CRRT IN PEDIATRICS

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2024/10/25

Continuous renal replacement therapy (CRRT) is the preferred method of renal support in critically ill children in the pediatric intensive care unit (PICU) as it allows for continuous and controlled fluid and solute clearance in hemodynamically unstable patients.

The advantages of this modality include the ability to promote both solute and fluid clearance in a slow continuous manner.

Data exist suggesting that approximately 25% of children in any PICU may have some degree of renal insufficiency; the true need for RRT is approximately 4% of PICU admissions.

Indications for CRRT

- The most common indications for CRRT in critically ill children are AKI and FO.
- Acid–base and severe electrolyte abnormalities are often associated with AKI
- Severe metabolic acidosis unresponsive to conventional medical therapy
- Other electrolyte abnormalities such as hyperkalemia, hyponatremia, and hyperphosphatemia

- In addition, there are a variety of non-renal indications for CRRT. Elimination of toxins in patients with inborn errors of metabolism is well established, although CRRT is mainly indicated for ammonia removal as well as in acute liver failure patients,

- The elimination of cytokines and inflammatory mediators in sepsis induced multi-organ dysfunction syndrome (MODS)

Most common indications for continuous renal replacement therapy initiation in critically ill children

Acute kidney injury with oligo/anuria (<0.5 ml/kg/h)
Fluid overload > 10%
Severe electrolyte imbalance refractory to medical treatment
Metabolic abnormalities (e.g., hyperammonemia refractory to medical treatment)
Severe metabolic acidosis
Uremic complications(e.g., encephalopathy, pericardial effusion, pulmonary edema)
Intoxications (e.g., drugs and toxins)
Septic shock with need of toxins clearance (e.g., endotoxins, cytokines)
Need to make room for more fluids for drug therapy and/or nutrition

Timing of initiation

identifying the optimal timing of initiation remains a difficult decision in clinical practice.

On the one hand, an early initiation strategy might result in improved outcomes, especially in patients with conditions with high risk for AKI and significant FO. On the other hand, CRRT is an invasive therapy and may be associated with complications especially in smaller children.

Additionally, the study by Cortina et al. showed that the odds of mortality increased by 1% for every hour of delay in CRRT initiation.

most experts would advise to consider initiation of CRRT in critically ill children with FO>10% when diuretics are unable to reverse or maintain fluid balance.

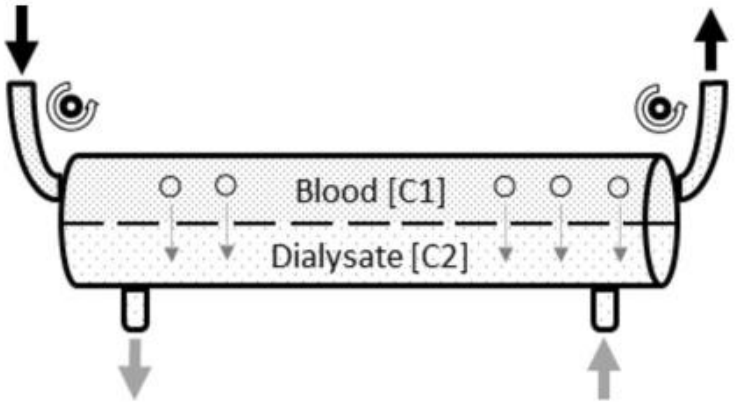
Vascular access

- The performance and delivery of CRRT depends heavily on an efficient vascular access.
- Vascular access is essential in achieving adequate blood flow rates, which prolongs circuit lifetime (CL) and thus reduces interruptions while optimizing the delivered CRRT dose.
- In order to minimize complications, KDIGO recommends placement of an adequate central line using ultrasound guidance.
- The most important factor ensuring low resistance during high blood flow rates is the location of the catheter tip and its diameter.

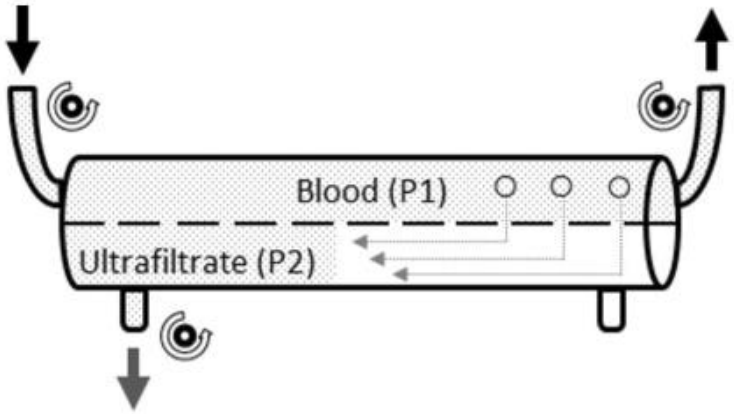
- The right internal jugular vein is recommended as the first choice
- The femoral vein is considered second choice
- KDIGO recommends that the subclavian vein should be avoided
- recent literature suggests that cannulation of the left brachiocephalic vein, using the supra- or infraclavicular ultrasound-guided approach, is an excellent choice in neonates and small infants

CRRT modality

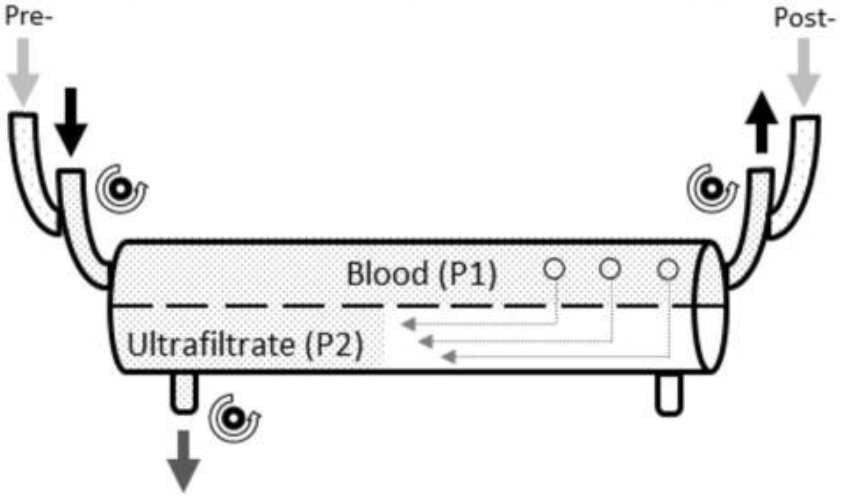
Continuous modalities are most frequently used in critically ill children as it allows for gentle fluid removal and minimizes fluid shifts and therefore is preferred in critically ill children at risk of severe hypotension or cerebral edema.



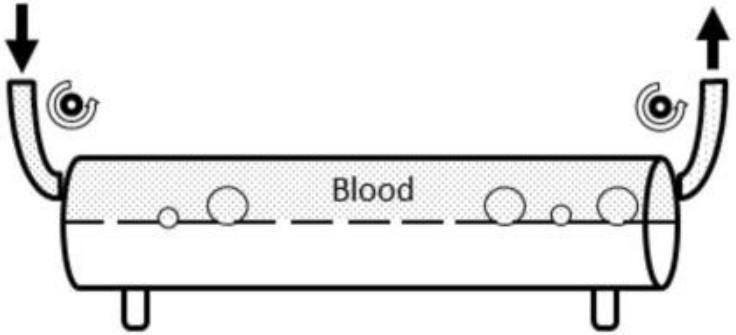
Diffusion: Movement of solutes according to their concentration ([C1] > [C2])



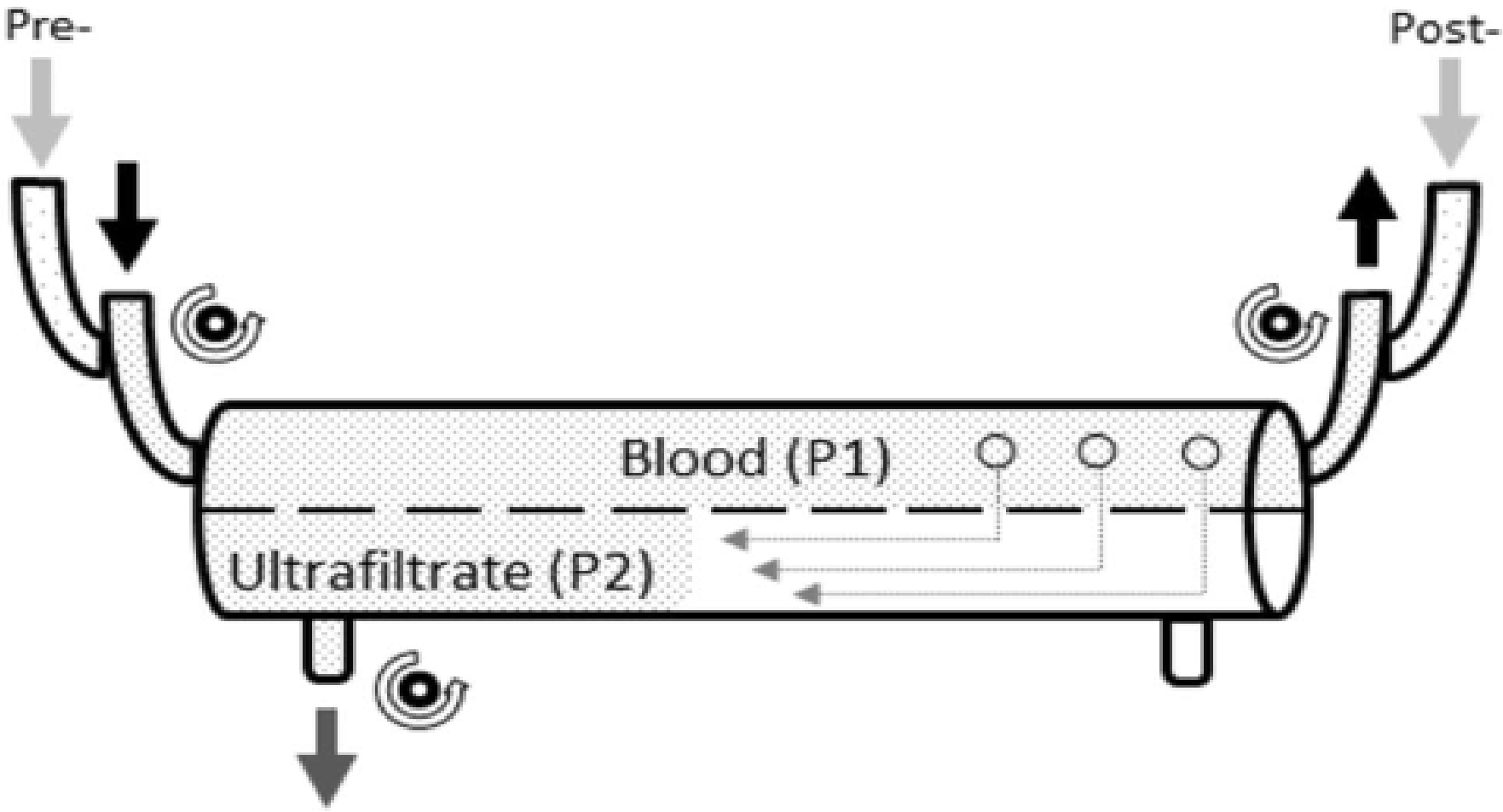
Ultrafiltration: Movement of plasmatic water (with solutes inside) according to pressure gradient (P1 > P2). The two solutions have the same concentration.



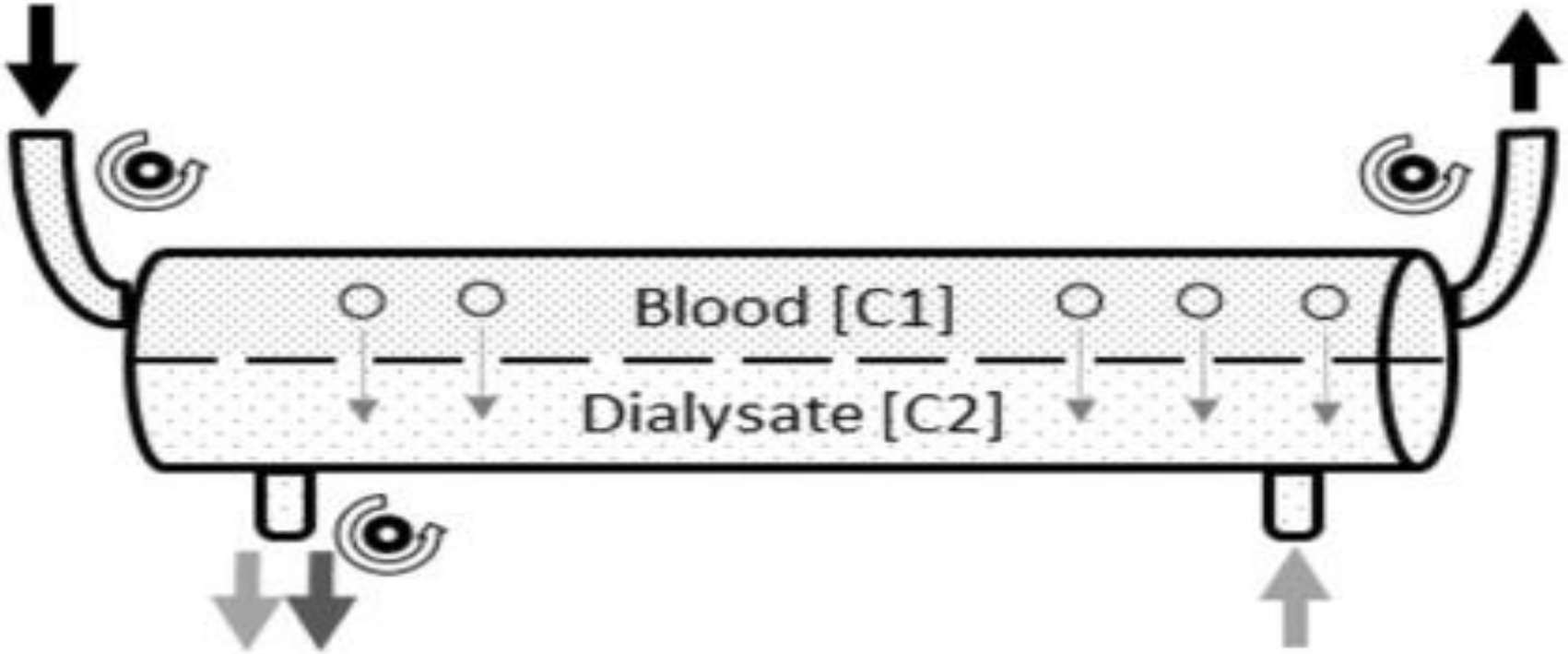
Convection: ultrafiltration + dilution of the blood pre- or post- filter with a volume of fluid (replacement fluid) equivalent to the one removed.



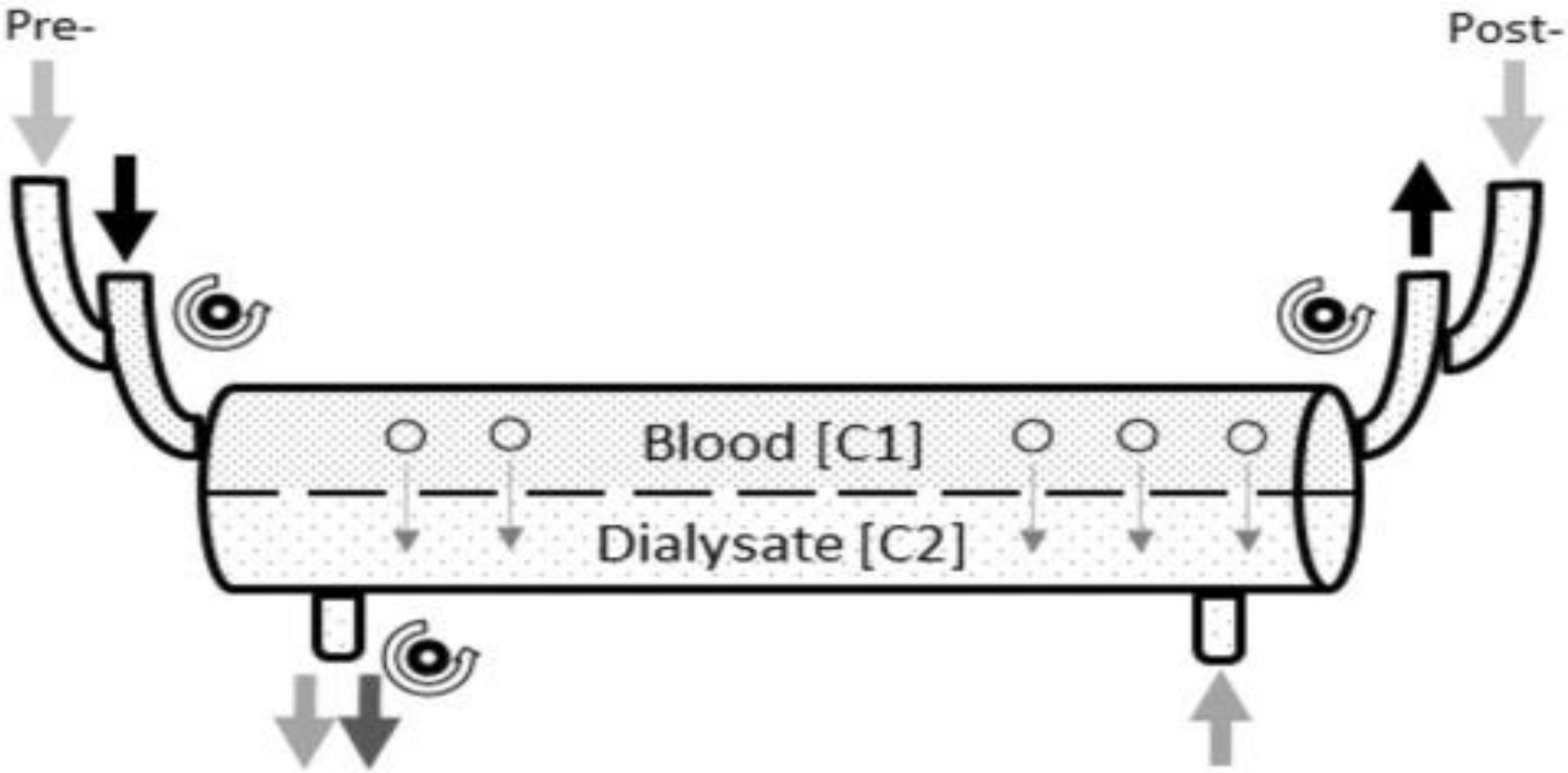
Adsorption: Adhesion of molecules (generally with a large molecular weight) to the filter surface.



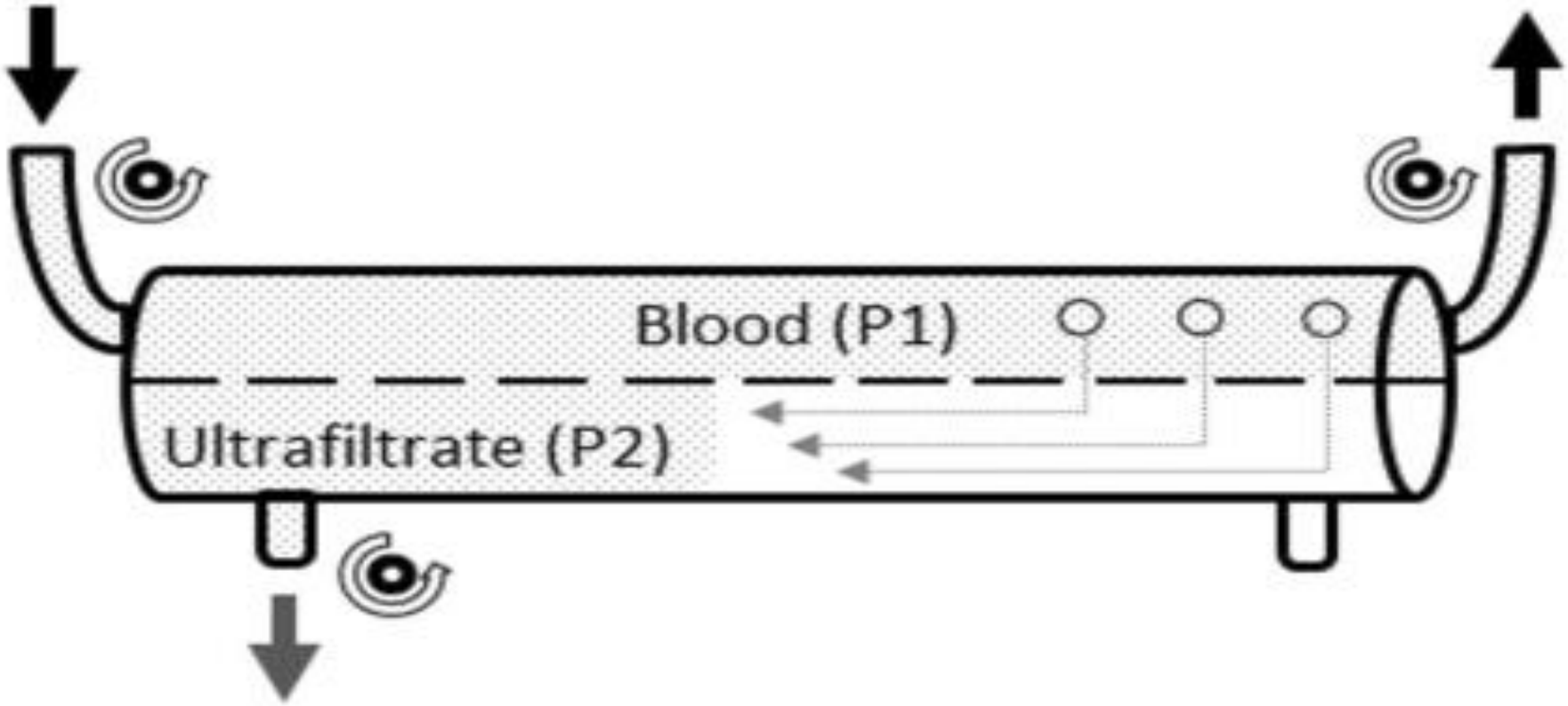
CVVH: Continuous veno-venous hemofiltration



CVVHD: Continuous veno-venous hemodialysis



CVVHDF: Continuous veno-venous hemodiafiltration



SCUF: Slow continuous ultrafiltration

Dosing of CRRT

- A prescribed dose of 30–35 ml/kg/h is considered standard volume CRRT dose.
- The prescribed dose in IRAN is 45-50 cc/kg/h.
- High-volume CRRT (up to 80 ml/kg/h) may be necessary to increase ammonia clearance in newborns with inborn errors of metabolism or children with acute liver failure.

Solutions

Drug formally called Normocarb, which was the first bicarbonate-based solution used in North America.

Modern physiologic solutions include bicarbonate levels of 22 to 35 mmol/dL depending on the needs of the patient. Often, these include physiologically normal sodium levels, 0 to 5 mmol/dL of potassium, 0 to 3.5 mg/ L of calcium, and 0 to physiologically normal levels of phosphorus, and no urea (BUN).

The solution used in iran called DUOSOL ,which is based on bicarbonate and maintains the electrolytes.

It is related to the company BBRAUN.

Method of anticoagulation

- The efficacy of CRRT is directly related to the longevity of the circuit as clotting of the circuit increases downtime, leads to blood loss of the patient, and may cause hemodynamic instability during de- and reconnection and increased costs.

Method	Dosing (D) and monitoring (M)	Advantage	Disadvantage
Unfractionated heparin	D: 10–20 IU/kg/h M: aPTT 45–60 s or 1.5–2 × NR; ACT 180–200 s	• Easily reversible with protamine • Low costs and widely available • wide experience as anticoagulant	• Risk of patients bleeding • Patients possibly developing heparin induced thrombocytopenia (HIT) • Unpredictable and complex pharmacokinetics resulting in dosing variability
Low Molecular Weight Heparin	D: Enoxaparin LD 0.15 mg/kg, MD 0.05 mg/kg/h M: Anti-Xa level (0.3–0.7 UI/mL)	• Less risks for HIT • Pharmacokinetics more predictable than unfractionated heparin	• Higher costs than unfractionated heparin • Less effective reversal with protamine
Regional citrate anticoagulation	D: starting dose 3 mmol/L[a] M: extracorporeal iCa 0.25–0.35 mmol/L; intracorporeal iCa 1.1–1.3 mmol/L	• Anticoagulation only of the extracorporeal circuit • Lower risks of bleeding • Longer filter life than heparin	• Need for training and strict protocols • Higher risks of citrate complications (electrolytes imbalance, citrate accumulation/toxicity) • Need for high dialytic dose (high volume of pre-filter fluid) • May need caution in patients with severe liver failure and lactic acidosis
Regional heparin and protamine	D: infuse 1 mg protamine post-filter for 100 IU Heparin M: circuit aPTT 45–60 s or 1.5–2 × NR; ACT 180–200	• Anticoagulation only of the extracorporeal circuit • Lower risks of bleeding	• Complex metabolism may lead to prolonged anticoagulation • Requires measurement of both circuit and patient APTT • Technically challenging (difficulty in estimating the amount of protamine required to antagonize post-filter heparin) • Possible side effects: hypotension, anaphylaxis, cardiac depression, leukopenia, and thrombocytopenia
Prostacyclin infusion	D: 2–8 ng/kg/min M: no monitoring tests	• No need for anticoagulation parameter monitoring since inhibits platelets aggregation • Easy to perform	• Possible hemodynamic impact, dose dependent (vasodilation, systemic hypotension, possible reflex tachycardia) • Possible raised intracranial pressure
Serine protease inhibitors—nafamostat mesilate, aprotinin	D: Depending on drug M: aPTT 45–60 s or 1.5–2 × NR; ACT 180–200 s	• Lower costs than regional citrate anticoagulation • Alternative to regional citrate anticoagulation if risk of citrate accumulation	• Only few studies available in pediatrics • Need for clotting parameter monitoring
Direct thrombin inhibitors—argatroban, bivalirudin	D: Depending on drug M: aPTT 45–60 s or 1.5–2 × NR; ACT 180–200 s	• Lower bleeding risk than unfractionated heparin in other context (e.g., ECMO) • Shorter half-life than heparin (bivalirudin the shortest) • Possible use in patients with HIT	• Only few studies available in pediatrics, evidences from adults • Non-reversible agents available

CRRT instruction for children

1.device mode(CRRT modality):

SCUF, CVVH, CVVHD or CVVHDF

2.normal saline type Prime :

Use blood for patient< 20 Kg and > 20 Kg use normal saline + 5000 U/L heparin.

3. Blood Flow rate :

Start from 3-5 cc/kg/min (minimum 50 cc/min and max 180 cc/min for adult and adolescents and 10 cc/kg/min in neonate)

4.Dialysis Solution Rate:

40-50 cc/kg/hour (max 2 L/ 1.73 m2/hour)

5.Ultra filtration Rate:

0-2 cc/kg/hour(usually start from minimum 0 and increase to max of 3 L/ 1.73 m2/hour)

6. Anticoagulation:

Heparin 10-20 U/kg bolus and then 5-20 U/kg/hour maintain to keep APTT between 1.5-2.5

7.Replacement Fluid Filter:

30-40 cc/kg/hour (max 4/5 L/hour)

8.Filtration Coefficient :

Less than 30%

9. Nutrition Adjustment:

Adjust oral or intravenous feeding to ensure a minimum intake of 2 grams of protein/kg/day

Dedicated neonatal and pediatric machines

- Most commercially available CRRT machines are not designed and not licensed for smaller children.

- Some concerns remain in small children with a body weight of less than 8 kg. Recently, a dedicated neonatal of infant dialysis machine called CARPEDIEM has become available and, according to the recent ESPNIC survey, is used in Europe by up to 15% centers.

Complications of CRRT

- Filter clotting
- Fluid imbalance
- Electrolyte abnormalities
- Metabolic acidosis or alkalosis
- Citrate toxicity
- Other solute imbalances
- Hypothermia
- Thrombocytopenia
- Hypotension Upon initiation of CRRT
- Hypoxemia

Contraindications

- Very few absolute contraindications to CRRT exist.
- Even in the presence of intracranial hemorrhage or systemic bleeding, CRRT can be safely performed by using no anticoagulation, using small doses of heparin with close serial monitoring of anticoagulation by aCT, or using regional anticoagulation provided by citrate/calcium.
- Although some centers consider an intracerebral hemorrhage an absolute contraindication to CRRT, others would use a regional circuit anticoagulation technique (citrate/calcium).

Liberation from CRRT

- when CRRT is no longer required either because intrinsic kidney function has recovered to the point that is adequate to meet patient needs, or because CRRT is no longer consistent with the goal of care

- The clinical indicators for discontinuation of CRRT include increased urinary output, no more fluid overload
- Clinician should consider “filter holiday” if spontaneous urine output is > 0.5 mL/kg/h and fluid status, acid–base status, and electrolytes are controlled.

In hospital outcomes

- In more recent studies, however, mortality seems to have decreased slightly . This effect may be caused by the overall increased use of CRRT among less sick children and/or earlier initiation of CRRT due to better recognition of AKI in critically ill children.
- several pediatric studies have shown that outcome is mainly related to the underlying disease, severity of illness, presence of MODS, and the degree of FO at CRRT initiation.

Long-term outcomes

- In a systematic review of pediatric AKI studies, the pooled long-term incidence of proteinuria was 13%,
- hypertension 7%,
- abnormal GFR (< 90 mL/ min/1.73m2) 28%,
- and end-stage kidney disease 0.4% .
- Together, these studies highlight the importance of kidney health surveillance after episodes of childhood AKI

Follow-up of AKI survivors

- The optimal timing and content of post-AKI follow-up care remains unclear. KDIGO guidelines suggest evaluating “patients 3 months after AKI for resolution, new onset, or worsening of pre-existing CKD” (ungraded recommendation)
- .Generally, children with severe AKI (stage 3 or receiving dialysis), prolonged AKI duration (≥ 7 days), and/or incomplete recovery should be re-assessed soon after the discharge and nephrologist referral should also be considered for these children.

Thanks for your attention