CRRT PRESCRIPTION

Shahram Taheri M.D.

Associate Prof.

MUI

CRRT: DEFINITION

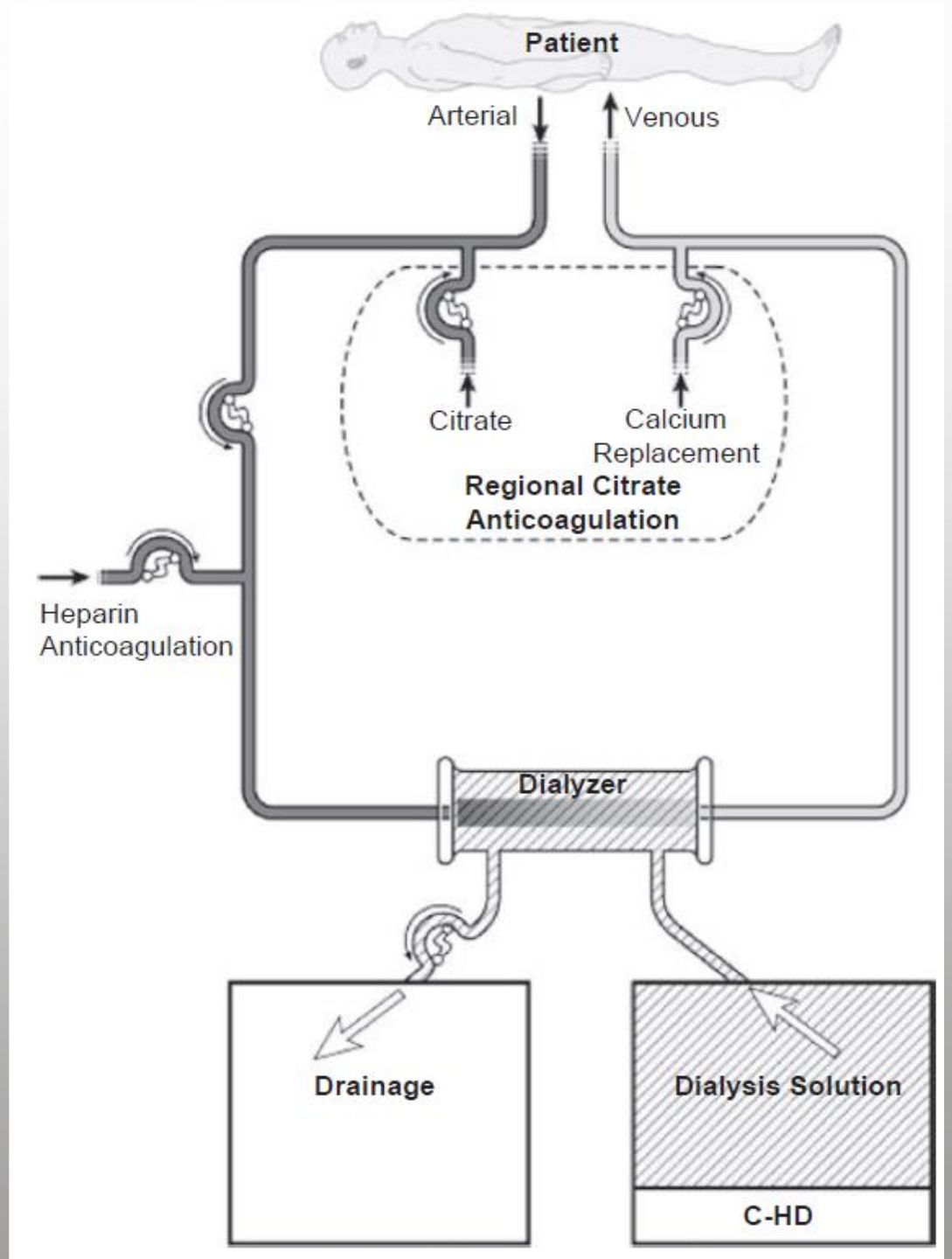
Continuous renal replacement therapy (CRRT) is a therapy indicated for continuous solute removal and/or fluid removal in the critically ill patient. It allows for slow and isotonic fluid removal that results in better hemodynamic tolerance even in unstable patients with shock and severe fluid overload. This process can be applied to both adults and children.

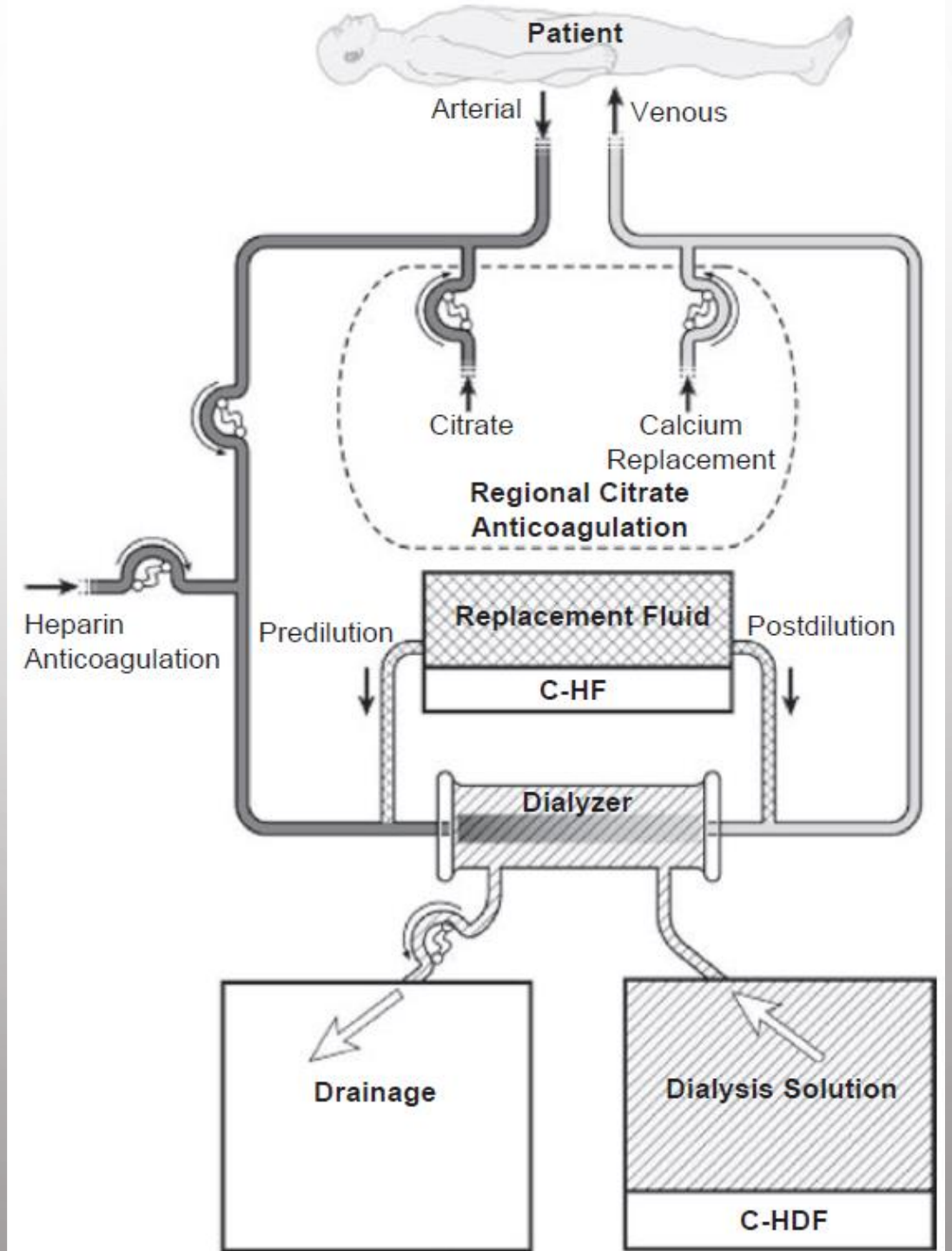
NOMENCLATURE

- Continuous hemodialysis (C-HD),
- Continuous hemofiltration (C-HF,)
- Continuous hemodiafiltration, (C-HDF).
- Slow continuous ultrafiltration (SCUF)
- Sustained low-efficiency hemodialysis (SLED)
- Hemodiafiltration are (SLED-F)
- SLED and SLED-F are collectively grouped as forms of prolonged intermittent renal replacement therapy, (PIRRT).
- Conventional intermittent treatment ,IHD (intermittent hemodialysis)

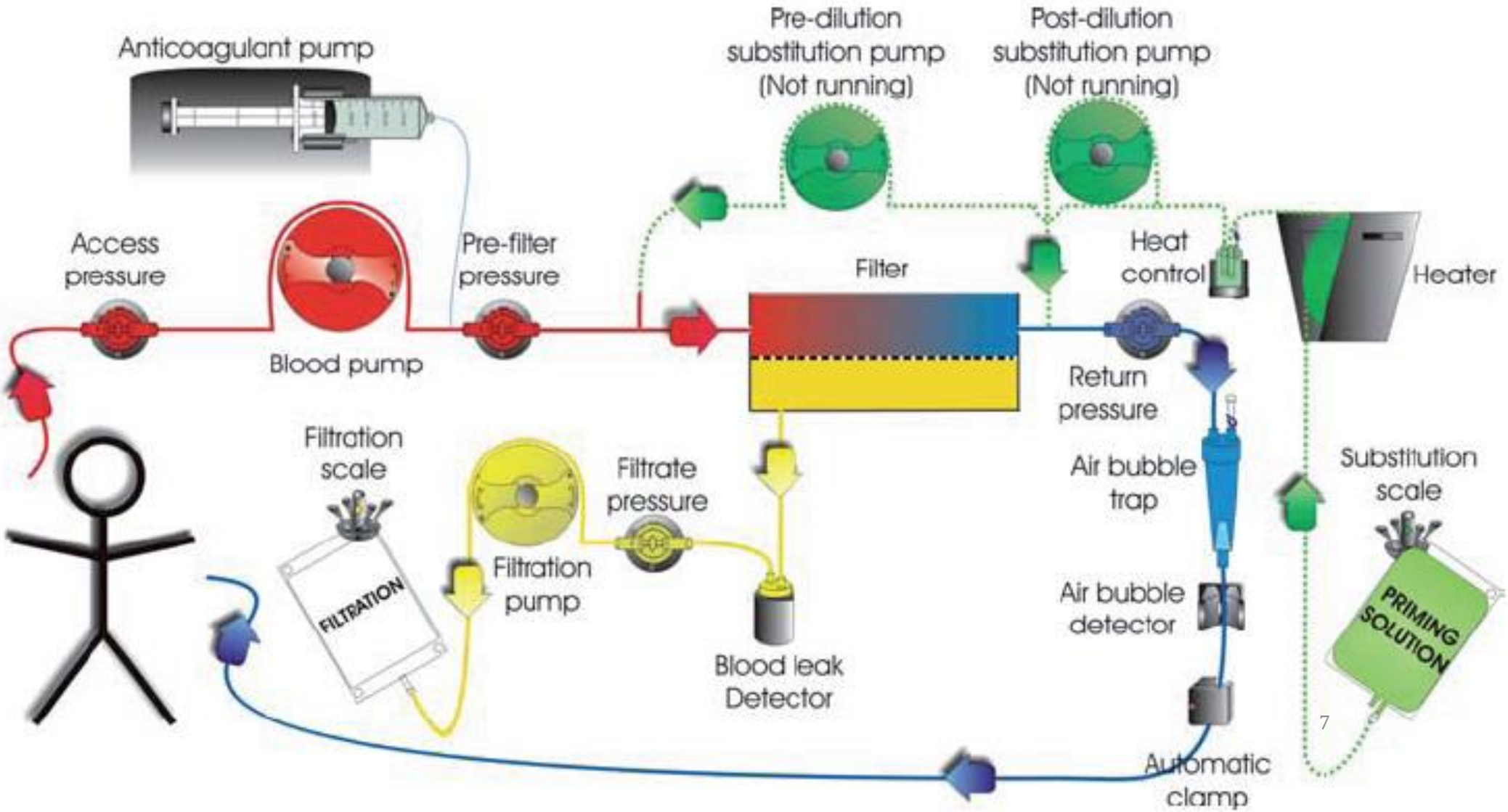
NOMENCLATURE

- One would insert “AV” or “VV” after the letter “C” to specify that the therapy was given using either an AV or a venovenous access, giving CAVHD or CVVHD (hemodialysis), CAVH or CVVH (hemofiltration), and CAVHDF or CVVHDF (hemodiafiltration} but today, most treatments are given using a venous catheter–based access, and so use of the “VV” has become superfluous.

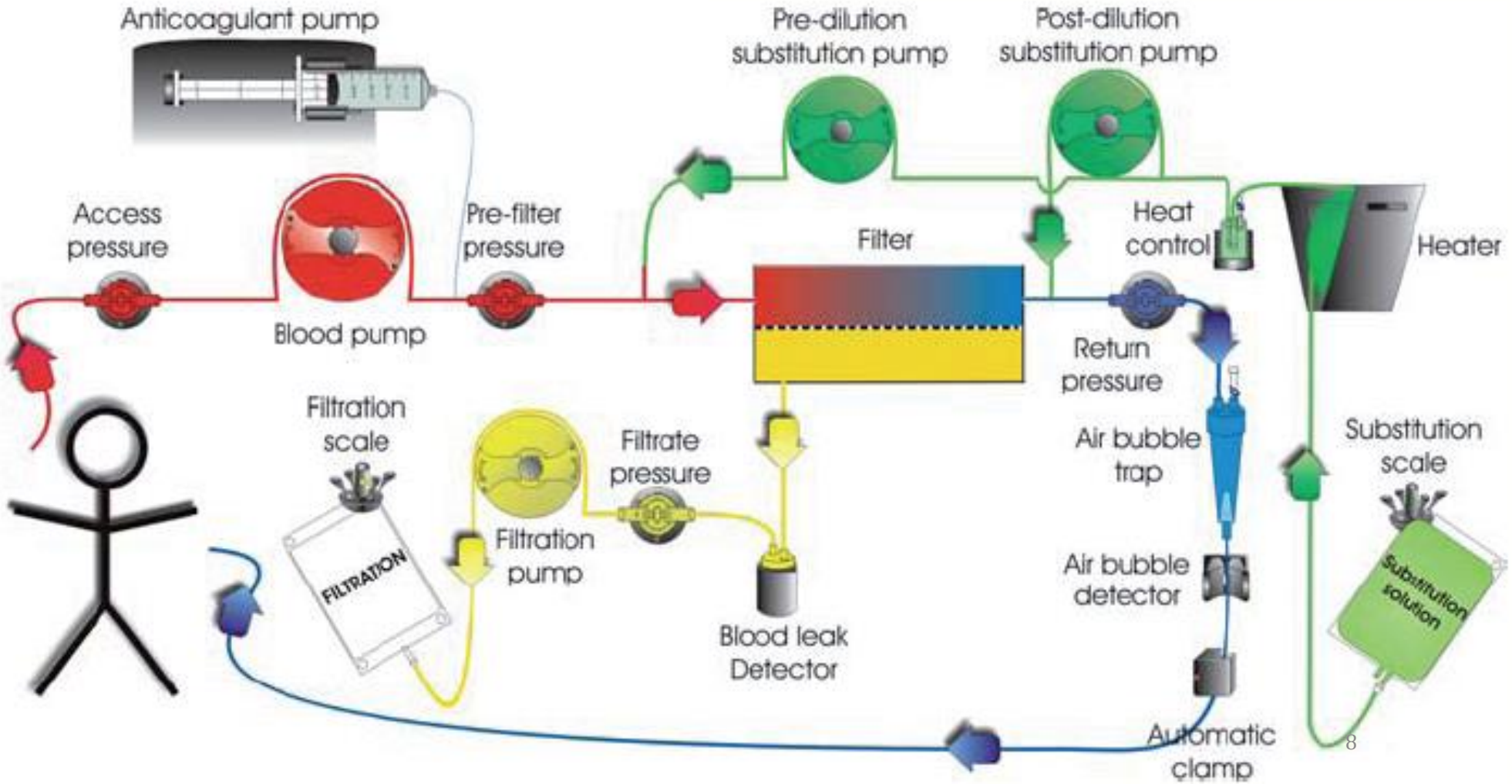

Patient
Arterial
Venous
Citrate
Calcium
Replacement
Regional Citrate
Anticoagulation
Heparin
Anticoagulation
Dialyzer
Drainage
Dialysis Solution
C-HD


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

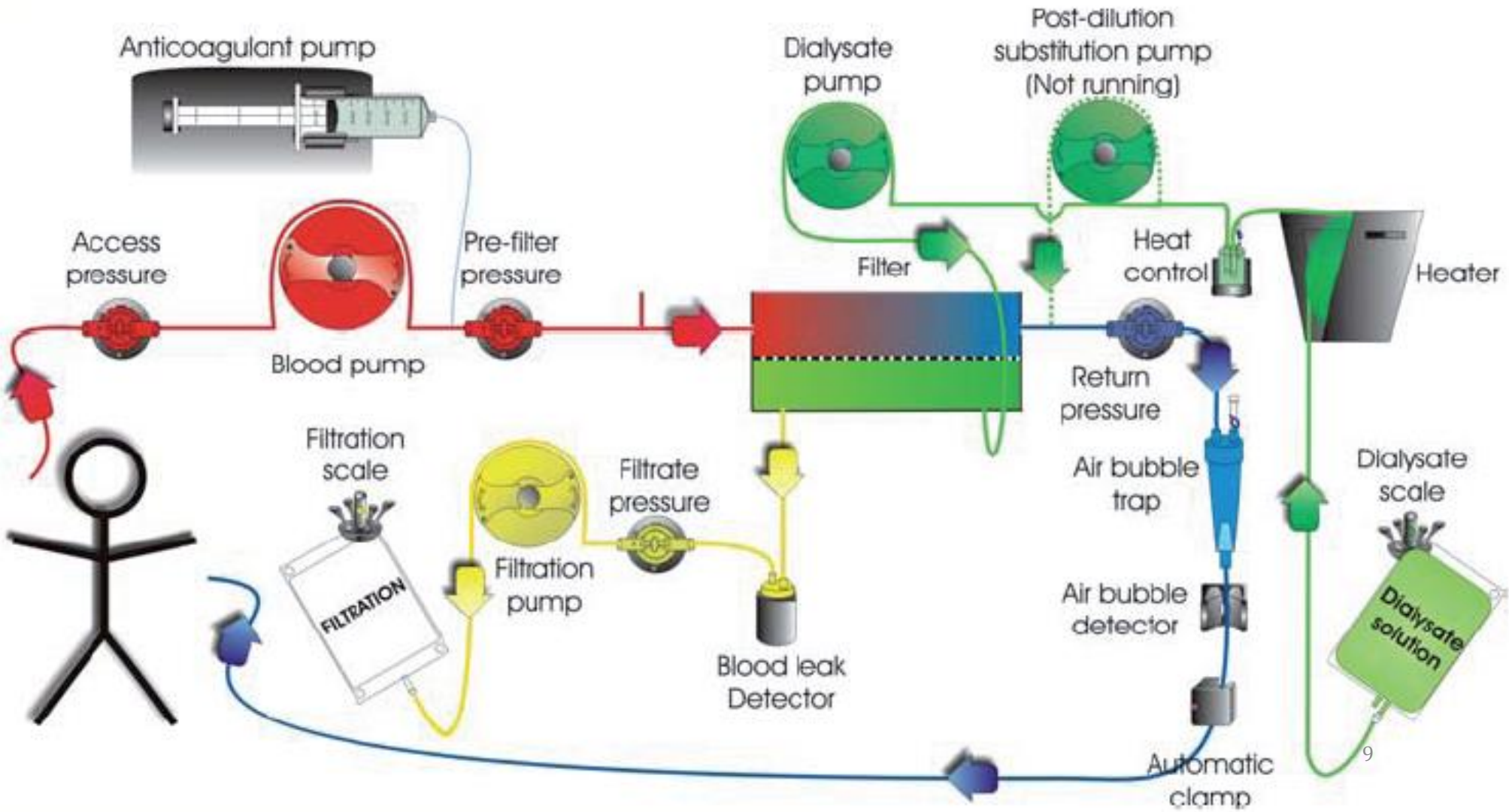
SLOW CONTINUOUS ULTRAFILTRATION[6] (SCUF)



CONTINUOUS VENO-VENOUS HEMOFILTRATION[7] (CVVH)



CONTINUOUS VENO-VENOUS HEMODIALYSIS[8] (CVVHD)



CONTINUOUS VENO-VENOUS HEMODIAFILTRATION[9] (CVVHDF)

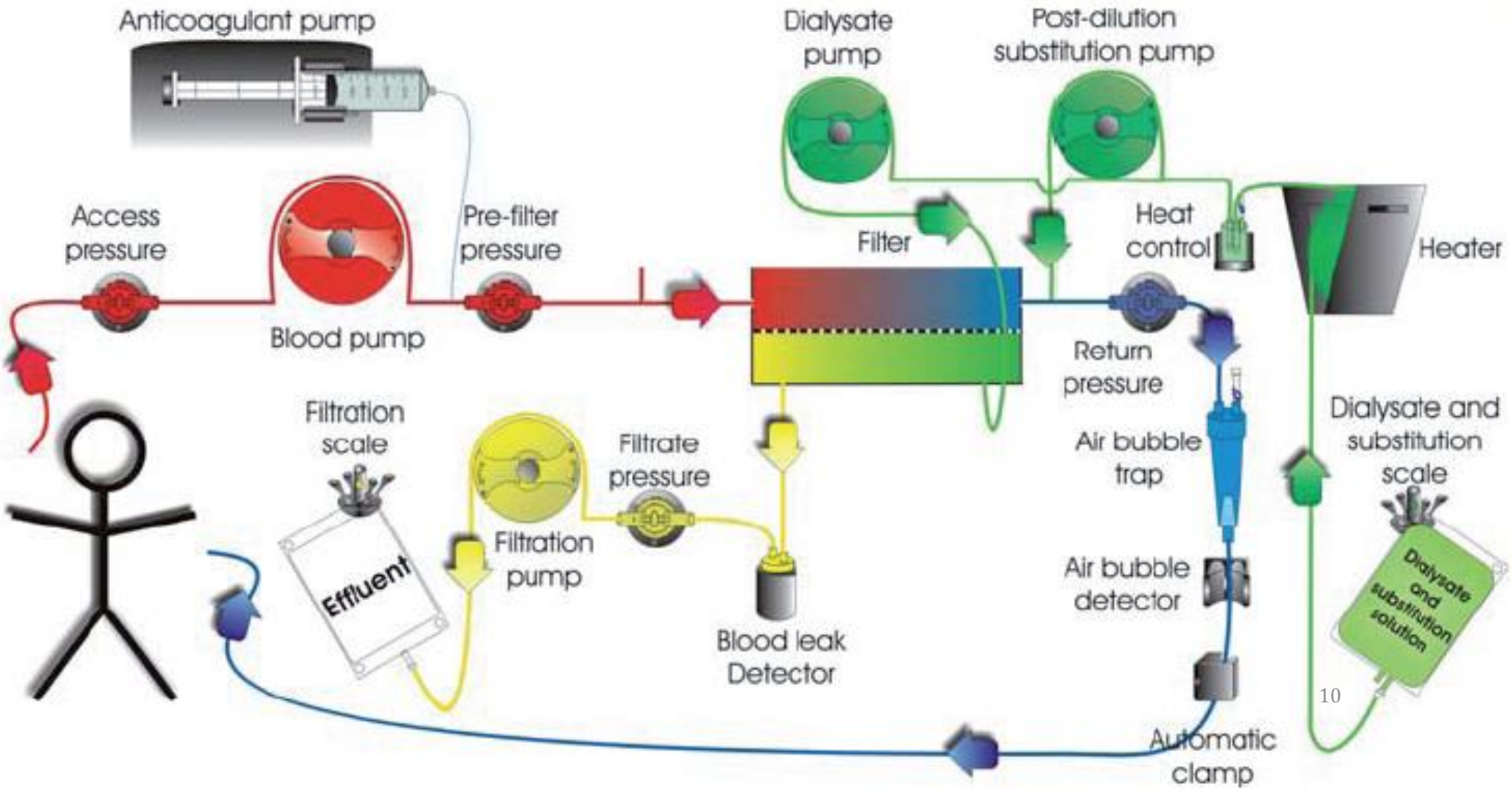


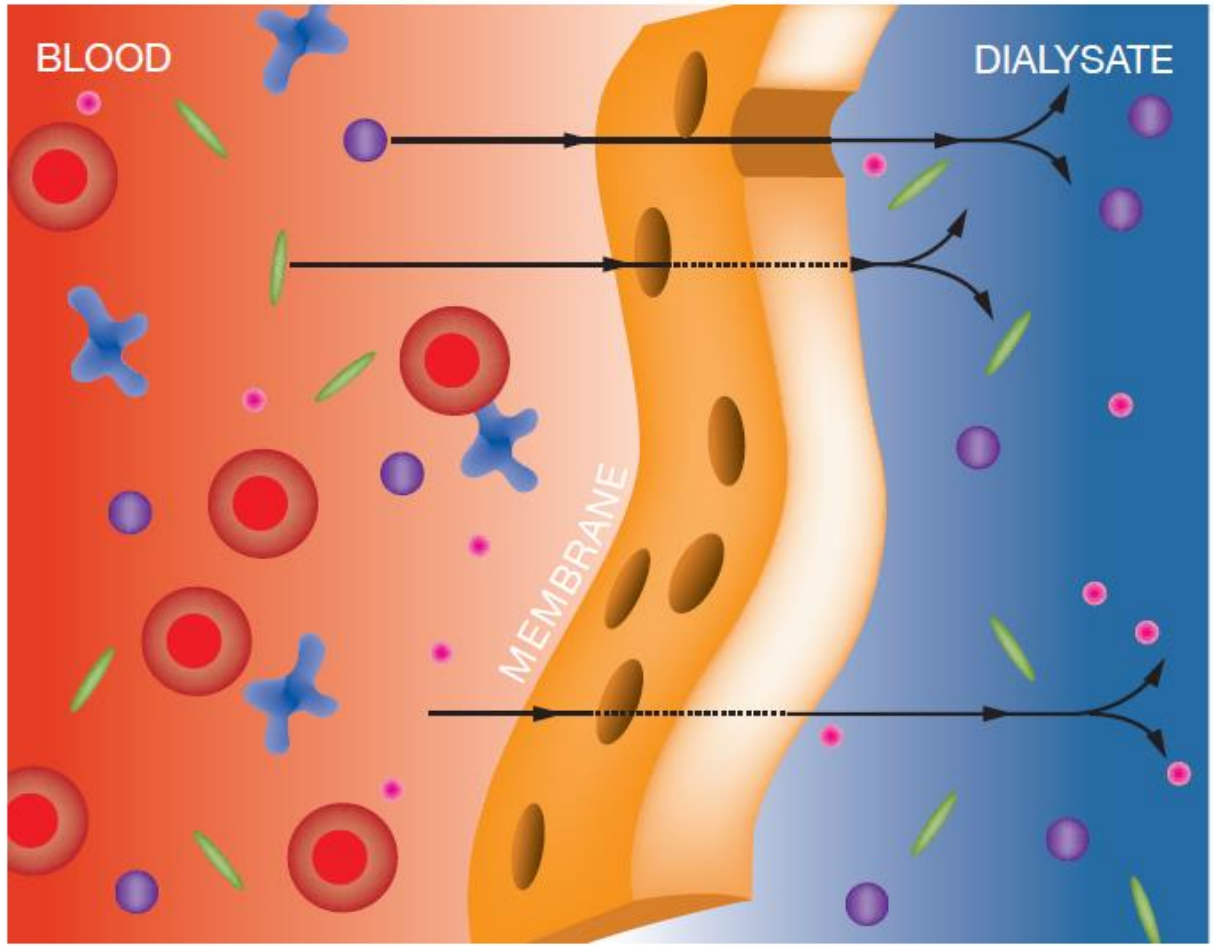
TABLE 15.1 Comparison of Techniques

	IHD	SLED	SCUF	C-HF	C-HD	C-HDF
Membrane permeability	Variable	Variable	High	High	High	High
Anticoagulation	Short	Long	Continuous	Continuous	Continuous	Continuous
Blood flow rate (mL/min)	250–400	100–200	100–200	200–300	100–300	200–300
Dialysate flow rate (mL/min)	500–800	100	0	0	16–35	16–35
Filtrate (L per day)	0–4	0–4	0–5	24–96	0–4	24–48
Replacement fluid (L per day)	0	0	0	22–90	0	23–44
Effluent saturation (%)	15–40	60–70	100	100	85–100	85–100
Solute clearance mechanism	Diffusion	Diffusion	Convection (minimal)	Convection	Diffusion	Diffusion + convection
Urea clearance (mL/min)	180–240	75–90	1.7	17–67	22	30–60
Duration (hr)	3–5	8–12	Variable	>24	>24	>24

DIFFUSION

Diffusion is the movement of solutes through a semi-permeable membrane from an area of higher concentration to an area of lower concentration until equilibrium has been established.

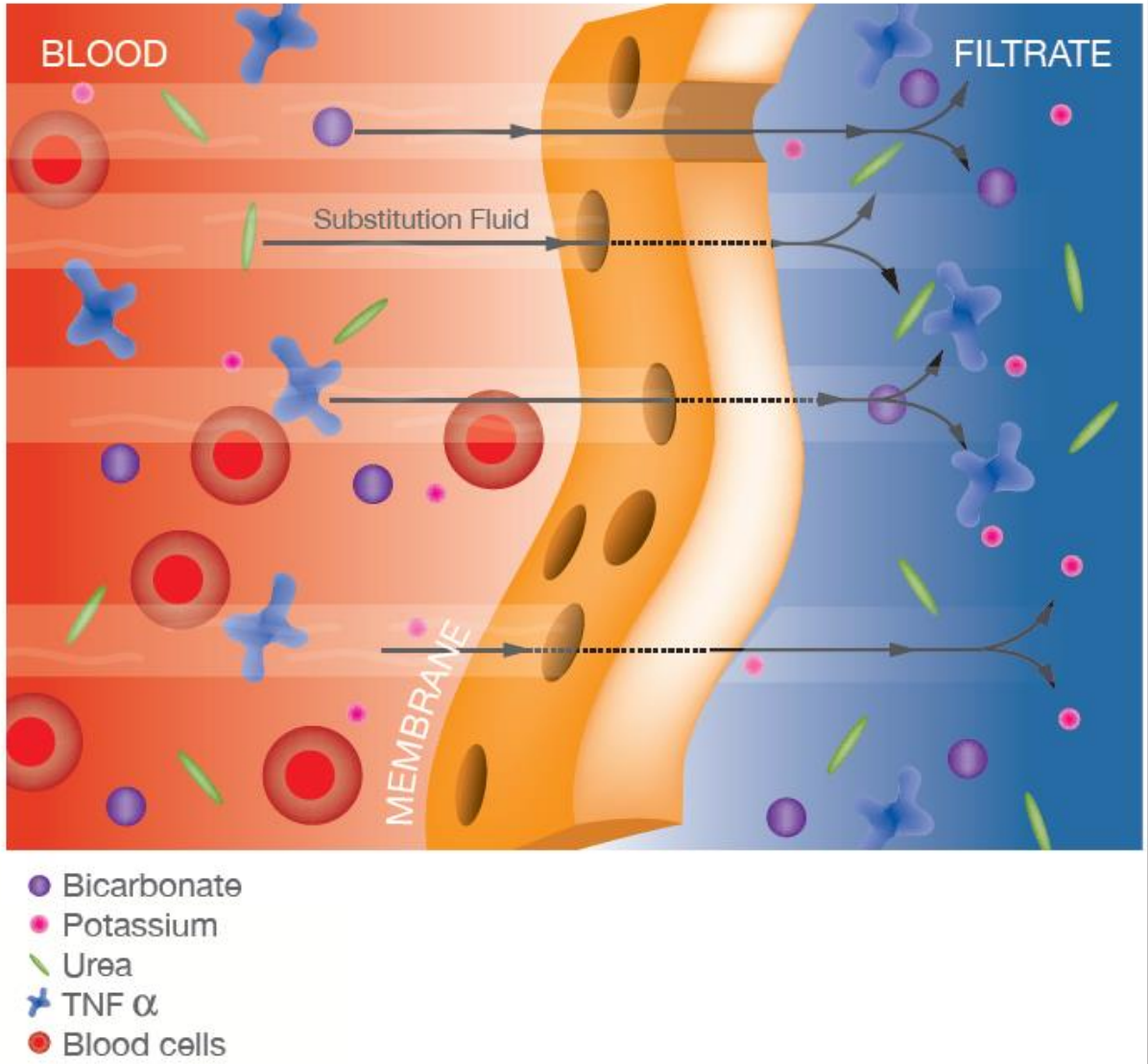
- Solutes move from a higher concentration to a lower concentration
- In CRRT, diffusion occurs when blood flows on one side of the membrane, and dialysate solution flows counter-current on the other side
- The dialysate does not mix with the blood
- Efficient for removing small molecules but not large molecules
- Molecular size and membrane type can affect clearances
- Diffusion occurs during hemodialysis



CONVECTION

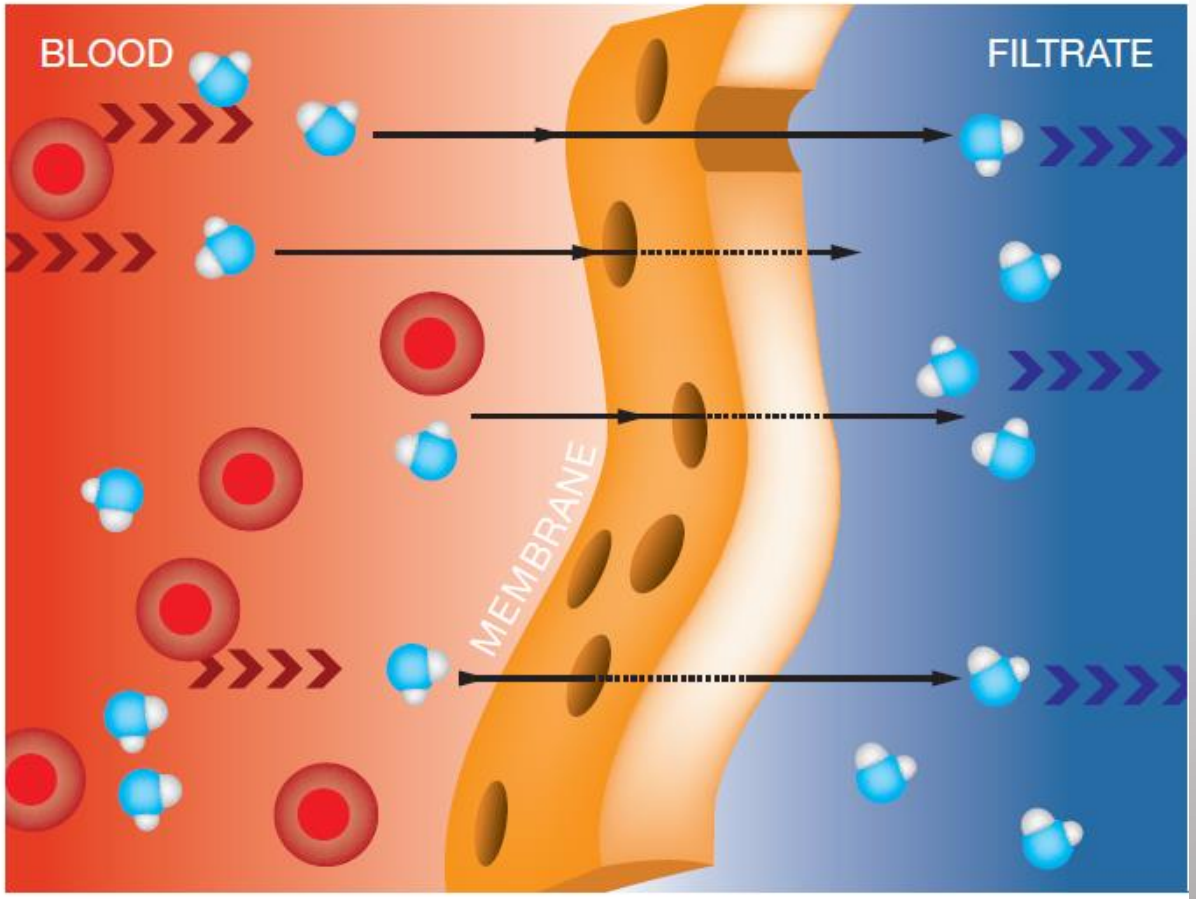
Convection is the one-way movement of solutes through a semi-permeable membrane with a water flow. Sometimes it is referred to as solvent drag.

- Efficient for both larger and smaller molecules
- The faster the substitution flow rate, the higher the clearance
- Pressure difference between the blood and ultrafiltrate causes plasma water to be filtered across. This causes solvent drag for small and large molecules across the membrane leading to removal from the blood. The ultrafiltrate containing the solute should be replaced by substitution solutions
- Substitution solutions must have near physiological levels of electrolytes and buffer, and be sterile



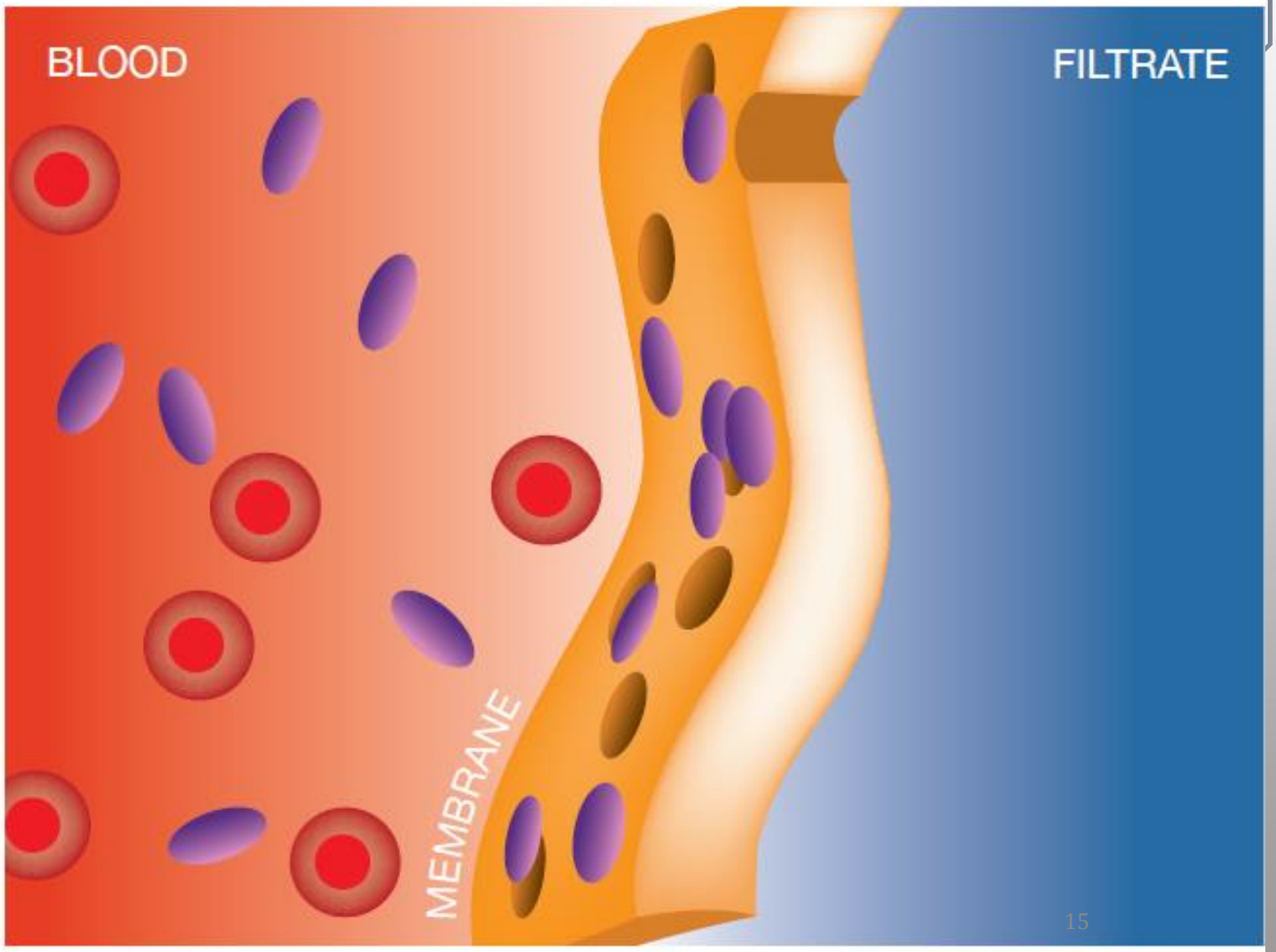
Ultrafiltration is the movement of fluid through a semi-permeable membrane along a pressure gradient.

- Positive and negative pressures affect ultrafiltration
- Positive pressure is generated on the blood side of the membrane and negative pressure is generated on the fluid side
- This gradient, positive to negative, influences the movement of fluid from the blood side to the fluid side, resulting in a net removal of fluid from the patient
- The ultrafiltration rate depends on the pressure applied to the filter, inside and outside the fibers
- Minimal solute clearance happens by convection during ultrafiltration



Adsorption is the adherence of solutes and biological matter to the surface of a membrane.

- High levels of adsorption can cause certain filters to clog and become ineffective
- Membrane type affects adsorptive tendencies /effectiveness
- Adsorption may also cause limited removal of some solutes (e.g., ß2 microglobulins) from the blood



CRRT GOALS[3,4]

- Removal of waste products
- Restoration of acid-base balance
- Correction of electrolyte abnormalities
- Hemodynamic stabilization
- Fluid balance
- Nutritional support
- Removal and/or modulation of septic mediators

TABLE 15.2

Potential Advantages of Slow Continuous Therapies

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 (postsurgery, 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.

TRAINING AND EQUIPMENT COSTS

- The use of continuous procedures requires an effort on the part of nursing staff in the ICU to become familiar with the procedures.
- In units with high staff turnover rates and in units where continuous therapies are done infrequently, use of prolonged intermittent therapies such as SLED may be a more practical option.
- In high-volume units where continuous therapies are a common part of the dialysis armamentarium, use of such therapies can aid in the fluid, solute, and nutritional management of the most challenging patients.

DIFFERENCES AMONG C-HD, C-HF, AND C-HDF IN CLEARANCE OF SMALL AND LARGE-MOLECULAR-WEIGHT SOLUTES

SOLUTE CLEARANCE WITH C-HD

- In 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.
- As a rule of thumb, BFR in C-HD should be at least three times the dialysate flow rate

SOLUTE CLEARANCE WITH C-HD

- .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 (MW) 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.

SOLUTE CLEARANCE WITH C-HD

- 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.

SOLUTE CLEARANCE WITH C-HD

- In terms of urea kinetics, this 40 L can be thought of as the familiar (K × t) measure of clearance.
- For a patient with a urea distribution volume of 40 L, such a prescription would translate to a daily Kt/V of 40/40 = 1.0 or about 7.0 per week.
- This compares favorably with an equivalent weekly Kt/V urea delivered by thrice-weekly IHD of about 2.7

SOLUTE CLEARANCE WITH C-HF

- C-HF is a purely convection-based blood cleansing technique.
- As blood flows through the hemofilter, a transmembrane pressure gradient between the blood compartment and the ultrafiltrate compartment causes plasma water to be filtered across the highly permeable membrane.
- As the water crosses the membrane, it sweeps along with it (nonprotein-bound) small and large molecules (pore size permitting) and thus leads to their removal from the blood.

SOLUTE CLEARANCE WITH C-HF

- The removed ultrafiltrate is replaced by a balanced electrolyte solution infused into either the inflow (predilution) or the outflow (postdilution) line of the hemofilter.
- Typically, about 20–25 mL/kg per hour of replacement fluid is infused. The filter outflow or “drainage fluid” is nearly 100% saturated with urea when postdilution mode is used.

FILTRATION FRACTION

- This is the fraction of plasma flowing through the hemofilter that is removed.
- Filtration fraction can be calculated as the ultrafiltration rate divided by the plasma flow rate. BFR × (1 – Hct).
- For example, if the BFR is 150 mL/min and the Hct is 33%, the plasma flow rate will be 0.67 × 150 = 100 mL/min. If the UF rate is 25 mL/min, then the filtration fraction is 25/97, or about 25%.

FILTRATION FRACTION

- The rule of thumb is to keep the filtration fraction at 25% or lower to avoid overconcentration of red cells and plasma proteins in the hemofilter.
- Overconcentration results in fouling of the membrane pores, which can impair UF efficiency and lower the sieving coefficient,
- Overconcentration can also increase the likelihood of clotting.

FILTRATION FRACTION

- To avoid overconcentration and keep filtration fraction below 25%, when a high replacement fluid infusion rate in postdilution mode is desired, the BFR needs to be increased above the usual 150 mL/min.
- Another way to keep the filtration fraction from increasing is to use predilution mode.

PREDILUTION MODE

- With predilution, there is slight lowering of the urea concentration of ultrafiltrate (usually 80%–90% of the corresponding plasma value),
- But this is outweighed by the ability to deliver an increased replacement solution infusion rate, enhancing overall middle-molecule clearances.
- We recommend using predilution whenever it is desirable to remove more than 25 L per day.

PREDILUTION MODE

- Predilution is also performed if the baseline blood viscosity is relatively elevated (e.g., if the hematocrit is >35%).
- A combination of pre- and postdilution has been advocated by some practitioners.

CALCULATING THE DILUTIONAL EFFECTS OF PREDILUTION MODE

- As an example, assume that the replacement fluid infusion rate is 25 mL/min and BFR is 150 mL/min.
- The amount of dilution of waste products in the blood entering the filter will be 25/(150 + 25) = 14%.

CALCULATING THE DILUTIONAL EFFECTS OF PREDILUTION MODE

- Assuming that 35 L per day of replacement fluid is used and that 5 L per day of excess fluid is removed, daily effluent volume will typically be about 40 L per day.
- In postdilution mode, (K × t) t will be 40 L.
- In predilution mode, (K × t) will be perhaps 15% less, 34 L, and so, assuming V = 40 L, then daily Kt/V with C-HF will be about 40/40 = 1.0 (postdilution) or 34/40 = 0.85 (predilution).

UREA CLEARANCE WITH C-HDF

- With C-HDF, the sum of the dialysis solution flow rate, replacement fluid infusion rate, and removal of excess fluid usually is set at a level similar to the outlet flow rate in C-HD or postdilution C-HDF.
- The clearance calculations are similar to those discussed above.
- The clearance of small molecules with C-HDF is similar to that with C-HD and C-HF when the daily effluent volumes are comparable.

SMALL- VERSUS MIDDLE-MOLECULAR-WEIGHT SOLUTE REMOVAL WITH C-HF VERSUS C-HD

- With C-HD, the outflow dialysate is not as highly saturated with larger-MW substances that diffuse slowly in solution and thus have a lower rate of diffusive transfer across the dialyzer membrane.
- In contrast, with C-HF, the plasma ultrafiltrate is almost completely saturated with both low- and middle-MW solutes, because the convective removal rates of small- and larger-MW solutes are similar.

SMALL- VERSUS MIDDLE-MOLECULAR-WEIGHT SOLUTE REMOVAL WITH C-HF VERSUS C-HD

- Hence, C-HF is more efficient than C-HD in terms of larger-MW toxin removal, including peptides, certain antibiotics, and vitamin B12.
- The theoretical advantage of C-HF is technically demanding to realize, as it can be challenging to ultrafilter >25 L from patients who cannot deliver the high BFRs required to prevent overconcentration.
- Also, fluid balancing becomes critical when the replacement fluid infusion rate is high.

SMALL- VERSUS MIDDLE-MOLECULAR-WEIGHT SOLUTE REMOVAL WITH C-HF VERSUS C-HD

- With high volume C-HF, any slowing of the BFR will result in transient
- hemoconcentration in the hemofilter, with attendant risk of clotting.
- On the other hand, it is easy to perform C-HD using dialysis solution flow rates of 50 L per day.
- For this reason, in daily practice, C-HD tends to be the more popular therapy, and if enhanced removal of middle molecules is desired, a replacement fluid component is added (C-HDF).

VASCULAR ACCESS

- Venovenous blood access
- Arteriovenous blood access

VENOVENOUS BLOOD ACCESS

- Vascular access is obtained 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 2012 KDIGO AKI guidelines recommend using uncuffed venous catheters for CRRT

VENOVENOUS BLOOD ACCESS

- The rationale is that insertion of an 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 (KDIGO, 2012)

CATHETER CHANGES

- CRRT catheters should be changed only when clinically indicated;
- catheters should not be changed according to some predetermined schedule in the hopes of minimizing the rate of catheter sepsis.
- The practice of routine, scheduled catheter changes, once popular, is not recommended by the Centers for Disease Control and Prevention (CDC), and studies do not support this approach

DIALYSATES AND REPLACEMENT SOLUTIONS

- CRRT fluids come premixed as commercially prepared sterile solutions.
- They are typically packaged in 2.5-L or 5-L bags;
- in some cases fluids are supplied in bags with two compartments that need to be mixed immediately prior to use.

COMPOSITION

- Buffers
- Sodium
- Potassium
- Phosphate
- Calcium and magnesium
- Glucose.

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

BUFFERS

- Lactate-based solutions
- Bicarbonate-based solutions
- Citrate-based solutions

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.

LACTATE-BASED SOLUTIONS

- 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.

LACTATE-BASED SOLUTIONS

- The 2012 KDIGO AKI guidelines suggest using bicarbonate-based solutions for all patients with AKI at a low level of evidence (2C),
- but recommend using such solutions more strongly for patients with liver failure and/or lactic acidosis (level of evidence 2B)
- And for patients in circulatory shock (level of evidence 1B).

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.

BICARBONATE-BASED SOLUTIONS

- Some solutions contain a small amount (3 mM) of lactate, left over from lactic acid used to acidify the final solution.
- There is no evidence that this small amount of lactate contributes to hyperlactatemia.
- When a high dialysis solution or replacement solution flow rate (e.g., >30 mL/kg/hour) is prescribed, use of lower bicarbonate solutions may help prevent metabolic alkalosis.

BICARBONATE-BASED SOLUTIONS

- 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.

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.

CITRATE-BASED SOLUTIONS

- 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).
- Therefore, it is not appropriate to use these solutions in C-HD where dialysate flow is countercurrent to blood, or C-HF/HDF with predominantly postfilter replacement.

SODIUM

- Commercially available CRRT fluids usually contain physiologic sodium concentrations at or close to 140 mM.
- When treating patients with severe, and especially longstanding, hyponatremia, where the goal is to slowly increase the serum sodium at a rate no greater than 6-8 mmol/L per day, the replacement fluid or dialysis solution needs to be diluted with water, to a concentrate just slightly greater than the predialysis sodium value.

POTASSIUM

- CRRT fluids with no potassium are suitable for initial treatment of AKI patients with severe hyperkalemia.
- Once serum potassium has decreased to a safe level, fluids containing 4 mM potassium are used to minimize arrhythmia risk and depletion of body potassium.
- Commercially made fluids come premixed with potassium concentrations of 0, 2, or 4 mM.
- The lower potassium content solutions also may be used as needed in patients who are highly catabolic with persistent hyperkalemia.

PHOSPHATE

- Hypophosphatemia during extended CRRT is common and can result in respiratory muscle weakness and prolonged respiratory failure in critically ill patients.
- Phosphate replacement for severe hypophosphatemia is routine, but frequent monitoring of serum phosphorus levels is necessary.

CALCIUM AND MAGNESIUM

- Most dialysis/replacement solutions contain 1.5–1.75 mM of calcium and 0.5–0.6 mM of magnesium, and their use usually allows maintenance of desired systemic levels.
- During RCA, citrate binds to and depletes serum calcium and magnesium.
- CRRT solutions used during RCA often contain no calcium to facilitate reduction of ionized calcium in the filter by citrate to allow adequate circuit anticoagulation.
- With RCA, separate systemic infusions of calcium and sometimes magnesium with strict monitoring protocols are thus necessary.

GLUCOSE

- Modern CRRT solutions are either glucose free, or contain physiologic glucose concentrations, usually 5.5 mM (100 mg/dL).
- Use of glucose-free fluids in CRRT is associated with hypoglycemia, and glucose-containing CRRT fluids are preferred; regular monitoring and administration of insulin is necessary to prevent hyperglycemia and to achieve a target serum glucose of 6–8 mM, a level that has been associated with the best outcomes.

GLUCOSE

- Another argument against use of glucose-free CRRT solutions is that substantial amounts of glucose can be removed from the body with their use, and this may adversely affect nutritional balance.

TEMPERATURE OF DIALYSIS SOLUTION/REPLACEMENT FLUID

- CRRT can be set up so that dialysis solution and replacement fluid are infused at room temperature.
- This is a departure from conventional dialysis, where dialysis solution is warmed.
- Use of room temperature fluid results in heat subtraction from the patient
- In fact, the hemodynamic benefits of CRRT appear to be due largely to such thermal cooling effects.

TEMPERATURE OF DIALYSIS SOLUTION/REPLACEMENT FLUID

- CRRT-associated heat subtraction may mask the presence of fever, thus reducing the reliability of body temperature as a marker for infection or inflammation.
- Whether this heat subtraction has an effect on the body's ability to resist infection has not been studied.
- One study done in a septic shock model using sheep suggested that warming of blood in the extracorporeal circuit increased survival rate.
- Current CRRT delivery systems have heating systems.

PRESCRIBING AND DELIVERING CRRT

- The suggested dose of CRRT in AKI is a delivered effluent volume of 20–25 mL/kg per hour (KDIGO AKI, 2012).
- This was, however, presented as an ungraded recommendation, and there is no evidence that lower levels of therapy give worse results.
- A handful of randomized controlled trials that suggested a use of a markedly higher effluent volume led to better outcomes, but these results were not confirmed.

PRESCRIBING AND DELIVERING CRRT

- One mechanistic analysis has suggested that use of a higher effluent volume results in only a very small increase in middle-molecule clearance (Hofmann, 2010) and that the best way to increase middle-molecule removal is to increase blood flow and membrane surface area.
- There is no evidence that convective therapies (C-H or C-HDF) lead to better outcomes than diffusion-based treatments (C-HD).

PRESCRIBING AND DELIVERING CRRT

- The adequate dose of CRRT remains an area where more research is needed.
- To deliver an effluent volume of 20–25 mL/kg per hour, one normally would need to prescribe a lower inflow fluid rate, as the effluent volume will also include 2–5 L per day of excess fluid removed from the patient.

PRESCRIBING AND DELIVERING CRRT

- However, technical problems often arise, yielding to interruption of therapy or reduction of efficiency due to partial clotting of the dialyzer, and so it is wise to prescribe a slightly higher inflow volume than the target.
- As noted above, when predilution mode is used, the infusion rate of the replacement fluid should be increased by about 15%–20%, depending on the ratio of predilution fluid infusion rate to blood flow.

EMPIRIC DOSING

- The intensity of treatment should be adjusted on the basis of clinical circumstances. CRRT intensity may need to be increased in highly catabolic patients, to facilitate nutritional support, in tumor lysis syndrome, or for drug intoxication where intermittent therapies are not tolerated.

EMPIRIC DOSING

- Based on information from the RENAL study and ATN study,
- the average serum urea nitrogen achieved should be less than
- 45 mg/dL (16 mmol/L).

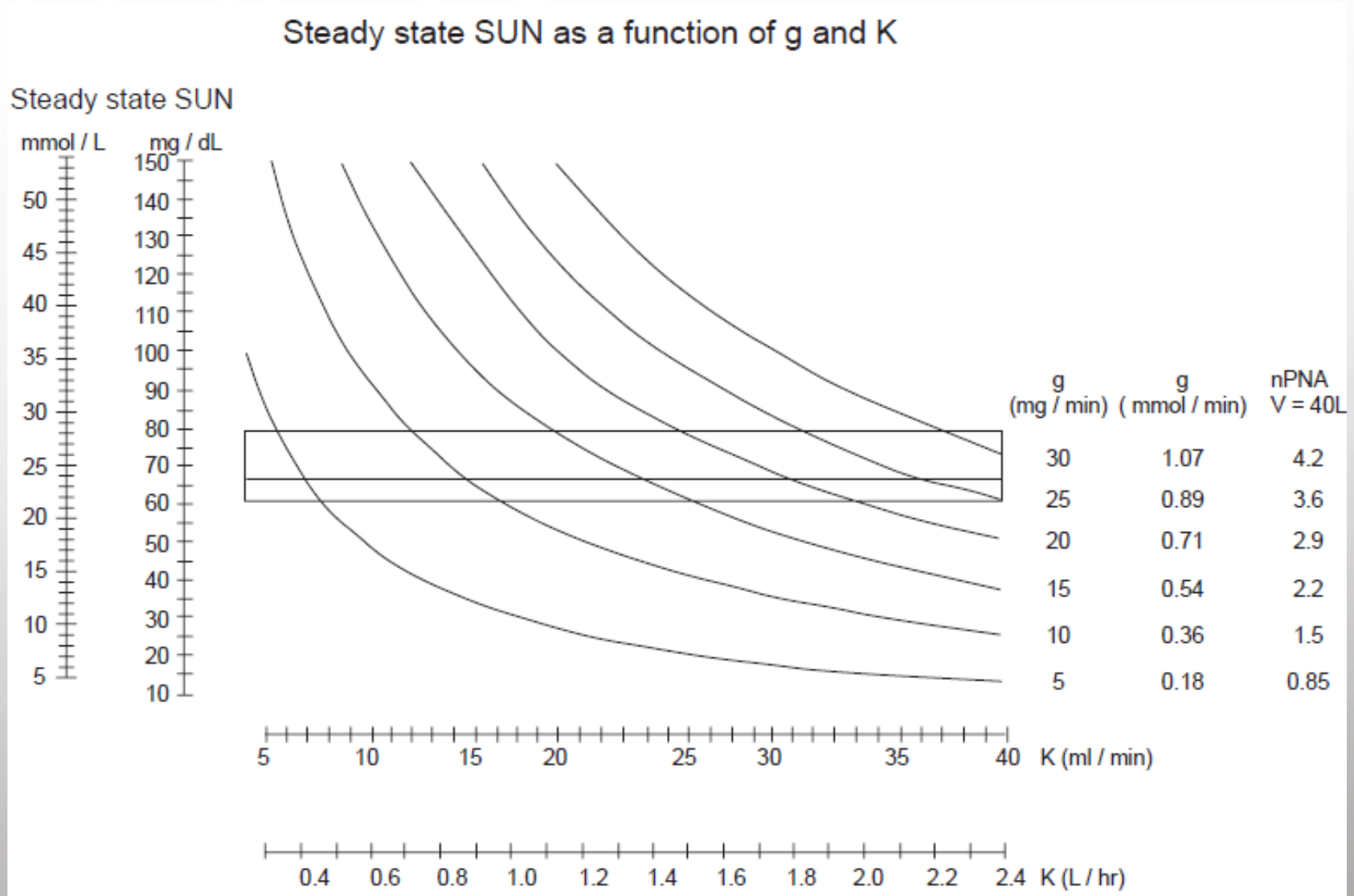


FIGURE 15.3 Estimated total extracorporeal urea clearance required to attain various steady-state serum levels of urea nitrogen. Clearance, on the bottom, is read from the intersection of the urea nitrogen generation level (g) and the steady-state goal serum urea nitrogen. (From Garred LJ. *Syllabus of the Second International Conference on CRRT*, San Diego, CA, Feb 9, 1997, p. 7.)

DOSING FOR SLED AND SLED-F

- Given the relative absence of dose-finding studies, there are no specific guidelines for the amount of SLED or SLED-F to give.
- The KDIGO AKI guidelines recommend that a weekly Kt/V of at least 3.9 be given when intermittent RRT (IRRT) is used, where the weekly Kt/V is defined simply as the sum of the treatments given each week.

DOSING FOR SLED AND SLED-F

- Usually, SLED is done for 6–12 hours, four to seven times per week, with a BFR of 200–300 mL/min and dialysis solution flow rate of 300–400 mL/min.
- Such a prescription far exceeds the 3.9 “weekly Kt/V” guideline recommended by KDIGO.

ANTICOAGULATION

- In most patients at low risk of bleeding, systemic heparin is routinely used as it is inexpensive and easy to implement.
- A patient already on systemic therapeutic anticoagulation for another indication (e.g., intra-aortic balloon pump) would not require additional anticoagulation.

ANTICOAGULATION

- Patients with severe thrombocytopenia or impaired coagulation should have a trial of anticoagulation-free CRRT.
- In immediate postoperative patients or patients at high risk of bleeding, heparin free CRRT or RCA can be used.
- In patients with nonimmune heparin-induced thrombocytopenia (HIT type I), RCA may be employed.

ANTICOAGULATION

- Systemic anticoagulation therapy is often required in patients with immune-mediated HIT type II, a disorder that is associated with venous or arterial thrombosis in addition to the thrombocytopenia.
- In such patients who also require CRRT, use of systemic anticoagulation with lepirudin or argatroban has been described.

HEPARIN

- After attachment of the primed hemofilter or dialyzer, if baseline clotting times are not elevated, 2,000–5,000 units of heparin are injected into the patient, ideally via the venous (outflow) blood line.
- One should then wait for 2–3 minutes to allow the heparin to mix with the patient's blood.
- Next, a constant infusion of heparin (at a rate of 500–1,000 units/hour) is begun via an intravenous infusion pump emptying into the arterial (inflow) blood line, and blood flow through the extracorporeal circuit is begun.

TABLE 15.5

Heparin Protocol for Continuous Therapies

1. *Initial therapy:* Heparin in priming and rinsing solution as described in text.
   At start of procedure, give 2,000–5,000 IU heparin to the patient via the venous line or other access. Wait 2–3 min for the heparin to mix with the circulation. Then start 500–1,000 IU/hr constant heparin infusion into the arterial (inlet) blood line.
2. *Monitoring:* PTT measured at the arterial and venous blood lines every 6 hr.
   Maintain arterial PTT 40–45 s.
   Maintain venous PTT >65 s.
   If arterial PTT >45 s, decrease heparin by 100 IU/hr.
   If venous PTT <65 s, increase heparin by 100 IU/hr, but only if arterial PTT <45 s.
   If arterial PTT <40 s, increase heparin by 200 IU/hr.

HEPARIN-FREE METHOD

- In patients with liver disease, in postoperative patients, in patients with active or recent bleeding, or in patients with HIT, CRRT can be performed without heparin.
- The filter will clot periodically and will need to be changed at more frequent intervals.
- If acute bleeding occurs while CRRT with heparin is being performed, the procedure can be continued even after heparin administration has been stopped.

HEPARIN-FREE METHOD

- When heparin is not given, several steps may be taken to reduce the likelihood of clotting.

1. With C-HD, the dialysis solution inflow rate is increased by 20–40%.

- The higher dialysate flow rate will compensate for the anticipated loss of clearance as the unheparinized dialyzer slowly clots.

HEPARIN-FREE METHOD

- When using the heparin-free method for C-HD, we usually do not infuse saline into the arterial blood line on a periodic basis, in contrast to what is commonly practiced in the case of heparin-free IHD for fear of introducing microbubbles into the filter, which may lead to clot formation.

HEPARIN-FREE METHOD

2. In C-HF done without heparin, the predilution mode is preferred because prefilter fluid replacement reduces the hemoconcentration within the hemofilter when plasma water is removed. Keeping the blood flows at 200 mL/min or higher may also prevent early or excessive clotting.

HEPARIN-FREE METHOD

- When heparin is not used in patients without coagulation disturbances, the dialyzers will usually clot within 8 hours.
- A sign of early clotting is a reduction to <0.8 in the ratio of dialysate to serum urea nitrogen levels.
- When the ratio is <0.6, clotting is imminent.

REGIONAL CITRATE ANTICOAGULATION

- Citrate chelates calcium (and magnesium) and impedes the coagulation cascade.
- Calcium citrate complexes are removed in the effluent and those that return to the circulation are metabolized by the liver and skeletal muscles.
- RCA may reduce bleeding risk in comparison with heparin for CRRT, with similar or better efficacy on circuit patency depending on the citrate dose administered.

REGIONAL CITRATE ANTICOAGULATION

- Citrate anticoagulation, by reducing local ionized calcium concentration, may also reduce neutrophil and complement activation in the extracorporeal circuit.
- For patients who have no contraindications to use of citrate, the KDIGO 2012 AKI guidelines recommend use of RCA for CRRT.

ANTICOAGULATION WITH LEPIRUDIN AND ARGATROBAN

- Lepirudin (recombinant hirudin) and argatroban are direct thrombin inhibitors.
- Lepirudin is eliminated mainly by the kidneys.
- The dose has to be adjusted according to residual renal clearance and dialysis clearance.
- It can be administered as a continuous infusion or as repetitive boluses.
- Typical doses are 0.005–0.025 mg/kg body weight per hour.

ANTICOAGULATION WITH LEPIRUDIN AND ARGATROBAN

- The anticoagulation effect is monitored by measuring the activated partial thromboplastin time (aPTT), aiming to keep it about 1.5–2.0 times normal, thereby ensuring anticoagulation without an excess of bleeding complications.
- After more than 5 days of lepirudin use, antilepirudin antibodies may develop.

ANTICOAGULATION WITH LEPIRUDIN AND ARGATROBAN

- These antibodies enhance the anticoagulation effects of lepirudin, and a reduction of the infusion dose may be needed to minimize bleeding risk.
- It is recommended that with prolonged use of lepirudin, daily aPTT measurements be taken.

ANTICOAGULATION WITH LEPIRUDIN AND ARGATROBAN

- Argatroban is eliminated predominantly by liver metabolism and biliary secretion, and for this reason may be a preferred agent in renal failure patients.
- Argatroban infusion is initiated at 0.5–1.0 mcg/kg/min, using lower doses in patients with hepatic dysfunction.

ANTICOAGULATION WITH LEPIRUDIN AND ARGATROBAN

- The anticoagulation effect is also monitored by measuring aPTT.
- The administration of fresh frozen plasma is required to reverse bleeding due to overdosage of lepirudin or argatroban. Hemofiltration with high-flux dialyzers can reduce the plasma concentration of hirudin.

TABLE 15.7

Dosing Parameters for Continuous Renal Replacement Therapy with Lepirudin or Argatroban

	Lepirudin	Argatroban
Infusion rate	Initiate at 0.005–0.01 mg/kg/hr	Initiate at 0.5–1.0 mcg/kg/min; start at lower doses in patients with hepatic dysfunction.
Monitoring test	aPTT	aPTT
Target	1.5–2.0 times normal	1.5–2.0 times normal

LOW-MOLECULAR-WEIGHT HEPARINS

- Monitoring anticoagulation requires measuring anti–factor Xa activity, but use of this measurement to guide LMWH heparin use in CRRT remains to be defined.
- LMWH is not readily reversible with protamine.
- In C-HDF, dalteparin can be given as a bolus of about 20 U/kg followed by an infusion of 10 U/kg per hour for adequate anticoagulation without an excess of bleeding.

LOW-MOLECULAR-WEIGHT HEPARINS

- In a study of C-HD, a dalteparin dose of 35 U/kg bolus followed by 13 U/kg per hour resulted in good filter patency rates, but there were bleeding episodes.
- At a lower dalteparin dose of 8 U/kg bolus and infusion of 5 U/kg per hour, circuit life was poor, so perhaps the optimal dose is somewhere in between.

LOW-MOLECULAR-WEIGHT HEPARINS

- Enoxaparin and nadroparin may be used, but the experience is limited.
- Nadroparin was compared with RCA for C-H; in patients who weighed >100 kg, nardroparin was given as a 3,800 IU bolus followed by continuous infusion at a rate of 456 IU/hour.

LOW-MOLECULAR-WEIGHT HEPARINS

- In patients ≤100 kg, the nardroparin dose was a 2,850 IU bolus followed by a 380 IU/ hour infusion.
- This was done without anti-Xa monitoring.
- Patients in the nadroparin arm suffered more bleeding complications than those treated with RCA