayed renal recovery
- Increased risk of immobilization and interference with physical rehabilitation

Patient-centered Factors

- Patient and family wishes and overall goals of care, including willingness to accept risk of long-term dialysis dependence
- Overall prognosis, including likelihood of patient survival

Health Care System Factors

- Availability of machines, disposable supplies, and nursing staff, especially during periods of strain on the health care system (eg, pandemics)
- Health care costs

Dose of Solute Clearance With CKRT

- Despite some early trials suggesting benefit with higher doses, 2 subsequent large RCTs, the VA/NIH ATN trial and the RENAL trial, found that higher doses of CKRT (35-40 mL/kg/h) had no benefit over lower doses (20-25 mL/kg/h) but were associated with somewhat higher rates of complications including hypophosphatemia and hypotension.

The risk of clotting

- related to hemoconcentration within the CKRT hemofilter is traditionally estimated by calculating the filtration fraction (FF),
- which is the ratio of total ultrafiltration rate over plasma water flow rate .
- To lower the risk of clotting, FF should be kept at ≤20%-25% either by maintaining adequate Qb or by preferential use of prefilter replacement fluid (with the potential exception of RCA, which anecdotally permits higher FF).

Continue……

- Although delivering 20-25 mL/kg/h is appropriate for most patients treated with CKRT in most circumstances, the dose should be serially reevaluated because critical illness dynamically evolves and doses of >25 mL/kg/h may occasionally be necessary.
- For example:
- in cases of rhabdomyolysis or tumor lysis syndrome, in which lack of clearance of potassium resulting from AKI is aggravated by extreme amounts of potassium being released into the circulation, CKRT doses of ≥40 mL/kg/h may be necessary to maintain metabolic control.

Vascular Access

- A 56-year-old man with (ESKD) on maintenance IHD via a left arm (AVF), diabetes, obesity with (BMI) 42 kg/m2, and congestive heart failure presents to the emergency department with dyspnea after missing several dialysis treatments due to malaise.
- He is diagnosed with an ST elevation myocardial infarction and cardiogenic shock and undergoes endotracheal intubation.
- infusions of epinephrine, norepinephrine, , 3-4+ pitting edema extending to the thighs, and a loud bruit and a strong thrill at his AVF.
- laboratory results include potassium, 6.2 mEq/L; (SUN), 98 mg/dL; lactate, 7.2 mmol/L; and arterial
- pH 7.12, PCO2, 48 mm Hg; and PaO2, 71 mmHg on 90% oxygen. The chest X-ray shows severe pulmonary

edema. The ICU resident begins to place a right internal jugular (IJ) temporary dialysis catheter but finds the vein to be occluded with thrombus.

Continue…..

- A well-functioning vascular access, in the form of either a temporary or tunneled cuffed dual-lumen hemodialysis catheter, is required for effective CKRT.
- In ESKD patients with a pre-existing AVF or arteriovenous graft (AVG), use of the AVF or AVG for CKRT should generally be avoided unless catheter placement proves impossible.
- Due to lower Qb and the continuous nature of CKRT, increased risks exist for needle dislodgment with possible exsanguination, access thrombosis, or permanent damage to the vascular access.

Anticoagulation

- Though the KDIGO guidelines for AKI recommend use of anticoagulation to prolonger filter life, a substantial proportion of centers (approximately 33%- 50%) start CKRT without anticoagulation, with the addition of anticoagulation if premature hemofilter clotting develops.
- The two most commonly used anticoagulants for CKRT are heparin and citrate.
- Heparin has the advantages of being inexpensive and familiar. Heparin can be provided via a separate infusion or within the CKRT circuit in the prefilter segment, with the latter being preferable as it increases intrafilter heparin concentration.
- However, heparin is not dialyzable and even prefilter heparin results in systemic anticoagulation (unless coupled with a reversal agent). Less commonly, heparin is used with the reversal agent protamine to produce regional anticoagulation. Not surprisingly, use of heparin anticoagulation without reversal is associated with increased bleeding risk.

RCA

- In contrast, RCA produces no systemic anticoagulant effect.
- In RCA, citrate is delivered in the pre-filter segment of the circuit, typically targeting a goal blood citrate concentration of 3-6 mmol/L, and chelates calcium to generate a low intra-filter ionized calcium concentration (typically <0.4 mmol/L) to inhibit the clotting cascade.
- Usually most of the citrate is removed in the CKRT effluent, though a variable but substantial proportion is delivered to the patient where it is metabolized primarily by the liver.
- To reverse the effect of citrate, to replace the calcium lost as citrate-calcium complexes, and to prevent life-threatening hypocalcemia in the patient, intravenous calcium is continuously infused into the return limb of the CKRT circuit or via a separate systemic infusion.

- total calcium should be monitored at least daily to monitor for citrate accumulation.
- Protocols have been developed specifically to minimize the risk of citrate accumulation when used in the setting of absent citrate metabolism. A more useful metric than is an organic anion normally metabolized primarily by the liver, and lactate elevations, regardless measures of hepatic function to determine the risk of citrate accumulation is lactate level. Like citrate, lactate ss of cause (eg, shock or liver disease),
- Imply impaired lactate metabolism and risk of impaired citrate metabolism. As a rough guide, serum lactate <4 mmol/L, 4-8 mmol/L, and >8 mmol/L suggest low, intermediate, and high risk, respectively, of citrate accumulation.

RCA OR HEPARIN

The most recent and largest of these was the multicenter RICH trial, which randomized nearly 600 patients to systemic heparin or RCA and found that RCA produced

- Significantly longer filter life by 15 hours
- Fewer bleeding events
- No significant difference in mortality

Complications of CKRT

Complications Related to Catheter Placement

- Hematoma, hemorrhage, or traumatic arteriovenous fistula
- Infection (CRBSI or local soft tissue infection)
- Vein thrombosis or stenosis
- Pneumothorax or hemothorax
- Air embolism
- Visceral injury

Complications Related to Extracorporeal Circuit

- Allergic reaction to dialyzer/hemofilter or circuit tubing (rare)
- Circuit thrombosis
- Hemolysis
- Air embolism
- Hypothermia
- Thrombocytopenia

Metabolic Disturbances

- Complications of regional citrate anticoagulation:
  - Citrate accumulation, ie, citrate toxicity or citrate lock (see text)
  - Citrate/buffer excess or citrate/buffer deficit (see text)
  - Isolated hypo- or hypercalcemia
  - Hypernatremia (if using formulation containing trisodium citrate)
  - Hypomagnesemia
- Hypophosphatemia, possibly aggravating respiratory muscle weakness
- Others: hypokalemia, hypocalcemia, hypomagnesemia
- Hypoglycemia (when using dextrose-free CKRT solutions)
- Euglycemic ketoacidosis (when using dextrose-free CKRT solutions)

Others

- Hypotension, especially with initiation or net ultrafiltration
- Inappropriate (excess or inadequate) medication dosing
- Inadequate nutrition due to nonselective clearance of amino acids and other micronutrients

complications of CKRT

- Most complications of CKRT can be categorized into metabolic disturbances, access-related complications, and those related to the extracorporeal circuit . Severe allergic reactions to the hemofilter or circuit tubing and circuit-related hemolysis have been described but are rare.
- Though anecdotally appreciated for years, recent observational data confirm an association between CKRT and thrombocytopenia in patients treated with CKRT.
- However, the degree of decline is usually relatively modest (ie, 33%-50% from baseline), and CKRT as the cause of thrombocytopenia should be considered a diagnosis of exclusion given the many other potential causes of thrombocytopenia in critically ill patients.

Hypophosphatemia

- severe hypophosphatemia can induce a variety of complications, including:

➢Muscle weakness, rhabdomyolysis, and myocardial depression.

➢Prolonged mechanical ventilation or an increased need for tracheostomy.

- Options include use of phosphate-containing CKRT solutions or the pre-emptive initiation of scheduled phosphate replacement as soon as the initial AKI-induced hyperphosphatemia is corrected.

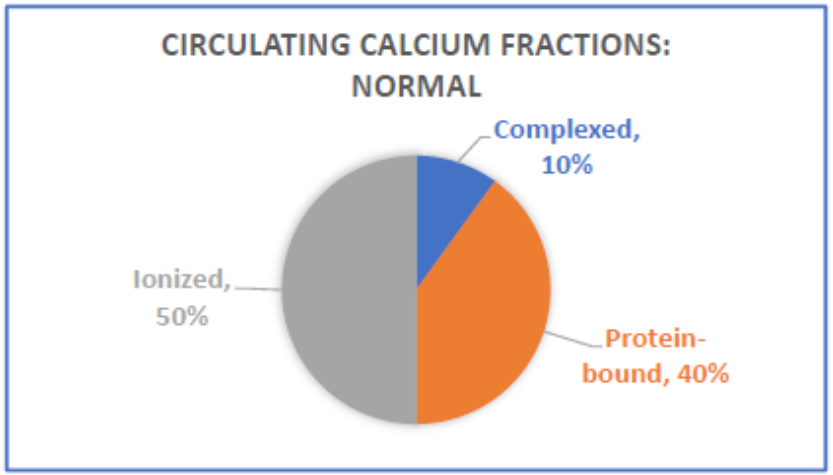
Euglycemic ketoacidosis

- Finally, in contrast to most other CKRT solutions which contain physiologic concentrations of glucose, the commercially available CKRT solutions containing phosphate are devoid of glucose, creating the potential for additional complications in patients not receiving nutrition or another glucose source—namely
- Hypoglycemia or euglycemic ketoacidosis.
- The latter manifests with unexplained anion gap metabolic acidosis, normal serum glucose, and ketonemia and requires treatment with infusions of dextrose and insulin.
- Thus, in patients on CKRT who develop high anion gap acidosis without elevated lactate or citrate accumulation, euglycemic ketoacidosis must always be considered.

Citrate accumulation

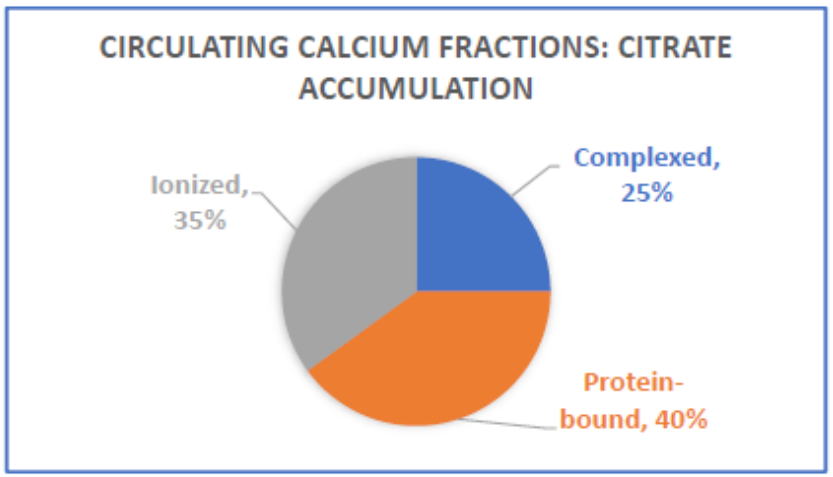
- The most feared complication of RCA is citrate accumulation, which is also referred to as citrate toxicity or citrate lock.
- As most clinical laboratories do not measure plasma citrate levels, the ratio of total calcium (tCa) to ionized calcium (iCa) is used as a surrogate measure of citrate levels. Because normally approximately 50% of total calcium is ionized, this ratio is usually 2-1
- Significant citrate accumulation will cause citrate-calcium complexes to accumulate, resulting in an increase in tCa and/or a decrease in iCa, with a tCa/iCa ratio of ≥2.5.
- Notably, correction of the total calcium for hypoalbuminemia is not generally recommended and, based on at least 1 study, likely unnecessary

A



Calcium Levels in Differing Units: Normal				
	%	mmol/L	mEq/L	mg/dL
iCa^{++}	50%	1.25	2.5	5
tCa^{++}	100%	2.5	5	10
tCa^{++}/iCa^{++}	2-to-1			

B



Calcium Levels in Differing Units: Citrate Accumulation				
	%	mmol/L	mEq/L	mg/dL
iCa^{++}	35%	0.96	1.92	3.84
tCa^{++}	100%	2.75	5.5	11
tCa^{++}/iCa^{++}	2.9-to-1			

Nutrition and Physical Rehabilitation

- CKRT may contribute significantly to the negative nitrogen balance that is typically seen with the inflammatory insults and catabolic states characteristic of critical illness. In contrast with intact kidneys, in which amino acids and small peptides are filtered at the glomerulus but fully reabsorbed by the proximal tubule, CKRT can lead to the nonselective loss of 10-20 g of amino acids daily along with other water-soluble micronutrients.
- Though additional data are needed, this amino acid removal by CKRT may plausibly aggravate ICU-acquired weakness.

Continue….

- To overcome this loss, daily nutritional targets of 25- 35 kcal/kg total calories and 1.5-2.5 g/kg of protein are recommended in patients receiving CKRT.
- Likewise, though many perceive CKRT to be a barrier to mobilization, observational studies have shown that cautious physical rehabilitation is feasible and safe in patients undergoing CKRT, and nephrologists should advocate that physical therapy is provided to CKRT patients who are otherwise appropriate candidates for early mobilization.

Monitoring CKRT Performance

- With mortality of approximately 50%, critically ill patients with AKI requiring CKRT are at high risk of adverse outcomes.
- Thus, to ensure patients receive the highest possible quality of care, quality assurance initiatives should be embedded into CKRT programs. Quality measures have only recently been developed and implemented in CKRT care.

Thank you


Thank
you!


THANK
YOU